Noninvasive Prenatal Screening

RESOURCE GUIDE FOR WOMEN

Society for
Women's Health Research

About SWHR

The Society for Women's Health Research (SWHR) is a national nonprofit and thought leader dedicated to promoting research on biological sex differences in disease and improving women's health through science, policy, and education. Founded in 1990 by a group of physicians, medical researchers, and health advocates, SWHR is making women's health mainstream by addressing unmet needs and research gaps in women's health. Thanks to SWHR's efforts, women are now routinely included in most major medical research studies and more scientists are considering sex as a biological variable in their research. Visit www.swhr.org for more information.

SWHR's Genetic Screening Programs

SWHR Science Programs identify research gaps and address unmet needs in diseases and conditions that exclusively affect women or that disproportionately or differently affect women. The Genetic Screening Programs in Expanded Carrier Screening and Noninvasive Prenatal Screening were launched in 2021 to address both barriers to access and reducing health disparities related to preconception and prenatal genetic screening for women. The programs engage genetic counselors and clinicians, medical professional society leaders, patients and patient advocates, diagnostic company scientists, and health care decision-makers to explore strategies to address knowledge gaps, unmet patient needs, and relevant policies that present barriers to equitable and quality care for women surrounding genetic screening.

Inside the NIPS Resource Guide for Women:

Acknowledgements

This resource guide was developed with the guidance of experts from the SWHR Genetic Screening Working Group.

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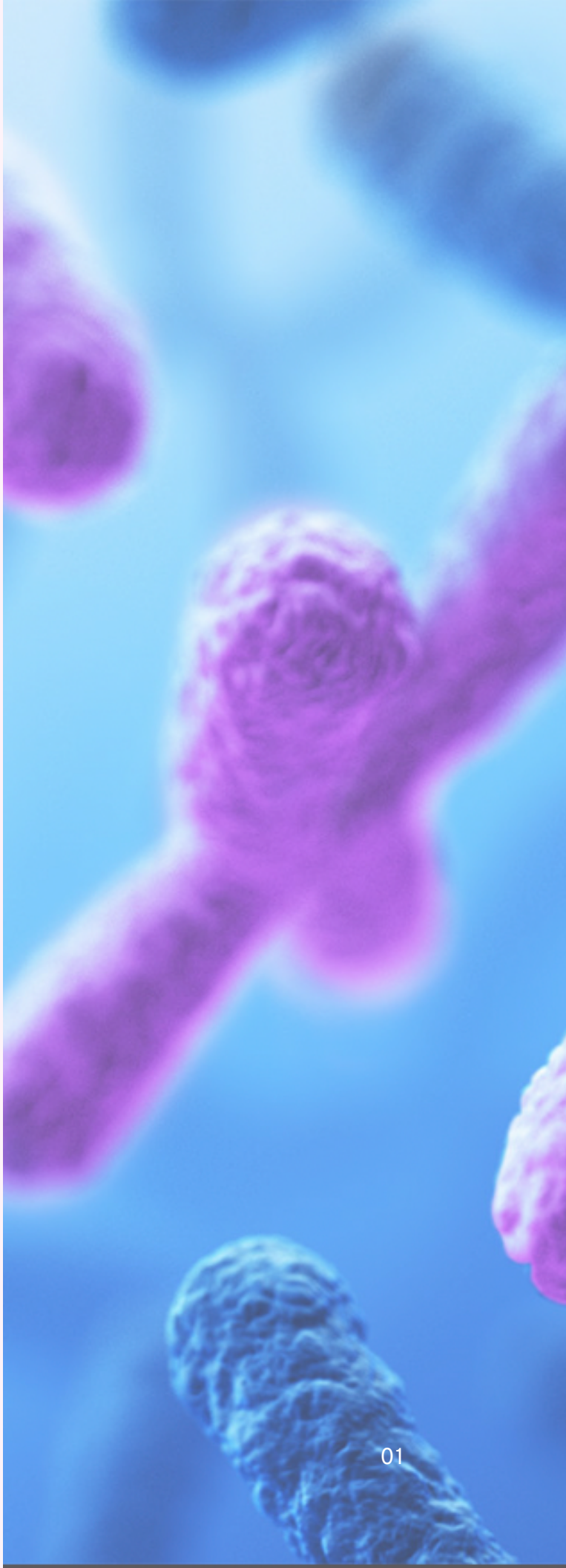
Understanding Genetic Screening and NIPS



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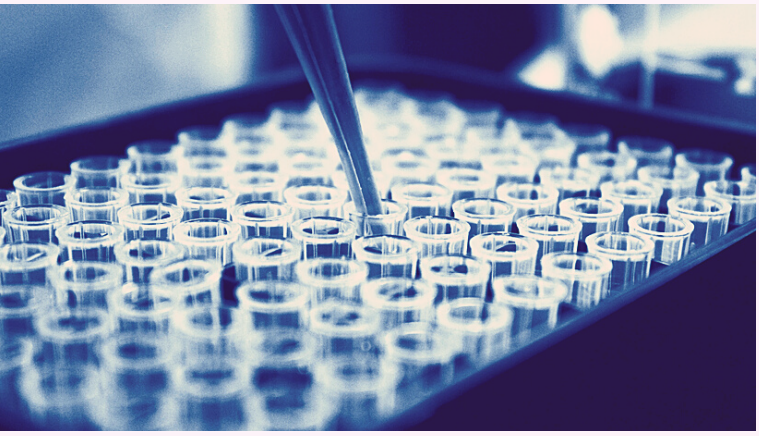
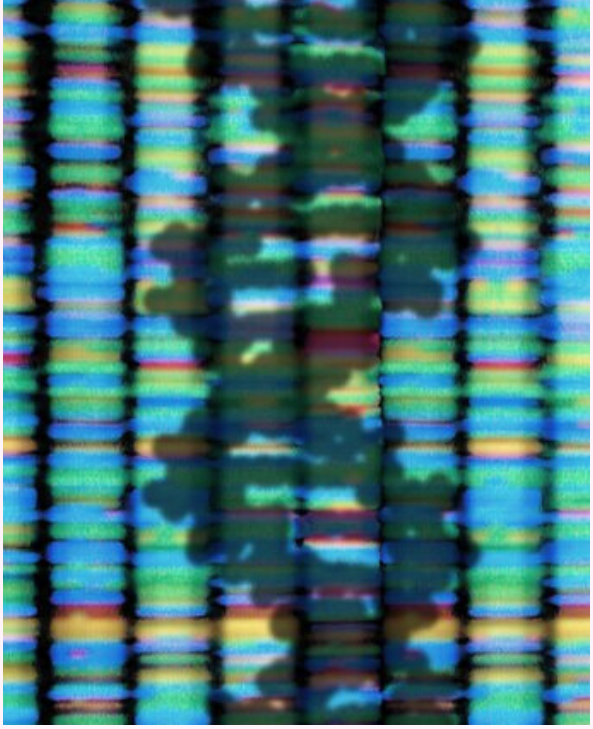
Each cell in the human body contains your genetic information, coded in strands of deoxyribonucleic acid (DNA). A complete set of DNA contains 46 **chromosomes**, combined from your biological parents – 23 from your mother and 23 from your father.

Variations or changes that have occurred in parent sperm and egg cells can sometimes result in clinically significant **chromosomal abnormalities**, such as an extra chromosome or a missing portion of a chromosome. These changes can affect the **fetus** (baby growing in the womb) during development or after birth. Occasionally, chromosomal changes can also happen after conception, when cells are rapidly dividing during fetal development.

1 in 150 live births have chromosomal abnormalities.[1]

The occurrence of certain types of fetal chromosomal abnormalities increases as a woman gets older and is not related to race or ethnicity. Depending on the type of change in the chromosome, they can significantly influence the baby's health and well-being, particularly if an entire chromosome is added or missing.





Genetic Screening

Screening for genetic disorders can be done using a number of different methods and varies depending on the type of disorder being screened. **Genetic screening** for chromosomal abnormalities often looks for specific sections of a person's DNA sequence to identify variations that are associated with certain genetic conditions. This screening is usually conducted with a blood sample or cheek swab, and can be done at different time points in a person's life, depending on what they are looking to assess. However, genetic screening is often associated with pregnancy and childbirth.

Prenatal genetic screening can offer expecting parents and those considering parenthood information about the chance of passing on certain conditions to their child, allowing women and their partners to make informed decisions about planning their family, pregnancy management, and future child-rearing. Screening can also be used to help those who are pregnant assess the risk of their baby having a chromosomal abnormality.

Different genetic screenings are available before, during, and after pregnancy – each offering unique insights:

- **Carrier screening** is used to determine the chance of **one or both parents** passing on certain inherited genetic conditions to a child. Ideally, this screening should be conducted before conception, but it can also be done during pregnancy. **Expanded carrier screening** includes a wider range of conditions than those included in carrier screening.
- **Noninvasive prenatal screening (NIPS)** is used to assess the risk of chromosomal **aneuploidy** – an irregular number of chromosomes – in the fetus. NIPS can be performed as early as 10 weeks into a pregnancy.
- **Newborn screening** is a national public health program that assesses all newborns for specific serious, but treatable conditions. Screening is typically performed 1-2 days after birth using blood taken by a small prick of a newborn's foot to test for metabolic, hormone, and hemoglobin (blood) disorders. Hearing and heart tests are also done to promote early detection, diagnosis, and treatment of certain defects. Newborn screening program requirements, the conditions screened, and screening methods may vary from state to state.

Genetic screening can also be used outside of pregnancy to assess risk for individuals with a personal or family history of certain cancers that have a hereditary component.

Noninvasive Prenatal Screening (NIPS)

Through the natural process of fetal growth and development during pregnancy, some of the tissue from the **placenta** (which contains similar DNA to fetal DNA) degrades, releasing that DNA into the mother's bloodstream. This **cell-free DNA (cfDNA)** can be examined by taking a blood sample from the mother and screening it for certain chromosomal changes. NIPS (also referred to as cfDNA screening) is considered noninvasive because the required blood draw poses minimal to no risk to mother or baby. Even though the blood draw is simple, NIPS should only be done after a woman is provided education and information about the process, risks, and benefits of NIPS, and gives her informed consent to proceed.

NIPS is not a required risk assessment, but experts agree that everyone should have access to this screening because of its accuracy in detecting pregnancies at increased risk for common chromosomal abnormalities in the fetus. As a result, NIPS may be considered more strongly under the following circumstances:

- If the mother is over the age of 35 at delivery
- A positive first or second trimester standard biomarker screening from initial blood work
- A fetal ultrasound that indicates an increased risk of aneuploidy
- A prior pregnancy with a **trisomy**
- If either parent has a chromosomal abnormality where there is an increased risk of fetal trisomy 13 (**Patau syndrome**) or trisomy 21 (**Down syndrome**)

Screening vs. Diagnostic Testing

Genetic screening, including NIPS, only provides information about the risk of certain genetic conditions like Down syndrome. Screening results should never be interpreted as a concrete determination of your or your baby's health; however, results can be used to inform conversations with your provider, make decisions about managing maternal and infant health, and determine whether to undergo diagnostic testing.

Screening is not the same as diagnostic testing.

Genetic screening results cannot provide a definitive diagnosis. NIPS results can provide information about the *likelihood* of your baby having a certain condition. Follow-up diagnostic tests help rule out false-positive or false-negative screening results.

It is important to talk to your health care provider about the purpose, potential risks, and benefits of genetic screening options before starting the process. A consultation with a genetic counselor, a specialist in genetics with advanced training in medical genetics and counseling, may also be very helpful before screening. For tips on how to have these conversations, visit the **Talking to Your Health Care Provider** section of the SWHR Noninvasive Prenatal Screening Resource Guide for Women.

Genetic Conditions Screened by NIPS

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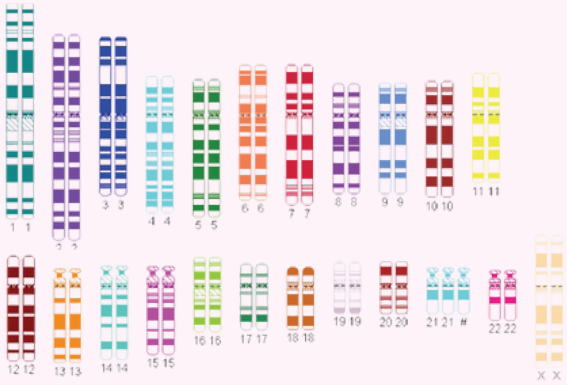
Most people have 23 pairs of **chromosomes** that, together, contain nearly all of their genetic information, or DNA. Sometimes, due to the genetic makeup of the parental sperm and egg prior to conception or through a variation that occurs during **fetal** development, a baby may have an extra or missing chromosome (**aneuploidy**). The most common type of chromosomal aneuploidy is a **trisomy** – when there are three copies of chromosome instead of the usual two.

Noninvasive prenatal screening (NIPS) can be used to assess the chance of a baby having a chromosomal aneuploidy, typically screening for the following, which are described in more detail below:

- Trisomy 21, which causes **Down syndrome**
- Trisomy 18, which causes **Edwards syndrome**
- Trisomy 13, which causes **Patau syndrome**

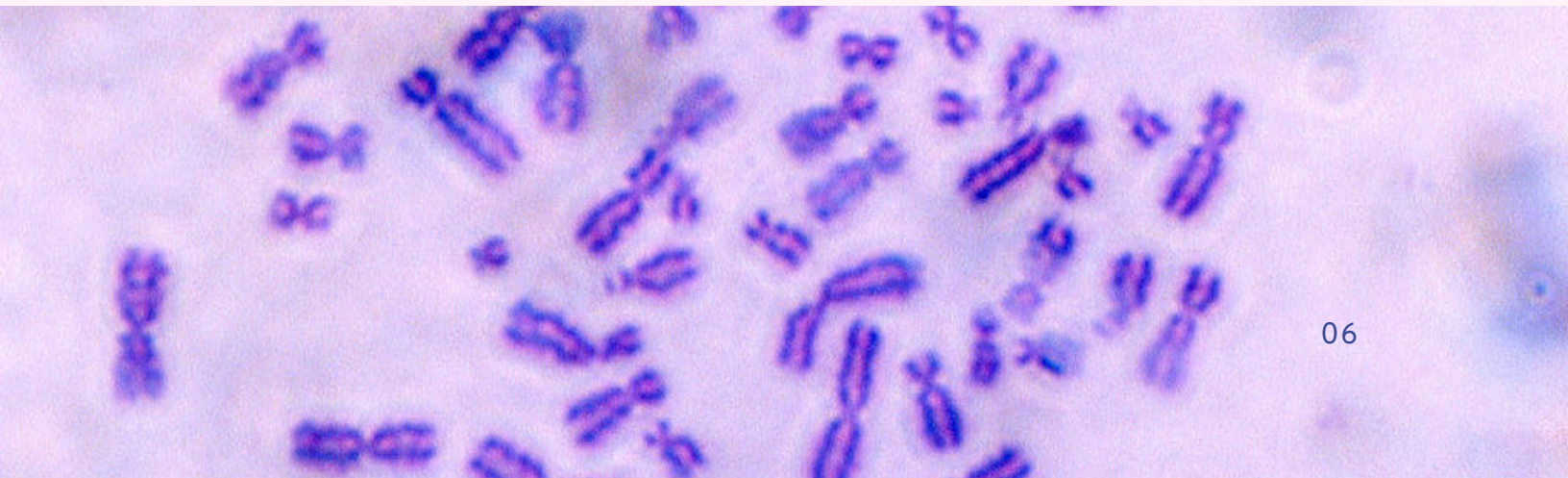
Other conditions that may be screened for by NIPS include changes to the number of sex chromosomes (e.g., Turner syndrome or Klienfelter syndrome) or conditions related to chromosomal **microdeletions** (when only a small piece of the chromosome is missing). However, the evidence and accuracy of NIPS to screen for these additional outcomes is limited.



I just want to know the sex.

Yes, NIPS can predict the sex of your baby before it is visible on an ultrasound, but this is NOT the purpose of NIPS. Before seeking out NIPS to determine the sex of your baby, consider ALL of the implications of undergoing screening, including what happens if you receive an abnormal result.

If you choose to undergo NIPS, talk to your health care provider and/or a **genetic counselor** about which conditions are appropriate to include in your screening. If the NIPS results indicate a high risk of an affected baby, confirmatory diagnostic testing (during pregnancy or after delivery) is highly recommended.



Down Syndrome (Trisomy 21)

Down syndrome is a condition that can result from someone having a full or partial extra copy of chromosome 21. This extra chromosome disrupts fetal development, resulting in features like reduced muscle tone, distinctive physical features, and intellectual and developmental disabilities. Down syndrome can increase the likelihood of developing hearing and vision problems or disorders of the endocrine or immune systems. However, with appropriate support and treatment, the life expectancy for someone with Down syndrome is over 60 years.

- Down syndrome occurs in about 1 in every 700 babies in the United States.[2]
- A prenatal ultrasound is expected to show a structural abnormality in 50% of fetuses confirmed with trisomy 21.[3]

Visit the National Down Syndrome Society to learn more about this condition.

Edwards Syndrome (Trisomy 18)

Edwards syndrome is a rare but serious condition that can result from having a full or partial extra copy of chromosome 18. Whether this chromosomal abnormality occurs in just some or all of the body's cells affects the severity of birth defects and intellectual disability. Pregnancies with trisomy 18 can spontaneously miscarry, and there is a high mortality rate for children with trisomy 18 immediately after birth. Between 5 and 10% of babies born with Edwards syndrome survive beyond the first year.

- Trisomy 18 occurs in 1 in 2,500 pregnancies in the United States.[4]
- A prenatal ultrasound is expected to show a developmental abnormality in the majority of fetuses confirmed with trisomy 18.[5]

Visit the Trisomy 18 Foundation to learn more about this condition.

Patau Syndrome (Trisomy 13)

Patau syndrome can result from someone having a full or partial extra copy of chromosome 13. It is the least common trisomy of the three commonly screened conditions, and it is the most severe. Neurological and heart defects and restricted growth in the womb contribute to the high mortality rate for children with trisomy 13, and long-term survival of babies born with Patau syndrome is rare.

- Trisomy 13 occurs in approximately 1 in 10,000 births.[6]
- A prenatal ultrasound is expected to show a developmental abnormality in more than 90% of fetuses confirmed with trisomy 13.[7]

Visit the National Organization for Rare Disorders (NORD) to learn more about this condition.

Always seek confirmation of a condition through follow-up diagnostic tests. Reproductive health care considerations and treatment decisions should never be made without receiving clinical and laboratory confirmation and, if possible, consulting with a genetics or maternal-fetal medicine health care provider.

Navigating the NIPS Screening Process

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Screening Process

NIPS can be conducted as early as 10 weeks into the pregnancy through a blood sample. Most NIPS panels will screen for trisomy 21 (**Down syndrome**), trisomy 18 (**Edwards syndrome**), and trisomy 13 (**Patau syndrome**). You may discuss with your health care provider if screening for sex **chromosome abnormalities**, **microdeletions**, or rare **aneuploidy** analysis are appropriate for your pregnancy.

Screening results usually arrive 1-2 weeks after the blood sample is taken. It can be beneficial to familiarize yourself with next steps after results come back.

To make the most of your consultation appointments, see the **Talking to Your Health Care Provider** section of the SWHR Noninvasive Prenatal Screening Resource Guide for Women.

Interpreting the Screening Results

If you get a negative screening result:
A negative result means that the screening **did not detect an increased risk** for the condition(s) screened. For a condition like Down syndrome, in which NIPS is a very reliable predictor, it is very unlikely (but not impossible) that women who receive a negative result will have a baby with Down syndrome.

If you get a positive screening result:
A positive result indicates that there is an **increased risk or suspicion** that the pregnancy is affected with a chromosomal abnormality. Because **genetic screening** is not definitive, it is important to consider a diagnostic test to confirm if the condition is present in the baby. Typical diagnostic tests include:

- **Chorionic villus sampling** – A procedure that involves taking a sample of tissue from the **placenta** for testing. Depending on the location of the placenta, tissue is taken by a tube is inserted through the vagina or a small needle inserted through the belly.
- **Amniocentesis** – A procedure that involves using a small needle to take a sample of the amniotic fluid from the sac that surrounds the **fetus** for testing.

DIAGNOSTIC TESTS TO CONFIRM A PRENATAL GENETIC CONDITION

	CHORIONIC VILLUS SAMPLING (CVS)	AMNIOCENTESIS
WHEN	Typically between 10 and 13 weeks of pregnancy	Typically between 15 and 20 weeks of pregnancy (ideally), but can be performed any time after 15 weeks
WHY	Can confirm if a fetus has a chromosomal condition	Can confirm a number of indicators of the fetus's health, including chromosomal conditions and neural tube defects
WAIT TIME	Typically 1-2 weeks	Typically 1-2 weeks, depending on the type of analysis being done

Although the chances are low, both CVS and amniocentesis come with a risk for bleeding, miscarriage, or preterm labor, so it is important to discuss the risks and benefits of these procedures with your health care provider or **genetic counselor**. Your health care team will be there to support you if the results from diagnostic testing come back positive. They can help walk you through expectations going forward, share useful resources, and connect you with community and support organizations for you and your family.

When you receive a positive NIPS result, your health care provider may refer you to a genetic counselor. A genetic counselor or maternal-fetal medicine specialist can help you assess your baby's risk of having a certain condition, discuss your options, and talk with you about any concerns you may have.

If you get an indeterminate result:
Sometimes screening results will not come back as positive or negative, meaning the result is indeterminate. This *may or may not* mean a chromosomal disorder is present. Naturally, these results can be confusing, so it is important to discuss your results with your health care provider or a genetic counselor. You will likely need to follow up with additional procedures, such as a fetal ultrasound and diagnostic testing.

Screening Accuracy

With any screening, it is possible to get results that do not represent what is actually happening with your baby.

A **false-negative** occurs when the screen shows a negative result, but the condition is actually present in the fetus.

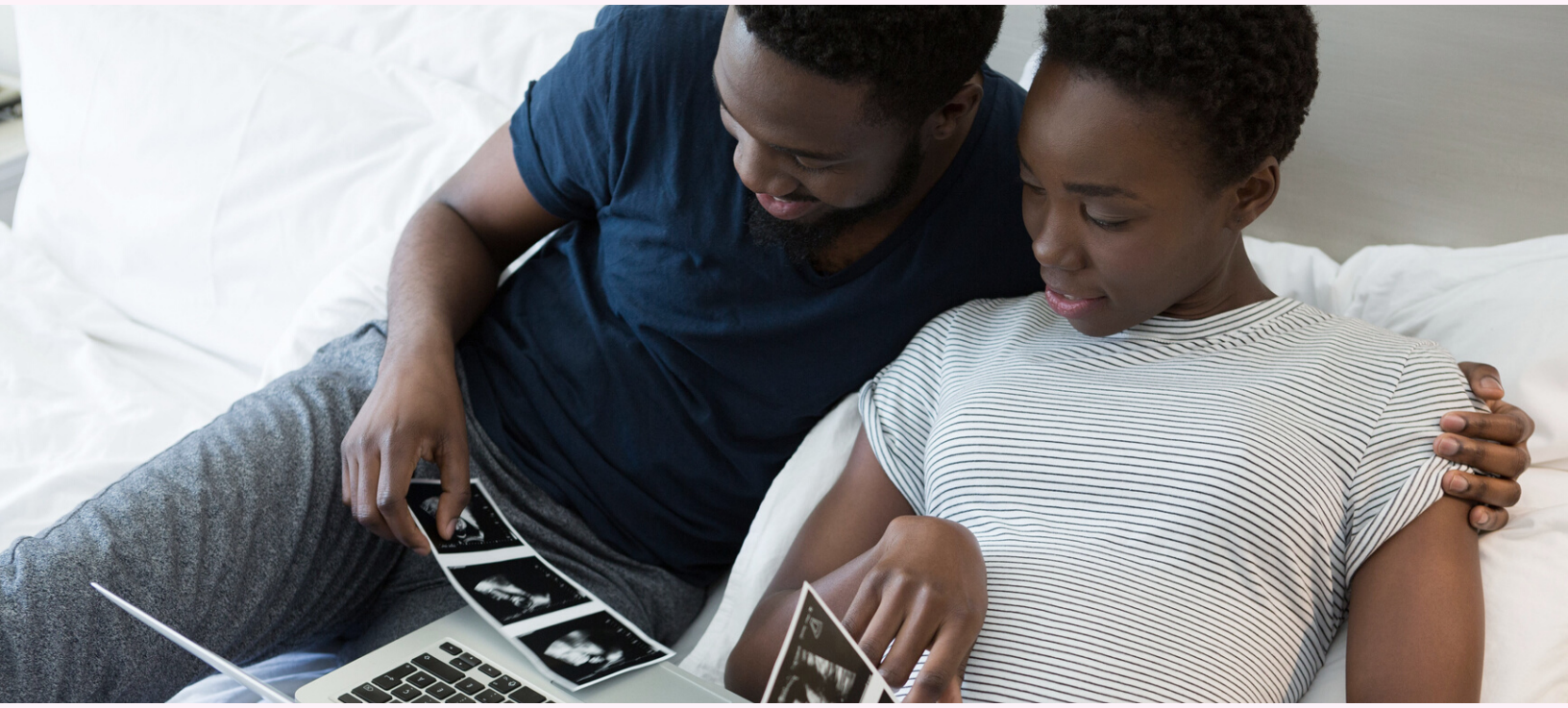
- False-negative results are uncommon, with rates as low as 1 in 10,000.[8]

A **false-positive** occurs when the screen shows a positive result, but the condition is not actually present in the fetus.

- The likelihood of a false-positive result is affected by several factors, including the conditions screened and if the pregnancy is considered high risk for those conditions.
- Often, the false-positive rate of screenings for trisomy 13, 18, or 21 is <1%.

It is important to remember that NIPS is just one of many tools that can be used to assess your and your baby's health during your pregnancy. Your health care provider will likely share your NIPS results in combination with results from other routine tests and screens, such as a prenatal ultrasound. Ultrasound results can provide additional context to NIPS results and may provide additional information about the overall health of the baby.

Microdeletions are typically associated with rare conditions; thus, screening has an increased chance of returning false-positive results.



Talking to Your Health Care Provider

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Consider Your Preferences

Before talking to your health care provider about prenatal **genetic screening** options, it may help to take some time to think about your personal values and preferences beforehand, so you can enter the conversation with an idea of the information you want to gather and desired outcomes. A few questions you may want to ask yourself and discuss with your partner include:

- What am I hoping to learn from genetic screening?
- What will I do with the information I gain?
- What follow-up testing and other care decisions should I consider in the event of a positive screening result?

Engage Relevant Health Care Providers

Obstetric Health Care Provider – a physician, nurse practitioner, or nurse midwife trained for routine pregnancy care and delivery

Maternal-Fetal Medicine Specialist – an obstetrician with specialized training to manage high-risk pregnancies and may become involved in your prenatal care after a positive fetal genetic diagnosis; also called a perinatologist

Genetic Counselor – a medical genetics and counseling professional with specific training to support health care providers and patients through the genetic screening and diagnostic testing processes, particularly in the case of positive screening or diagnostic test results

Geneticist – a biologist or medical doctor who is trained to evaluate and diagnose fetal conditions based on relevant exams and genetic test results

Understand the Process

Health care providers need your **informed consent** to perform the blood draw for genetic screening. This means they need to dedicate time to discuss what genetic screening means and help you make your decision about whether or not to undergo the genetic screening process.

Sometimes providers may go through this conversation quickly, as it is one of many steps in providing pregnancy care, but you should feel empowered to take the time that you need to address any questions or concerns beforehand. Don't be afraid to ask for more time to discuss or deliberate.

Questions for Your Health Care Provider

Before screening:

- Based on my personal history, pregnancy history and family history, what are my risk factors for the conditions screened by **noninvasive prenatal screening (NIPS)**?
- What conditions do you recommend including in my screening panel?
- When should I be screened?
- What are the steps in the screening process?
- What happens if my results come back normal? What if they indicate high risk?
- How long will it take to receive my screening results?
- How accurate will the results be?
- Should I speak to a genetic counselor before screening? If so, how can I find one?
- Will my insurance cover the cost of screening and follow-up tests?

After screening:

- What do my NIPS screening results mean?
- Do I need additional diagnostic testing?
- If so, what are my options? What are the pros and cons of each option?
- When should I undergo diagnostic testing?
- What are the chances that my NIPS results are a **false-positive** or **false-negative**?
- What happens after diagnostic testing? How long will it take to receive those results?
- Given my results, should I speak to a genetic counselor?

Questions for Your Genetic Counselor

Your genetic counselor should be able to answer many, if not all, of the questions provided on the previous page. They may also be particularly well-equipped to discuss:

- Your risk factors and if your pregnancy is considered high risk for certain conditions
- The meaning of a positive NIPS result for both you and your baby
- The accuracy of your NIPS results and likelihood of a false-positive or false-negative result
- If your baby is diagnosed with a condition, details about the condition and managing expectations for your and your baby's health
- Recommendations to community resources and support groups

Depending on when you seek out a genetic counselor, they may be able to coordinate with your regular health care provider on screening results, additional procedures, and planning for the rest of the pregnancy.

Genetic Screening Key Terms

Aneuploidy – Having extra or missing chromosomes, resulting in a change in the number of chromosomes in the cell

Cell-free DNA (cfDNA) – Small pieces of DNA that often circulate in the blood stream during natural cellular processes

Chromosomal abnormality – A change in DNA that affects the structure or number of chromosomes, and can sometimes affect the cell's ability to function or survive

Chromosome – A DNA molecule that is tightly packed with the genetic material for each cell; every cell should contain 23 pairs of chromosomes, 46 in total

Down syndrome – A condition that results from the body's cells having a full or partial extra copy of chromosome 21

Edwards syndrome – A condition that results from the body's cells having a full or partial extra copy of chromosome 18

False-negative – When the outcome of a screen incorrectly indicates that the result is negative, when the real result is positive

False-positive – When the outcome of a screen incorrectly indicates that the result is positive, when the real result is negative

Fetus – An unborn baby, from eight weeks after conception until birth

Genetic counselor – A healthcare professional who has received training in medical genetics and counseling. Genetic counselors help individuals and families assess the risk of genetic conditions, understand genetic screening results, and determine best approaches for care.

Genetic screening – A test used to identify changes in DNA structure or sequence in a fetus or in an adult that can be passed on to their future children

Informed consent – A principle in medical ethics and law, in which patients are provided with sufficient and understandable information, including possible risks and benefits, and the freedom of choice in advance of making a decision about their medical care

Noninvasive prenatal screening (NIPS)– A type of genetic screening that is used to assess the risk of chromosomal abnormalities in fetal DNA; also known as noninvasive prenatal testing (NIPT) or cell-free DNA (cfDNA) testing

Microdeletion – A chromosomal abnormality where a tiny piece of the chromosome is missing

Patau syndrome – A condition that results from the body's cells having a full or partial extra copy of chromosome 13

Placenta – An organ that develops and attaches to the uterus during pregnancy to facilitate the exchange of nutrients, oxygen, and waste between mother and baby

Trisomy – Having an extra (third) copy of a certain chromosome, instead of two

NIPS Resources and Select References

Organizations and Support for NIPS

- American College of Medical Genetics and Genomics: Find a Genetic Clinic or Counselor
- American College of Obstetricians and Gynecologists: Genetic Disorders FAQ and Cell-Free DNA Prenatal Screening Test Fact Sheet
- March of Dimes: Prenatal Tests
- National Society of Genetic Counselors: AboutGeneticCounselors.org and Find a Genetic Counselor Directory
- Society for Maternal Fetal Medicine: Prenatal Screening Using Cell-Free DNA and Find an MFM Specialist

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- Created with imagery designed by Freepik; double helix image by Peter Artymiuk

NIPS Patient Checklist

Having a conversation with your health care provider or genetic counselor about noninvasive prenatal screening (NIPS) can be overwhelming. The checklist below can be used to guide conversations to help you fully understand the screening process before you make a decision to proceed or not. Some items you may have completed already.

☐ **I understand the purpose of the screening.**
- Do you know why you are going to be screened?
- Do you understand what the results will tell you?

☐ **I have received a description of genetic condition(s) that will be screened.**
- Do you know which chromosomal conditions will be included in your screening panel?
- Do you know what it means if those conditions are present in the fetus?

☐ **My provider has reviewed the potential benefits and risks of screening with me.**
- Consider the screening technique and process.
- Consider the potential outcomes and your resources to handle them.

☐ **We have explored potential results and what they might mean.**
- Do you understand the accuracy of NIPS for the conditions being screened?
- What happens if results are positive, negative, or indeterminate?
- Discuss the potential for unanticipated results (e.g., non-paternity, diagnosis unrelated to conditions being screened).

☐ **My provider has explained how the blood sample and genetic information will be used.**
- Will the sample be discarded after testing or retained by the lab for research?
- Do you have details about your privacy policies, including access to the sample and genetic information?

☐ **I have determined the cost of NIPS and if my insurance requires pre-authorization.**
- You may need to call your insurance company for more information.

☐ **My provider has confirmed how results will be shared.**
- Should you expect a phone call, text, or a message through a patient portal?
- When can you expect to receive your results?

☐ **We have discussed what happens after I receive my results.**
- Will you need to schedule a follow-up appointment?
- Do you need to ask for additional resources or community support information?