Non-invasive prenatal testing \(NIPT\)

What NIPT is and why it is used

NIPT is a prenatal screening test performed on a blood sample from the pregnant person. The sample contains circulating cell-free DNA, often called cfDNA. During pregnancy, a portion of this cfDNA comes from placental cells, which usually reflect the fetal chromosomal complement. By analyzing patterns in this DNA, the test estimates whether there is an increased probability of certain chromosomal abnormalities.

The best-established use of NIPT is screening for aneuploidy, meaning an abnormal number of chromosomes. The most common targets are trisomy 21, also known as Down syndrome; trisomy 18, or Edwards syndrome; and trisomy 13, or Patau syndrome. Some panels also include screening for sex chromosome aneuploidies, such as monosomy X or Klinefelter syndrome, and some laboratories offer expanded panels for selected microdeletions or rare autosomal trisomies.

Importantly, NIPT does not examine every gene or every possible fetal condition. It is not a comprehensive fetal genome test, and it does not replace detailed ultrasound assessment, routine obstetric care, or diagnostic testing when a definitive answer is needed.

How the test works

Most NIPT platforms use massively parallel sequencing, targeted sequencing, or related next-generation sequencing methods. These technologies count or compare fragments of cfDNA from specific chromosomes. If there is a relative excess of DNA fragments from chromosome 21, for example, the pattern may suggest an increased risk of trisomy 21.

The fetal or placental component of cfDNA is often called the fetal fraction. A sufficient fetal fraction is necessary for reliable interpretation. Fetal fraction is influenced by gestational age, maternal weight, placental biology, and other clinical factors. If the fetal fraction is too low, the laboratory may report a no-call, inconclusive, or test-failure result rather than a low-risk or high-risk result.

Because the DNA assessed is largely placental in origin, rare biological discrepancies can occur. Confined placental mosaicism, vanishing twin, maternal chromosomal variation, organ transplantation, malignancy, or technical factors may affect interpretation. These situations are uncommon, but they help explain why NIPT remains a screening tool rather than a diagnostic test.

When NIPT is usually offered

NIPT is commonly available from about 10 weeks of gestation onward, when the amount of placental cfDNA in the bloodstream is usually sufficient for analysis. Timing may vary by laboratory, pregnancy type, and local clinical guidelines.

Historically, NIPT was first used mainly for pregnancies considered at higher risk for chromosomal abnormalities, such as those with advanced maternal age, a prior pregnancy affected by aneuploidy, abnormal ultrasound findings, or a high-risk result from traditional serum screening. In many healthcare systems, it is now offered more broadly as an option for singleton pregnancies and, in some settings, twin pregnancies. However, performance characteristics may differ in multiple gestations, donor egg pregnancies, and pregnancies with a vanishing twin.

The decision to have NIPT is optional. Some people want as much information as

possible early in pregnancy; others prefer not to screen for chromosomal conditions unless an ultrasound finding arises. Both responses are valid. The role of clinicians is to provide balanced information, not pressure.

What results can mean

NIPT results are often reported as low risk, high risk, positive, negative, increased risk, or decreased risk, depending on the laboratory. Some reports also provide a positive predictive value, or PPV, which estimates the probability that a high-risk result is truly affected in the specific clinical context.

Low-risk result: This means the screened chromosomal conditions were not detected at an increased level. It substantially lowers risk for the conditions included on the panel, but it does not eliminate risk.
High-risk result: This means the DNA pattern suggests an increased probability of a specific chromosomal condition. It is not a diagnosis. Diagnostic confirmation is usually recommended before any irreversible pregnancy decision.
No-call or inconclusive result: This may occur because of low fetal fraction, sample issues, or biological factors. Depending on the situation, options may include repeating NIPT, having an ultrasound, using a different screening approach, or considering diagnostic testing.

The meaning of a high-risk result depends partly on the condition being screened and the baseline chance of that condition in the pregnancy. For common trisomies, particularly trisomy 21, NIPT generally has high sensitivity and specificity. However, the PPV is not the same for every condition. For rarer conditions, a positive result is more likely to be false positive than for more common conditions, even when the test is technically accurate.

Screening versus diagnosis

The distinction between screening and diagnosis is central to informed decision-making. A screening test estimates risk. A diagnostic test examines fetal or placental cells more directly and can usually confirm whether a chromosomal condition is present.

Diagnostic options include chorionic villus sampling, usually performed in the

first trimester, and amniocentesis, typically performed later. These procedures are invasive and carry small procedure-related risks, which should be discussed with a maternal-fetal medicine specialist or other qualified clinician. They can provide chromosomal analysis through methods such as karyotyping, chromosomal microarray, or targeted testing, depending on the clinical question.

If NIPT is high risk, confirmatory testing is generally advised before making major medical decisions. If ultrasound identifies structural anomalies, diagnostic testing may be recommended even if NIPT is low risk, because many structural conditions are not caused by the chromosomal abnormalities screened by standard NIPT.

What NIPT does not screen for

NIPT is powerful, but its scope is limited. A standard NIPT panel does not rule out all genetic syndromes, single-gene disorders, neural tube defects, congenital heart defects, placental complications, growth problems, or birth differences detectable by ultrasound.

For this reason, routine prenatal care remains important. First-trimester ultrasound may help confirm dating, viability, and the number of fetuses. A nuchal translucency scan, detailed anatomy ultrasound, maternal serum alpha-fetoprotein, and other assessments may be recommended depending on gestational age and local practice. Screening for infections, blood type, anemia, diabetes risk, and other pregnancy-related conditions also remains separate from NIPT.

People who had preconception carrier screening, IVF with embryo testing, or earlier genetic counseling may still be offered NIPT. These tests answer different questions. For example, carrier screening evaluates parental risk for passing on certain inherited conditions, while NIPT primarily evaluates fetal risk for selected chromosomal copy-number abnormalities.

Benefits and limitations to weigh

Many people value NIPT because it can be performed early, requires only a blood draw, and has strong performance for common trisomies. It may reduce the number of people who undergo invasive diagnostic procedures after a lower-risk

screening result. It can also provide information that helps families and clinicians plan further evaluation, delivery location, neonatal care, or emotional preparation.

Limitations deserve equal attention. False positives and false negatives can occur. Results may create anxiety, especially when they are high risk or inconclusive. Expanded panels may identify rare findings with less certain predictive value. Some results can raise unexpected issues, such as suspected sex chromosome differences, mosaicism, or maternal findings, which may require careful counseling.

Before testing, it can help to ask: Which conditions are included? How will results be reported? What is the laboratory's performance for each condition? What follow-up is recommended after a high-risk result? Would the information change pregnancy management, preparation, or decision-making? These questions are not only technical; they are deeply personal.

Emotional and ethical considerations

Prenatal screening can bring relief, uncertainty, grief, or decisional conflict. None of these reactions is wrong. A low-risk result may be reassuring, but it may not erase all worry. A high-risk result can feel overwhelming, especially while waiting for confirmatory testing. Support from clinicians, genetic counselors, partners, family, or trusted community resources can be important.

Ethically, NIPT should be offered with informed consent. That means understanding the voluntary nature of testing, what is being screened, possible outcomes, privacy considerations, costs, and follow-up options. Some people may choose not to receive information about fetal sex or sex chromosome conditions. Others may decline expanded screening because the uncertainty feels more burdensome than helpful.

If a result suggests an increased risk of a chromosomal condition, a genetic counselor can help explain the result in context, discuss diagnostic testing, review ultrasound findings, and connect families with condition-specific resources. The goal is not to direct a single choice, but to support informed, values-consistent care.