

NIPT accuracy timing and limitations



What NIPT is actually testing

NIPT analyzes cell-free DNA fragments in the pregnant person's bloodstream. A portion of these fragments comes from the placenta and is often used as a proxy for fetal chromosomal status. This is why many clinicians prefer the term cell-free DNA screening: the sample is maternal blood, and the fetal component is usually placental DNA rather than DNA obtained directly from fetal cells.

Most standard NIPT panels screen for common autosomal aneuploidies: trisomy 21, associated with Down syndrome; trisomy 18, associated with Edwards syndrome; and trisomy 13, associated with Patau syndrome. Many tests also offer fetal sex prediction and screening for sex chromosome aneuploidies, such as monosomy X or Klinefelter syndrome. Some laboratories provide expanded screening for selected microdeletions or rare autosomal trisomies, but the clinical performance of these broader panels is more variable.

Because NIPT estimates probability rather than directly confirming fetal chromosomes, results are typically reported as low risk, high risk, increased risk, atypical, or no result. The exact wording varies by laboratory. A low-risk result can substantially reduce the likelihood of the screened conditions, but it does not rule out all genetic disorders, structural

anomalies, single-gene conditions, or pregnancy complications.

Best timing: why many tests start at 10 weeks

Many NIPT platforms can be performed from approximately 10 weeks of gestation. This timing is not arbitrary. Early in pregnancy, the proportion of placental cell-free DNA in the maternal bloodstream, called the fetal fraction, may be too low for reliable analysis. As gestation advances, fetal fraction generally increases, improving the chance that the laboratory can generate an interpretable result.

Testing too early can increase the likelihood of a no-call or inconclusive result. This does not necessarily mean something is wrong, but it can create uncertainty and may require a repeat blood draw. Accurate pregnancy dating also matters. If ovulation occurred later than expected or the pregnancy is not as far along as estimated by last menstrual period, the fetal fraction may be lower than anticipated.

NIPT timing should also be considered alongside other first-trimester evaluations. Nuchal translucency ultrasound, first-trimester combined screening, early anatomy assessment, and routine prenatal labs may provide complementary information. For example, ultrasound can identify structural findings or dating discrepancies that NIPT alone cannot evaluate. Some patients choose NIPT because of its strong screening performance; others combine it with ultrasound-based assessment after discussing the benefits and limits with their care team.

How accurate is NIPT for common trisomies?

NIPT performs best for trisomy 21. In many clinical settings, sensitivity and specificity for trisomy 21 are very high, often above those of traditional serum screening. Sensitivity refers to how well a test identifies pregnancies affected by the condition; specificity refers to how well it identifies pregnancies not affected by the condition. High sensitivity reduces, but does not eliminate, the chance of a false negative. High specificity reduces, but does not eliminate, the chance of a false positive.

Performance for trisomy 18 is also generally strong, though often slightly

lower than for trisomy 21. Performance for trisomy 13 tends to be lower and more variable. This variation reflects biological and technical factors, including differences in placental mosaicism, fetal fraction, and the relative rarity of the condition.

It is also essential to distinguish sensitivity and specificity from positive predictive value. Positive predictive value, or PPV, is the probability that a high-risk result truly represents an affected fetus. PPV depends heavily on the baseline chance of the condition, which is influenced by factors such as maternal age, gestational age, ultrasound findings, and prior screening results. A test can have excellent sensitivity and specificity but a modest PPV for rare conditions, especially in a lower-risk population.

Why a positive NIPT result needs confirmation

A high-risk NIPT result can be emotionally overwhelming, but it should not be treated as a definitive diagnosis. Diagnostic testing is usually needed to confirm fetal chromosomal status. The two main diagnostic options are chorionic villus sampling, typically performed in the first trimester, and amniocentesis, typically performed later. These tests analyze fetal or placental cells in a more direct way and can provide a karyotype, chromosomal microarray, or other targeted testing depending on the clinical question.

Confirmatory testing is especially important before making major pregnancy-management decisions. The reason is that NIPT may detect a placental chromosomal pattern that is not present in the fetus, a phenomenon known as confined placental mosaicism. It may also be affected by a vanishing twin, maternal chromosomal variation, maternal copy-number variants, organ transplant history, or, rarely, maternal malignancy. These are not common scenarios for every patient, but they illustrate why screening and diagnosis are different categories.

Genetic counseling can be very helpful after a positive, atypical, or inconclusive result. A counselor can explain the condition-specific PPV, review ultrasound findings, discuss diagnostic testing options, and help you think through next steps without pressure. This support can make a difficult waiting period feel more structured and less isolating.

False negatives and the meaning of a low-risk result

A low-risk NIPT result is reassuring for the specific conditions included in the screen, particularly when fetal fraction is adequate and the report is otherwise straightforward. However, low risk does not mean no risk. False negatives can occur, though they are uncommon for trisomy 21. Potential contributors include low fetal fraction, placental mosaicism, sample or laboratory factors, and biological differences between placental and fetal chromosomes.

Low-risk NIPT also does not exclude many other conditions. It does not replace a detailed anatomy ultrasound, which assesses fetal structures such as the heart, brain, spine, kidneys, abdominal wall, and limbs. It also does not screen for most single-gene disorders, neural tube defects, congenital infections, metabolic conditions, or all chromosomal rearrangements. Depending on the test, some triploidy, microdeletions, or rare chromosomal abnormalities may not be assessed or may be assessed with limited accuracy.

If ultrasound later shows a structural anomaly, growth concern, or other unexpected finding, clinicians may recommend additional evaluation even if NIPT was low risk. This can feel confusing, but it reflects the fact that different tests answer different questions.

No-call and low fetal fraction results

A no-call result means the laboratory could not provide an interpretable screening result. One common reason is low fetal fraction. Fetal fraction can be influenced by early gestational age, higher maternal body mass index, sample handling, medication or medical conditions, and characteristics of the placenta. Sometimes a repeat sample after one to two weeks yields a result because fetal fraction has increased.

In some contexts, low fetal fraction itself may be associated with an increased risk of certain aneuploidies or placental dysfunction, but interpretation depends on the laboratory method, gestational age, ultrasound findings, and the patient's overall clinical picture. A no-call result should not be dismissed automatically, but it also should not be assumed to indicate an affected pregnancy.

Common next steps may include verifying gestational age, repeating NIPT, considering first-trimester or second-trimester screening, obtaining a targeted ultrasound, or discussing diagnostic testing. The best path depends on the reason for the no-call result, the patient's preferences, and the degree of clinical concern.

Limitations in twins, IVF pregnancies, and expanded panels

NIPT can be used in many twin pregnancies, but interpretation is more complex. Fetal fraction is shared across the pregnancy, and if one twin is affected, the signal may be diluted. Determining which twin is affected may not be possible from screening alone. Vanishing twin, where a demised co-twin contributes residual cell-free DNA, can increase the chance of discordant or false-positive results.

In pregnancies conceived through IVF, including those with preimplantation genetic testing, NIPT may still be offered. However, PGT and NIPT evaluate genetic risk in different ways and at different stages. PGT assesses cells biopsied from an embryo before transfer, while NIPT evaluates placental cell-free DNA during pregnancy. Neither replaces diagnostic testing when definitive fetal chromosomal information is needed.

Expanded NIPT panels deserve special caution. Screening for microdeletions, rare autosomal trisomies, or genome-wide copy-number changes may detect clinically relevant findings, but the PPV is often lower than for trisomy 21 because these conditions are rarer. Expanded results can also create ambiguous counseling situations, including findings that may relate to the placenta or pregnant person rather than the fetus. A more comprehensive test is not always a clearer test.

How to interpret NIPT results in context

The most useful interpretation of NIPT combines the laboratory result with clinical context. Important factors include gestational age, fetal fraction, whether the pregnancy is singleton or multiple, maternal age, ultrasound findings, family history, prior pregnancy history, and what exact conditions the panel included. Even the same "high-risk" label can have different

implications depending on which condition is flagged.

Before testing, it can help to ask what you want the information for and what you would do with different possible results. Some people want early reassurance. Others want time to prepare for a child with special medical needs. Some want to know whether diagnostic testing should be considered. There is no single emotionally correct approach, and patients should be supported without judgment.

Good pretest counseling should include what the test screens for, what it does not screen for, the possibility of no-call results, whether fetal sex or sex chromosome findings will be reported, and how positive results are confirmed. If you receive a result that feels frightening or unclear, contacting your obstetric clinician or a genetic counselor promptly is appropriate.