

NIPT results interpretation and false positives



What an NIPT result is actually measuring

NIPT, also called cell-free DNA screening, looks at small fragments of DNA circulating in maternal blood. Most of that signal reflects placental DNA, which is usually representative of the fetus but is not always identical to it. That distinction is why the test is best understood as screening versus diagnostic testing: it estimates risk, but it does not directly diagnose the fetal chromosome makeup.

In practical terms, a low-risk result lowers the probability of the conditions included in the panel, but it does not rule out every genetic syndrome, structural anomaly, or single-gene disorder. A high-risk result raises concern, yet it still needs confirmation because the screen can be positive even when the fetus is unaffected. The positive predictive value is not fixed; it changes with the specific condition, the pregnancy's starting risk, and the quality of the sample. That is one reason the same report can feel very different to two patients with different backgrounds.

One useful way to think about NIPT is as a refined probability test. It is often more accurate than older serum screening methods, but it still sits one step before diagnosis. If the wording on the report feels opaque, ask your

clinician which chromosome or condition was flagged, whether the result is considered low, moderate, or high risk, and whether the laboratory reported any limitations such as low fetal fraction.

Why false-positive NIPT results happen

A false positive means the screen suggests a chromosome abnormality when the fetus does not actually have that condition. Because the assay mostly analyzes placental DNA, one of the most important explanations is confined placental mosaicism, a situation in which the placenta and fetus do not share the same chromosomal pattern. The placental signal can therefore look abnormal even when fetal cells are normal.

Other biologic sources are also well recognized. Maternal copy-number variation or maternal mosaicism can add extra DNA signal from the pregnant person rather than the fetus. A vanished twin can leave behind residual DNA that changes the result, which is why vanishing twin and NIPT interpretation can be complicated early in pregnancy. Rarely, maternal conditions such as malignancy may create unusual cfDNA patterns that mimic fetal aneuploidy. These explanations are uncommon, but they matter because they remind us that a positive screen is not always a fetal finding.

Placental factors: confined placental mosaicism, placental aneuploidy, or placental DNA that differs from fetal DNA.

Maternal factors: copy-number variation, mosaicism, or rarely an occult maternal malignancy.

Pregnancy factors: a vanished twin or, less often, other multi-fetal biology.

Technical factors: low fetal fraction, sample handling issues, sequencing noise, or bioinformatic thresholds that classify a borderline sample as high risk.

Because NIPT is highly dependent on the quality and proportion of cfDNA in the sample, a result can also be less reliable when the fetal fraction is low. That is one reason some reports are labeled no-call or inconclusive rather than simply positive or negative.

How to interpret a positive result without panicking

The most important interpretive step is to separate the emotional meaning of a positive screen from the statistical meaning. A report that says high risk is not the same as a diagnosis of trisomy 21, trisomy 18, trisomy 13, or a sex chromosome condition. It means the chance is elevated enough to justify more careful evaluation. The clinical question is not, "Is this result perfect?" but, "How likely is it to be true in this specific pregnancy?"

That likelihood changes with pretest probability. For example, a positive result in a pregnancy already considered higher risk because of maternal age, prior history, or ultrasound findings will generally have a different interpretation than the same result in a pregnancy with no additional risk factors. The specific chromosome abnormality also matters; some findings have stronger predictive value than others. This is why clinicians often review the full report instead of focusing on a single color-coded label.

It can help to ask three focused questions: What exactly was screened? How strong is the evidence that the fetus is affected? And what could explain a discordant result if the fetus is normal? Those questions keep the discussion anchored in probabilities rather than fear. They also create space for a shared decision about the next test, which may include ultrasound review, additional counseling, or diagnostic sampling.

What confirmatory testing can clarify

After a positive screen, the next step is usually confirmatory diagnostic testing after NIPT. The two standard diagnostic options are chorionic villus sampling and amniocentesis, and the choice depends on gestational age, the specific NIPT finding, and the clinical picture. Both procedures analyze fetal or placental tissue directly, which is why they can answer the question that screening cannot: whether the fetus truly has the chromosome condition in question.

There is an important nuance here. Chorionic villus sampling samples placental tissue, so if confined placental mosaicism is suspected, the placenta may still differ from the fetus. In some situations, that makes amniocentesis for fetal chromosome diagnosis especially useful because amniotic fluid more directly reflects fetal cells. Your care team will decide which diagnostic pathway is most appropriate rather than assuming every positive screen requires the same

follow-up.

Ultrasound also remains part of the evaluation. Structural findings, growth concerns, or soft markers can shift the probability toward or away from a true fetal condition. A normal ultrasound cannot exclude all chromosome abnormalities, but it can provide important context. Conversely, an abnormal ultrasound can make a positive screen more concerning. The key point is that confirmation is not just about repeating a blood test; it is about using the right diagnostic method for the question being asked.

If you are offered invasive testing, it is reasonable to ask about timing, what conditions the test can detect, how results are reported, and how the laboratory handles mosaic or borderline findings. Clear answers often make the decision feel less abstract.

A calm next-step conversation with your care team

When NIPT results are unexpected, the conversation with your clinician matters as much as the report itself. Ask for a plain-language summary of the result, including whether the abnormality appears to be a whole-chromosome finding, a sex chromosome finding, or a more complex pattern. If the report mentions limitations, low fetal fraction, or no-call territory, ask how those details affect confidence in the result.

This is also a good time to ask whether prenatal genetic counseling would be helpful. Genetic counselors can explain the likely meaning of the result, compare diagnostic options, and help you understand what the test can and cannot predict. They can also review the possibility of placental, maternal, or twin-related explanations in a way that is both precise and emotionally grounded.

Many people also find it helpful to prepare a short written list before the appointment. Include questions such as: What is the most likely explanation for this result? What diagnostic test do you recommend and why? Could a vanishing twin, placental mosaicism, or maternal finding explain the screen? What will we learn from ultrasound, and how soon can results return? Having those questions in front of you can reduce the feeling of being swept along by medical jargon.

Finally, give yourself permission to feel unsettled while the picture is incomplete. A false positive is not a failure on your part, and an abnormal screen does not mean you have done anything wrong. The goal is careful confirmation, not immediate certainty.