
IT'S TIME FOR
Expanded
NIPT
EXPANDED SCREENING WITH
UNPARALLELED ACCURACY
AS
EARLY
AS
WEEK
10
NIPT=
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prenatal
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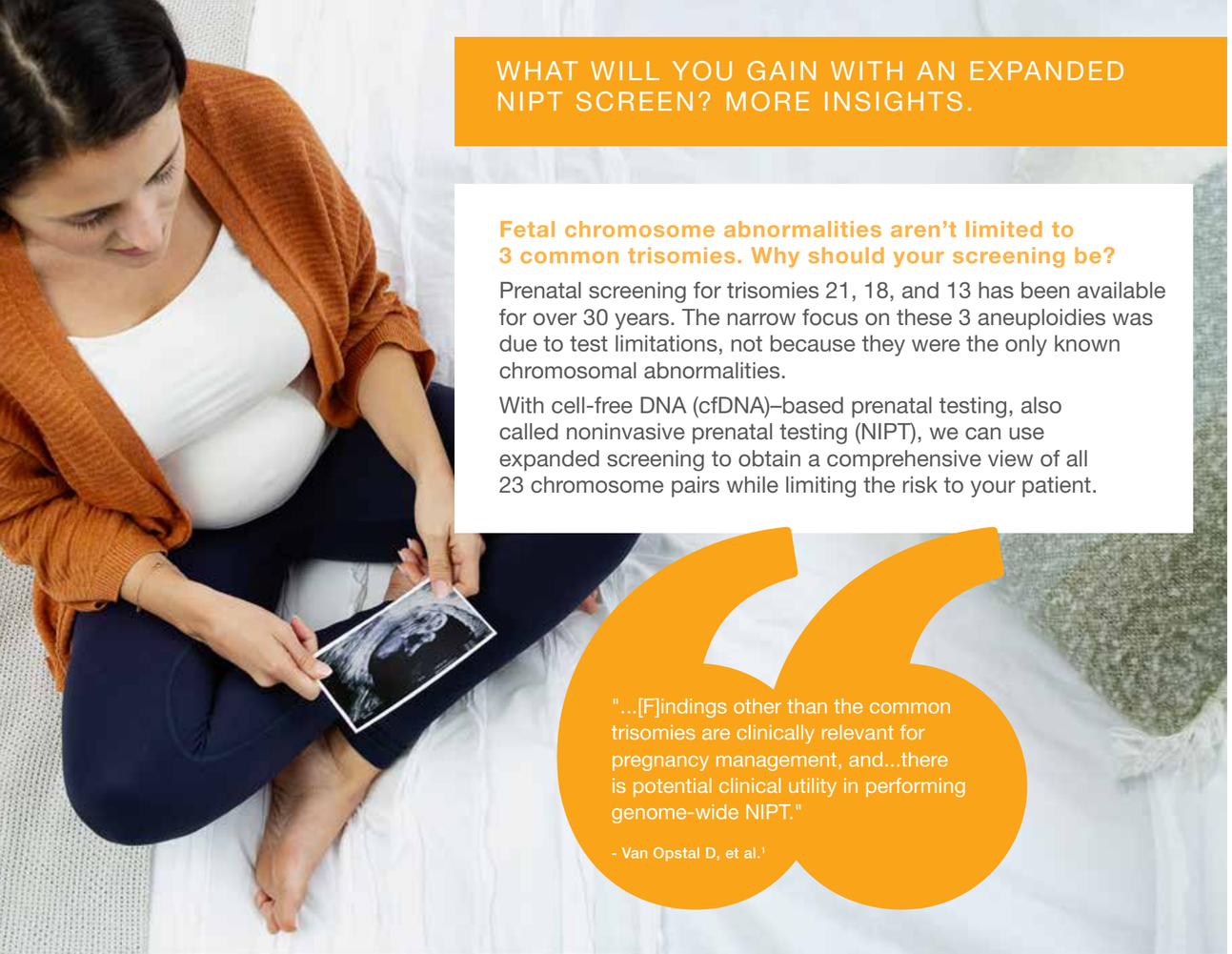


WHAT WILL YOU GAIN WITH AN EXPANDED NIPT SCREEN? MORE INSIGHTS.

Fetal chromosome abnormalities aren't limited to 3 common trisomies. Why should your screening be?

Prenatal screening for trisomies 21, 18, and 13 has been available for over 30 years. The narrow focus on these 3 aneuploidies was due to test limitations, not because they were the only known chromosomal abnormalities.

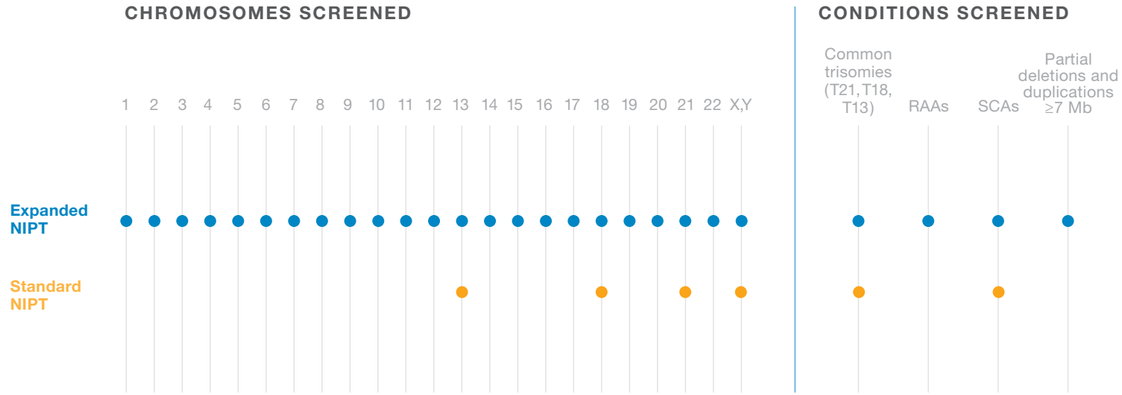
With cell-free DNA (cfDNA)–based prenatal testing, also called noninvasive prenatal testing (NIPT), we can use expanded screening to obtain a comprehensive view of all 23 chromosome pairs while limiting the risk to your patient.

"...[F]indings other than the common trisomies are clinically relevant for pregnancy management, and...there is potential clinical utility in performing genome-wide NIPT."

- Van Opstal D, et al.[1]

GAIN EXPANDED NIPT INSIGHTS

NIPT gives you valuable information about the chromosomal status of the fetus as early as 10 weeks' gestation.[2,3] Newer tests take advantage of next-generation sequencing (NGS) to bring a whole-genome sequencing (WGS) approach to NIPT, expanding test options beyond chromosomes 21, 18, and 13 to include rare autosomal aneuploidies (RAAs), sex chromosome aneuploidies (SCAs), and partial deletions and duplications, also referred to as copy number variations (CNVs), ≥7 Mb in size. Traditional, targeted tests do not screen for these additional chromosomal abnormalities, which have been associated with clinically relevant outcomes such as developmental delays, intellectual disabilities, structural anomalies, and adverse pregnancy outcomes.[4,5]



RARE IS MORE COMMON THAN YOU THINK

While called rare, rare autosomal aneuploidies (RAAs) are more prevalent than you may expect. Their combined screen positive rate in early pregnancy is estimated to be 0.44%.[4,5]

Compare that to the estimated combined 0.56% screen positive rate of trisomies 21, 18, and 13.[6] This means that **you may be missing something if you're not looking at the whole genome.**

Why Expanded NIPT screening?

EXPANDED SCREENING						
	Common aneuploidies			SCA	Additional chromosomal conditions	
Screened condition	Trisomy 21	Trisomy 18	Trisomy 13	Sex chromosome aneuploidy	RAAs	Partial deletions and duplications ≥7 Mb
Clinical association	Down syndrome	Edwards syndrome	Patau syndrome	Turner syndrome, Klinefelter syndrome, others	Early miscarriage, fetal anomalies, growth restriction, UPD, stillbirth	Fetal anomalies, developmental delay, others
Screen positive rate, all risk[6,7]	0.39%	0.13%	0.04%	0.39%	0.34%*	0.1%
Total screen positive rate	0.56%[6]			0.39%[6]	0.44%[7]	

Expanded NIPT may increase the overall screen positive rate.

cfDNA Screening Observed NIPT Screen Positive Rate at FIRST Trimester.
UPD=uniparental disomy; RAA=rare autosomal aneuploidy.

*This study included only rare autosomal trisomies. The screen positive rate for all RAAs, which also includes monosomies, is expected to be marginally higher than the rate reported for rare autosomal trisomies.

WHY RAAs AND CNVs MATTER

A positive RAA or CNV NIPT result can represent the fetal and/or placental genome. Either way, a positive result indicates an increased risk for fetoplacental disease and is associated with clinical relevance in half of the cases.[4,7,8] Even if the RAA or CNV is mosaic in nature, an abnormality within the fetus and/or placenta may manifest itself.

Possible implications of RAA- or CNV-positive results include:

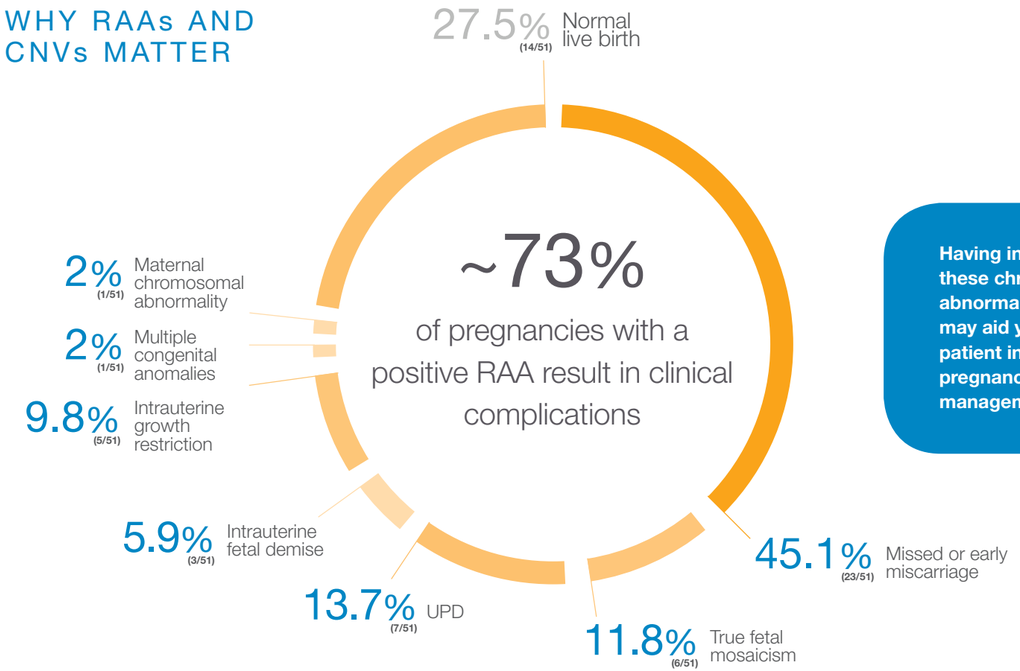
Risk of miscarriage—early screening may help in understanding the cause of a miscarriage and often reassures about the recurrence risk for a future pregnancy with a chromosomal abnormality.

Risk of fetal anomalies—RAAs and CNVs may have an adverse effect on organ and brain development, resulting in structural anomalies, developmental delays, and intellectual disability; even if the RAA is only present in the placenta, uniparental disomy in the fetus can lead to adverse effects on development.

Risk of adverse outcomes—if the RAA or CNV is confined to the placenta, the fetus may be chromosomally normal, but problems with the placenta may result in poor fetal growth and/or preterm labor.

CNV=copy number variation; RAA=rare autosomal aneuploidy; UPD=uniparental disomy.

WHY RAAs AND CNVs MATTER



Having insight into these chromosomal abnormalities earlier may aid you and your patient in making pregnancy and delivery management decisions.

RAAs were detected using expanded NIPT in 51 cases. Cases may fall into more than one category, therefore the total may exceed 100%.[4] This study included only rare autosomal trisomies. The screen positive rate for all RAAs, which also includes monosomies, is expected to be marginally higher than the rate reported for rare autosomal trisomies.

CNV=copy number variation; RAA=rare autosomal aneuploidy; UPD=uniparental disomy.

VERISEQ™ NIPT SOLUTION V2: SUPERIOR PERFORMANCE, MORE CONFIDENCE

To provide your patients with the best care possible, you need information from an NIPT screen you can trust. The VeriSeq™ NIPT Solution v2 combines low failure rates, highly accurate results, and low false-positive rates, making it one of the most reliable NIPT screens available.[9]

It covers all 23 pairs of chromosomes, which is more than any other available prenatal screening solution, providing the most comprehensive view of the fetal genome for broad insights early in the pregnancy. You can test as early as 10 weeks' gestation, so you'll get results early in the pregnancy.

	Trisomy 21 Down syndrome	Trisomy 18 Edwards syndrome	Trisomy 13 Patau syndrome	RAA	Partial deletions and duplications
Sensitivity	>99.9%	>99.9%	>99.9%	96.4%	74.1%
Specificity	99.90%	99.90%	99.90%	99.80%	99.80%

Disclaimer: Sensitivity and specificity of the VeriSeq™ NIPT Solution v2 for detecting trisomies 21, 18, and 13 in a basic screen for singleton pregnancies (excluding known mosaics).

Source: VeriSeq™ NIPT Solution v2 package insert, May 2019.

Data on file, Illumina, Inc. 2020.

WHAT DOES A POSITIVE RESULT MEAN?

It is important to note that NIPT is a screening test, not a diagnostic test. Any positive result needs to be confirmed with diagnostic testing. NIPT results should not be used as the sole basis for pregnancy management decisions.

If your patient does receive a positive NIPT result, refer them to a health care professional with appropriate expertise to discuss the reported abnormalities, what further testing and evaluations are appropriate, and potential clinical implications. Testing options can include (but are not limited to):

Detailed ultrasound evaluation to confirm fetal viability, identify possible structural anomalies in the fetus, and/or to determine if the pregnancy is at risk for complications such as intrauterine growth restriction

Diagnostic testing via chorionic villus sampling or amniocentesis to determine if the positive NIPT result is indicative of a true fetal chromosomal abnormality, fetal mosaicism, fetal uniparental disomy, or placental mosaicism

Additional specialized testing (in some cases)

Limitations of the test:
NIPT based on cfDNA analysis from maternal blood is a screening test; it is not diagnostic. False-positive and false-negative results do occur. Test results must not be used as the sole basis for diagnosis. Further confirmatory testing is necessary prior to making any irreversible pregnancy decision. A negative result does not eliminate the possibility that the pregnancy has a chromosomal or subchromosomal abnormality. This test does not screen for polyploidy (eg, triploidy), birth defects such as open neural tube defects, single-gene disorders, or other conditions, such as autism. There is a small possibility that the test results might not reflect the chromosomal status of the fetus, but may instead reflect chromosomal changes in the placenta (ie, confined placental mosaicism) or the mother that may or may not have clinical significance.

cfDNA=cell-free DNA.

EARLIER INSIGHTS, EARLIER PLANNING

Advanced technology. Increased understanding. More information. Chromosomal abnormalities occur across the genome at a collective rate that is clinically relevant. NIPT with expanded screening, powered by WGS, provides a comprehensive view of all the chromosomes in the fetal genome, yielding knowledge beyond the common aneuploidies. Now, you and your patients can obtain more insights earlier to aid in pregnancy and delivery management.

Is NIPT with expanded screening right for my patients?

When you need more insight into the genetic risks of a pregnancy, or it is a clear patient preference, NIPT with expanded screening may be the right choice for you.

Expanded NIPT may also be considered in patients with increased risk of chromosomal abnormalities, based on medical history or other clinically relevant findings.

WGS=whole-genome sequencing.

References

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6. Liang D, Cram DS, Tan H, et al. Clinical utility of noninvasive prenatal screening for expanded chromosome disease syndromes. *Genet Med.* 2019;21:1998–2006.

7. Pertile MD. Genome-wide cell-free DBA-based prenatal testing for rare autosomal trisomies and subchromosomal abnormalities. In: Page-Christiaens L, Klein H-G, eds. *Noninvasive Prenatal Testing (NIPT): Applied Genomics in Prenatal Screening and Diagnosis*. London, United Kingdom: Academic Press Elsevier; 2018:97-123.

8. Benn P, Malvestiti F, Grimi B, Maggi F, Simoni G, Grati FR. Rare autosomal trisomies (RATs): a comparison of the detection through cell-free DNA and chorionic villus sampling [epub ahead of print]. *Ultrasound Obstet Gynecol*. 2019;54(4):458-467.

9. Data on file, Illumina, Inc 2019.

Intended use

The VeriSeq™ NIPT Solution v2 is an in vitro diagnostic test intended for use as a screening test for the detection of genome-wide fetal genetic anomalies from maternal peripheral whole blood specimens in pregnant women of at least 10 weeks' gestation. VeriSeq™ NIPT Solution v2 uses whole-genome sequencing to detect partial duplications and deletions for all autosomes and aneuploidy status for all chromosomes. The test offers an option to request the reporting of sex chromosome aneuploidy (SCA). This product must not be used as the sole basis for diagnosis or other pregnancy management decisions. The VeriSeq™ NIPT Solution v2 includes: the VeriSeq™ NIPT Workflow Manager v2 for the VeriSeq™ NIPT Microlab STAR, the VeriSeq™ NIPT Sample Prep Kits, and the VeriSeq™ Onsite Server v2 with the VeriSeq™ NIPT Assay Software v2. The VeriSeq™ NIPT Solution v2 is intended to be used with a next-generation sequencer.

NIPT based on cfDNA analysis from maternal blood is a screening test; it is not diagnostic. Test results must not be used as the sole basis for diagnosis. Further confirmatory testing is necessary prior to making any irreversible pregnancy decision.

cfDNA=cell-free DNA.

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Expanded NIPT

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Learn more at illumina.com.

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