

ACMG Publishes Evidence-Based Clinical Practice Guideline Recommending Noninvasive Prenatal Screening Become the Standard Screening Option for All Pregnant Individuals

BETHESDA, MD — December 16, 2022 | The American College of Medical Genetics and Genomics (ACMG) has released a new Evidence-Based Clinical Practice Guideline (EBG), ["Noninvasive prenatal screening for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics."](#)

Noninvasive prenatal screening with cell-free DNA (cfDNA), also referred to as NIPS, was introduced into clinical practice in 2011. NIPS involves a blood test performed any time after 10 weeks of pregnancy. By analyzing small fragments of circulating DNA in the mother's blood that primarily originate from the placenta, the test can be used to detect several chromosomal disorders including Down syndrome. The use of NIPS as an alternative to traditional biochemical and ultrasound-based screening tests has rapidly expanded in recent years but access to NIPS remains uneven in the United States.

Based on a Systematic Evidence Review published in May 2022, the new guideline makes a strong recommendation for the use of NIPS over traditional screening methods for all pregnant individuals with singleton and twin gestations, to screen for fetal trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome) as well as fetal sex chromosome abnormalities (aneuploidy). The guideline replaces the 2016 ACMG Position Statement, which recommended that all pregnant individuals have access to NIPS and be made aware of its superior sensitivity for detecting common trisomies.

"Our workgroup was able to make a strong recommendation that NIPS should replace traditional screening for the common fetal trisomies for all individuals with singleton or twin pregnancies. This recommendation was supported by the rigorous evidence review conducted by ACMG that demonstrated NIPS' clearly superior screening characteristics across virtually all studies. This is the first professional practice guideline that is based on such a thorough analysis of the current literature," said Jeffrey S. Dungan, MD, FACMG, the first author of the new guideline.

To develop the new guideline, an ACMG working group considered the results of the recent Systematic Evidence Review, which analyzed the performance, psychosocial impact, and cost-effectiveness of NIPS compared to traditional screening methods. The Evidence-Based Guideline working group also considered additional emerging evidence published after the Systematic Evidence Review, as well as relevant information from conference presentations, grey literature (which is content produced outside of traditional publishing and distribution channels), and their own extensive clinical experiences with prenatal screening. Recommendations were made based on the quality and certainty of evidence.

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The new guideline includes strong recommendations for clinicians to use NIPS over traditional screening methods for all pregnant individuals who desire such screening. This applies for the common trisomies in singleton and twin pregnancies, as well as for sex chromosome abnormalities in singleton pregnancies. The group cites evidence that, for singleton pregnancies, the detection rate of NIPS for Trisomy 21 is 98.8%, for Trisomy 18 is 98.83%, for Trisomy 13 is 92.85% and for sex chromosome abnormalities is 99.6%.

The high accuracy of these tests, as well as their low false positive rates, means that fewer pregnant individuals have to undergo invasive diagnostic procedures. Moreover, obtaining a reliable result early in pregnancy is a major advantage of NIPS compared to traditional methods, which require multiple tests and/or ultrasound exams over the course of the first two trimesters of pregnancy.

The new guidelines also include a conditional recommendation, based on moderate certainty of evidence, that NIPS for 22q11.2 deletion syndrome, the most common pathogenic copy number variant, be offered to all pregnant individuals.

At this time, ACMG concluded that there is insufficient evidence to recommend routine screening for other copy number variants, which are changes to smaller sections of chromosomes rather than entire chromosomes. ACMG also concluded that there is insufficient evidence to recommend NIPS for the identification of rare autosomal trisomies—duplications of chromosomes other than 13, 18, 21, X or Y. These recommendations, the team said, were mostly due to a lack of clinical evidence in the current literature.

With the release of this Evidence-Based Clinical Practice Guideline, ACMG affirms the principles of counseling for NIPS that have previously been endorsed, including providing up-to-date, balanced and accurate information and personalized, patient-centric counseling. Pre-test counseling should include a discussion of the optional and screening nature of NIPS and what results may mean. Post-test counseling should emphasize the reduction, but not elimination, of risk with negative results and the recommendation for diagnostic confirmation of the NIPS results after positive tests.

Dungan added, “NIPS has been available from a number of clinical labs for more than 10 years but has not been routinely offered to all pregnant individuals. One factor behind this is the inconsistent insurance coverage across various populations and insurance plans. We believe that our new evidence-based guideline provides a clear and valid rationale to provide coverage for all pregnant individuals who opt for NIPS.”

About the American College of Medical Genetics and Genomics

Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is a prominent authority in the field of medical genetics and genomics and the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics. The only medical specialty society in the US that represents the full spectrum of medical genetics disciplines in a single organization, the ACMG provides education, resources and a voice for more than 2,500 clinical and laboratory geneticists, genetic counselors and other healthcare professionals. ACMG's mission is to improve health through the clinical and laboratory practice of medical genetics as well as through advocacy, education and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health. *Genetics in Medicine* and the new *Genetics in Medicine Open*, a gold open access journal, are the official ACMG journals. ACMG's website, www.acmg.net, offers resources including policy statements, practice guidelines, and educational programs. The ACMG Foundation for Genetic and Genomic Medicine works to advance ACMG educational and public health programs through charitable gifts from corporations, foundations and individuals.

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