Screening vs Diagnostic: Understanding Non-Invasive Prenatal Screening

Non-invasive prenatal screening (NIPS) is a category of lab tests used during pregnancy by health care providers to assess whether a pregnant patient may be carrying a fetus at increased risk of having a genetic disorder. These tests are used most often to look for conditions caused by the presence of an extra or missing copy of a chromosome, and, in some cases, they can be used to identify deletions (microdeletions) or duplications (microduplications) of a part of a chromosome.

NIPS monitors for conditions that can cause cognitive impairment, shortened life expectancy and/or other birth defects. NIPS utilizes a blood draw taken from the expectant patient, making it a "non-invasive" procedure. Most DNA is found inside the nucleus of the cell. However, cell-free DNA (cfDNA) used in NIPS is fragments of DNA from placenta cells that naturally are shed into a pregnant patient's blood during pregnancy.[i] Before the introduction of NIPS, providers used maternal serum screening (MSS), which uses biochemical analysis of certain protein markers and not cfDNA. Compared to NIPS, MSS has a higher rate of false positives, which leads to more patients being identified as "high risk" and being referred for costly, invasive and higher risk diagnostic procedures.[ii,iii]

How and when is NIPS performed?

NIPS can be used early in the prenatal screening and diagnostic journey. The screening tests often are administered in the first trimester, usually at around 10 weeks of pregnancy.[iv] The results are interpreted by a patient's health care provider and provide information to help assess whether additional testing would be recommended. If a pregnancy is identified as being at increased risk for a chromosomal abnormality, next steps would be discussed with the patient, including confirmatory and diagnostic testing and consultation with a genetic counselor.

Who should receive NIPS?

The American College of Obstetrics and Gynecology (ACOG) and the Society for Maternal Fetal Medicine (SMFM) recommend that all pregnant patients be offered the option of prenatal screening for fetal chromosomal abnormalities, which can occur regardless of maternal age, baseline risk, race or ethnicity.[v] ACOG and SMFM currently do not recommend routine screening with cfDNA for microdeletions and microduplications.[v] Ultimately, choices about prenatal screening are made by patients in close consultation with their health care provider.

What are the benefits of NIPS?

Chromosomal abnormalities can have profound consequences on the life and health of a child. Detecting this information early on in pregnancy can help health care providers recommend specialized care, before and after delivery. Knowledge of the presence of chromosomal abnormalities can be a powerful tool to prepare for delivery. This allows for the appropriate level of care at a facility with access to neonatal specialists, social workers and counseling. In addition, the availability of a non-invasive blood test to screen for common chromosomal abnormalities can help a large majority of patients avoid more invasive tests that have associated risks, including infection and miscarriage. Multiple studies have confirmed a significant reduction in invasive prenatal procedures since the introduction of NIPS (greater than 50% reduction).[vi,vii,viii]

Understanding the difference between screening and diagnostic tests

Screenings are used throughout a patient's lifetime to detect potential health conditions, even if the patient currently is not exhibiting any symptoms of disease. A screening test provides information about the chance a person may be affected with a condition, and diagnostic tests are used to confirm the presence or absence of a condition. Generally, the goal of screening is to identify who in a population should consider diagnostic testing, especially when this testing may be invasive or carry risks of its own.

In contrast to screening, diagnostic tests are performed upon a health care provider's recommendation when a patient's health, medical history or previous screen warrants further investigation. These tests can lead to a diagnosis of a medical condition by the patient's health care provider.

NIPS – like all screening tests – is not a diagnostic test and does not provide definitive results for any genetic condition. These risk assessments help identify pregnancies at elevated risk of having chromosomal abnormalities. The results of these screening tests can help health care providers and genetic counselors develop appropriate medical management plans with their patients.

Diagnostic tests for chromosome abnormalities during pregnancy include chorionic villus sampling (CVS) and amniocentesis. These are used to determine, with as much certainty as possible, whether a specific genetic disorder or condition is present in a fetus. These tests are invasive, in contrast to NIPS, and carry a heightened risk for miscarriage related to the procedure.

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[i] https://medlineplus.gov/genetics/understanding/testing/nipt/

[ii] https://www.illumina.com/clinical/reproductive-genetic-health/nipt/labs/nipt-vs-conventional-aneuploidy-screening.html

[iii] Delzell, John E. "What can we do to prepare patients for test results during pregnancy?" *West J Med* vol. 173, 3 (2000): 183-184. doi: 10.1136/ewjm.173.3.183 (PMID: 10986182)

[iv] https://swhr.org/wp-content/uploads/2022/01/SWHR-Genetic-Screening-Poster-FINAL-2022Jan.pdf

[v] Rose, Nancy C. MD; Kaimal, Anjali J. MD, MAS; Dugoff, Lorraine MD; Norton, Mary E. MD; American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. "Screening for Fetal Chromosomal Abnormalities" *Obstetrics & Gynecology* vol. 136, 4 (2020): 48-69. doi: 10.1097/AOG.0000000000004084 (PMID: PMID: 32804883)

[vi] Van Den Bogaert, Kris et al. "Outcome of publicly funded nationwide first-tier noninvasive prenatal screening." *Genetics in medicine : official journal of the American College of Medical Genetics* vol. 23,6 (2021): 1137-1142. doi:10.1038/s41436-021-01101-4 (PMID: 33564150)

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medicine." *American journal of perinatology* vol. 31,9 (2014): 759-64. doi:10.1055/s-0033-1359717 (PMID: 24338115)
[viii] Robson, Stephen J, and Lisa Hui. "National decline in invasive prenatal diagnostic procedures in association with uptake of combined first trimester and cell-free DNA aneuploidy screening." *The Australian & New Zealand journal of obstetrics & gynaecology* vol. 55,5 (2015): 507-10. (PMID: 26259499)