JUNO™ diagnostics

Equitable Non-Invasive Prenatal Screening in the United States

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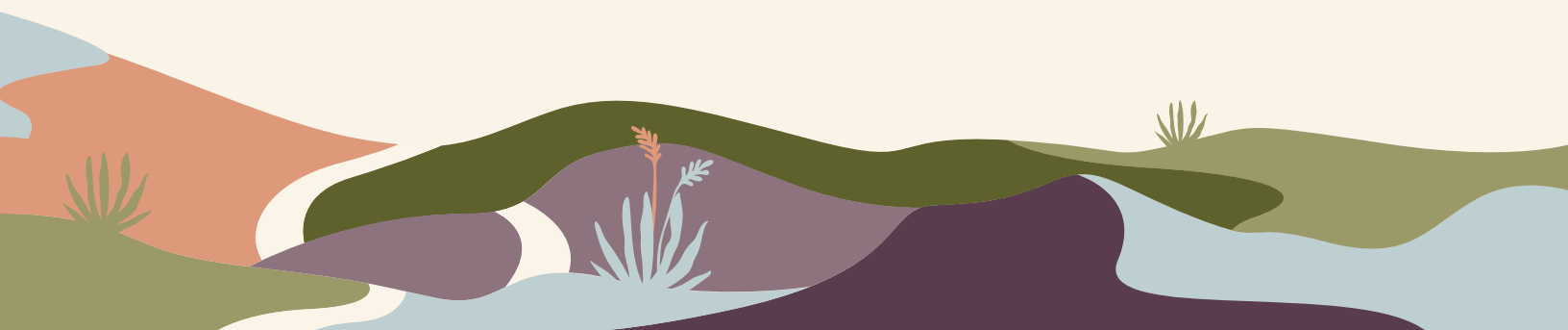

Introduction

Maternal serum screening has long been the standard for fetal aneuploidy screening, with high-risk results requiring diagnostic confirmation through chorionic villus sampling (CVS) or amniocentesis.

Non-invasive prenatal screening (NIPS), also known as non-invasive prenatal testing (NIPT) or circulating cell-free DNA (cfDNA) screening, has consistently demonstrated lower false-positive rates and higher detection rates for common aneuploidies than traditional serum screening methods, including first trimester screening (FTS), serum integrated screening, sequential screening, and quad or penta screening.[1]

Due to its superior sensitivity and specificity compared to maternal serum screening, NIPS offers a higher standard for fetal aneuploidy screening. By reducing the occurrence of unnecessary prenatal diagnostic procedures, patients are less likely to encounter their associated risks, including possible pregnancy loss.[1] The American College of Obstetricians and Gynecologists (ACOG) issued a practice bulletin on fetal aneuploidy screening in 2020, and recommended that all patients be offered the option of NIPS through cfDNA analysis.[2]

Yet, in the United States, disparities in access to comprehensive health insurance, tailored patient education and counseling resources, and affordable genetic screening products form barriers to the equitable implementation of NIPS for all who may benefit.

In this white paper, we explore the issue of equitable access to NIPS, including:

- **A breakdown of the current state of NIPS accessibility in the U.S.**
- **Current research on the accuracy of NIPS compared to traditional serum screening**
- **An overview of current trends in NIPS utilization**
- **A brief cost analysis of NIPS adoption across patient populations**
- **Expert predictions on the future of prenatal genetic screening**

Why does equitable access to NIPS matter?

- NIPS was commercially introduced for fetal aneuploidy screening in 2011. Using next-generation sequencing and bioinformatics algorithms, NIPS offers a more accurate option to assess fetal aneuploidy information than traditional serum screening.[3] It also allows screening for additional aneuploidies that cannot be detected through FTS and other serum screening paradigms, including fetal sex chromosome aneuploidy.

- NIPS requires only a blood sample collected from the pregnant person in order to analyze chromosomal information from the pregnancy without any procedural risks for pregnancy loss.

- NIPS products typically screen for the most common aneuploidies observed at the time of live birth: trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome).[4] They often also include evaluation for sex chromosome aneuploidies as well as the presence or absence of Y chromosome material.[5]

- NIPS is used for screening, not diagnostic purposes. While the terms NIPS, NIPT, and cfDNA screening are often used interchangeably, in this white paper we use 'NIPS' to acknowledge the screening nature of this technology.

Barriers to equitable fetal aneuploidy evaluations in the U.S.

Both the American College of Obstetricians & Gynecologists (ACOG)[2] and the American College of Medical Genetics and Genomics[6] (ACMG) agree that healthcare providers should counsel all patients - not just those with high-risk* pregnancies - about NIPS and other prenatal screening and diagnostic testing options. However, many pregnant individuals do not have the opportunity to make an informed decision about the full spectrum of their prenatal screening and testing options.[2]

This disparity primarily stems from three sources:

- **The lack of universal insurance coverage for NIPS**
- **The out-of-pocket cost of genetic screening and testing**
- **The hesitancy of some healthcare providers to offer or recommend NIPS to their patients given the above factors**

Most (but not all) private insurance companies cover NIPS across risk stratifications, but many state Medicaid programs deny NIPS coverage for women with average-risk pregnancies.[7, 8]

- **Only 20 states offer NIPS coverage in all pregnancies.**
- **Twenty-five states, including Texas, Colorado, and New York, only cover NIPS for high-risk pregnancies.**
- **Five states and the District of Columbia deny NIPS coverage completely, even to those with pregnancies at high risk for aneuploidy.**

When a person's health insurance plan denies coverage of NIPS, or payment for the cost of screening is only provided after meeting one's deductible or co-insurance, pregnant people and their families may encounter out-of-pocket costs for NIPS in excess of $1,000. The lack of affordable NIPS effectively cements a barrier to equitable care between those who can afford such out-of-pocket costs, or those with access to comprehensive health and maternity care insurance, and those who do not enjoy such benefits.[9]

To date, healthcare providers have been forced to decide whether and how to counsel patients on this universally beneficial, selectively costly screening option. Some physicians and genetic counselors may be hesitant to recommend NIPS to patients whose insurance status, income, or geographic location make testing unaffordable or otherwise virtually inaccessible.[9] Eliminating the barriers created by the cost of NIPS is essential to promoting equitable reproductive care in the U.S. and worldwide.

For insurance purposes and within the medical community, "high-risk" typically describes pregnancies at maternal age >35 at delivery, those with high-risk results from maternal serum screening or prenatal ultrasound examinations, and those with specific risk factors for aneuploidy including a family or prior pregnancy history of chromosome variations.

Why is NIPS an improvement over traditional FTS?

A 2015 study published in The New England Journal of Medicine found that NIPS for trisomy 21 offered higher sensitivity, higher positive predictive value (PPV), and significantly lower false-positive rates than FTS.[10] These findings were confirmed in a meta-analysis inclusive of data from multiple NIPS laboratories published later in the same year.[11]

When screening for trisomies 21 and 18—and, to a lesser degree, trisomy 13 —NIPS demonstrates far superior detection rates (>99%) and far lower false-positive rates (<1%) than FTS. These findings have been consistent across study cohorts comprised of both high-risk pregnancies and average-risk pregnancies.[12]

One 2016 study found that the increased accuracy of NIPS over FTS decreased the need for invasive diagnostic procedures by 88%, thereby reducing the possibility of iatrogenic fetal loss by 94% when compared to the downstream need for invasive procedures following FTS.[13]

The positive predictive value (PPV) of NIPS varies with each condition screened.When the background chance for a condition is extremely low, a screen-positive NIPS result confers a lower PPV than a screen-positive NIPS result for a much more common condition. Furthermore, in very rare cases, NIPS results may prompt further evaluation of the pregnant person.

Despite these limitations, NIPS represents a technological advancement that is superior to traditional methods of fetal aneuploidy screening.[14] Yet, the widespread application of NIPS is limited by the associated cost-making NIPS not a question of choice, but instead, one of access.

Trends in NIPS

Current trends in prenatal testing and screening have demonstrated a massive shift from invasive diagnostic testing through chorionic villus sampling (CVS) and amniocentesis to non-invasive screening methods.[15] Many reasons exist for patient preference of NIPS as a first-tier screening evaluation, including its highly sensitive and specific evaluation for fetal aneuploidy, as well as its non-invasive nature without associated risk for pregnancy loss. Not only does NIPS offer a highly reliable evaluation for select fetal aneuploidies, but it also does not require advanced training of a physician/sonographer team to complete the procedure.

The American College of Medical Genetics and Genomics (ACMG) has stated that NIPS can replace traditional serum screening for trisomies of chromosomes 21, 18, and 13 scenarios.[6] Additionally, NIPS is currently the only method of non-invasive screening for sex chromosome variations and certain copy-number variants (CNVs), thus increasing the potential for its application in a variety of clinical scenarios.

Standardized use of NIPS has spread across the globe due to both its accuracy and potential to decrease the need for invasive prenatal diagnosis.[15] However, about half of state Medicaid programs do not cover NIPS for average-risk pregnancies.[8] Cost remains the primary barrier preventing equitable access to safe and reliable fetal aneuploidy screening through NIPS.[7]

Cost Analysis of NIPS in U.S. Health Insurance Plans

As a screening tool, NIPS is cost-effective and not associated with complications such as fetal loss, as is the case with prenatal diagnosis.[13] Experts in healthcare economics predict that NIPS cost per unit will continue to decrease as technology advances.[12]

Cell-free DNA-based NIPS has become increasingly popular among healthcare providers and expecting parents, but insurance coverage does not yet reflect this increased utilization. In 2022, much uncertainty exists surrounding the incorporation of NIPS into both private and public insurance plans.

Recent studies have demonstrated that pregnant people with public insurance are about 3.5 times more likely than those with private insurance to choose NIPS as initial screening for fetal aneuploidy.[9] This discrepancy is largely due to the high deductibles, co-insurances, co-payments, and insufficient coverage of many private insurance plans. Self-pay prices for NIPS can range from around $300 to over $1,000, depending on the availability of assistance programs for those facing financial hardship.[9]

The Future of NIPS

NIPS is a dynamic field with research and technological advancement continually driving new applicability across diverse patient populations and varied clinical contexts. Provider-offered NIPS should be the standard for fetal aneuploidy screening in all pregnancies, not only those considered high-risk.[2]

Without parallel growth in NIPS accessibility alongside advances in NIPS applications and accuracy, inequitable opportunities for NIPS utilization increases the potential for disparities in access. Access to high-quality, affordable NIPS, such as the JunoDx Hazel™ NIPS, is essential to ensure equitable and robust prenatal genetic screening opportunities for everyone.

JunoDx™ aims to provide equitable non-invasive prenatal screening in all pregnancies by eliminating long-standing barriers to care such as cost. For more information on offering your patients affordable and accessible NIPS, schedule a call with JunoDx™ at support@junodx.com.

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