

Improving Inequities in Prenatal Screening: Time to Modernize Guidelines

Presented by:

Edie Smith, DNP, CNM, WHNP-BC, AGN-BC

Medical Science Liaison III

Myriad Women's Health

Summer Pierson, MS, CGC

Senior Manager, Provider Engagement and Relationships Myriad Women's Health

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Edie Smith, DNP, CNM, WHNP-BC, AGN-BC Medical Science Liaison III Myriad Women's Health





Disclosures

All presenters are employees of Myriad Genetics





Agenda

- Current Landscape
- Carrier Screening
- Non-invasive Prenatal Screening
- Working Together to Reduce Disparities





Objectives

- Describe various professional resources that provide support for genetic risk assessment in midwifery practice
- Implement current guideline recommendations into clinical practice.
- Recognize barriers to patient access to important actionable genetic information
- Identify & engage with others dedicated to improving patient access to actionable genetic information





ACNM Mission

To support midwives, advance the practice of midwifery, and achieve optimal, equitable health outcomes for the people and communities midwives serve through inclusion, advocacy, education, leadership development and research.





Guidance that Shapes Midwifery Practice

- ACNM Scope of Practice
- ACNM Core Competencies
- National Guidelines & Position Statements & Opinions
 - ACOG
 - ACMG
 - NPWH
- Individual State Regulations





One way to address inequities is to get comfortable with genetics









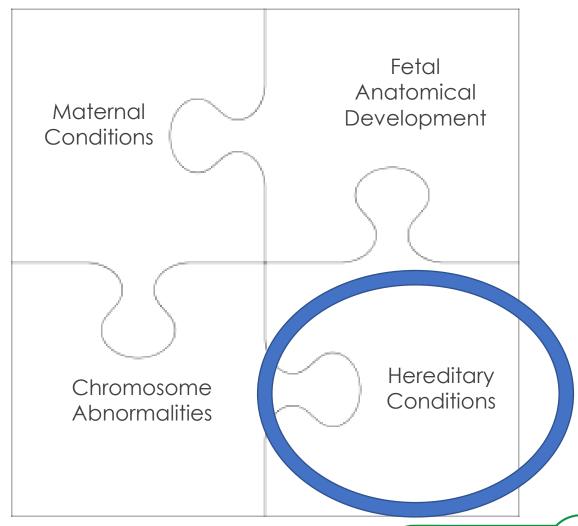
Summer Pierson, MS, CGC Sr. Mgr. Provider Engagement & Relationships Myriad Women's Health





Screening is Essential for Healthy Outcomes

The major goal of prenatal care is to help ensure the birth of a healthy baby while minimizing risk to the mother.







Carrier Screening

"...the goal of preconception and prenatal carrier screening is to provide couples with information to optimize outcomes based on their personal values and preferences."

A Joint Statement of the American College of Medical Genetics and Genomics (ACMG), American College of Obstetricians and Gynecologists (ACOG), National Society of Genetic Counselors (NSGC), Perinatal Quality Foundation, and Society for Maternal-Fetal Medicine (SMFM).

-from Expanded Carrier Screening in Reproductive Medicine—Points to Consider





When patients have information, they use it!



Retrospective analysis of at-risk couples 2017: 64 couples 2018: 391 couples

Preconception

77%

Pursued alternative reproductive options

Prenatal

Pursued or planned for prenatal diagnosis

37%







What's preventing people from getting the information they need?

Our practice, our guidelines, our insurance coverage





The History of Carrier Screening in the US







Historically: US Guidelines Based on Ethnicity

	Caucasian	Ashkenazi Jewish	African/ AA	Asian	Hispanic	Mediterr.	Southeast Asian
Cystic Fibrosis		• •	• •	• •	• •	• •	• •
Spinal Muscular Atrophy				• •	• •	• •	• •
Tay Sachs Disease							
Canavan Disease							
Familial Dysautonomia							
Bloom Syndrome							
Gaucher Disease							
Fanconi Anemia Type C							
Mucolipidosis IV							
Niemann-Pick Disease Type A							
Sickle Cell Anemia							
Thalassemia							





Assumptions that need to be true for ethnicity-based screening to be effective

Ethnicity data is always easily obtained

No Ethnicity provided: ~15% in both studies

Historical ethnicitybased disease risk literature is complete Guidelines exist for ~7-8 ethnicities Published data on ~10- 15 ethnicities No Ethnicity provided: ~15% Other Ethnicity: ~1-6% Multi-ethnic: ~3-25%

Self-reported ethnicity is consistent and accurate

Self-reported ethnicity is an imperfect indicator of genetic ancestry





Pitfalls of Ethnicity Based Screening

1 out of **7**

new marriages is between spouses of different ethnic backgrounds





40%

of Americans can't correctly identify the ethnicity of all four grandparents





The current status quo is leaving affected pregnancies unidentified

At-Risk Couple Rate:

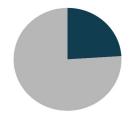
1 in 44 - 1 in 22 couples

Affected Pregnancies:

1 in 300 - 1 in 175

Individually rare, collectively common

Northern European



24% of affected pregnancies identified

Ashkenazi Jewish



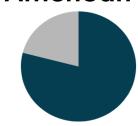
25% of affected pregnancies identified

Hispanic



13% of affected pregnancies identified

African American

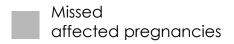


79% of affected pregnancies identified

East Asian



24% of affected pregnancies identified









Current Guidelines Do Not Address Limitations of Self-Reported Ethnicity

- Data demonstrate a discrepancy between self-reported ethnicity and genetic ancestry.
- Ethnicity-based carrier screening is <u>recommended</u>, but <u>nearly</u> impossible to execute and be consistently accurate.
- There are no recommendations on management of individuals who self-report blended ethnicity, or individuals who are adopted, or are otherwise uncertain of their ethnicity.





How can providers help bridge the current gaps?

What panel you offer Which lab you offer Advocacy





Considerations when evaluating carrier screening panels

Panel Design

- Criteria for inclusion
- At-Risk Couple Rate (ARC)
- Bigger = better?

Detection Rate

- Targeted genotyping
- Gene sequencing
- Specialty assays for complex genes

Variant Curation

- ACMG classifications
- Curation pipelines
- Variants of uncertain significance

The *goal* of carrier screening is to inform people about their risk of having children with autosomal recessive and X-linked recessive disorders, to allow for informed decision making about reproductive options.





- Advocate for expanded carrier screening
 - Help educate policy makers
 - Write to state Medicaid Directors requesting coverage of CPT 81443, expanded carrier screening
 - Speak Up
 - Participate in oral testimony at medical policy meetings and other venues
 - Share Your ECS Experience
 - Highlight your experience using expanded carrier screening and how it has empowered you and your patients

Collaboration is Key

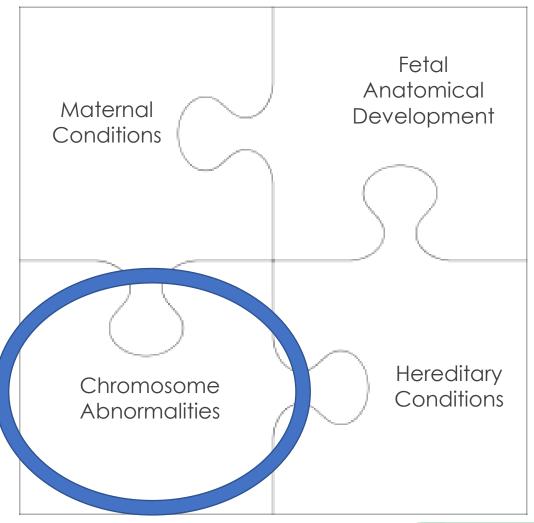






Screening is Essential for Healthy Outcomes

The major goal of prenatal care is to help ensure the birth of a healthy baby while minimizing risk to the mother.







ACOG now supports NIPS in average risk patients and recognizes its superior performance





ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician-Gynecologists

NUMBER 226

(Replaces Practice Bulletin 163, May 2016, Reaffirmed 2018)

Committee on Practice Bulletins—Obstetrics, Committee on Genetics, and Society for Maternal-Fetal Medicine. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics and Committee on Genetics, and the Society for Maternal-Fetal Medicine in collaboration with Nancy C. Rose, MD, and Anjali J. Kaimal, MD, MAS, with the assistance of Lorraine Dugoff, MD, and Mary E. Norton, MD, on behalf of the Society for Maternal-Fetal Medicine.

Screening for Fetal Chromosomal Abnormalities

"Cell-free DNA is the most sensitive and specific screening test for the common fetal aneuploidies."

Level A recommendation

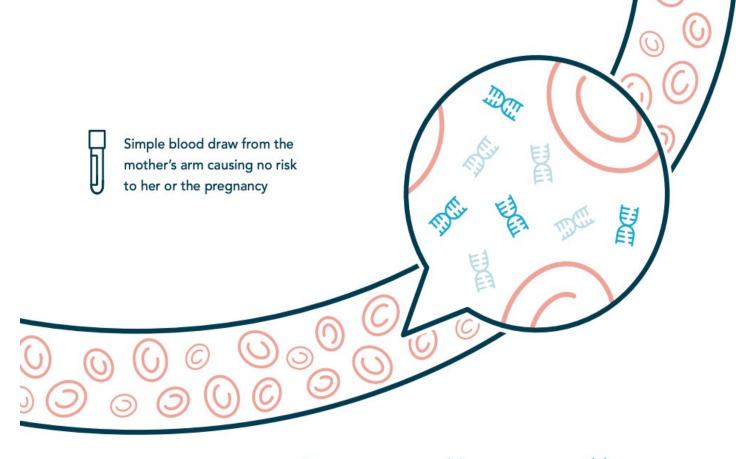
2020 ACOG/SMFM Practice Bulletin #226 on
screening for fetal aneuploidy





NIPS Refresher

- Fetal Fraction:
 Percentage of circulating DNA attributed to the fetus.
- The DNA identified as "fetal" originates from trophoblastic cells from the placenta.
- cffDNA co-mingles with maternal cfDNA in maternal circulation.





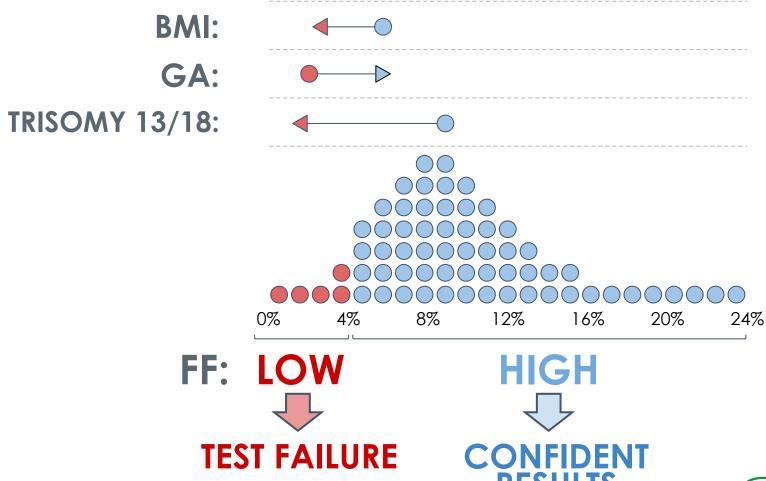








IMPACT AND DRIVERS OF LOW FETAL FRACTION IN NIPS

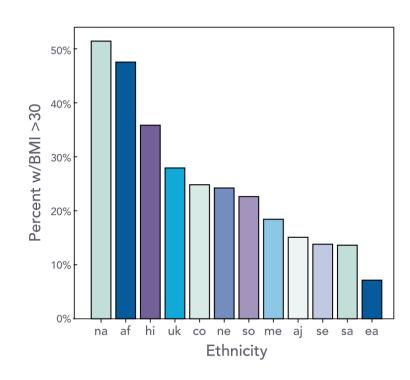






DUE TO LOW FETAL FRACTION, BMI CAN RESULT IN DISPARITIES IN CARE FOR PREGNANCY MANAGEMENT

- ~50% of pregnant patients present as overweight or obese to their OBGYN (BMI>25)¹. Further complicating the problem is that BMI is not evenly distributed across ethnicities².
- Current strategies to manage patients with high BMI include maternal serum screening or offering NIPS later in a patient's pregnancy. This creates a disparity in care.



- 1. Arroyo-Johnson C, Mincey KD. Obesity Epidemiology Worldwide. Gastroenterol Clin North 463 Am. 2016 Dec;45(4):571–9
- 2. Muzzey *et al.* (2019). Noninvasive prenatal screening for patients with high body mass index: Evaluating the impact of a customized whole genome sequencing workflow on sensitivity and residual risk. Prenatal Diagnosis. doi/abs/10.1002/pd.5603





How can providers help bridge the current gaps?

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Considerations when evaluating carrier screening panels

Panel Options

- Common Trisomies
- Sex Chromosome Abnormalities
- Expanded
 Aneuploidies
- Microdeletion Panels
- Genome Wide CNV

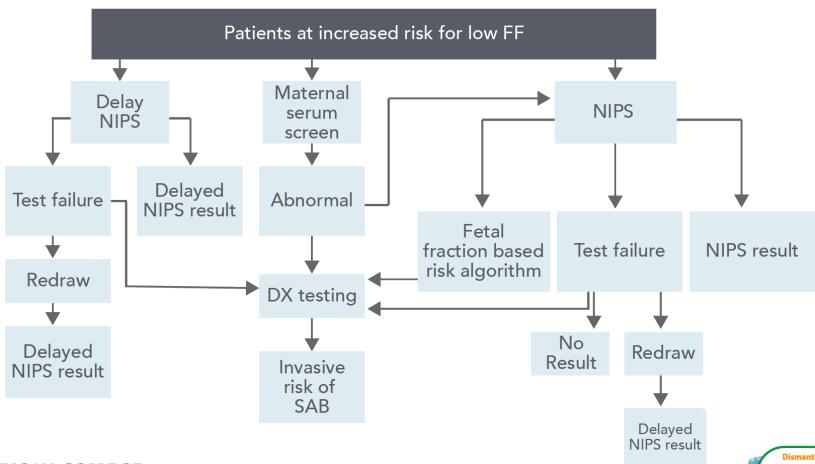
Time to Actionable Result

- TAT
- No Call Rate
- Opt. In vs Opt. Out options
- Management of specimens with low fetal fraction
- Positive Predictive Value Reporting





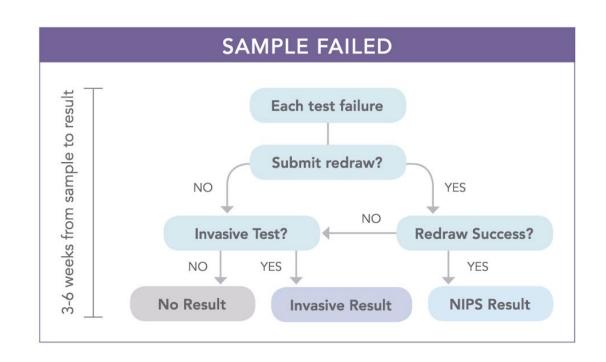
STRATEGIES TO DEAL WITH LOW FETAL FRACTION LEAD TO WORKFLOW CHALLENGES AND DISPARITY IN CARE







EVERY FAILED OR DELAYED SAMPLE CAN INCREASE PATIENT ANXIETY AND/OR LIMIT CLINICAL OPTIONS



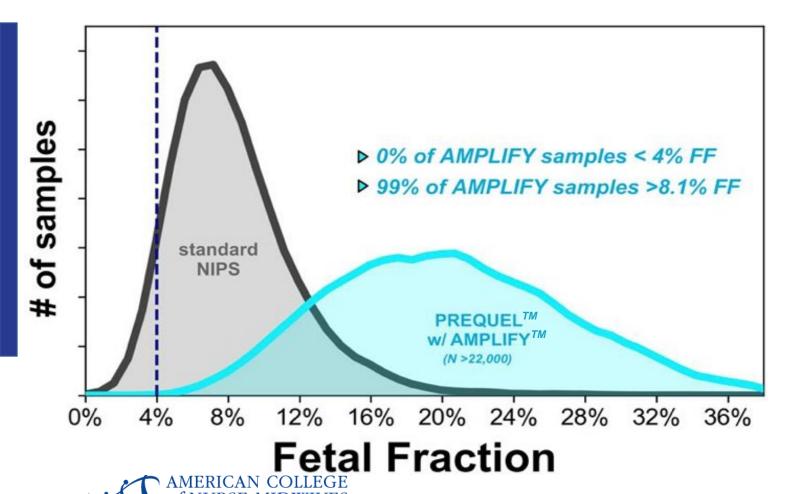
Patient anxiety







IMPACT OF FFA IN A REAL-WORLD CLINICAL LABORATORY SETTING



With women, for a lifetime[®]

- >20K clinical lab samples
- Test failure rate 0.16%
- Average FF with AMPLIFY: 20.5% (without AMPLIFY 8.1%)



HOW DOES AMPLIFY SET THE STAGE FOR FUTURE INNOVATIONS?

Higher fetal fraction amplification allows for increased sensitivity for small changes to the genome, including:

- Higher sensitivity for the microdeletion syndromes, like 22q deletion.
- Increased resolution allows for the increased accuracy in the calling of novel deletions and duplications throughout the genome, which can help in the diagnostics of other syndromes.

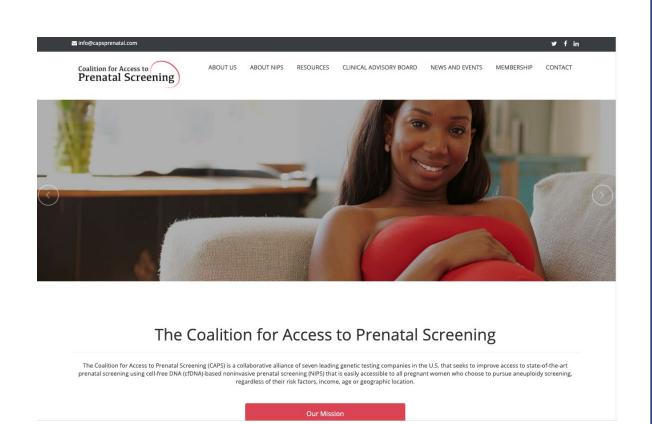




Advocate for NIPS

- Help educate policy makers
 - Write to state Medicaid Directors
 requesting coverage of NIPS for all
- Speak Up
 - Participate in oral testimony at medical policy meetings and other venues
- Share Your Experiences
 - Highlight your experience using NIPS and how it has empowered you and your patients

Collaboration is Key



www.capsprenatal.com



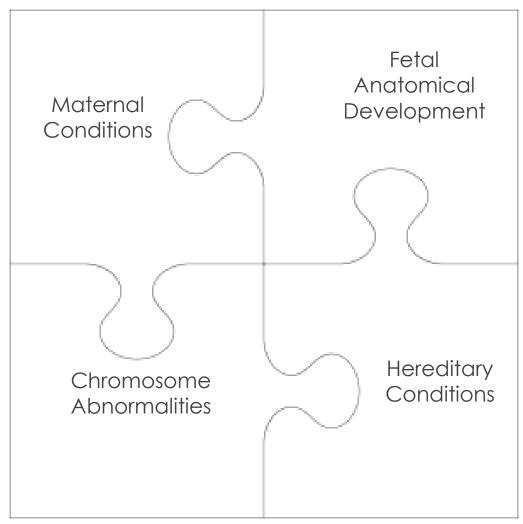


Answer the question: "Will my baby be healthy?" with consistent confidence:

NIPS is has superior performance across all pregnancies, including average risk patients.

Technology exists to minimize potential care inequities that result from low fetal fraction specimens.





ECS outperforms family history, basic screening and ethnicity-based screening in finding pregnancies at risk for serious heritable conditions.







Conclusion

- Significant advancements and improvements in genetic risk assessment and testing
- Genetics practice in the care of patients and families is constantly evolving - we need to keep abreast!
- Opportunity to collaborate given our shared passion and shared goal of improving equity and access
- A call to action!





What Questions do you have?

- <u>summer@myriad.com</u>
- edith.smith@myriad.com
- www.capsprenatal.com
- www.accesstoecs.com





Abstract

Background/Statement of the Problem: Professional guidelines can have a profound impact on reproductive health. In many cases, prenatal genetic screening is often only recommended for specific groups or those who have been historically recognized as high risk. Unfortunately, this approach results in missed opportunities to identify those who have equal or greater risk and results in a disparity in how prenatal genetic screening is conducted both preconceptionally and prenatally. For example, carrier screening guidelines are typically ethnicity based (1, 2) and many individuals are only screened for cystic fibrosis and spinal muscular atrophy even though they may be at risk for more than these two conditions. Additionally, noninvasive prenatal screening is not recommended for obese individuals, thus eliminating certain ethnic groups who are prone to higher BMIs for detection of aneuploidies.(3) Overall Statement of Purpose /

Objective: Current guidelines result in inequitable prenatal genetic screening across ethnicities and require a discussion around needed changes to promote equitable care.

Brief Summary of Methods: Previously published and data-driven analyses were examined to determine how current guidelines cause inequitable prenatal genetic screening across ethnicities.

Key Findings Multiple studies demonstrate that ethnicity-based carrier screening fails to effectively identify carriers and at-risk couples. In one study of nearly 350,000 individuals across ethnicities, guidelines-based screening identified only 6% of affected conceptuses among East Asians, 21% among Hispanics, 35% in Northern Europeans, and 45% in Ashkenazi Jews (4). This inequity occurs for several reasons. Ethnicity is often unknown or inaccurate, with substantial discordance between self-reported ethnicity and genetic ancestry. Additionally, the U.S. population is increasingly ethnically admixed (5,6). Furthermore, incongruency exists in carrier rates among ethnicities and conditions recommended for screening: for seven of 16 conditions included in ethnicity-based screening guidelines, the majority of carriers are not in the ethnic population covered by guidelines (5). In all studies, expanded carrier screening, more effectively identified at-risk couples compared to ethnicity-based screening.

Guidelines recommend against offering NIPS to those who are significantly obese and recommend against reporting results (a "no-call") when fetal fraction is below 4%(3). One study identified significant obesity (BMI >30) in ~50%, 45%, and 35% of pregnant women who were Native American, African American, and Hispanic, respectively compared to 25% in Northern European women(7). According to guidelines, these women should be offered a less accurate aneuploidy screening test than those who have BMI <30. In another study, maternal ethnicity was independently associated with low fetal fraction; those of African American and South Asian ethnicities were 1.72 and 1.99 times as likely to experience no-call results than those of other ethnicities(8). Additionally, females with a test failure have delayed results and fewer pregnancy options, disproportionately impacting certain racial and ethnic groups. Despite the emergence of NIPS technology that provides accurate results at low fetal fraction(9), guidelines have yet to be updated, creating ethnic disparities in access to aneuploidy screening.

Conclusions / Implications for Practice Current prenatal screening guidelines disproportionately limit access to care for individuals of certain ethnicities. Evidence supports the modernization of guidelines to improve equitable care.



