Improving Inequities in Prenatal Screening: Time to Modernize Guidelines

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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
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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
37% Pursued or planned for prenatal diagnosis
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

- 1970: Tay Sachs for AJ
- 1988: CF recommended by NIH
- 2001: Limited CF by ACOG
- 2009: Expanded carrier screening available
- 2013: ACMG position statement
- 2015: ECS joint statement
- 2017: ACOG Opinions #690, 691
Historically: US Guidelines Based on Ethnicity

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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 ethnicity-based 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

Hispanic
- 13% of affected pregnancies identified

East Asian
- 24% of affected pregnancies identified

Ashkenazi
- Jewish
- 25% of affected pregnancies identified

African American
- 79% of affected pregnancies identified

Identified
- Missed affected pregnancies

Internal data on ~400,000 patients; Haque I, et al. JAMA. 2016;316(7):734-742.
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 **recommended**, but nearly 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

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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
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.

“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

BMI:  

GA:  

TRISOMY 13/18:  

0% 4% 8% 12% 16% 20% 24%

FF:  

LOW

TEST FAILURE

HIGH

CONFIDENT RESULTS
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). Further complicating the problem is that BMI is not evenly distributed across ethnicities.

• 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.

How can providers help bridge the current gaps?

What panel you offer
Which lab you offer
Advocacy
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
- 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
IMPACT OF FFA IN A REAL-WORLD CLINICAL LABORATORY SETTING

- >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.
**Collaboration is Key**

- **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

[www.capsprenatal.com](http://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?

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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.