**RESULTS**

- Without FFA, the percent of patient samples having less than 4% FF varied by ethnicity; for example, 6.36% of samples from patients with African ancestry (N=27,151 samples) had less than 4% fetal fraction, versus just 2.42% of samples from patients with East Asian ancestry (N=8,039 samples; Figure 2).
- With FFA, the percentage ≤4% FF fell to less than 1% across all ethnic groups (Figure 2).
- Further, patients with high BMI benefited from the incorporation of FFA.
- Without FFA, 12.95% of samples from patients with obesity (obesity classes I-III) (N=88,415) had fetal fractions <4%. Low FF was most pronounced in patients with class III obesity (21.15%), followed by class II obesity (12.43%) and class I obesity (6.89%; Figure 3).
- With FFA, only 0.28% of samples from patients with obesity (obesity classes I-III; N=81,027) had FF ≤4%, greatly reducing the chance of test failure. Notably, FFA increased FF effectively even in patients with class III obesity, with only 0.66% of these patients experiencing a test failure after FFA was implemented (Figure 3).

**CONCLUSION**

These results indicate that NIPS with FFA improves disparate FF distributions, thereby providing more equitable risk assessment regardless of patient ethnicity and supporting weight-neutral clinical care.

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**METHODS**

- We retrospectively analyzed results from 496,494 samples from individuals with BMI > 18.5 that underwent NIPS with Myriad's Prequel prenatal screen from December 2016 through July 2022.
- 279,038 patient samples underwent standard screening (without FFA), and the remaining 217,456 underwent screening after the launch of FFA.
- The dotted line denotes a fetal fraction of 4%.

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**Figure 1. Fetal fraction distribution prior to FFA and after FFA Implementation**

- **Figure 2. Proportion of samples with fetal fraction ≤4% stratified by patient self-reported ethnicity**

- **Figure 3. Proportion of samples with fetal fraction ≤4% stratified by BMI**

**PURPOSE**

- Noninvasive prenatal screening (NIPS) using cell-free DNA (cfDNA) identifies pregnancies at increased risk for fetal chromosomal abnormalities.
- NIPS accuracy is significantly impacted by fetal fraction (FF), the proportion of cfDNA originating from the placenta.
- Low FF, commonly defined as FF <4%, is correlated with early gestational age, pregnancies affected with trisomy 18 or 13, and high body mass index (BMI).
- Guidelines therefore recommend against offering NIPS to those who are significantly obese and recommend against reporting results (a “test failure”) when FF is below 4%.
- Further, as BMI is not evenly distributed across ethnicities, certain ethnic groups are disproportionately impacted by test failures.
- A whole-genome sequencing (WGS)-based NIPS that employs a FF amplification (FFA) technology for all samples has been shown to increase FF by 3.9-fold for samples with low FF (Figure 1).
- Here, we examined the impact of FFA on the performance of NIPS across obesity classes and ethnicities.

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**Figure 1. Fetal fraction distribution prior to FFA and after FFA Implementation**

**Figure 2. Proportion of samples with fetal fraction ≤4% stratified by patient self-reported ethnicity**

**Figure 3. Proportion of samples with fetal fraction ≤4% stratified by BMI**

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* Fetal fraction distributions reflect Myriad Prequel prenatal screen from December 2016 to July 2022. The dotted line denotes a fetal fraction of 4%.