Poster #270

Fetal Fraction Amplification in Prenatal cell-free DNA screening supports equitable care for ethnically- and BMI-diverse patients.

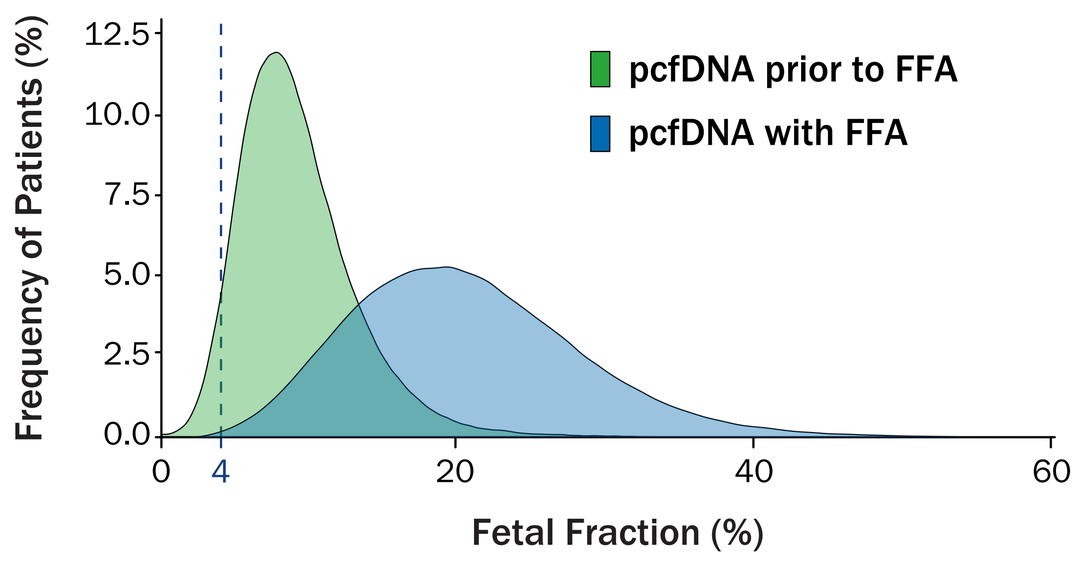
Lauren Eisemann, MS, CGC; Gabriel Lazarin, MS, CGC; Summer Pierson, MS, CGC; John Guittar, PhD; Devika Chawla, PhD; Katie Johansen Taber, PhD

All authors were employed by Myriad Genetics, Inc. at the time of this study

Background

- Prenatal cell-free DNA screening (pcfDNA) accuracy is heavily dependent on fetal fraction (FF). 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 pcfDNA 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 pcfDNA 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 (**Fig 1**).
- Here, we examined the impact of FFA on the performance of pcfDNA across obesity classes and ethnicities.

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



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

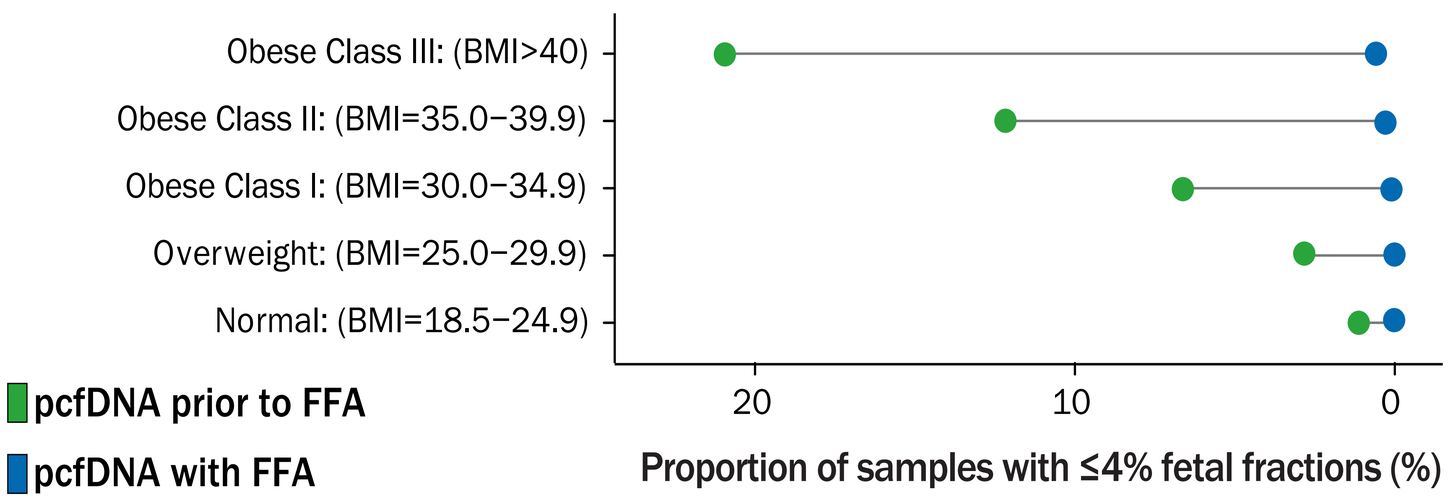
Methods

- We retrospectively analyzed results from 496,494 samples from individuals with BMI > 18.5 that underwent pcfDNA 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.
- We compared the percent of samples with <4% FF before and after the launch of FFA, stratified by self-reported ancestry and by BMI.

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). With FFA, the percentage ≤4% FF fell to less than 1% across all ethnic groups (Figure not shown).
- 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%; **Fig 2**).

Figure 2. Proportion of samples with fetal fraction ≤4% stratified by BMI



- 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 (**Fig 2**).

Conclusion

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