

Supporting Equitable & Weight Neutral Care in Fetal Aneuploidy Screening

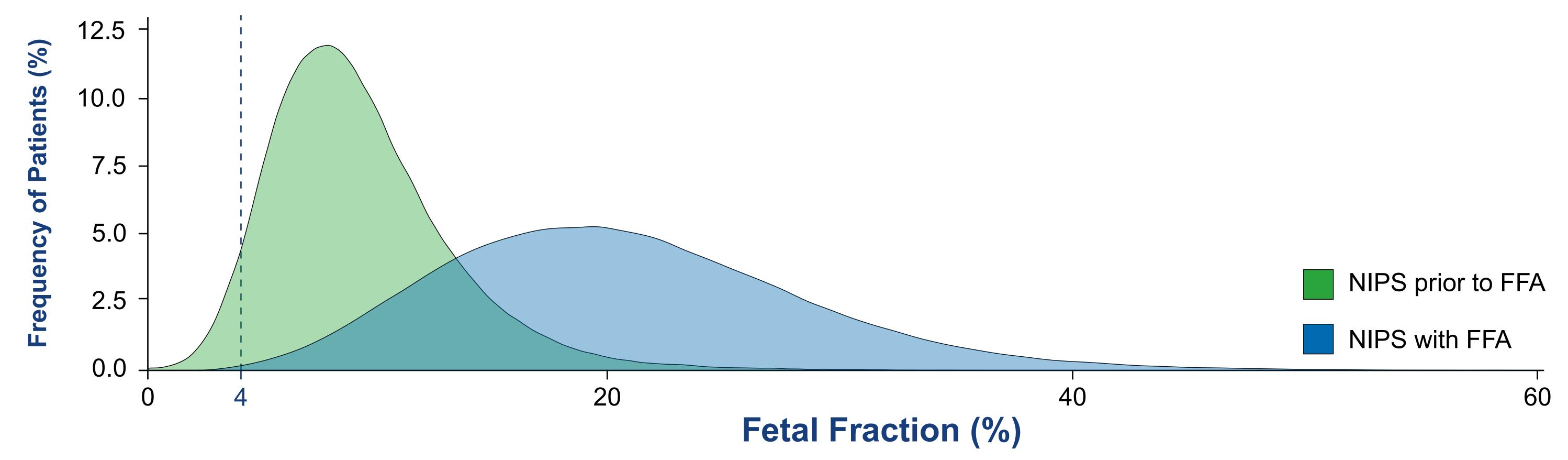
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All authors were employed by Myriad Genetics, Inc. at the time of this study

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.

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%.

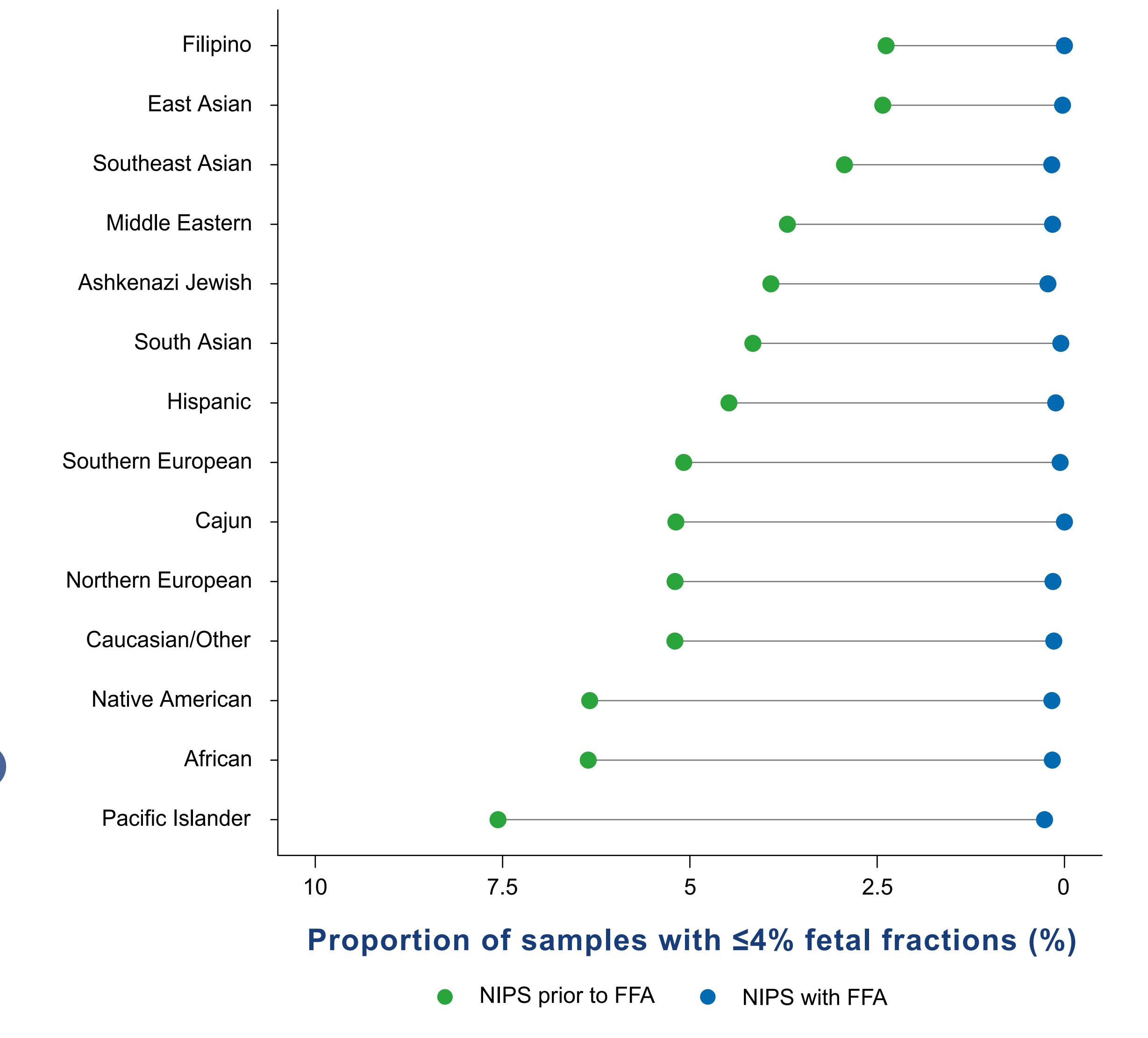
METHODS

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

• 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**).

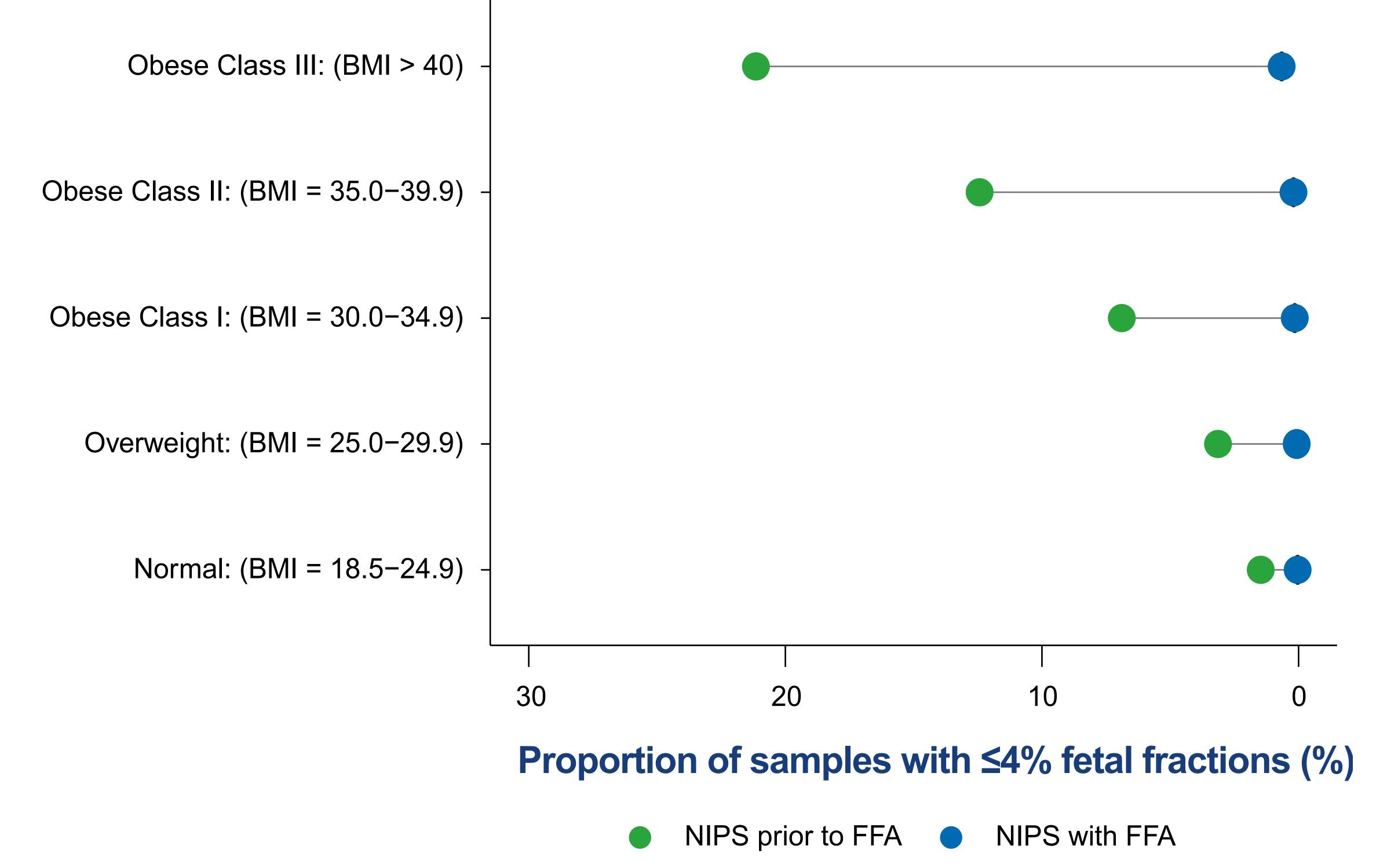
• With FFA, the percentage ≤4% FF fell to less than 1% across all ethnic groups (Figure 2).

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



RESULTS





- 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.