

# A noninvasive prenatal screen with >4% fetal fraction in all samples: Clinical laboratory experience

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

## INTRODUCTION

- For millions of pregnant patients, noninvasive prenatal screening (NIPS) based on cell-free DNA (cfDNA) detects whether their pregnancies are at elevated risk for fetal chromosomal abnormalities.
- Fetal fraction (FF), the proportion of cfDNA originating from the placenta, can impact the accuracy of NIPS, and many laboratories fail samples with low FF, commonly defined as FF <4%.
- FF has been shown to negatively correlate with body mass index (BMI), pregnancies with trisomy 18 or 13, and early gestational age, resulting in higher test failure rates in these populations.
- A whole-genome sequencing (WGS)-based NIPS that employs FF amplification (FFA) technology for all samples has been shown to increase FF by 3.9-fold for samples with low FF.<sup>1</sup>

## METHODS

- We retrospectively analyzed results from patients who underwent NIPS with FFA during a two-month period.
- The FFA technology increased FF by preferentially sequencing short cfDNA fragments, known to be enriched for fetal-derived cfDNA. FF was assessed for patients who received a screening result (N= 19,433).
- BMI data were available for 12,579 patients.

## RESULTS

Figure 1. Fetal Fraction Amplification (FFA) increases FF as compared to standard NIPS.

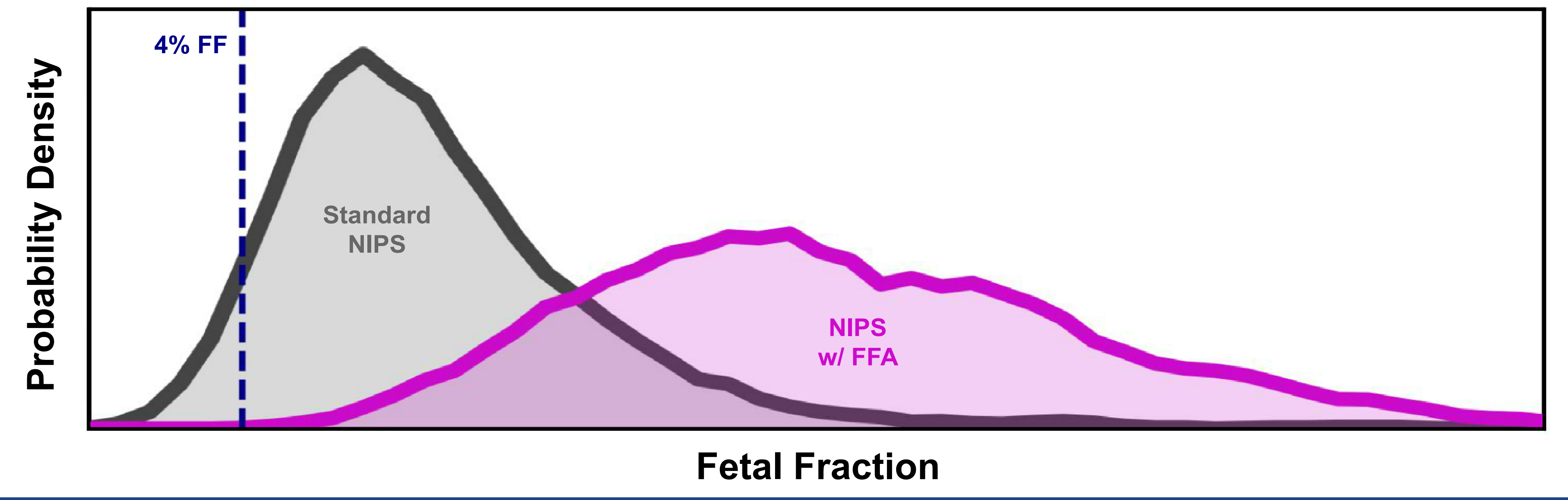


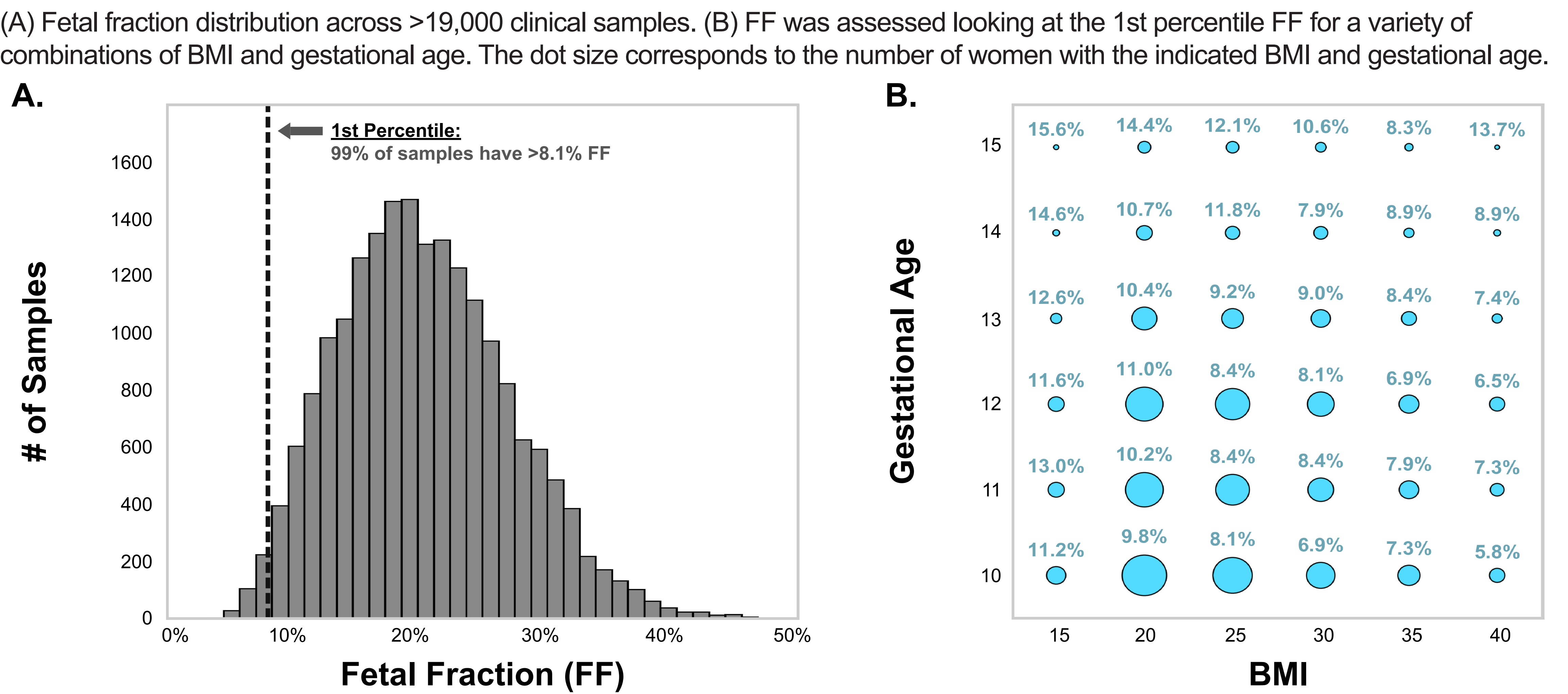
Table 1. Actual patient cases.

Patient	Gestational Age	BMI	Other Lab Result (FF)	Prequel with AMPLIFY Result (FF)
A	13 weeks	25	Failed due to “Low FF”	Positive T21 (6%) & later confirmed with amnio
B	10 weeks	25	Failed (2%)	Negative (20%)
C	10 weeks	39	Failed (3%)	Negative (9%)
D	11 weeks	>40	Failed (3%)	Negative (12%)
E	12 weeks	45	Failed (2%)	Negative (9%)

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- Median maternal age was 31 years and median gestational age was 12 weeks.
- Fetal fraction increased overall by >2-fold with FFA as compared to standard NIPS without FFA (Fig 1).
- No patients had FF results <4%. Ninety-nine percent of patients had FF >8.1% (Fig 2A).
- In patients with multiple risk factors for low FF, both high BMI and early gestational age draw, FF remained abundant. For example, the average FF was 13.1% among patients with BMI ≥40 with samples drawn at 10 weeks gestation (Fig 2).
- Five samples were identified as having had a previous test failure due to low FF in outside laboratories, including one that had failed to identify Down syndrome (Table 1).

Figure 2. FFA performance in >19,000 clinical samples.



## CONCLUSION

- A commercial NIPS using FFA for all samples provides confident results regardless of a patient’s risk factors for low FF. FFA provides ample FF, preventing unnecessary test failures in NIPS.
- This innovative technology identifies pregnancies at risk for chromosome abnormalities regardless of patient BMI.

**REFERENCES:** 1. Welker, N. C. et al. High-throughput fetal fraction amplification increases analytical performance of noninvasive prenatal screening. *Genet. Med.* (2020) doi:10.1038/s41436-020-01009-5