

Prenatal Cell-free DNA Screening for Fetal Aneuploidy in Pregnant Women at Average or High Risk: Results from a Large US Clinical Laboratory

Background

- The American College of Medical Genetics and Genomics recommends informing all pregnant women that noninvasive cell-free DNA (cfDNA) prenatal screening is the most sensitive screening option for detecting fetal aneuploidies, including trisomies 21, 18, and 13.¹
- QNatal Advanced is a cfDNA screening assay developed at Quest Diagnostics. It uses a high-yield method of cfDNA preparation, massively parallel sequencing, and a correction algorithm for GC content. To reduce false-positive rates, karyograms are generated when test results initially specify affected chromosomes.²
- Most studies that examine the accuracy of cfDNA prenatal screening assays, including QNatal Advanced,² have done so in high-risk populations, but recent studies indicate such assays may also perform well in the general population.³⁻⁵
- **Objective:** The investigators of this study extended evaluation of QNatal Advanced to include pregnant women at average risk as well as those at high risk for fetal aneuploidy.

Methods

- The analysis included 75,658 specimens from 72,176 pregnant women who consented to QNatal Advanced screening for fetal aneuploidy, performed at Quest Diagnostics.
- High risk was defined as meeting any of the following criteria: advanced age (≥ 35 years), abnormal ultrasound and/or positive maternal serum screen (MSS) result, or a personal or family history of fetal aneuploidy.
- The cfDNA extraction, massively parallel sequencing, and bioinformatics analysis were conducted as described previously.²
- Results were evaluated for concordance with pregnancy outcomes, and performance characteristics of the screening assay were evaluated.

Results

- Results were available for 69,794 unique pregnancies, of which 13% were average risk and 87% were high risk.
- Results were positive for fetal aneuploidy in 1.9% of pregnancies.
- The positive predictive value (PPV) was 98.1% for trisomy 21, 88.2% for trisomy 18, and 59.3% for trisomy 13. PPV was 69.0% for sex chromosome abnormalities and 75.0% for microdeletions.
- The overall PPV of QNatal Advanced for fetal aneuploidies was 87.2%.
- Sensitivity was 97.9% and specificity was 99.9%.

Conclusions

- In a population that included pregnant women at average risk or high risk of fetal aneuploidy, QNatal Advanced provided highly accurate discrimination between affected and unaffected pregnancies.
- The strong performance of this laboratory-developed assay reflects advanced bioinformatics, expert scientific review, and specialized coordination of follow-up studies.

Article published in the journal *Molecular Genetics & Genomic Medicine*

Authors

Carrie Guy, Farnoosh Haji-Sheikhi, Charles M Rowland, Ben Anderson, Renius Owen, Felicitas L Lacbawan, Damian P Alagia

Affiliations

Quest Diagnostics, San Juan Capistrano, CA

Citation

Guy C, Haji-Sheikhi F, Rowland CM, et al. *Molec Genet Genom Med*. Published online January 31, 2019.

Webpage

<https://onlinelibrary.wiley.com/doi/full/10.1002/mgg3.545>

References

1. Gregg AR, Skotko BG, Benkendorf JL, et al. *Genet Med*. 2016;18:1056-1065.
2. Strom CM, Anderson B, Tsao D, et al. *PLoS One*. 2017;12:e0167130.
3. Norton M, Jacobsson B, Swamy G, et al. *New Engl J Med*. 2015;372:1589-1597.
4. Zhang H, Gao Y, Jian F, et al. *Ultrasound Obstet Gynecol*. 2015;45:530-538.
5. Taneja PA, Snyder HL, de Feo E, et al. *Prenat Diagn*. 2016;36:237-243.