753

Updated Clinical Laboratory Experience: Over 50,000 Average Risk cfDNA Tests

Jason Chibuk, Jenna Wardrop, Theresa Boomer, Samantha Caldwell, Eyad Almasri and Ron McCullough
Sequenom® Inc., Laboratory Corporation of America® Holdings

Integrated GENETICS
LabCorp Specialty Testing Group
sequenom

I. Introduction

The use of cell free DNA (cfDNA) screening for fetal aneuploidy has been well established in high risk pregnancies, and more recently has been expanded to the average risk obstetric population per recent ACMG guidelines.[1] Here we provide an update to our initial laboratory experience[2] and compare the laboratory and clinical performance of >50,000 average risk MaterniT® 21 PLUS samples to the total MaterniT® 21 PLUS experience in >600,000 samples.[3]

II. Methods

Maternal blood samples submitted to Sequenom Laboratories® for MaterniT® 21 PLUS testing were subjected to DNA extraction, library preparation, and genome-wide massively parallel sequencing as previously described.[4] Samples that did not meet the ACOG Committee Opinion #640 criteria were considered average risk and included in this analysis.[5]

III. Results

Table 1. Demographics

	Average Risk	Total Tested Population[3]
Number of Samples	55,526	>600,000
Average Maternal Age (years)	29.3	35.0
Average BMI	26.3	27.2
Average Gestational Age	12w6d	14w2d
Median Fetal Fraction	9.2%	10.2%
Non Reportable Rate (Technical)	0.21%	0.53%
Non Reportable Rate (QNS)	0.73%	0.95%

Table 2. Positivity Rate

	Average Risk	High Risk
Trisomy 21	0.24%	1.23%
Trisomy 18	0.08%	0.39%
Trisomy 13	0.08%	0.19%
Common Aneuploidy Cumulative Positivity Rate	0.39%	1.81%

Image 1. Maternal Age Distribution – Average Risk Cohort

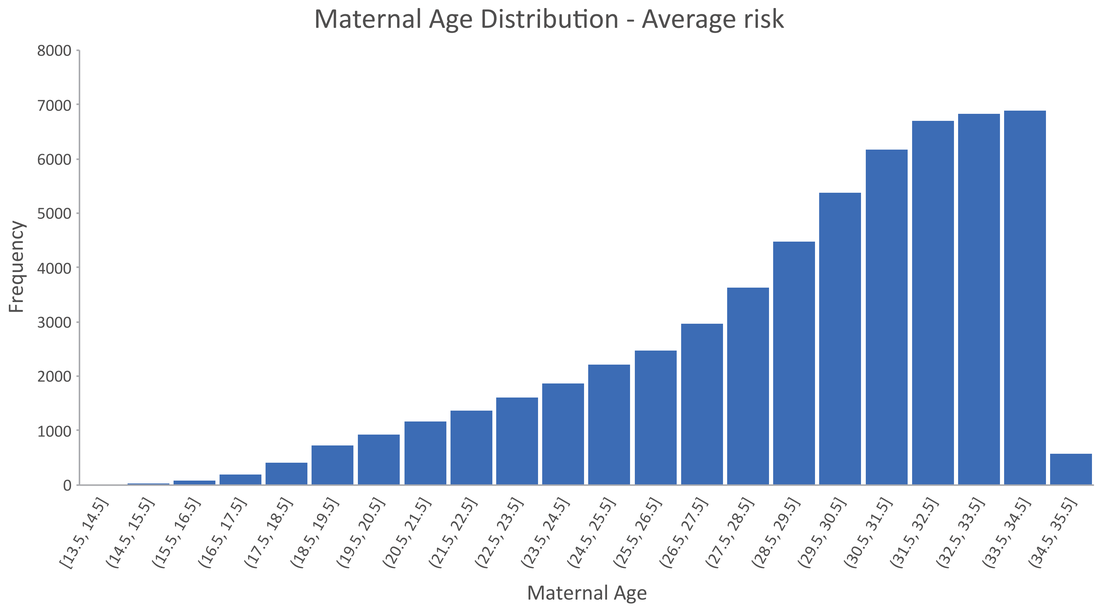

Table 3. Average Risk Outcomes

Chromosome	MaterniT® 21 PLUS samples reported as negative	MaterniT® 21 PLUS samples reported as positive	False negative results communicated to Sequenom Laboratories®	False positive results communicated to Sequenom Laboratories®
21	54,875	131	0	0
18	54,964	42	0	1
13	54,961	45	0	3

Table 4. Average Risk vs. High Risk Performance

	Average Risk	High Risk[3]	Average Risk	High Risk[3]	Average Risk	High Risk[3]
Chromosome	Relative Observed Sensitivity	Relative Observed Sensitivity	Relative Observed Specificity	Relative Observed Specificity	Relative Observed Analytical PPV	Relative Observed Analytical PPV
21	>99.9%	99.4%	>99.9%	>99.9%	>99.9%	99.2%
18	>99.9%	98.6%	>99.9%	>99.9%	97.6%	97.5%
13	>99.9%	99.3%	>99.9%	>99.9%	93.3%	93.1%

IV. Conclusions

Over 55,000 average risk MaterniT® 21 PLUS samples have been ordered. The positivity rate in the average risk group is lower than in high risk (0.39% vs. 1.81%), as expected in these differing patient populations.[3] The average risk samples were tested at a slightly younger gestational age (12w6d vs 14w2d), which was expected given that high risk indications of positive serum screening or abnormal ultrasound tend to be identified later in pregnancy. Overall, performance in the average risk cohort much resembles that seen in high risk pregnancies. When compared to current serum biochemical screening protocols, expanding cfDNA screening into the average risk population allows markedly improved screening performance of common aneuploidies.

V. References

1. Gregg AR, Skotko BG, Benkendorf JL, et al., Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics. *Genet Med* 2016; 18:1056-1065.
2. Caldwell S et al., Expanding Noninvasive Prenatal Testing (NIPT) to Average Risk: MaterniT® 21 PLUS Performance in the Average Risk vs. High Risk Population. Poster presented at the *Society of Maternal Fetal Medicine Annual Meeting*; 2017 January 23-28; Las Vegas, NV.
3. Khanna A et al., Over a half million noninvasive prenatal tests: a clinical laboratory experience. Poster presented at: *American Congress of Obstetricians and Gynecologists Annual Meeting*; 2017 May 6-9; San Diego, CA.
4. Jensen TJ, Zwiefelhofer T, Tim R, et al., High-throughput massively parallel sequencing for fetal aneuploidy detection from maternal plasma. *PLoS One* 2013; 8(3):e57381. doi:10.1371/journal.pone.0057381. Epub 2013 Mar 6.
5. ACOG practice committee opinion number 640: Cell-free DNA screening for fetal aneuploidy. *Obstet Gynecol* 2015; 126:e31-37.

LabCorp

©2018 Laboratory Corporation of America® Holdings. All rights reserved. rep-1176-v1-0318

MaterniT® is a registered trademark of Sequenom, Inc. Sequenom, Inc. is a wholly owned subsidiary of Laboratory Corporation of America® Holdings.
Integrated Genetics is a brand used by Esoterix Genetic Laboratories, LLC, a wholly owned subsidiary of Laboratory Corporation of America® Holdings.
Poster presented at the *ACMG Annual Clinical Genetics Meeting*; 2018 April 10-14; Charlotte, NC.