Complex chromosomal rearrangements revealed through Genome-wide cfDNA: 40,000 samples

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I. Background

Genome-wide cell-free DNA prenatal screening continues to increase our insight into placental findings not previously recognized. Here we present data from the first two years of clinical testing for expanded cfDNA screening, including genome wide aneuploidy detection and subchromosomal copy number variants (CNVs) larger >7 Mb, with specific attention to complex chromosomal rearrangements.

II. Methods

Maternal blood samples submitted for genome-wide cfDNA testing were subjected to DNA extraction, library preparation, and whole-genome massively parallel sequencing as described by Jensen et al.1 Sequencing data were analyzed using a novel algorithm as described by Lefkowitz et al.2

III. Results

41,634 samples were submitted to the clinical laboratory between August 2015 and November 2017.

MaterniT® GENOME: Overview of positive cases | Aug 31, 2015 - Nov 2, 2017 | (n=1,957 positives)

MaterniT® GENOME Complex CNVs: Individual Chromosome Findings | (n=83 positives) | (n=168 segments)

MaterniT® GENOME Complex CNVs: Testing indications of positive cases | (n=83 positives)

Table 1. MaterniT® GENOME Complex CNV samples’ key metrics.

IV. Conclusion

Genome-wide cfDNA prenatal screening with subchromosomal CNV detection has allowed noninvasive technology to reach the subset of patients at highest risk for chromosomal imbalance, many previously unaware. These high risk families can benefit from early identification or added reassurance, prior to diagnostic testing. While the nature of cfDNA placental screening can find and report CPM, certain complex chromosomal rearrangements have an extremely high fetal concordance rate, with 90% being diagnostically confirmed, partially confirmed, or highly likely given supportive clinical details and family histories. Collectively, the superior performance of cfDNA screening in this unique subset of high risk patients speaks to the clinical feasibility and utility of including CNVs in early cfDNA screening in pregnancy.

V. References