CLINICAL IMPACT OF ADDITIONAL FINDINGS DETECTED BY GENOME-WIDE NON-INVASIVE PRENATAL TESTING: FOLLOW-UP RESULTS OF THE TRIDENT-2 STUDY

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Background & Aim

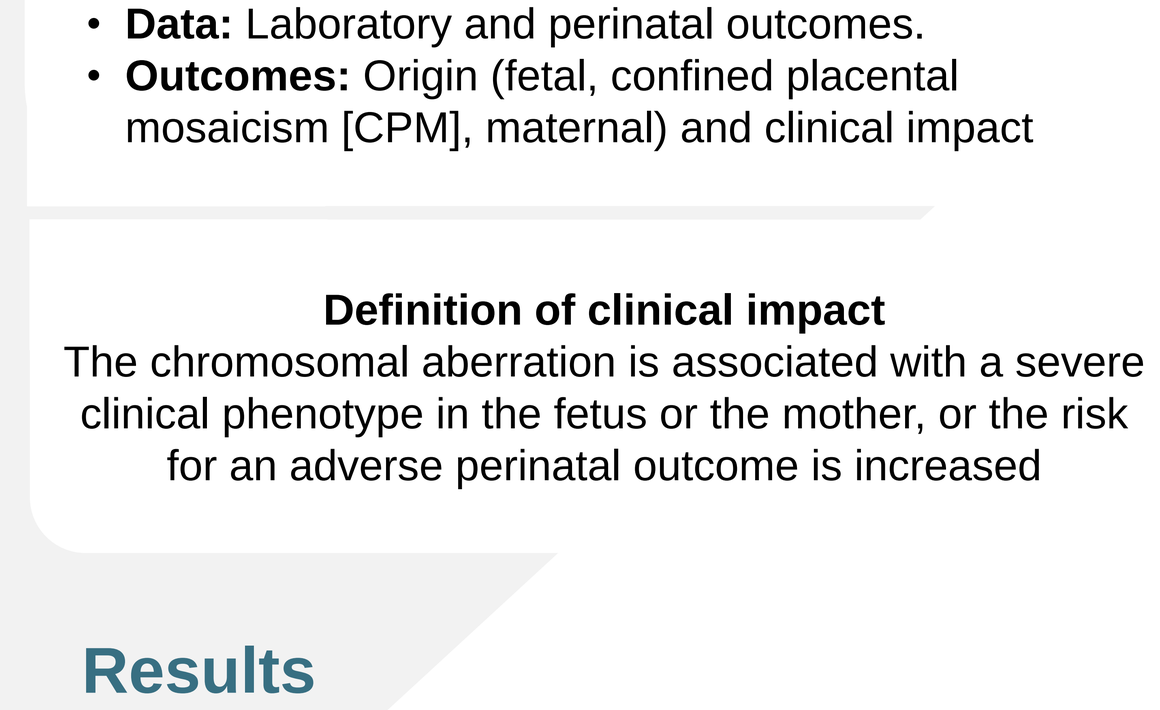
Genome-wide prenatal testing (GW-NIPT) is increasingly being used in clinical practice. However, the clinical utility of this test is still topic of heavy debate. We present follow-up results of the TRIDENT-2 study to determine this clinical impact.

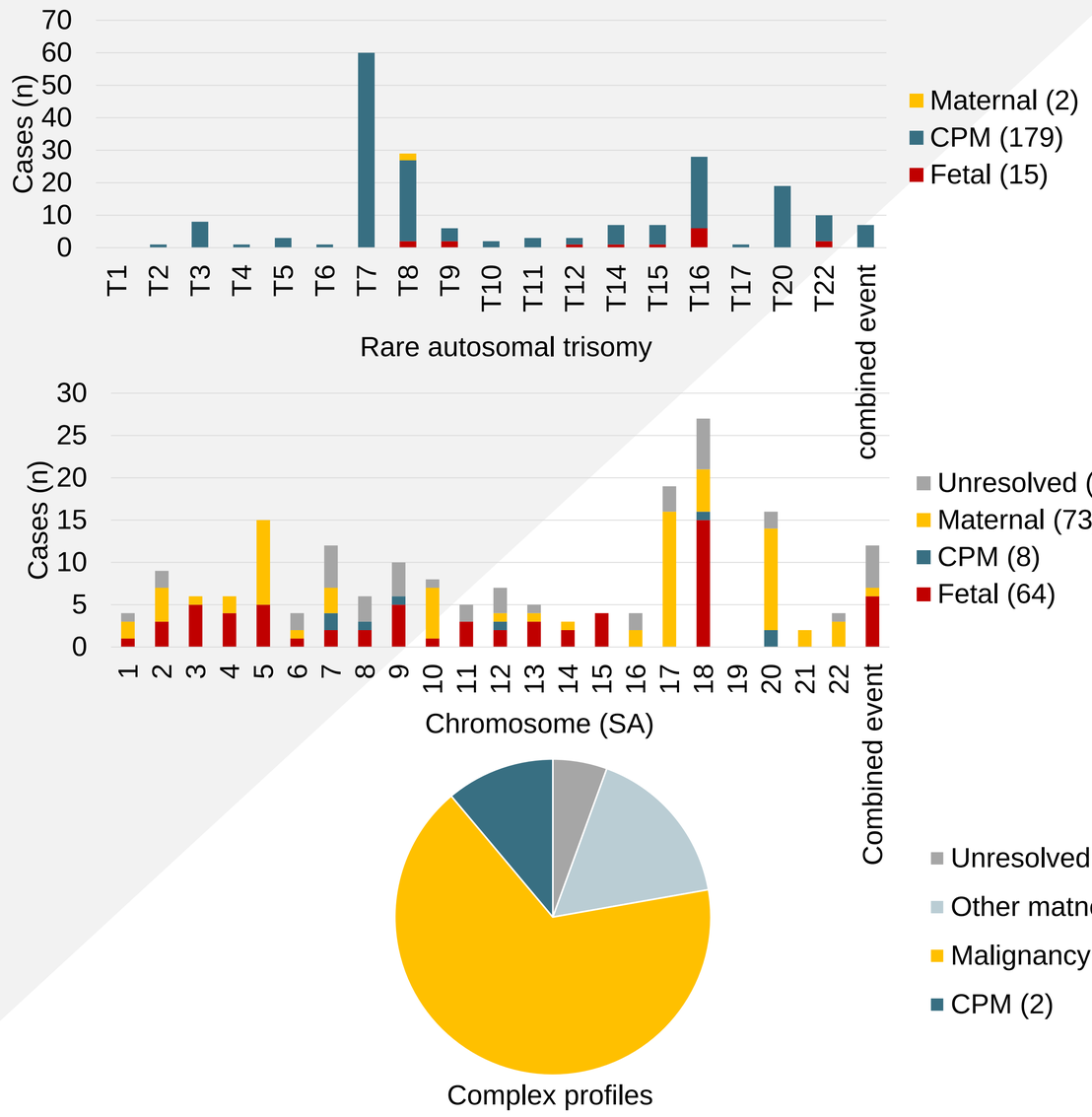
Method

- **Study setting:** All pregnant women in the Netherlands are offered GW-NIPT with a choice of receiving either full screening or screening solely for common trisomies (TRIDENT-2)
- **Study cohort:** All cases (402/110,739; 0.36%) with additional findings detected between April 2017-2019
- **Data:** Laboratory and perinatal outcomes.
- **Outcomes:** Origin (fetal, confined placental mosaicism [CPM], maternal) and clinical impact

Definition of clinical impact
The chromosomal aberration is associated with a severe clinical phenotype in the fetus or the mother, or the risk for an adverse perinatal outcome is increased

Results





- Most fetal chromosomal aberrations were pathogenic and associated with severe clinical phenotypes (61/79; 77.2%)
- CPM pregnancies are at increased risk for adverse perinatal outcomes
- Of the 90 maternal findings, 12 (13.3%) were malignancies and 33 (36.7%) (mosaic) pathogenic copy number variants, mostly associated with mild or no clinical phenotypes

Adverse perinatal outcomes	CPM	CPM (T16 excluded)	Dutch (obstetric) population
Pre-eclampsia	8.5%*	6.0%*	0.5%
Birth weight <p2.3	13.6%*	8.9%*	2.5%
Birth weight p2.3-p10	13.0%*	12.0%*	7.4%
NICU admission	6.2%*	5.1	3.1%

*Significantly different from Dutch (obstetric) population p<.05

Conclusions

- The majority of additional findings have clinical impact
- This large cohort study provides crucial information for the decision if and how to implement GW-NIPT in screening programs
- The challenging interpretation and counselling of additional findings can be improved when our data are used

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