Population-based analysis of atypical chromosomal abnormalities according to nuchal translucency measurement: an individual record linkage study of 81,244 women

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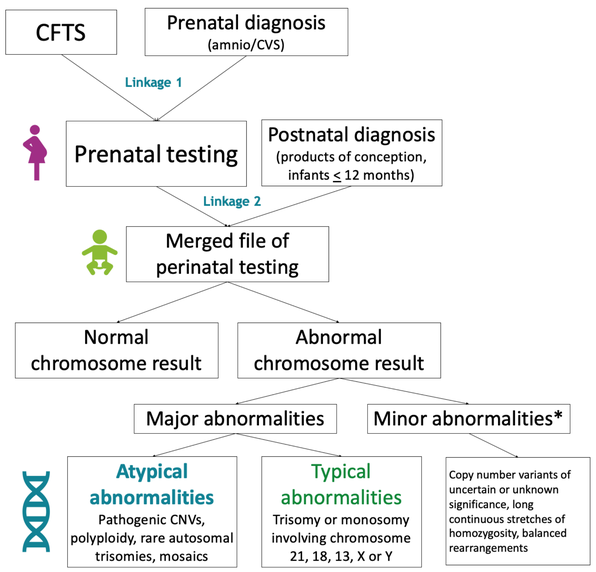
Introduction

- The American College of Obstetricians and Gynecologists recently recommended offering genetic counselling and diagnostic testing for enlarged NT at > 3.0mm, regardless of prior negative screening with noninvasive prenatal testing (NIPT).
- The aim of this study was to perform a population-based individual record-linkage study of women undergoing combined first trimester screening (CFTS) and prenatal or postnatal diagnosis to analyse the frequency and type of chromosome abnormalities according to NT measurement.

Methods

- A retrospective study of women resident in Victoria, Australia, who underwent CFTS from January 2015 to December 2016.
- CFTS results were matched to prenatal diagnostic procedures and postnatal cytogenetic results from products of conception and infants up to 12 months of age, using probabilistic record linkage.
- An atypical chromosome abnormality was defined as any major chromosome abnormality, other than whole chromosome aneuploidy involving chromosomes 21, 18, 13, X and Y.

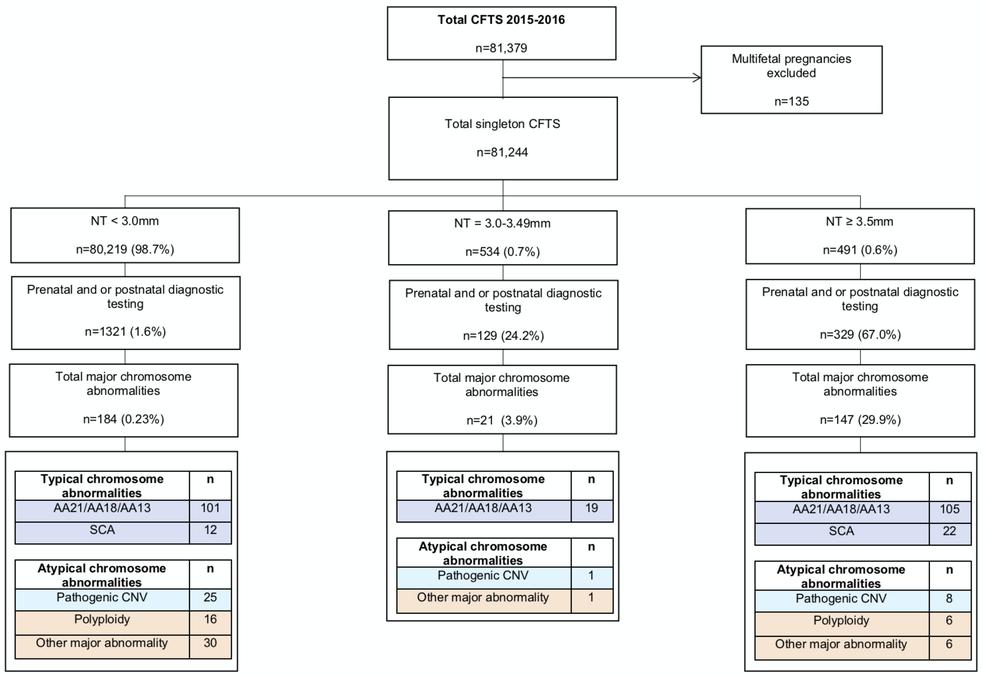
Fig 1. Overview of linkage process and classification of chromosome results



Results

- **A total of 81,244 singleton pregnancies undergoing CFTS were included and linked to prenatal and postnatal diagnostic testing results**
  - A total of 1779 pregnancies underwent prenatal or postnatal diagnostic testing, of which 89.60% were performed by chromosomal microarray.
  - The frequency of total major chromosome abnormalities was significantly higher in the group with NT > 3.5mm (29.94%) compared with NT 3.0-3.4mm, (3.93%) or NT < 3.0mm (0.09%) (P< 0.001) respectively.
- **There were 93 atypical chromosome abnormalities in the total screened cohort.**
  - On a population-scale, 98% of atypical chromosome abnormalities occured in fetuses with NT < 3.0mm or > 3.5mm.
  - The risk of an atypical chromosome abnormality in fetuses with NT 3.0-3.4mm (1 in 270) was similar to previously reported risks in pregnancies undergoing diagnostic testing without an ultrasound abnormality. (ref)

Fig 1. Flowchart of prenatal and postnatal chromosome analysis by nuchal translucency



Results

- When defining thresholds for offering diagnosis with chromosomal microarray at 11-13 weeks, both an NT threshold of 1.9MoM and a fixed threshold of 3.0mm captured 22/93 (23.7%) of fetuses with an atypical chromosome abnormality.
- However, the gestation-specific threshold of 1.9 MoM had better specificity than 3.0 mm.
- The positive predictive value of an enlarged NT for any atypical chromosome abnormality was 1 in 47 for NT > 3.0mm and 1 in 32 for NT > 1.9 MoM.

Conclusions

- Approximately one in four fetuses with an atypical chromosome abnormality has an enlarged NT.
- If a NT threshold below 3.5mm is to be considered for offering diagnostic testing with CMA after low risk NIPT, a gestation specific NT threshold of 1.9MoM is superior to a fixed threshold of 3.0 mm, capturing the same number of atypical abnormalities for 31% fewer ‘screen positives’.

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