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Clinical Experience for Noninvasive Prenatal Screen in Twins

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Background

- Noninvasive prenatal screening (NIPS) based on cell-free DNA (cfDNA) is rapidly displacing traditional methods of aneuploidy screening in clinical practice.
- There are limited studies assessing NIPS performance in twins.
- Here we describe the clinical performance of a whole genome sequencing-based NIPS in twin pregnancies.

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Methods

- Retrospective analysis of results from 59,362 patients who underwent NIPS
- 1,257 pregnancies (2.1 percent) with twin gestations
- Fetal fraction (FF) was measured but was not used as a stand-alone reason for test failure.
- Sought twin pregnancy outcomes for all screen positive and for 19% of those who screened negative. Outcomes also accepted by voluntary report.
- Concordance of results determined with respect to pregnancy outcome.

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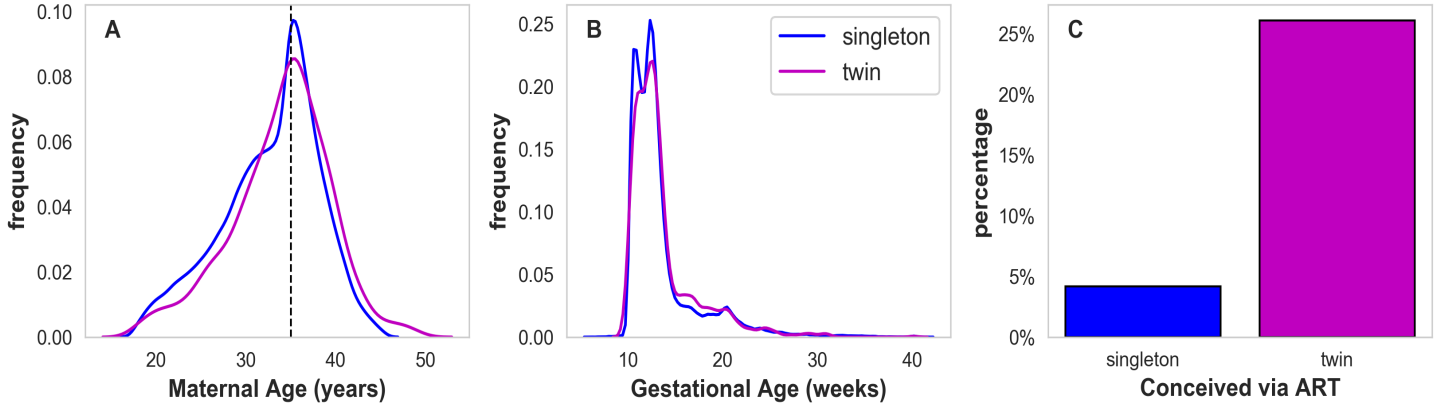
Results

- The total patient cohort included both average-risk (42%, n=25,086) and high-risk patients (56%, n=34,276).
- Though maternal age and gestational age were significantly higher in twin pregnancies compared to singleton pregnancies ($p<0.01$, one-sided Kolmorogov-Smirnov-test), the respective distributions were highly similar.
- Twin pregnancies were more commonly conceived via assisted reproductive technologies (ART) than singleton pregnancies



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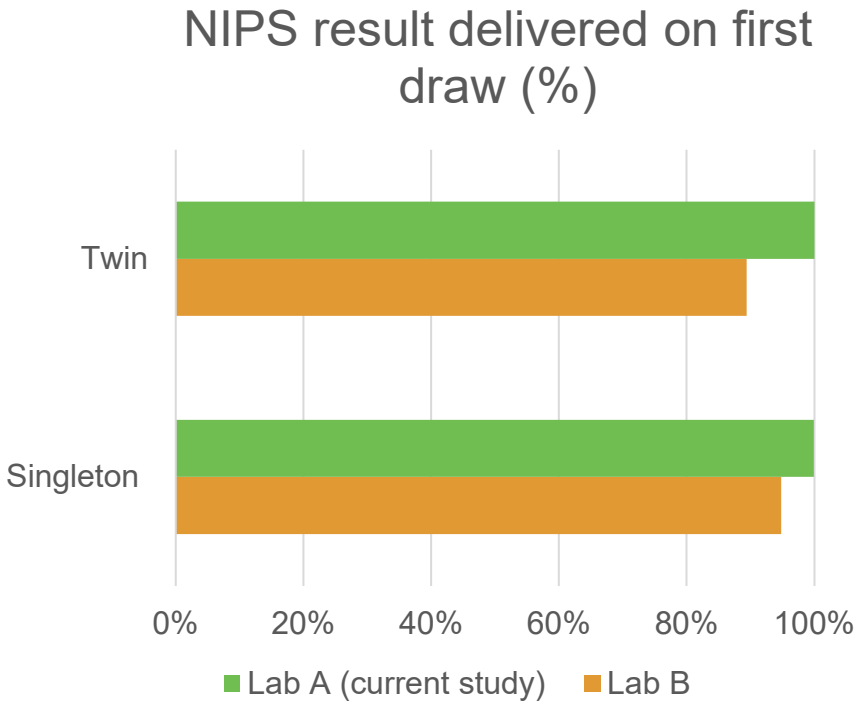
Results

- In both twin and singleton pregnancies, patients received a result in >99.9% of pregnancies
- The rate of test failure in the current study of this customized WGS-based NIPS is lower than for some other NIPS laboratories.[1,2]



References 1. Ryan, A. *et al.* (2016) 'Validation of an Enhanced Version of a Single-Nucleotide Polymorphism-Based Noninvasive Prenatal Test for Detection of Fetal Aneuploidies', *Fetal diagnosis and therapy*, 40(3), pp. 219–223. 2. Norwitz, E. R. *et al.* (2019) 'Validation of a Single-Nucleotide Polymorphism-Based Non-Invasive Prenatal Test in Twin Gestations: Determination of Zygosity, Individual Fetal Sex, and Fetal Aneuploidy', *Journal of clinical medicine research*, 8(7). doi: 10.3390/jcm8070937.

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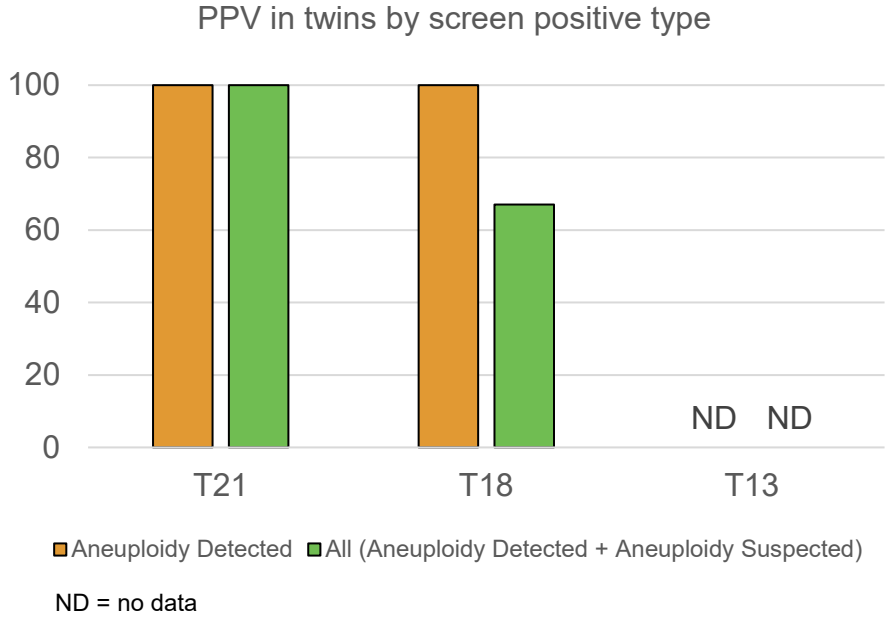
Results

- In both twin and singleton pregnancies, patients received a result in >99.9% of pregnancies
- The screen positive rate in twin pregnancy was 0.8% (N=10)
- 1 screen-positive result was borderline (aneuploidy suspected)
- Informative outcomes were received for 70% of screen-positive results (N=7):
- Two true positives (TPs) via diagnostic confirmation
- Four TPs by ultrasound findings and/or pregnancy loss
- One false positive (aneuploidy suspected) confirmed via amniocentesis
- No twins screened positive for Trisomy 13.
- No false negatives were reported.



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Conclusion

- Clinical experience demonstrates that NIPS in our laboratory using a highly customized whole-genome sequencing approach achieves high PPV while maintaining a low test-failure rate in twin pregnancies.

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