

# Non-invasive prenatal testing (NIPT): Laboratory experiences of PrenaTest®

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## OBJECTIVES

Non-invasive prenatal testing (NIPT) is an emerging new option in prenatal care. According to the International Society for Prenatal Diagnosis (ISPD) NIPT is an advanced screening method for women at increased risk of common fetal aneuploidies (1). The commercially available PrenaTest® has been introduced in Europe in August 2012 with focus on Germany, Switzerland and Austria and exhibits sensitivities and specificities around 99%. The laboratory experiences from routine application of NIPT service are reported, and test accuracy, quality parameters as well as patient profiles are discussed.

## METHOD

PrenaTest® for common fetal trisomies is done by massively parallel sequencing (MPS) of cell-free DNA from maternal plasma (Figure 1) (2,3). Presented data were collected during laboratory routine from August 2012 to January 2013 for the detection of trisomy 21 only, and from February 2013 onwards for the detection of trisomies 13, 18 and 21.

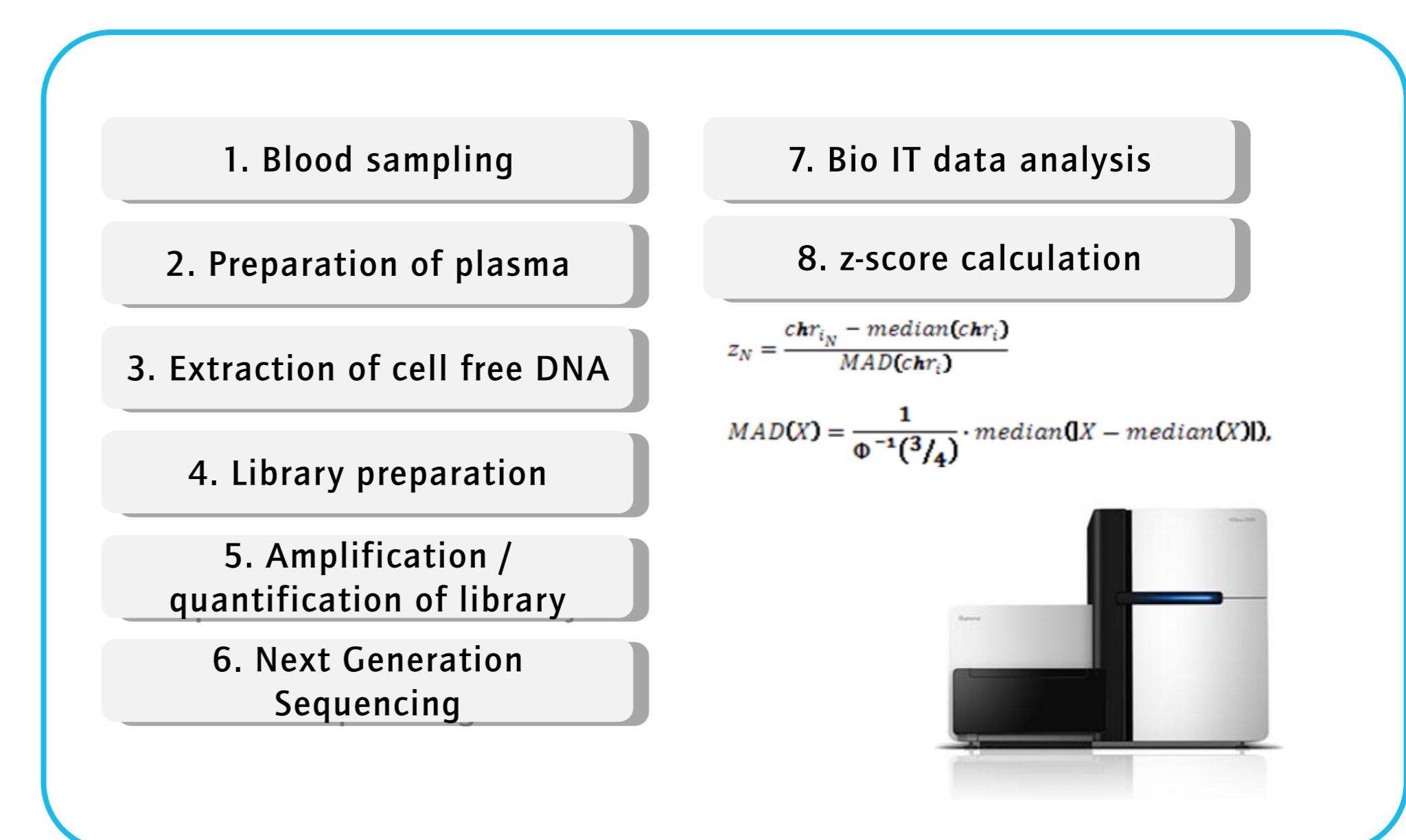


Figure 1: Analysis workflow. Median Absolute Deviation (MAD) based z-score – is computed based on the chromosomal abnormalities observed in the sample set using an euploid reference set.

## RESULTS

Within the past eighteen months over 8200 successfully PrenaTest® analyses have been reported, with 98.0% negative results, 1.7% positive for trisomy 21, 0.3% positive for trisomy 18 and 0.1% positive for trisomy 13 (Figure 2). Remarkably, in the routine application the incidence of positive cases has decreased considerably in comparison to the overall incidence in the clinical trials for the PrenaTest® (from 11.6% to 2.0%) (3).

According to *ad hoc* feedback from the ordering specialists there were one false-negative result for trisomy 18 and 13 false-positive results up to now. Further analysis revealed that one discordant positive T21 case was caused by a fetus papyraceus as determined by investigation of the placenta after birth, the other discordant T21 case was reported back by the responsible doctor as a known case of a vanishing twin (4). For one discordant positive T18 case, the fetus had a euploid karyotype after amniocentesis, but placental material exhibited 80% cells with trisomy 18 in FISH analysis (confined placenta mosaic).

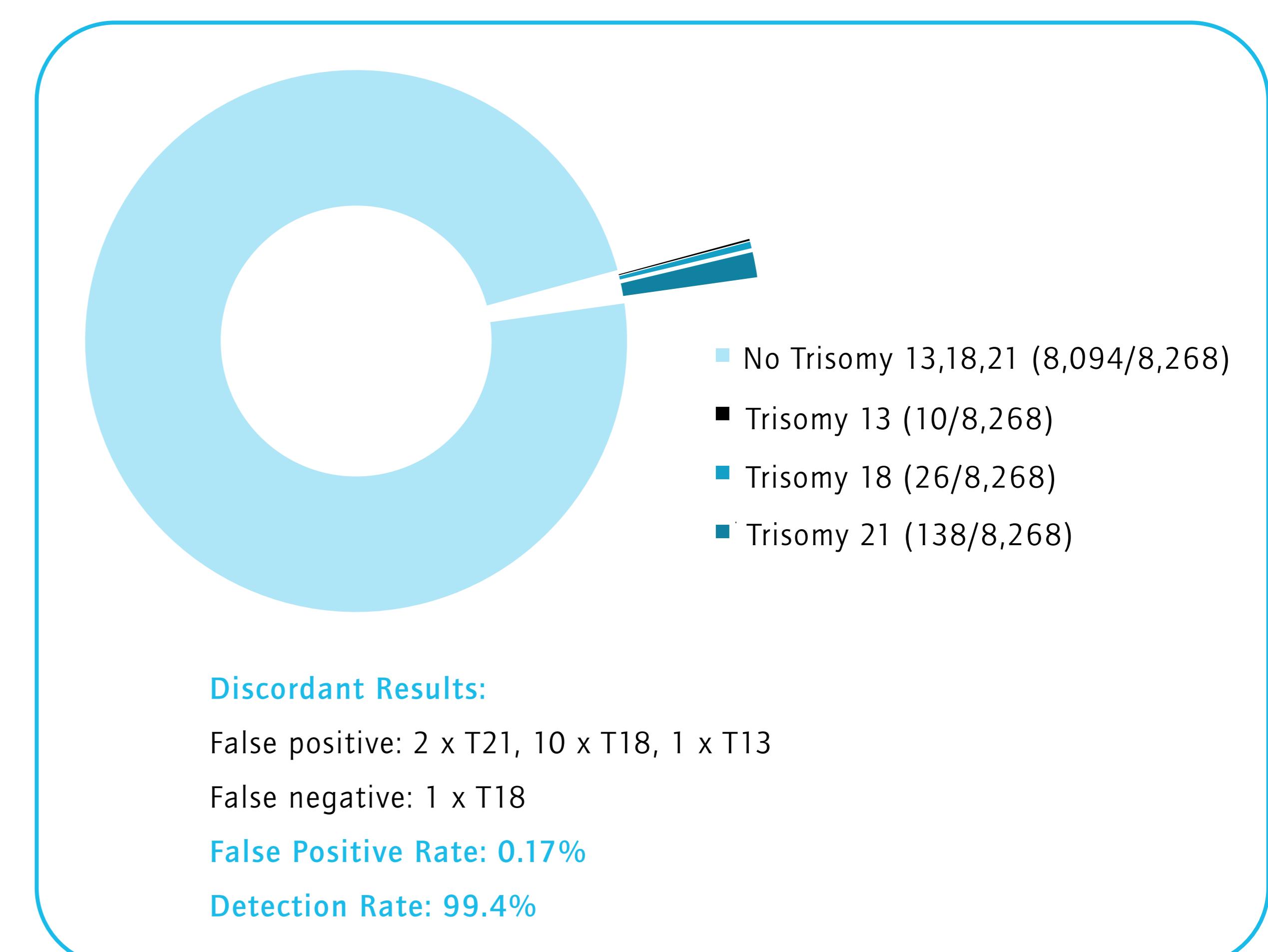


Figure 2: Results of successfully analysed samples using PraenaTest®

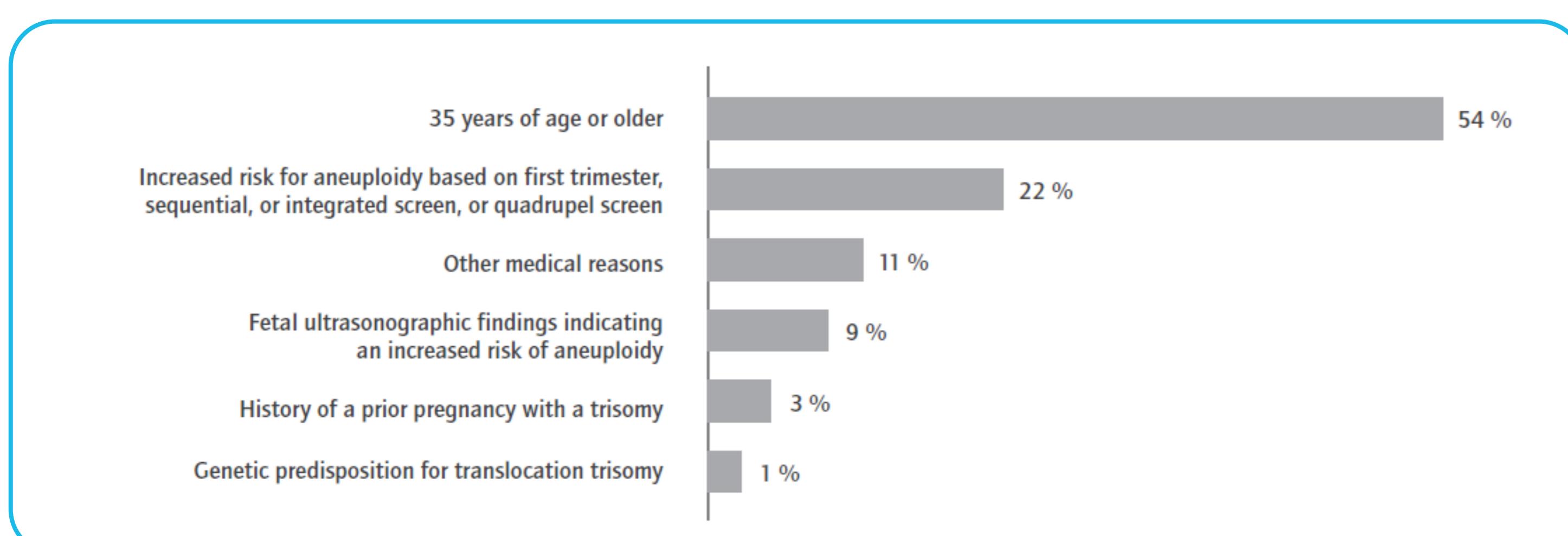


Figure 3: Summary of clinical indications for application of PraenaTest®

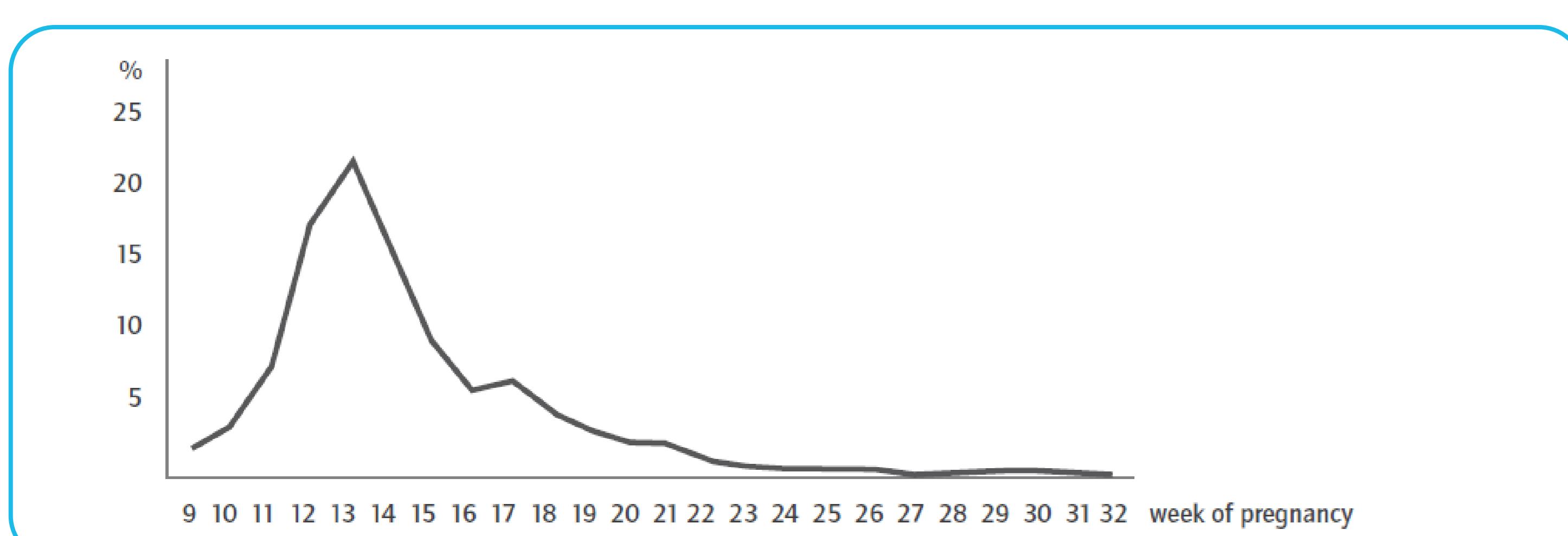


Figure 4: Overview about week of pregnancy of women who ordered PraenaTest®

## REFERENCES

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## CONCLUSION

In the near future, to characterize the limitations of NIPT more precisely, it is important to analyse thoroughly the discrepancies between NIPT results and the results of conventional karyotyping. It is intriguing that the majority of discordant results of NIPT and invasive diagnosis seem in fact to be the consequence of fetal vs. extra fetal cytogenetic discrepancies or due to undiscovered vanished twins. These findings suggest that biological reasons rather than methodical failures play the major role, emphasising the highly important collaboration between geneticists and gynaecologists specialized in ultrasonography and further analysis of discordant results.

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