

## Introduction

To assist women and their partners in making reproductive choices, prenatal screening for Down syndrome and other common autosomal aneuploidies is offered to pregnant women in Belgium. Non-invasive testing (NIPT) for Down syndrome (trisomy 21) and other common autosomal aneuploidies (trisomy 18 and 13) based on sequencing of cell-free DNA (cfDNA) in maternal plasma is a valuable technique for prenatal screening of high and low risk populations.<sup>1,2,3</sup>

## Application of NIPT

The use of NIPT for prenatal screening in a general Belgian obstetric population results in the smallest number of missed diagnoses of fetal trisomy 21.<sup>4,5</sup> Moreover, the number of invasive tests that are performed as a result of a positive screening test is much lower than using the combined first trimester screening (cFTS) as the primary screening instrument.<sup>6</sup>

Therefore, NIPT is currently the best choice as a first tier prenatal screening tool for trisomy 13, 18 and 21.

## Good clinical practice with NIPT as a screening tool

- NIPT is the first tier screening tool for prenatal screening for fetal trisomy 13, 18 and 21.
- Pre-test counselling with information about the different screening options and their possibilities and limitations is required.
- Informed consent has to be obtained.
- NIPT does not replace the first trimester fetal ultrasound for measurement of the nuchal translucency (NT) and identification of fetal malformations; fetal ultrasound should be performed before NIPT screening to ascertain whether there is an indication for another prenatal test or for additional genetic counselling.
- In case of ultrasound abnormalities, including NT >95 percentile, invasive techniques (chorionic villus sampling or amniocentesis) are indicated.
- Acquiring pre-NIPT family history by means of pedigree information is standard practice to make sure that no other prenatal test is indicated.
- Referral of a patient with a positive NIPT for invasive prenatal diagnosis by amniocentesis is necessary.
- Accreditation of genetic labs offering NIPT and regular peer review on a national level (Prenatal Working group of the Belgian Society of Human Genetics) is required.
- If NIPT is used beyond the scope of trisomy 13, 18 and 21, appropriate genetic counselling is required.

- NIPT should be performed with caution:
  - in case of a multiple pregnancy or a pregnancy with a vanishing twin
  - if the patient has (had) cancer
  - if the patient recently had heparin therapy or a blood transfusion
  - if the patient has had immunotherapy, a stem cell transplant or an organ transplantation
- It is recommended to postpone NIPT analysis to 14 weeks for pregnant women with a BMI  $\geq$  30 in order to increase the chance of an interpretable result.
- Incidental findings (= findings which are not directly related to the indication for which the NIPT was performed, e.g. an fetal aneuploidy of a chromosome other than 13, 18 and 21 or a genetic anomaly in the mother) should be handled according to the “Belgian guidelines for managing incidental findings detected by NIPT”.<sup>7</sup> In case of incidental findings that are likely to be valid and have obvious clinical utility, referral for genetic counselling is required.
- The fetal fraction (= proportion of fetal cell-free DNA) is determined as a standard quality control parameter that is taken into account while interpreting all NIPT results.

## References

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2. Daley R, Hill M, Chitty LS. Non-invasive prenatal diagnosis: progress and potential. *Arch Dis Child Fetal Neonatal Ed.* 2014; 99:426-430
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5. PUBLICATIE VAN DE HOGE GEZONDHEIDSRAAD nr. 8912 Implementatie van niet-invasieve prenatale genetische screening van trisomie 21 (Syndroom van Down) in de Belgische zorgpraktijk 07.05.2014
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7. Website: Belgian guidelines for managing incidental findings detected by NIPT (BeSHG): <https://www.college-genetics.be/fr/pour-les-professionnels/recommandations-et-bonnes-pratiques/guidelines.html>

## Version history

Version	Date prepared by BeSHG Prenatal Workgroup	Date approved by College of Medical Genetics	Updates
V2014	21.11.2014	05.12.2014	New document: no history available.
V2017	26.01.2017	03.02.2017	Review of the reference list (reference 3 added, references 5-7 removed). Fetal fraction was added as a quality control parameter.
V2023	14.12.2023	02.02.2024	Reference 6 was added. Reference 7: website was updated. Guideline on not reporting sex chromosomal abnormalities was removed. Recommendation was added to postpone NIPT analysis to 14 weeks in pregnant women with BMI $\geq 30$ to increase the chance on an interpretable result.