NIPT: non-invasive prenatal test
Risk calculation for trisomy 21 (Down syndrome)

Information for Patients

What is Trisomy 21 or Down Syndrome?
A fetus with trisomy 21, commonly known as Down syndrome, has three copies of chromosome 21 instead of the normal two copies. Trisomy 21 occurs in about 1 out of 700 live-born babies and is the most frequent chromosomal abnormality. The main feature is intellectual disability, although in a minority of cases a congenital heart defect or other physical abnormality may be detected via ultrasound examination. The risk for trisomy 21 increases with the age of the mother, rising sharply from the age of 36 years.

For those who wish to know if they are at increased risk of having a fetus with trisomy 21, the two current options for risk determination are the combined test (blood biochemical screening + ultrasound evaluation) and the NIPT (non-invasive prenatal test).

What is the Non-invasive Prenatal Test (NIPT)?
During pregnancy, DNA fragments from the fetus can be found circulating in the blood of the mother. By measuring these DNA fragments of the fetus in the maternal circulation, the number of copies of chromosome 21 can be determined allowing for detection of trisomy 21 in the fetus. The blood collection for this test can be carried out as from 11 weeks of gestation, because from then on there is sufficient fetal DNA present in the maternal blood. The blood collection does not confer any risk to the pregnancy nor to the mother.

There are several situations where NIPT can be considered:

- You have a combined test result which indicates an increased risk for trisomy 21 (>1/300).
- You have had a previous pregnancy with a fetus affected with trisomy 21.
- You are over 36 years of age and thus have an increased risk of a fetus with trisomy 21.
- You have reasons other than those listed above for considering NIPT. You should discuss this with your doctor since, for other specific genetic disorders, an alternative type of genetic testing may be more appropriate.

NIPT is not possible in cases of:
- A dizygotic twin pregnancy (non-identical twins) or multiple pregnancies
- A blood transfusion, stem cell therapy, immunotherapy, or transplantation within 3 months prior to the NIPT
NIPT is **not recommended**:

- When ultrasound abnormalities are present in the fetus (including a nuchal translucency >3.5mm).
- When the weight of the mother prior to the pregnancy exceeded 100 kg since in these cases NIPT would give an unreliable result in more than 1 in 10 pregnancies.

NIPT is **not able to detect**:

- Mosaicism (not all the cells have a trisomy)
- Small chromosome abnormalities (microdeletions or microduplications)
- Monogenic (single gene) disorders (such as cystic fibrosis or fragile X)

The NIPT performed in the Centre for Human Genetics in UZ Leuven is accredited (ISO 15189).

**WHAT ARE THE POSSIBLE RESULTS OF THE NIPT?**

1. The NIPT indicates a **low risk**. A normal result is given and means that no indication was found for the presence of trisomy 21 in the fetus. As NIPT is a screening test and not a diagnostic test, a normal result cannot 100% exclude trisomy 21. The NIPT has a sensitivity of 99.9%: out of 1000 fetuses with trisomy 21 the NIPT will identify 999 of these.

2. The NIPT indicates a **high risk**. The abnormal result given is a strong indication but not a guarantee that the fetus has trisomy 21. Where the NIPT indicates an abnormal number of chromosomes 21, this result should be confirmed by an invasive test (chorionic villus sampling or amniocentesis) – by carrying out this diagnostic examination directly on fetal material, you will have complete certainty as to whether or not the fetus has trisomy 21.

3. The NIPT is **inconclusive or has failed**. This occurs in up to 5% of samples and may be due to blood collection before the eleventh week of pregnancy when there is insufficient circulating fetal DNA in the mother’s blood; may be due to obesity in the mother where there is an increased amount of maternal DNA fragments in the circulation; or may be due to technical reasons. When the NIPT is inconclusive or has failed due to technical issues, the NIPT can be repeated once without incurring extra costs, alternatively you may choose to perform another test.

4. The NIPT will detect the sex of the fetus, other chromosome aberrations such as trisomy 18 or trisomy 13, or a clinically relevant chromosome abnormality in the mother. In these cases, the Centre for Human Genetics or your gynaecologist will discuss these results with you.

**HOW MUCH DOES THE NIPT COST?**

The cost of the test is **€390**. Currently, NIPT is not reimbursed by the health insurance system. The patient is therefore completely responsible for payment.

The result will be reported within a **maximum of 3 weeks** of blood collection. Your doctor will inform you of the results.

If you have any further questions after reading this information, you may contact your gynaecologist or a Human Genetics Centre.