Module 2:
Patient selection and performance criteria

St George's University Hospitals NHS Foundation Trust

Module 2 will cover:

- How early in pregnancy can NIPT be done?
- How is the NIPT test result calculated?
- The advantages and disadvantages of NIPT
- NIPT in multiple pregnancies
- NIPT in IVF, egg or ovum donation?
- Why may NIPT not work?

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How Early in Pregnancy can NIPT cfDNA Screening be Done?

- Feto-placental cfDNA is present in the maternal circulation from 4-5 weeks.
- Adequate quantities of cfDNA for NIPT appear at about 10 weeks gestation.
- An ultrasound scan is required to confirm gestation prior to NIPT screening.

How is a NIPT Screening Result Calculated?

- The a-priori risk is the maternal age risk of a specific trisomy or the first trimester combined test, if available.
- The a-priori risk is modified by the likelihood ratio generated by the cfDNA analysis to calculate a final result.
- The NIPT test is given as a risk score i.e. I:X. A risk score of 1:150 (or greater) is used as the ”cut-off” for a high risk result.
- It is best practice to refer to “risk” as “chance” when speaking with expectant parents.

What are the Advantages of NIPT?

- SAFE: uses a sample of the mother's blood (no risk of miscarriage)
- ACCURATE: Most NIPT tests have a detection rate of over 99% compared to around 85% for the combined test
- FAST: results available in 4-5 working days
- LOCAL: samples sent to a local laboratory
- COST EFFECTIVE: NIPT reduces the number of false positive results, thereby reducing the number of unnecessary invasive tests
- COMPREHENSIVE: includes maternal age or first trimester combined test result within the NIPT result
- QUALITY: CE-marked IVD

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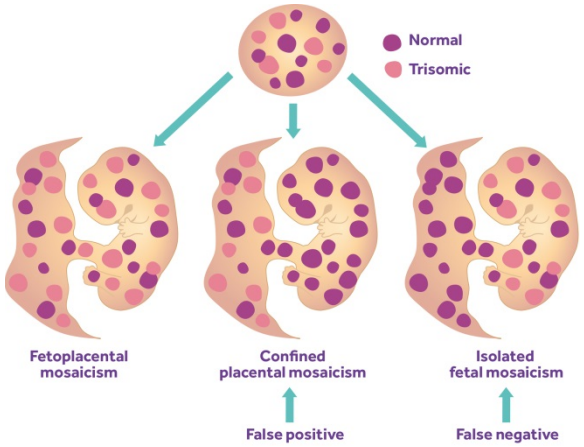
What are the disadvantages of NIPT?

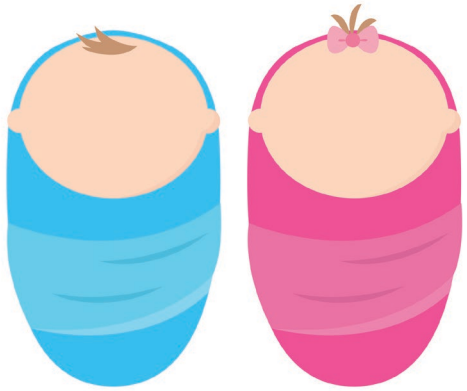
- It is a screening test NOT a diagnostic test.
- NIPT cannot differentiate between DNA from the placenta or fetus. In the presence of rare ‘confined placental mosaicism’, NIPT screening could show a false positive result.
- Small chance of test failure and a re-draw may be required.



What about Multiple pregnancies?

- For monochorionic twins (MCDA), the sensitivity and specificity is as for singleton pregnancy (as the babies are always genetically identical).

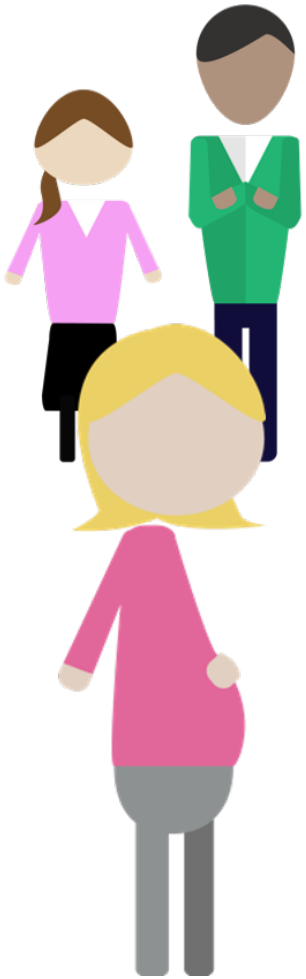
- For dichorionic diamniotic (DCDA), the sensitivity and specificity are reduced to about 95%.



- NIPT is unable to distinguish the twin origin of the cfDNA so is unable to identify which twin is affected.

- NIPT cannot be used in higher order multiple pregnancy (triplets, quads).

IVF, Egg Donor and Surrogate Pregnancies



- Some, but not all, NIPT's take maternal age for the a-priori risk.
- The SAFE test uses the age of the egg donor at the point of donation, to give the most accurate screening result.
- This ensures an accurate and individualised risk result for egg donation and surrogacy pregnancies.

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When may NIPT not work?

Maternal trisomy

- As NIPT cannot distinguish between the maternal or placental cfDNA, any extra genetic material from trisomy 21, 18 or 13 in the mother is likely to cause a screen positive result.

Maternal Malignancy

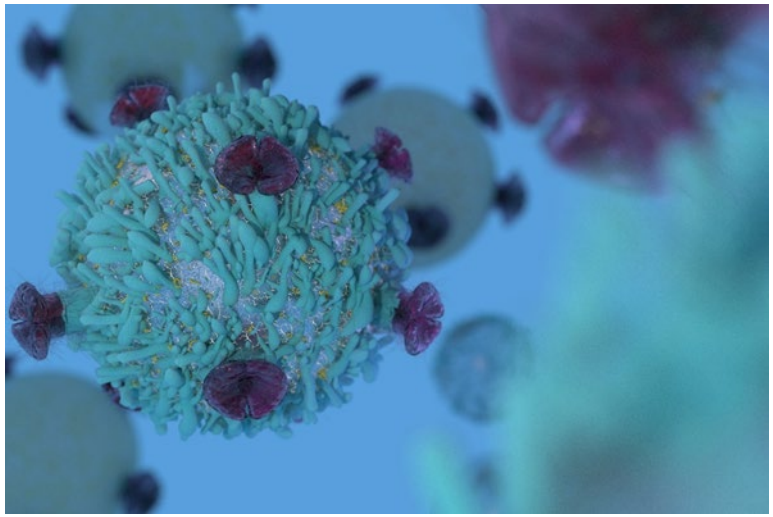
- Malignant tumours shed cfDNA fragments, and therefore can affect an NIPT result.
- Pregnant women with cancer cannot have an NIPT.

Blood Transfusions

- Cell-free DNA screening is not advised in women that have had a blood transfusion within the past 3 months.

- This is because the transfused blood in the circulation could potentially affect an NIPT result due to exogenous (transfused) DNA remaining in the circulation.

Transplants, Stem Cell Therapy or Immunotherapy



- NIPT is not suitable for individuals who have had transplant surgery or immunotherapy.
- There may be a small chance of cell free DNA circulating from the donor which can affect the NIPT result.