Module 1:
NIPT cell-free DNA introduction

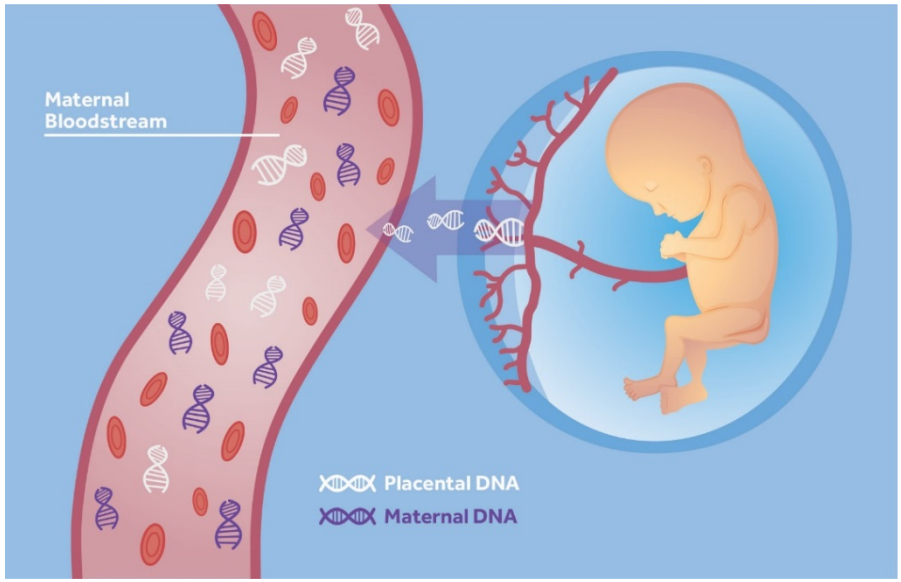
St George's University Hospitals
NHS Foundation Trust

Module 1 will cover:

- What is placental cfDNA?
- How is cfDNA used to screen for chromosomal aneuploidies?
- How accurate is cfDNA screening?
- NIPT recommendations for use within the NHS

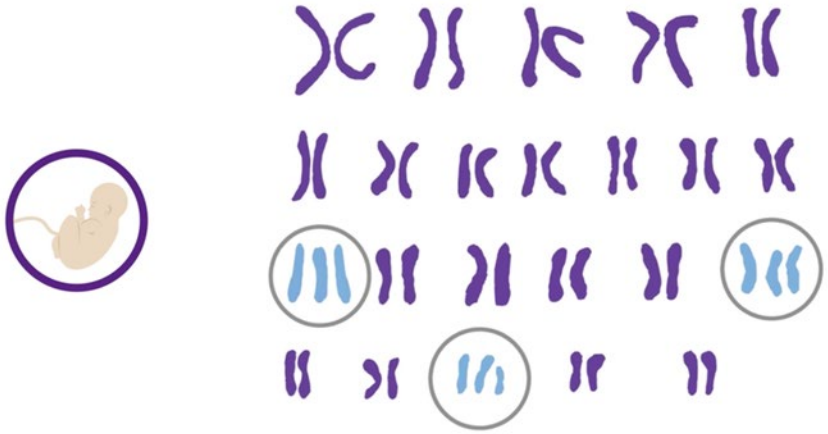
the SAFE test
St George's Antenatal Fetal Evaluation

What is placental cfDNA?



- During pregnancy the cells that make up the placenta, shed cell-free DNA into the maternal blood circulation.
- Maternal blood contains a mixture of placental and maternal cfDNA.
- Approximately 10% of the circulating cfDNA comes from the placenta.

How is cfDNA used to screen for trisomies?



- Trisomy 21 (Down's Syndrome)
- Trisomy 18 (Edwards' Syndrome)
- Trisomy 13 (Patau's Syndrome)

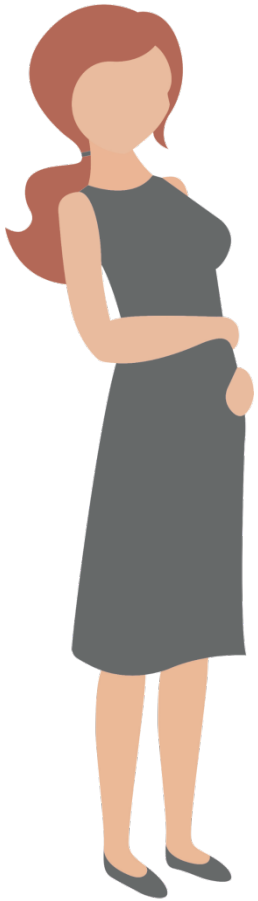
- Chromosomes are made up of long strands of DNA that contain information that determine the baby's growth and development.
- Trisomic syndromes occur when a person has an extra chromosome over and above the normal two strands.
- During NIPT small fragments of placental cfDNA are sequenced and counted.
- Extra chromosomal material indicates the presence of a trisomy.

How accurate is cfDNA screening?

- Most NIPT tests have a detection rate of over 99% compared to around 85% for the combined test.
  - This is a population statistic that provides information on the proportion of cases that have been correctly identified out of the total number of cases truly affected by a condition.
- Most NIPT tests have a false positive rate of less than 1% compared to the combined test with a false positive rate of 3%.
  - This is the proportion of people who do not have a condition but have been identified as a screen positive/high chance.
- NIPT enables greater clarity in the management of pregnancy.

Positive Predictive Value (PPV)

- Positive Predictive Value (PPV) and Negative Predictive Value (NPV) are more beneficial for a patient following a high chance result from the combined test.
  - PPV is the number of truly positive cases that have been reported as a screen positive/high chance result.
  - NPV is the number of truly negative cases that have been reported as a screen negative/low chance result.
- PPV statistics vary between populations (high chance vs. general), the condition being screened for and NIPT tests.
- Most reviews recommend that NIPT is most suitable following a high chance combined or quadruple screening test.



What are the recommendations for use within the NHS?

- The National Screening Committee (NSC) has recommended that NIPT is offered to women who have a high chance result (≥1:150) of trisomy on combined or quadruple testing.
- The recommendation is on the basis of the effectiveness of NIPT at reducing the demand for unnecessary invasive prenatal diagnosis.
- As a healthcare professional, it is important to understand who is eligible for the test, its benefits and limitations.