



UK National
Screening Committee

Frequently asked questions – cell free fetal DNA (cffDNA) testing for Down's syndrome and other trisomies

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Cell free fetal DNA (cffDNA) testing, sometimes known as Non-Invasive Prenatal Testing (NIPT), is a test that can identify pregnant women who are at higher risk of having a baby with certain genetic and chromosomal conditions, such as Down's syndrome (also known as Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13).

The test detects DNA fragments in a sample of blood taken from the mother. Most of the DNA fragments are from the mother but some are from the unborn baby, these fragments are called cell free fetal DNA (cffDNA). CffDNA is detectable from around 7 weeks of pregnancy and the amount of detectable DNA is thought to rise as the pregnancy continues.

What trisomy screening are women currently offered during pregnancy?

All pregnant women in England are offered the combined test for Down's syndrome as part of the NHS Fetal Anomaly Screening Programme (FASP). This programme also includes first trimester screening for Edwards' syndrome and Patau's syndrome.

The main aim of FASP is to offer all pregnant women in England a minimum of two ultrasound scans. The screening process for trisomy abnormalities; Down's syndrome, Edwards' syndrome and Patau's syndrome includes:

- a dating scan at 8 to 11 weeks of pregnancy, this usually happens at the same time as the combined test
- the combined test which involves a blood test and a Nuchal Translucency (NT) ultrasound scan in the first trimester of pregnancy, normally at 12 weeks
- second trimester screening, between 14 and 20 weeks, is offered for Down's syndrome if the woman missed the first trimester offer. The second trimester blood test is not as accurate as the combined test. Similarly, for women who miss the offer of first trimester screening for Edwards' syndrome and Patau's syndrome, a second trimester ultrasound scan is offered to check for abnormalities.

Women will be given two risk scores from the combined test, one for Down's syndrome and one for both Edwards' syndrome and Patau's syndrome.

Pregnant women who are shown to be at a higher risk (more than a 1 in 150 chance) of having a baby with one of these conditions are then offered follow-up diagnostic tests. These diagnostic tests can tell whether the baby will have Down's syndrome (or Edwards' syndrome or Patau's syndrome) but they are invasive and carry a small (1 in 100) risk of miscarriage.

How does cffDNA testing differ from the current screening tests?

CffDNA tests are thought to be more accurate than the combined test and studies have shown that it correctly identifies more cases of Down's syndrome in pregnancy. The improved accuracy is important as cffDNA itself does not carry any risk of miscarriage and can give parents-to-be higher quality information about their baby's risk of Down's syndrome.

Although cffDNA is thought to be very accurate, there is still a chance that it would incorrectly identify a pregnancy as high risk of Down's syndrome. For this reason it should not replace the current diagnostic test used in FASP. Its improved accuracy compared to the combined test does mean that fewer women will go on to have the invasive diagnostic test when their baby does not in fact have Down's syndrome.

Should cffDNA testing replace the current combined screening test?

There is the potential for cffDNA to replace the current combined screening test in the future. However, as the technology stands, the number of tests which don't give a result would mean that more women would be offered invasive testing than now.

Also, cffDNA may be very accurate when identifying which babies are at a higher risk of Down's syndrome, but there is not enough evidence to be sure of its accuracy when looking for Edwards' syndrome and Patau's syndrome.

The UK NSC will continue to keep emerging evidence under review.

Why has the UK NSC not already recommended introducing cffDNA testing as part of screening?

There are a number of considerations to be made before the UK NSC can make a formal recommendation on using cffDNA within the UK setting. These include:

- The tests had only been used in women at high risk so there was no international research to show it would work for all women in day to day practice within NHS.
- Availability of equipment and resources – cffDNA testing is a relatively new technology and the UK does not yet have the resources to support a full screening programme using this method. Many of the tests that are currently offered within the UK are sent abroad for processing.
- Which women should be offered cffDNA? As the test takes around 2 weeks to process the results, this wait may cause unnecessary anxiety for parents-to-be when their baby is at very low risk of having a condition. Therefore, it is not clear whether all pregnant women should be offered cffDNA, or just those identified as at higher risk through the combined test.
- What happens to those women who have cffDNA testing but the test fails? Research shows that between 1% and 4% of women will not get any results from cffDNA. This can happen for a variety of reasons, including some cases where there is not enough of the baby's DNA present in the mother's blood sample. Inconclusive results may cause further anxiety and delays for women who may need to decide whether to have the diagnostic test without the cffDNA result. The UK NSC must make sure there is support in place to help these women.

Is cffDNA testing already available within the NHS?

CffDNA testing is not currently part of routine English screening programmes. Some NHS Trusts have piloted the test and a number of maternity units do offer cffDNA testing privately.

The UK NSC is currently working with experts who are researching the use of cffDNA in routine screening practice in England. The UK NSC will review the results of this research, when available, to make a recommendation on whether the test can be safely introduced as part of FASP.

Although there is evidence that cffDNA testing will lead to a reduction in the number of women undergoing invasive diagnostic tests unnecessarily, the UK NSC must be sure that there are safe and quality care and support routes in place within the NHS before recommending its use.

For more information

The UK National Screening Committee (UK NSC) reviews the evidence for screening for conditions against strict criteria, which you can find here: www.screening.nhs.uk/criteria

Details of the review process can be found here: www.screening.nhs.uk/evidencereview

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