

Screening for Down's syndrome, Edwards' syndrome and Patau's syndrome in twin pregnancies

1. Introduction to twins and screening

Twin pregnancies account for 1.6% of all pregnancies in the UK.

In order for women to be able to make a fully informed decision about entering the screening pathway they need to understand the stages in the pathway prior to deciding whether to have screening or further tests.

Decision making for women around the offer of screening for these conditions in a twin pregnancy is more complicated than in singleton pregnancies. This is because non-invasive prenatal testing (NIPT) is not offered in a twin pregnancy as part of the screening pathway. Invasive testing in a twin pregnancy carries a higher risk of miscarriage than a singleton pregnancy and there are risks associated with selective termination of one affected fetus.

Screening for Down's syndrome, Edwards' syndrome and Patau's syndrome is not offered in triplets or higher multiple pregnancies.

The accuracy of the screening tests and the risks associated with invasive testing will be different for:

- dizygotic (70% of all twins) - arise from two separate eggs that are fertilised by separate sperm and are non-identical
- monozygotic twins (30% of all twin pregnancies) - occur when a single fertilised egg later divides into two embryos. These twins usually share the same genetic material (are identical).¹

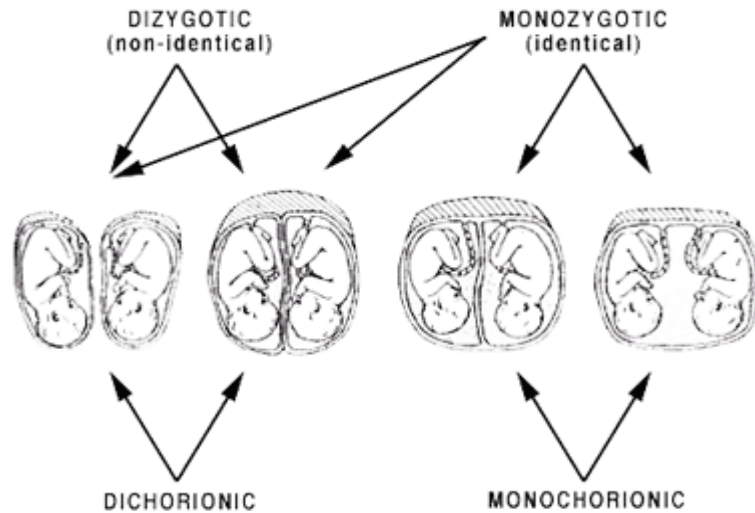


Diagram 1

Lambda λ sign = dichorionic

T sign = monozygotic ²

Monochorionic twins are almost always monozygotic (identical).

Dichorionic twins in most cases (around 90%) are dizygotic and are therefore usually non-identical. However around 10% of dichorionic twins are identical (monozygotic).

2. Ultrasound Measurements in Twin Pregnancy

It is the largest of the two crown rump length (CRL) measurements that is used for estimation of gestational age for the purpose of standardizing the biochemical measurements. For combined testing in twins, both should have a CRL of 45mm or more and the larger CRL should be not be greater than 84mm. **ie if one twin has a CRL of more than 84mm screening cannot be performed.**

3. Tests available in a twin pregnancy NHS Wales

Combined screening (11^{+2} - 14^{+1}) and invasive procedures (CVS, 11^{+0} - 13^{+6}) and amniocentesis (>15 weeks gestation) are part of the screening pathway for twins.

4. Tests not available for twins in Wales

Quadruple screening should not be offered to women with twin pregnancies. This is because this test does not perform well in twins with a detection rate of only 40-50% for a 3% screen positive rate.

NIPT (non-invasive prenatal testing) should not be offered in a twin pregnancy. There is insufficient evidence of how the test performs in twins and this is not included in the recommendations by UK National Screening Committee.

NIPT cannot be offered if this pregnancy was **ever** a twin pregnancy (e.g. if a second fetal pole or pregnancy sac has been seen on scan). This is because the free fetal DNA may still be present in the maternal blood from the demised twin potentially giving an inaccurate result.

5. Combined testing in monozygotic twins

5.1 Accuracy

The sensitivity (affected fetus identified by the test) of combined screening in monozygotic twins is comparable to or better than in singleton pregnancies. The specificity (women that have a negative result where the fetus does not have the condition) is slightly lower than in singleton pregnancies.

5.2 Calculation of chance using nuchal translucency (NT) and biochemistry

The prior risk in screening, which takes into account things such as maternal age, smoking status, and ethnicity, also takes into account the twin pregnancy. This risk is adjusted by a factor of 0.6 for monozygotic twin pregnancies.³

The expected amount of free Beta hCG and PAPP-A are also adjusted for the type of twin pregnancy.

The chance of the pregnancy being affected is calculated by taking the mean of the two NT measurements.

If either twin has a CRL of greater than 84.0mm a combined screening test cannot be offered.

If the CRL and NT measurement can only be obtained for one twin the laboratory will provide a result based on that measurement and the result will state that this will be less accurate for the pregnancy than if the two measurements were available.

5.3 Result

The result of screening in a monochorionic twin pregnancy will be:

- A chance of Down's syndrome 1:xxx for the **pregnancy** and
- A chance of Edwards'/ Patau's syndrome 1:xxx for the **pregnancy**

5.4 Invasive procedures in monochorionic twins

Monochorionic twins will almost always have the same karyotype, but it is not impossible to have a chromosomal abnormality in one twin, and not the other.

An invasive test in a twin pregnancy carries an increased risk of miscarriage of around 2%.

6. Combined testing in dichorionic twin pregnancies

6.1 Accuracy

The sensitivity (affected fetus identified by the test) of combined screening in dichorionic twins is comparable to or better than in singleton pregnancies. The specificity (women that have a negative result where the fetus does not have the condition) is slightly lower than in singleton pregnancies.

If dichorionic twins are monozygotic (around 10% of cases of dichorionic twins), the accuracy of the chance result for these women will be affected. This is because the biochemistry calculation will have made the assumption that the twins are non-identical based on the chorionicity. This will affect the accuracy of the result for the woman who has a monozygotic twin pregnancy which is dichorionic. **There is no way of telling zygosity unless the twins have different genders, which cannot be defined on scan at this gestation.**

6.2 Calculation of chance using NT and biochemistry

The chance of a dichorionic twin pregnancy being affected by one of the syndromes is higher than for a singleton pregnancy as each fetus has the same risk as a singleton pregnancy and there are two fetuses. This means that the calculation of chance for the pregnancy needs to be adjusted for this. Therefore the prior risk, which takes into account things such as maternal age, smoking status etc, is also adjusted for the type of twin pregnancy. The risk is adjusted by a factor of 1.2 for dichorionic twin pregnancies.⁴

The chance of each fetus being affected is calculated using the NT measurements for each fetus in a dichorionic a twin pregnancy as it is assumed they will be non-identical twins.

The calculation of the chance of a pregnancy being affected by one of the syndromes will also be adjusted because of the increase in the expected amount of the biochemical markers for twin pregnancies. This will be affected by the chorionicity of the twins.

If either twin has a CRL of greater than 84.0mm combined screening test cannot be offered.

If the CRL and NT measurement can only be obtained for **one** twin the laboratory will provide a result based on that measurement and the result will state that this will only be accurate for the twin that was measured.

6.3 Result

The result of screening in a dichorionic twin pregnancy will be:

- A chance of Down's syndrome 1:xxx for **each twin**
- A chance of Edwards'/ Patau's syndrome 1:xxx for **each twin**

7. Higher chance screening results

Women with a higher chance screening result in a twin pregnancy should have a face to face appointment with the health board nominated professional for screening in a twin pregnancy.

The woman should have a full discussion about the result; options for invasive testing; benefits and harms of invasive testing; and options if a condition is diagnosed. This should include information about risk of miscarriage and risks of selective termination of pregnancy in a dichorionic twin pregnancy.

8. Invasive procedures

An invasive test in a twin pregnancy carries an increased risk of miscarriage around 2% as there will need to be two samples of either amniotic fluid or chorionic villi collected.

If the woman chooses an invasive procedure this must be performed in a unit where the obstetrician can perform a selective termination of pregnancy if required. This is to enable the twins to be identified at the time that the invasive procedure is performed. This will reduce the risk of termination of the unaffected twin if the woman chooses to have a selective termination.

9. Risks associated with selective termination of pregnancy

In a twin pregnancy where one fetus is affected and the other fetus unaffected, the woman may decide to have a selective termination of the affected fetus.

The risk of miscarriage of the unaffected twin below 25 weeks gestation following a selective termination is around 9% higher than in a continuing twin pregnancy. In pregnancies following selective termination the birth of babies is earlier than for continuing twin pregnancies.^{5 6}

There is a risk of neurodevelopmental morbidity for the surviving twin. This risk is 2% in dichorionic twins and 26% in monochorionic twins.⁷

There is a very small risk that the unaffected twin could be terminated by the health professional carrying out the procedure.

Crib sheet for Health Board nominated professional for discussing this screening

Discuss:

- Screening is a choice and the woman can decide to change her mind at any point in the pathway and will be supported in all of her decisions.
- Type of twins identified on scan if known.
- Screening is more complicated in twin pregnancies.
- NIPT is not available on the NHS in Wales for twin pregnancies.
- The risk of miscarriage from an invasive procedure is around double the risk for a singleton pregnancy.
- Options following an invasive procedure with an abnormal result.

Specific information if a monochorionic twin pregnancy:

- These are much more rare and as the twins are very likely to be identical both will be either affected or unaffected.
- The "chance" result for the combined test will be for the pregnancy being affected by either Down's syndrome or Edwards'/ Patau's syndrome.
- If only one twin could be measured then a less accurate result for the pregnancy will be issued if the woman wishes to continue on the screening pathway.
- If the combined test cannot be obtained, quadruple testing is not offered in Wales.
- If the combined test result is higher chance for Down's syndrome or Edwards'/Patau's syndromes an invasive procedure will be offered – either CVS or amniocentesis – dependant on gestation and maternal choice.
- The risk of miscarriage from the invasive procedure should be discussed.
- If the invasive procedure shows that the pregnancy is affected by one of the conditions, the woman should understand that in most cases she will be offered a termination of the pregnancy for both twins.

Specific information if a dichorionic twin pregnancy:

- These are the most common type of twins and as the twins are likely to be non identical, therefore each twin could be either affected or unaffected.
- The chance result for the combined test will be for each fetus being affected by either Down's syndrome or Edwards'/ Patau's syndrome.
- If only one twin could be measured, and the woman wishes to continue on the screening pathway then a result will be issued for only one fetus.
- The combined test is slightly less accurate in dichorionic twins because a small number of dichorionic twins are identical but the test assumes they are all non identical.
- If the combined test cannot be obtained quad testing is not offered in Wales.
- If the combined test result is higher chance for Down's syndrome or Edwards'/Patau's syndromes an invasive procedure will be offered – either CVS or amniocentesis – dependant on gestation and maternal choice.
- If an invasive test diagnoses one affected baby and the other unaffected, the woman may decide to have a selective termination of the affected baby. In this instance the invasive procedure should be performed by the person who will also perform the selective termination of pregnancy.
- The risk of miscarriage from the invasive procedure should be discussed.
- If the invasive procedure identifies that one fetus has Down's, Edwards' or Patau's syndromes, the woman should understand that in most cases she will be offered a termination of the affected fetus and that this can carry risks for the unaffected fetus and these should be explained.

¹ Ob-gyn ultrasound online. Accessed from <http://www.fetalsono.com/teachfiles/choram.lasso>

² Multiple Births Foundation Accessed from: <http://www.multiplebirths.org.uk/identical.asp>

³ Cuckle H, Wilson C. "Twins - Risk per fetus or per pregnancy." Down's Screening News 13:1:8, 2006.

⁴ Cuckle H, Wilson C. "Twins - Risk per fetus or per pregnancy." Down's Screening News 13:1:8, 2006.

⁵ Mheen, L. et al (2015) Pregnancy outcome after fetal reduction in women with a dichorionic twin pregnancy. Human Reproduction, Vol.30, No.8 pp. 1807–1812

⁶ Wimalasundera, RC. (2010) Selective reduction and termination of multiple pregnancies. Seminars in Fetal & Neonatal Medicine 15 (2010) 327-335

⁷ Mackie, F, Morris, RK & Kilby, M 2016, 'Fetal brain injury in survivors of twin pregnancies complicated by demise of one twin: A review' Twin Research and Human Genetics, vol 19, no. 03, pp. 262-267. DOI:10.1017/thg.2016.39