Fetal Anomaly Screening - Down's, Edward's and Patau's Syndrome

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

Guidance on antenatal screening tests available for all pregnancies and the management of high chance results.

This guideline is for use by the following staff groups:

Midwives, sonographers performing screening ultrasound scans and obstetric doctors.

Lead Clinician(s)

Aldonna Morrison	Lead Midwife Sonographer
Emma Davis	Lead Antenatal and Newborn Screening Midwife
Approved by Maternity Governance Meeting on:	21st April 2023
Review Date: This is the most current document and should be used until a revised version is in place	21st April 2026

Key amendments to this guideline

Date	Amendment	Approved by:
April 2023	Full Guideline Review. Changes to documentation to include digital notes.	Maternity Governance Meeting

Description of Screening Programme

Down's (Trisomy 21/T21), Edwards' (Trisomy 18/T18) and Patau's (Trisomy 13/T13) syndromes Screening is part of the NHS Fetal Anomaly Screening Programme (FASP). This pathway has been reviewed in line with the national standards for fetal anomaly screening.

The screening policy is to offer screening to assess the risk of the baby being born with Down's, Edwards' or Patau's syndromes. The eligible population is identified through maternity antenatal care services and includes the total number of pregnant women booked for antenatal care excluding women who miscarry, opt for termination or transfer out between booking and testing (ie prior to testing), and women who book later than 14 weeks and 1 day of pregnancy.

For Down's syndrome screening, the eligible population are women with singleton and twin pregnancies $<20^{+0}$ weeks of pregnancy confirmed by ultrasound scan and for Edwards' and Patau's syndromes screening using biochemical markers the eligible population are women with singleton and twin pregnancies $\leq 14^{+1}$ weeks of pregnancy confirmed by ultrasound scan.

Introduction

Screening for Trisomy T21, 18 and 13 is well established in England. The primary aim of screening is to enable parents to make informed choice concerning their pregnancy outcome. The purpose of this guideline is to ensure that appropriate tests, methods and limitations of screening for the above conditions are outlined.

The test of choice for both singleton and twin pregnancies is first trimester Combined screening. As part of this test, patients can choose from the following options:

- Not to have screening
- To have screening for T21 and T18 / T13
- To have screening for T21 only
- To have screening for T18 / T13 only

For women having first trimester screening (Combined screening), dependant of their screening choice, up to two risks will be reported:

- A risk for T21 and a risk for T18/T13
- A risk for T21 only or T18/T13 only

The test of choice for both singleton and twin pregnancies in second trimester is Quadruple (QUAD) testing. As part of this test, patients can choose from the following options:

- Not to have screening
- To have screening for T21 only

For women having second trimester screening (Quadruple screening) one chance result will be reported:

- A chance result for T21 only

1st trimester screening (Combined test) The optimal time to perform the combined test is between 11 weeks 2 day to 14 weeks 1 day of gestation, which corresponds to a CRL of 45.0mm to 84.0mm. The test uses maternal age, the nuchal translucency ultrasound measurement (NT) and two biochemical tests, free beta HCG and PAPP-A, together with the

gestational age calculated from the crown rump length (CRL) measurement, to calculate the risk of the pregnancy being affected by T21 or T18/T13.

If the ultrasound measurement shows that the CRL is less than 45.0mm, the woman should be recalled for a further scan to measure the NT. If the CRL is greater than 84.0mm, the second trimester quadruple test should be offered.

Women should be made aware that whilst the screening programme, dependant on their screening choice, aims to assess the risk of the baby being born with T21/13/18. Other complications may also be identified due to out of range results i.e.:

- Low PAPP-A

In the event of a low PAPP-A result being identified via combined screening, the pathway for serial growth scans would be triggered including the need for Aspirin. The patient will be informed of the result and management plan via a detailed patient information leaflet sent out by the screening team. This is included with the letter from Birmingham Women's Hospital which reports the low chance findings for the chromosomal testing. Please refer to the identification of low PAPP-A pathway and allocation of pregnant women to high risk care and serial growth scans pathway.

A Nuchal Translucency of ≯ ≥ 3.5mm may indicate potential complications other than Down's syndrome. Therefore, a local fetal medicine referral should be made and blood for combined screening should still be taken with consent.

Women with a previous pregnancy affected by confirmed T21, T18 or T13 are eligible for NIPT via the joint genetics service between WHAT and BWH. At booking these women should be referred to the antenatal screening team via Badgernet who will then arrange for this to happen (in these cases, combined screening is not required as a primary screening choice for the three trisomy's). However, women with a previously affected pregnancy with any genetic condition can also choose to directly have diagnostic/invasive testing.

Twin Pregnancy- the combined test will be offered for twin pregnancies. If the nuchal translucency is not measurable on a first attempt a 2nd attempt should be offered within the screening time frame. If a combined test is unable to be performed then a quad test can be offered following specialist discussion (quad testing detection rate is less in twin pregnancy's than in a singleton pregnancy).

For women screened using the combined test, where a dichorionic twin pregnancy is identified, the chances will be reported for each fetus. In a monochorionic twin pregnancy, both fetuses are either affected or unaffected so the chance will be the same and a single 'pregnancy' chance will be reported.

Please note where there are triplets or more, biochemistry cannot be offered as there is no Software programme available to assess risk. In this situation nuchal translucency measurement only will be used to assess the risk calculation.

NB: In cases of vanishing twin, where one sac contains a non-viable fetus, only a nuchal translucency measurement and maternal age will be used to ascertain the risk calculation (biochemistry would be unreliable) unless the woman prefers to have a quadruple screening test at 15 weeks.

Definitions

Title	Definition
Down's Syndrome genetic makeup	The structure of each human cell is made up of 46 chromosomes in 23 pairs. Down's syndrome there is an extra chromosome 21 making 47 in total. This gives three number 21 chromosomes, hence the medical terminology Trisomy 21. The extra genetic material gained from this gives the characteristics of Down's syndrome
Standard or Regular Trisomy 21	Most cases arise when the chromosomes donated by the mother or father have Failed to divide correctly. This type is called Standard or Regular Trisomy 21 and Accounts for 95% of people with this condition. Regular Trisomy 21 is not hereditary but it is known from statistical analysis that if a woman has a child with this type of condition then the risk will be higher of it occurring in the next pregnancy.
Other types of Down's Syndrome	Other types of Down's syndrome occur due to translocation of genetic material between chromosome 21 and another chromosome (e.g. Chromosomes 14 and 21 known as Robertsonian translocation). This type occurs in 4% of cases
Mosaicism	The remaining 1% occurs when there is Mosaicism – where normal and Trisomy 21 cells are found within the individual.
Edwards syndrome	In trisomy 18 there is an extra copy of chromosome 18 in each cell. Complete trisomy 18 is fatal. Babies with partial and mosaic trisomy 18 may survive to adulthood, but this is rare.
Patau's syndrome	With trisomy 13 there is an extra copy of chromosome 13 in each cell. Complete trisomy 13 is fatal. Babies with partial and mosaic trisomy 13 may survive to adulthood, but this is rare.
Combined test (CT)	This screening combines a nuchal translucency (NT) scan with biochemical testing, and gives results at an earlier gestation
Quadruple screening	This is a single blood test using four biochemical markers.

Prevalence

Down's syndrome occurs in approximately 1:394 births. (NCARDRS, 2019) This figure is similar in all populations and is an overall population risk. The incidence rises sharply with maternal age. It affects both boys and girls equally. Approximately 70% of Down syndrome babies are born to women under 35 therefore maternal ages should not be the sole screening factor.

Table to show incidence of Trisomy 21 with rising maternal age

Age of mother	Risk	Risk in percentage
20 years	1:1500	0.066
30 years	1:800	0.125
35 years	1: 270	0.37
40 years	1:100	1.0
45 and over	1:50 and greater	2.0

Detection Rate of Screening Tests

These figures are provided by Birmingham laboratory quarterly and by DQASS (Down's syndrome screening Quality Assurance Support Service).

FASP (22/23) defines the national cut off set at 1 in 150 at term for both first and second trimester screening tests. A woman with a risk of 1 in 150, or greater (1 in 2 – 1 in 150), of having a pregnancy affected by T21, T18/T13 in the first trimester or T21 only in the second trimester will be considered to be in the 'higher risk' group and offered an invasive test.

Excludes increased nuchal translucency (NT) measurement only – FASP policy (22/23) stipulates all women who accept first trimester screening must have all components of the screening test completed- NT and biochemistry.

Detection Rates (DR) performance thresholds: **for singleton pregnancies**

- T21 Standardised DR 85%
- T13/18 Standardised DR 80%
- T21/ 13/18 Standardised DR 80%
- Quadruple Standardised DR 80%

Detection Rates (DR) performance thresholds: **for twin pregnancies**

- T21 Standardised DR 85% For Monochorionic
- T13/18 Standardised DR 80% For Monochorionic
- T21/T13/ T18 Standardised DR 80% for Monochorionic
- T21 Standardised DR 85% For Diamniotic
- T13/18 Standardised DR 80% For Diamniotic
- T21/T13/ T18 Standardised DR 80% for Diamniotic
- Quadruple Standardised DR 80% in Monochorionic twin pregnancies
- Quadruple Standardised DR 40-50% in Diachorionic Twin pregnancies

Process of Screening

1) 1st Contact and Booking appointment with Community Midwife (ideally before 10 weeks)

- Information offered, about screening for T21/13/18 ("Screening tests for you and your baby booklet'- NHS screening programmes via Badgernet). This will provide the opportunity for further discussion before embarking on screening.
- The screening pathway for both screen positive and screen negative results
- The decisions that need to be made at each point along the pathway and their consequences
- The fact that screening does not provide a definitive diagnosis and a full explanation of the risk score obtained following testing
- Balanced and accurate information about the above conditions.

All pregnant women should be offered screening for T21/13/18. This offer and acceptance/decline should be documented on the Badgernet maternity information system (the NSC leaflet 'Screening Tests for You and Your Baby' should be given at the point of offer). Women should understand that it is their choice to embark on screening. Ideally a cooling off period should elapse between the offer and decision.

2) A dating scan appointment is generated from the Community Midwives referrals to the appropriate hospital.

3) On attending the dating scan appointment the trained ultra-sonographer will re-offer combined screening.

4) If screening is accepted the Nuchal translucency will be measured as part of the Combined Test.

5) Combined screening test bloods taken directly after the USS which will be entered into documented in the hand held records.

6) If Nuchal Translucency is unable to be measured at that appointment, a second appointment within the screening window should be offered. If the pregnancy is greater than 14+1 a Quad test will be offered and appointment for the Quad clinic will be generated with the patient still present.

7) It is the responsibly of the person taking screening bloods for either combined or quad tests to deliver the sample to the laboratory. The person who is responsible for the individual screening clinics should also ensure that the blood samples have been delivered to the laboratory in a timely manner. The air pod transporting system for blood samples should not be used.

8) Following completion of screening process information will be given as to how results will be reported.

Management of Screening Test Results:

Low chance results:

Results reviewed on a daily basis by the screening team. All women should be notified of their screening test result by letter within two weeks of the test being taken. The results will also be entered in the Badgernet maternity information system. These will then be made available to be viewed on the individuals' badger notes app.

Community Midwife to check that results have been received by patient and document on Badgernet at 16 week routine antenatal appointment.

High chance results:

Birmingham Women's Hospital Regional laboratory directly informs the Screening team of the high chance result via the antenatal screening results generic email account. In turn the screening team will acknowledge receipt of the high chance result with a return email. Women are informed of the result within 3 working days of the receipt of result and offered a face to face discussion with a relevant specialist midwife.

The midwife will discuss the options available:

- Whether to have no further testing
- Whether to have a diagnostic test.
- Whether to have Non Invasive Prenatal Testing (NIPT) This was made available within the NHS national screening programme as of April 1st 2021

Discussion should include sufficient information to ensure that the woman is aware of the purpose, benefits, limitations and risks of undergoing a diagnostic test.

Discussion details and results to be documented on Badgernet maternity information system.

Diagnostic Testing:

Chorionic Villi sampling (CVS) - 10+0-13+6 weeks

- Woman's decision is documented on Badgernet
- Referral to tertiary Fetal Medicine Unit -Birmingham Women's Hospital via e-mail.
- Following referral for diagnostic testing, Birmingham FMU will share information with the Screening Team to ensure appropriate pregnancy management/delivery of the baby and monitoring of screening outcomes.

Amniocentesis - 15 weeks onwards

- Woman's decision is documented on Badgernet
- Appointment to be made at WRH ideally within 3 working days of women receiving high risk results (gestation dependent).
- Please refer to Amniocentesis policy for full process.
- If appointments unavailable at WHAT within a reasonable time frame please refer to the tertiary Fetal Medicine Unit at Birmingham Women's Hospital via email.

Management of Diagnostic Test Results:

Normal result:

- The woman will continue with pregnancy and outcome is obtained at delivery.

Abnormal result:

- Abnormal results are reported by the Regional Cytogenetic Laboratory (Birmingham Women's Hospital) to the Antenatal Screening Team via email (read receipt in place).
- The woman is given the opportunity to discuss the results with health professionals who are knowledgeable about Down's, Edwards' and Patau's syndromes. This will include the offer of a termination of pregnancy or continuing support through pregnancy.
- If the woman chooses not to undergo termination of pregnancy and continues with her pregnancy a referral to appropriate paediatric and support services should be made (see appendix 3-Paediatric alert referral) for on-going care.
- If termination of pregnancy is chosen, this should be undertaken in line with the Abortion Act 1967 and Medical Management of Termination (14+0-20+) policy and WAHT-GYN-001/ Medical management of termination (20+ weeks).
- Abnormal results will be reported to West Midlands Congenital anomaly register (WMCAR) now (NCARDRS) by the Antenatal Screening team via e-mail

<u>NIPT (non-invasive pre-natal testing)</u>

- NIPT will be an additional option, for those women who have a higher chance (1 in 2 to 1 in 150) of having a baby with Down's syndrome, Edwards' syndrome or Patau's syndrome following combined or quadruple screening. NIPT can be offered in single and twin pregnancies
- as part of the Down's syndrome, Edwards' syndrome and Patau's syndrome screening pathway, NIPT can be offered and performed up to 21 weeks and 6 days (21+6) of pregnancy

NIPT in twin pregnancies:

- There is a small amount of evidence related the performance of NIPT to detect Down's syndrome, Edwards' syndrome, and Patau's syndromes in twin pregnancies. The offer of NIPT has been extended to eligible women who are pregnant with twins.

Women need to be aware that NIPT as part of the NHS screening pathway will:

  - Only screen for Down's syndrome, Edwards' syndrome and Patau's syndrome
  - Not detect other chromosomal or genetic conditions
  - Not assess fetal sex

- NIPT is a screening test and false positive and false negative results can occur.
- Invasive prenatal diagnosis is required if the woman wants a definitive result.
- Women with IVF or donor egg pregnancies are eligible for the offer of NIPT. The relevant details must be recorded accurately on the request form.

Failsafe Mechanisms:
Worcester Royal Hospital, Evesham, Kidderminster and the Alexandra Hospital

- The designated Midwife in charge of the combined/quad clinic will generate a list of all Combined and Quad test samples. This list is sent to the local laboratories and screening team via secure email. (see appendix 3 -Fail Combined and Quad failsafe list).
- On receipt of the sample the local laboratory will return the list to the screening team via email acknowledging receipt of all samples.
- The screening team will be informed of any missing samples. These will be followed up as a matter of urgency.
- In exceptional circumstances, if a blood sample is taken in a community clinic, the health care professional taking the blood must inform the screening team and Biochemistry so they are aware the sample is expected.
- All results are checked daily, via direct access to Birmingham Clinical Chemistry results system, against the check lists to ensure all patients have received a reportable result.
- Blood samples are sent to Birmingham Women's Laboratory via courier Monday to Friday.

At the mandatory routine 16 week antenatal appointment, the midwife must check that all screening results have been received by the lady and have been inputted into Badgernet. If there is no documented evidence of results then it is the responsibility of all healthcare professionals at every point of contact to ensure that a reportable screening result is documented. If there is any uncertainty regarding these results the Antenatal Screening Coordinator should be informed to investigate further.

Training-Ultra sonographers

All professionals involved in the provision of ultrasound screening for Down's, Edwards' and Patau's syndromes should comply with the training requirements detailed in the FASP ultrasound practitioner's handbook':

NHS FASP recommends that any person undertaking a Fetal Anomaly ultrasound scan on pregnant women, for the purpose of screening and diagnosis of a related condition should hold, as a minimum, one of the following:

- Completion of NT and CRL online screening resources (CEM 21) annually
- Certificate/Diploma (as appropriate) in Medical Ultrasound (CMU/DMU) of the College of Radiographers (CoR) with evidence of appropriate continuous professional development (CPD)
- Post Graduate Certificate in Medical Ultrasound (PgCert) approved and validated by a Higher Institute of education and accredited by the Consortium for Sonographic Education (CASE) or equivalent. The qualification should be relevant to obstetric ultrasound practice

- Royal College of Obstetricians and Gynaecologists (RCOG) Royal College of Radiologists (RCR) Diploma in Obstetric Ultrasound or the Advanced Training Skills Module (ATSM)

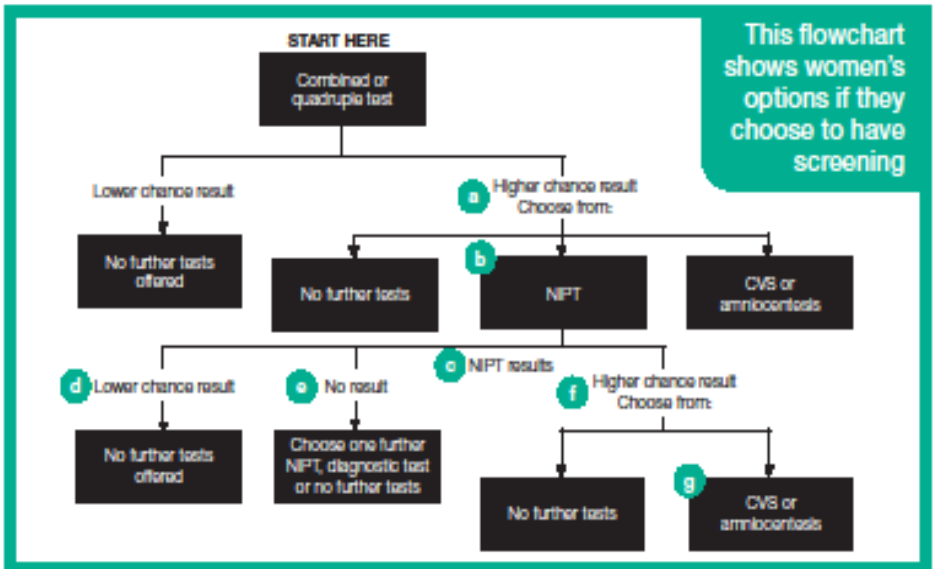
http://www.fetalanomaly.screening.nhs.uk/Combinedscreeningresources

The NSC Continuing Professional Development website for Antenatal and Newborn Screening

www.e-lfh.org.uk

Non-invasive prenatal testing (NIPT)

for Down's syndrome, Edwards' syndrome and Patau's syndrome



Whatever results women get from any of these screening or diagnostic tests, they should be offered care and support in the decision that is right for them.

As part of the NHS screening pathway for Down's syndrome, Edwards' syndrome and Patau's syndrome, NIPT:

- can be offered to women who have received a higher chance result from combined or quadruple screening
- can be offered to women with single and twin pregnancies
- might be less accurate in twin pregnancies
- can be offered until 21^{+6} weeks of pregnancy
- does not screen for other conditions or fetal sex
- is not suitable for everyone

Find out more in the e-learning module at
https://portal.e-lfh.org.uk/Component/Details/671159

As part of the NHS screening pathway, NIPT is not suitable for women:

with triplet or higher order pregnancies
who currently have cancer, unless in remission
who have received a blood transfusion in previous 4 months
who have had bone marrow or organ transplants
who have had stem cell therapy
having immunotherapy in the current pregnancy
with a vanished twin pregnancy (an empty second pregnancy sac or a second pregnancy sac containing a non-viable fetus)
with Down's syndrome, or a balanced translocation or mosaicism of Down's syndrome, Edwards' syndrome or Patau's syndrome

NIPT:
presents a potential delay of 2 weeks in the screening timeframe
gives a correct result for most women
can give false positive (higher-chance result when the baby does not have the condition) and false negative (lower-chance result when the baby does have the condition) results

Depending on her choice, a woman could get:
separate results for all 3 conditions
one result for Down's syndrome only
one result for Edwards' syndrome and one result for Patau's syndrome

Most women will receive their NIPT result within 2 weeks.
NIPT results will be reported as either higher or lower-chance.
Most women who have NIPT will get a lower-chance result.
Sometimes, NIPT will not produce a result.
NIPT does not give a definite diagnosis.
Prenatal diagnosis is required if the woman wants a definitive diagnosis following a higher-chance NIPT result.

Appendix 2: Contact Details

NAME	ROLE	CONTACT NUMBER
Emma Davis **~~Nicola Wilcox~~** **Karen Lloyd** **Sadie Stringer** **Cassie Taft**	**Antenatal and Newborn Screening Team, based at Worcester Royal Hospital**	**01905 768945** **wah-tr.antenatalscreeningresults@nhs.net**
FETAL MEDICINE UNIT-BIRMINGHAM	**TERTIARY REFFERAL UNIT**	**0121 6272683** **f.medicine@nhs.net**
CLINICAL CHEMISTRY LAB-BIRMINGHAM	**DOWN'S SCREENING LAB**	**0121 6272730** **bwh-tr.clinchem@nhs.net**

Appendix 3

Combined and Quad Test Sample Checklist

For attention of Tracy Stock or Charlotte Dixon (WRH)
For attention of Claire Todd, Lisa Richardson or Tina Waldron (ALEX)
Copies of this form must be emailed to wah-tr.AntenatalScreeningResults@nhs.net
wah-tr.dutyBMS@nhs.net

Date	Name	Hospital Number	Date of Birth	Where Sample was Taken	Received in Lab	Result letter Sent

The lab will email confirmation of receipt of all samples to screening team generic email account.

Checked by midwife 1 …… **Checked by midwife 2 ……**

Received in lab by / confirmation emailed by ……..

Signature……

Monitoring

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the Policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	Data Feeding into national audit	Audit collection Data	Continuously	Antenatal Screening Team	National Audit	Quarterly & Yearly

Contribution List

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This key document has been circulated to the following individuals for consultation;

Designation
All Staff in Maternity – via the Maternity Newsletter in March 23

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Maternity Governance Meeting