Trust Guideline for Antenatal Screening for Trisomy 21, Trisomy 18 and Trisomy 13

A Clinical Guideline

For use in:	Maternity Services
By:	Midwives, Obstetricians
For:	Women requesting antenatal screening for major trisomies - Down syndrome, Edwards syndrome and Patau syndrome
Division responsible for document:	Women / Children
Key words:	Down syndrome, Edwards syndrome, Patau syndrome, major trisomies, combined test, quadruple test
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Supported by:	The Maternity Guidelines Committee
Assessed and approved by the:	Maternity Guidelines Committee & NMCP Board
Date of approval:	19/10/2022
Ratified by or reported as approved to (if applicable)**:**	NMCP board
To be reviewed before: This document remains current after this date but will be under review	15/06/2024
To be reviewed by:	Richard Smith
Reference and / or Trust Docs ID No:	AO25 id 836
Version No:	8
Compliance links: *(is there any NICE related to guidance)*	NICE CG62
If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

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Version and Document Control:

Version Number	Date of Update	Change Description	Authors
7	15/06/2021	Confirmation of pathway for vanishing twin and pathway for raised AFP	Richard Smith and Alison Evans
8	19/10/2022	The guideline has been updated to reflect the new CT/QT request pathway (1. Combined Screening Test and Quadruple Screening Test Screening Request Pathway) attached. Furthermore, added a minor revision to the already approved Appendix 1 A025 - Antenatal Screening for Down, Edwards and Patau syndromes pathway (also attached) to ensure all related pathways are consistent.	Richard Smith Charlotte Aldous

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Quick reference guideline

This guideline is to be used when offering women antenatal screening for Down, Edwards and Patau syndromes

- All pregnant women to be offered screening for Down, Edwards and Patau syndromes.
- Women have different options for screening
    - Combined test – can choose to be screened for all 3 major trisomies, Down syndrome only or Edwards/Patau syndrome only.
    - Quadruple test – screens for Down syndrome only, cannot screen for Edwards or Patau syndrome as not enough research evidence linked to quadruple screening. Edwards and Patau syndrome screening in the 2nd trimester is the fetal anomaly scan at 18+0 – 20+6 weeks.
- The combined test can be performed when the baby's crown rump length (CRL) is between 45.0mm and 84.0mm. This is between 11^{+2} and 14^{+1} weeks. The nuchal translucency (NT) measurement is needed to calculate the chance result. The blood sample can be taken from 10 weeks.
- If the NT cannot be measured, or the CRL measurement is greater than 84.0mm, the woman is offered the quadruple test. If accepted, this test can be performed

when the baby's head circumference (HC) is between 101.0mm and 172.0mm. This is between 14^{+2} and 20^{+0} weeks. The blood sample can be taken from 14^{+2} weeks

- Women found to be higher chance for any of the syndromes to be offered the options of non-invasive prenatal testing (NIPT) and prenatal diagnosis Non-Invasive Prenatal Testing (NIPT) for Down, Edwards and Patau Syndromes Trustdocs ID 18818
- NICU alert system to identify babies at higher chance where prenatal diagnosis and NIPT are declined

Objective/s

The objective of the guideline is to ensure all women are offered Antenatal Screening for Down, Edwards and Patau syndrome and are able to give informed consent. Where a result is shown to be higher chance, appropriate information should be given to allow decision-making about prenatal diagnosis.

Rationale

The UK National Screening Committee (UKNSC) has stated that the 1st trimester Combined test is the preferred method of screening as it supports screening being completed in one stage without the need for more than one attendance. It will also give a risk before 14+2 weeks of pregnancy allowing earlier decision-making for parents. It meets the NSC outcome of a detection rate (DR) for Down syndrome of greater than 75% of affected pregnancies with a screen positive rate (SPR) of less than 3%(1). The recent revision of the NICE clinical guideline on "Antenatal care: routine care for the healthy pregnant woman" also advises that the 1st trimester Combined test is used (2).

Where it is not possible to offer the Combined test, the UKNSC recommend the Quadruple test is the preferred second trimester screening test for Down syndrome but Edwards and Patau syndrome should be screened for as part of the 18+0 – 20+6 weeks fetal anomaly scan. The Quadruple test can be performed between 14+2 and 20 +0 weeks (note the optimum time is after 15+0 weeks, so those booking an appointment specifically for the Quadruple test should be seen on or after 15+0.)

A cut-off of 1 in 150 is used for all syndromes on both tests to detect higher and low chance. (3)

Screening should only be performed after documented verbal consent (ie. completion of the serum screening request form, M43). If the woman declines the test, this should be recorded in the hand held notes and on E3 (the maternity IT system).

Broad recommendations

- To offer all eligible women screening for Down, Edwards and Patau syndrome.
- To offer women with higher chance results options for prenatal diagnosis in a timely manner.

To utilise the NICU alert system where prenatal diagnosis is declined in a higher chance result.

Management

Ideally women should have access to screening information prior to making a decision about a test. The NHSE "Screening tests for you and your baby" information is available to women via the link on the NNUH electronic self-referral form, this gives access to all screening information in different languages and formats to allow accessibility for all. Where it has not been possible for a woman to access this due to language or vulnerability issues, signposting to the link or a hard copy can be given at the time of the face-to-face booking appointment with the community midwife.

All antenatal screening tests should be discussed at the booking appointments with the midwife, including screening for Down, Edwards and Patau syndromes. If the patient provisionally opts for the Combined Test, this should be indicated on the antenatal booking workflow on the maternity IT system and on the maternal serum screening request on the ICE requesting system. The Combined Test/ Quadruple Test (CT/QT) ICE electronic request will explicitly specify the choice of trisomy screening the patient wishes to proceed with. Incorrect or missing data on the ICE request form may lead to delay or incorrect results. Although antenatal clinic staff will endeavour to assist patients attending appointment without a completed ICE request form or without a full understanding of the test, the responsibility of consenting the patient for trisomy screening ultimately lies with the health professional conducting the booking appointment. All CT request forms will be printed off ICE by the Antenatal Screening Team daily and taken to Antenatal Clinic ready for the patients planned ultrasound appointment.

Some women may decline trisomy screening. It is imperative to discuss the rationale for offering trisomy screening with the woman fully to ensure an informed decline is confirmed. This must be recorded on the E3 Booking workflow and the patient informed how to arrange trisomy screening if they wish to opt into this pathway. Patients must be fully apprised of the cut-off timeframes for trisomy screening (11+2-14+1 for Combined Screening and 14+2-20+0 for Quadruple testing) and it is good practice to document this conversation at the end of the E3 Booking workflow.

Action by reception staff

The dating (NT) scan appointment is made by the receptionist from information received within the automated referral sent following completion of the E3 booking workflow. It should be booked between 11+2 and 14+1 weeks of pregnancy inclusive (crown rump length 45 to 84 mm inclusive). This will require timely booking appointments (ideally by 8 weeks) to take place at least three weeks prior to optimum window for scanning. On arrival at the appointment, the antenatal clinic receptionist will check the woman wishes to proceed with trisomy screening and provide the patient with her CT ICE request form following confirming the patients identity. If the patient has changed her address the request form should be re-printed by the ANC Midwife to ensure results are posted to the correct address. All CT ICE requests will be kept securely in a specified folder, safely stored by the ANC receptionist.

If the woman is unsure whether she wishes to proceed with trisomy screening, even if there is a completed request form, an Antenatal Clinic midwife will be asked to counsel the woman to ensure informed consent.

Before the scan, the sonographer will confirm with the woman whether she wishes to opt for screening, including women who have declined at booking, in which case the nuchal translucency (NT) will be measured at the same time as the dating scan. Women who decline screening should be asked whether they wish to be informed of any obvious abnormality including an NT measurement of 3.5mm or more. (Those who decline will be offered a dating scan without NT measurement). The sonographer will check and complete the part of the request form relating to bleeding in pregnancy and attach an extra copy of the report to the request form for either combined or quadruple testing.

If the NT is ≥3.5mm, the patient should be referred to Fetal Medicine for review, but the Combined test should still be completed. Those who declined screening but where the NT is incidentally found to be ≥3.5mm should still be referred to Fetal Medicine because of the increased risk of other abnormalities.

<u>If the NT is not obtainable</u> but the gestation is correct, the patient will be offered a re-scan, including a transvaginal scan, later that day. If the NT is still not obtainable the patient will be advised they can have a quadruple test with the community midwife 14+2 – 20+0 and this will be documented on the scan report. The sonographer will leave a copy of the report for the Antentatal and newborn screening team who will ensure the community midwife is informed via Medicom re need for quadruple test.

<u>If the gestation is too early</u>, the patient should be re-booked for the appropriate gestation.

<u>If the gestation is too late</u> (ie. ≥14+2 weeks, head circumference must be > 101mm), then the Quadruple test can be offered between 14+2 and 20+0 weeks. For convenience, this can still be done on the same day as the scan, remembering that the optimum time for the Quadruple test is after 15 weeks.

Where a patient can only be offered the Quadruple test due to gestation or unobtainable NT, she should be informed that the test cannot screen for Edwards or Patau syndromes but that screening for these are part of the Fetal Anomaly Scan at 18+0 – 20+6 weeks gestation.

After 20+0, no screening is available, other than the fetal anomaly scan.

After scan:

The sonographer will inform the woman to wait in the waiting area and will place the request form in the Antenatal Clinic Phlebotomist's tray. The woman will be given her hand held notes following her scan unless she is attending a face to face Antenatal clinic appointment.

Phlebotomist

The phlebotomy staff will weigh the patient and take 5ml of clotted blood (yellow top bottle). Samples will be sent by the pod system and need to be spun down the same day.

If samples are sent after 5pm (by antenatal clinic staff), the pathology reception need to be notified on extension 5419. The phlebotomist is required to weigh and record weight on the ICE CT/QT form.

Please see Appendix 1 for the Combined Screening Test and Quadruple Screening Test Screening Request Pathway detailing each professionals responsibility in the requesting process for trisomy screening.

Results

The results will be issued by the biochemistry department. The Combined test will provide a result for Down syndrome and a joint result for Edwards and Patau syndromes. The Quadruple test will give a result for Down syndrome only. Low chance patients will be notified by letter directly from the laboratory. The letter will state that the patient should file the result (ie. the letter) in her hand-held notes. Higher chance results will be saved in a shared folder on the "S" drive and the Antenatal and Newborn Screening (ANS) team emailed via the generic **nnu-tr.ANS@nhs.net** address, to inform them there is a result to action. The ANS midwives will contact the patient directly and discuss options within 3 working days of the result being reported, in line with UK NSC standards.

Trisomy screening can sometimes identify significant coincidental findings such as low Pregnancy Associated Plasma Protein-A (PAPP-A) from a Combined test and raised Alpha-fetoprotein (AFP) from a quadruple test.

Low PAPP-A (< 0.415 MoM) is a risk factor for placental issues in a pregnancy. See Trust guideline for the assessment of fetal growth and referral and management of large for gestational age foetuses. No 8882v7 for full pathway. The screening team will contact the woman, discuss the result and arrange an initial growth scan around 28 weeks gestation.

A raised AFP can be an indicator of a neural tube or abdominal wall defect. If 2.5 MoM or above (5.0 MoM for twins), the screening team will contact the woman and offer an early detailed ultrasound scan in the Fetal Medicine Dept.

Multiple pregnancies

Combined screening is the recommended screening test for twin pregnancies. It is essential that women with a twin pregnancy are fully counselled re Down, Edwards and Patau syndrome screening prior to accepting the test, i.e. discuss issues of one twin only being higher chance , increased complication risks of prenatal diagnosis and options such as selective feticide.

These women should be seen in the Specialist twin Antenatal Clinic for discussion, this may require the woman being given a further appointment on another day. The NT will be measured for each twin and this, together with the blood sample will give a result. It is important to be sure of chorionicity as there will be either individual twin results for a dichorionic pregnancy or one result for a monochorionic pregnancy. If it is an IVF pregnancy, details of this, i.e. age of donor eggs/frozen embryos etc. must be on the request form.

If the NTs are unobtainable or the gestation too late for the Combined test, the Quadruple test can be offered in twin pregnancies but will only give one overall result of the pregnancy being affected – it cannot give individual twin results if dichorionic.

For higher multiple pregnancies, i.e. triplets etc. it is not possible to offer Combined or Quadruple tests. In these cases, the woman can only be offered a NT measurement for each fetus. The laboratory will then calculate a result for each fetus using NT and maternal age alone.

Due to the limitations of screening for multiple pregnancies, if a NT is unobtainable the patient should be recalled the same day to try to achieve a measurement and if still unobtained, must be offered another appointment on another day, where gestation allows.

Vanishing twin

Where there is a surviving fetus but evidence of initial multiple pregnancy, this can influence what screening should be offered.

Where there is an empty gestation sac noted, the Combined test can still be offered. Where there is evidence of a gestation sac containing a fetal pole with no fetal heart, then combined screening cannot be offered due to the analytes being influenced by the demised twin. Fetal anomaly screening programme recommendation is to offer these women a quadruple test but latest Down syndrome Quality Assurance Support Service (DQASS) detection rates show that the quadruple test performs less well than NT and age alone for vanishing twins (NT and age alone 80% detection rate, QT 77% detection rate - DQASS vanishing twin data Oct 2019) . Where an NT is obtainable, NT and age alone is the test of choice at NNUH, if an NT is unobtainable, the woman can be offered a quadruple test with her community midwife. The woman should be informed at the time of the scan, the findings of vanishing twin, and be advised of her trisomy screening options by someone qualified to discuss this scenario – i.e. sonographer, Screening midwife, senior doctor in Antenatal Clinic.

Screening Safety Incidents

Due to the nature and characteristics of screening tests, safety incidents within screening programmes require special attention and management. (Ref. no. 5) Where an incident occurs along any of the antenatal and newborn screening pathways the ANSC should be informed and the PHE document “Managing Safety Incidents in NHS Screening Programmes: updated Jan 2018” referred to.

Clinical audit standards

NSC KPI data FA1 – completion of serum screening request forms
DQASS 6 monthly audit of Laboratory and sonographer performance

Summary of development and consultation process undertaken before registration and dissemination

During the development of this guideline, advice has been sought from obstetricians with fetal medicine subspecialty, sonographers and the laboratory lead for screening for Down, Edward and Patau syndrome.

This version has been endorsed by the Clinical Guidelines Assessment Panel.

Distribution list / dissemination method

R Smith	Consultant Obstetrician, Fetal Medicine Specialist, Chair of Antenatal Screening Steering Group
G Sveronis	Consultant Obstetrician, Chair of Guidelines Committee
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A Chipchase	Consultant Biochemist , Lead for Down, Edwards and Patau syndrome screening

References / source documents

1. www.nice.org.uk/nicemedia/pdf/CG062NICEguideline.pdf. Accessed 24/04/09

2. Fetal Anomaly Screening Programme Standards 2015-16: UKNSC

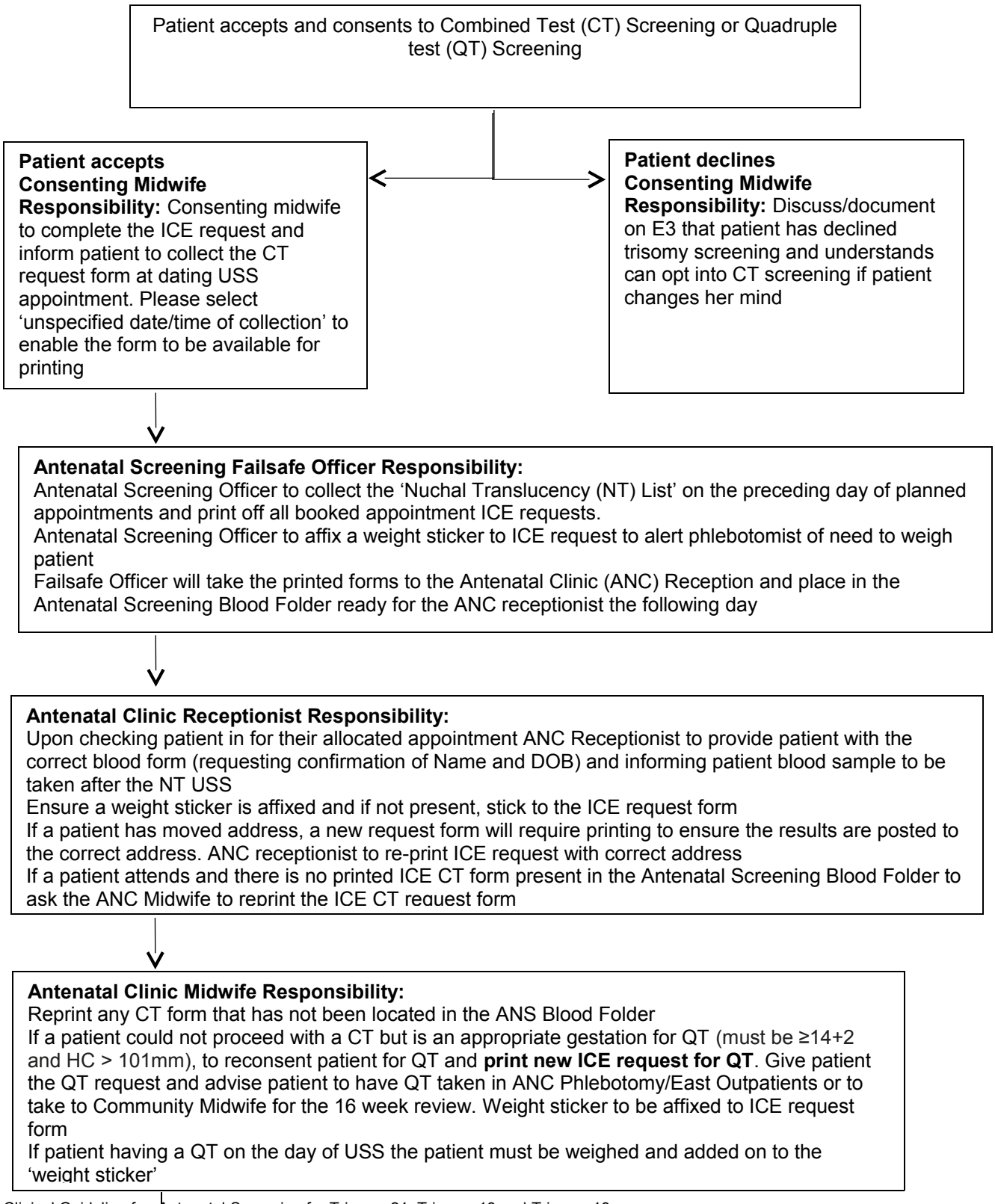
3. Fetal anomaly screening programme: Down's syndrome, Edwards' syndrome and Patau's syndrome screening Handbook for Laboratories. August 2018

4. PHE Managing Safety Incidents in NHS Screening Programmes: August 2017 (updated Jan 2018)

Non-Invasive Prenatal Testing (NIPT) for Down, Edwards and Patau Syndromes
Trustdocs Id 18818

Appendix 1 Combined Screening Test and Quadruple Screening Test Screening Request Pathway.

Combined Screening Test and Quadruple Screening Test Screening Request Pathway



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Ultrasonographer Responsibility:
Staple USS report to CT ICE request and request patient attends ANC Phlebotomy/East Phlebotomy today to complete CT Screening
If patient not eligible for CT and requires QT (regardless of gestation) to request ANC midwife to consent patient for QT and reprint QT form.
If gestation (≥14+2 and HC > 101mm) allows request patient attends ANC Phlebotomy/East Phlebotomy today to complete QT Screening
If the patient is too early for NT, sonographer to request patient to bring CT form to subsequent USS

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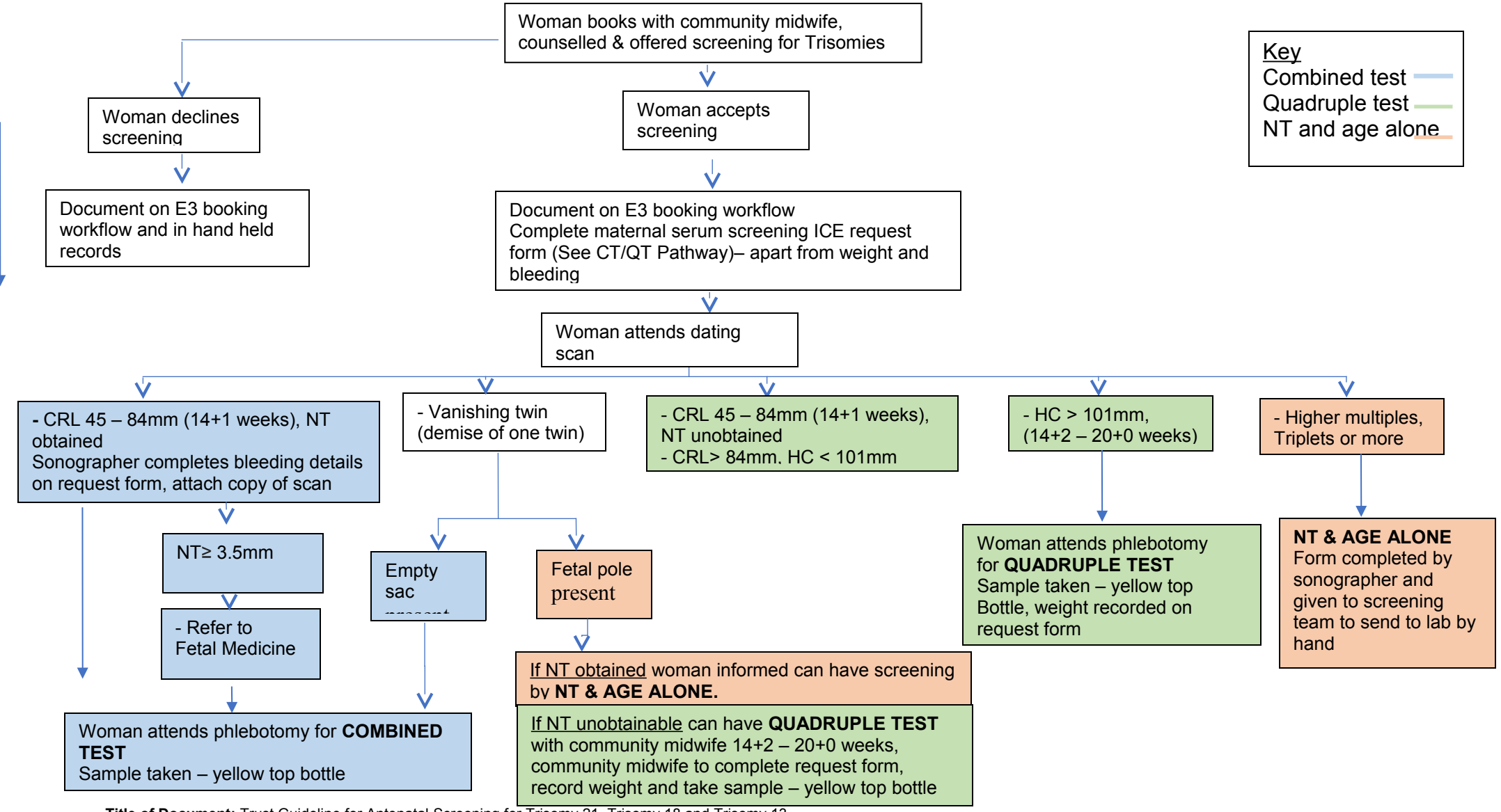
Phlebotomy Responsibility:
Weigh patient and document this on the affixed sticker
Yellow topped bottle to be used when extracting blood sample
Date/time/name on the ICE request and blood bottle
Send sample to the laboratory for screening

Appendix 2 – Antenatal screening for Down, Edwards and Patau syndromes pathway

Antenatal Screening for Down, Edwards and Patau syndromes



Low chance result
Woman should receive letter within 10-14 days – to contact ANC or Screening team if not received

Higher chance result (should be offered appt within 3 working days)
Woman contacted directly by Antenatal Screening team – counselled re result and offered appointment to discuss result or appointment arranged for prenatal diagnosis/ Non-Invasive Prenatal Test (NIPT)