NIPT for fetal trisomy 21 risk assessment is now available and is rapidly replacing other screening tests. In singleton pregnancy, it has a much higher detection rate and lower false-positive rate than the current best screening tests (i.e. combined nuchal translucency screening). In a 2014 meta-analysis, the weighted pooled detection rate for trisomy 21 in singleton pregnancies was 99% for a false-positive rate of 0.8%.[36] The corresponding values in twin pregnancies were 94.4% and 0%. However, the reported number of trisomy 21 cases in the twin pregnancies included was small (three studies; 18 cases). Since this meta-analysis, two more publications have reported promising detection rates.[37,38] The largest published study[38] comparing NIPT in twins versus singletons (515 twin pregnancies versus 1847 singletons) demonstrated that failed test rates (failure to get a result) were higher compared with singletons (5.6% versus 1.7%). The studies do not differentiate detection rates and failed test rates according to chorionicity. As in monochorionic twinning the fetuses share the same genetic material in the vast majority of cases (i.e. are genetically identical), the performance of NIPT should be similar to that in singletons. Clinicians should be aware of the latest guidance from the National Screening Committee.

Evidence level 1+

Please see section 11 for invasive diagnostic testing in twin pregnancy.

6.2 *What is the optimum method of screening for structural abnormalities in monochorionic twin pregnancies?*

All monochorionic twins should undergo a routine detailed ultrasound scan between 18 and 20^{+6} weeks of gestation which includes extended views of the fetal heart anatomy (as recommended in the Fetal Anomaly Screening Programme screening of a singleton fetus).

C

Structural abnormalities, particularly cardiac abnormalities, are more common in twin and higher order pregnancies than in singleton pregnancies. This is mainly because of the higher incidence of abnormalities in monozygotic twins (owing to the unusual nature of the cleavage of the conceptus) compared with dizygotic twins.[39] Monozygotic twins are monochorionic in 70% of cases; hence the higher rates of abnormality in monochorionic twins. Abnormalities specific to monozygotic twins are often midline (such as holoprosencephaly, neural tube defects and cardiac abnormalities).[39] As one cannot determine monozygosity using ultrasound, both monochorionic and dichorionic twins have the same recommended second trimester ultrasound screening regimen, which is in line with the NICE guideline.[1,6]

Evidence level 4

A Scandinavian study of twin pregnancies[26] where women had a package of scans (nuchal translucency scan, anomaly scan at 19 weeks of gestation, fetal echocardiography at 21 weeks of gestation and a cervical length scan at 23 weeks of gestation) found that 0.5% of the fetuses had cardiac anomalies, 80% of which were detected at the 19–20-week anomaly scan (i.e. before fetal echocardiography) and therefore, concluded that formal fetal echocardiography by a cardiologist is not justified.

Evidence level 2+

Limited published evidence suggests that detection rates of fetal anomalies on ultrasound scan for twin pregnancies are similar to published data for singletons.[26,40–42] Therefore, routine anomaly screening by a trained screening sonographer between 18 and 20^{+6} weeks of gestation is appropriate[1,43] and should include extended cardiac views as per the NHS Fetal Anomaly Screening Programme current screening protocols.[43]

Evidence level 4

The management of monochorionic pregnancies where one fetus has a congenital abnormality is complex because of shared circulations within the placenta. Timely diagnosis facilitates management by allowing time to prepare,

optimisation of fetal surveillance depending on the anomaly, involvement of multidisciplinary specialists (e.g. genetics team, paediatric cardiologist, paediatric surgeons) and appropriate birth planning (place, timing and mode), including access to intrauterine management where it is possible. Management of discordant abnormalities is addressed in section 11.

Selective termination of a single fetus in a monochorionic pregnancy should be assessed and carried out in a centre with expertise and experience in performing such prenatal procedures. In addition, increased prenatal surveillance, the potential for referral to a tertiary specialist centre and the adverse risks to the pregnancy must be discussed in a timely fashion.

6.3 What is the optimum ultrasound regimen for monochorionic twin pregnancies?

Fetal ultrasound assessment should take place every 2 weeks in uncomplicated monochorionic pregnancies from 16^{+0} weeks onwards until delivery (Appendix III). D

At every ultrasound examination, liquor volume in each of the amniotic sacs should be assessed and a deepest vertical pocket (DVP) depth measured and recorded, as well as the umbilical artery pulsatility index (UAPI). Fetal bladders should also be visualised. Although first presentation of TTTS is rare after 26^{+0} weeks of gestation, it can occur and therefore, scans should be performed at 2-weekly intervals in uncomplicated monochorionic twins until delivery (Appendix III). ✓

From 16^{+0} weeks of gestation, fetal biometry should be used to calculate an EFW and the difference in EFW calculated and documented. As the risk of sGR extends to delivery, this should be performed at 2-weekly intervals until delivery. D

There are a number of serious pathologies in monochorionic twin pregnancy that need to be screened for routinely. Ultrasound is required to make these diagnoses and therefore, serial ultrasound is required at regular intervals.

Ultrasound examinations between 16 and 26 weeks of gestation focus primarily on the detection of TTTS.[1] After 26 weeks, when first presentation of TTTS is relatively uncommon (but may occur), the main purpose is to detect sGR or concordant growth restriction, and more rarely TAPS or late-onset TTTS. The 2011 NICE guideline suggested that surveillance of uncomplicated monochorionic twins should occur at intervals of every 2 weeks from 16^{+0} weeks of gestation until delivery.[1] One of the prime reasons for performing serial ultrasound scans in monochorionic twins between 16 and 26 weeks is to detect TTTS. Thus, the development of discordance in liquor volumes within the amniotic sacs is pivotal to the process of detection and diagnosis.[44] After 26 weeks, TTTS may still occur and in addition, sGR may also be associated with discordant liquor volumes. For this reason, this guideline has been modified to include the recommendation that ultrasound surveillance is performed from 16 weeks until delivery at 2-weekly intervals. This is different from the NICE guidance published in 2011 (but undergoing revision). Evidence level 2+

There are no comparative studies of assessment techniques or regimens to assess fetal growth and wellbeing, and to detect late-onset TTTS (after 26 weeks). Few twin pregnancies were included in the randomised trials of umbilical artery Doppler velocimetry to detect FGR and these were not specifically monochorionic.[45]

Since 2011,[1] the international research community has evaluated the risk of other complications, especially sGR, and it is now recommended that, in addition to screening for TTTS, from 20 weeks of gestation, screening for sGR should be included.[19]

Evidence level 2–

This ultrasound screening should include, as a minimum, fetal biometry measurements (head, abdominal and femur measurements), measurement and recording of DVP depth of both sacs, and evaluation of fetal bladders (i.e. size and visibility). From 16^{+0} weeks of gestation, EFW should be calculated and documented (Appendix III). In addition, if at any point in time there is evidence of significant growth discordance or a suspicion of TTTS, then UAPI, middle cerebral artery peak systolic velocity (MCA PSV) and pulsatility index, and ductus venosus Dopplers should be performed. From 16 weeks of gestation, umbilical artery Doppler velocities should be evaluated, and the presentation of positive, absent or reversed velocities noted and documented. From 20 weeks of gestation, UAPI should be performed even in the absence of signs of TTTS or growth discordance (uncomplicated monochorionic twins) and plotted on standard charts. This may be best performed in a multiple pregnancy clinic.

The STORK population-based data set was analysed to evaluate fetal biometry in the second and third trimesters of 323 monochorionic twin pregnancies. It was found that ultrasound biometry showed 'a small but statistically significant reduction in fetal growth in twin pregnancies relative to that in singletons, particularly in the third trimester, with a more marked difference for MCDA than for dichorionic diamniotic (DCDA) pregnancies'.[46] For each variable, the mean value for DCDA twins was close to the reported value in singletons at 20–30 weeks of gestation and showed a decrease relative to singletons beyond 30 weeks. Fetuses in MCDA twin pregnancies displayed lower mean measurements than those in DCDA pregnancies throughout the gestational age range considered. In addition, this group found that algorithm formulas for calculation of EFW that include a combination of head, abdomen and femur measurements perform best in both singleton and twin pregnancies (Hadlock 2 formula).[47]

Evidence level 2+

6.4 *What are the optimum methods of screening for specific complications of monochorionic twin pregnancies?*

6.4.1 Screening for TTTS

Screening for TTTS by first trimester nuchal translucency measurements should not be offered. C

Women with monochorionic twin pregnancies should be asked to report sudden increases in abdominal size or breathlessness to healthcare professionals in their secondary or tertiary centres as this may be a manifestation of TTTS. ✓

Screening for TTTS should be by ultrasound examination from 16^{+0} weeks onwards, at 2-weekly intervals, noting and recording fetal biometry and liquor volumes (DVP). Fetal bladders should also be visualised. ✓

A large, prospective, Scandinavian, five-centre study that reported on 74 monochorionic pregnancies diagnosed before 15 weeks of gestation[26] did not find that measurement of nuchal translucency predicted the development of TTTS. Women with monochorionic pregnancies were scanned every 2 weeks between 12 and 23 weeks of gestation to detect TTTS. DNA testing was used to assess zygosity after delivery. TTTS was diagnosed in 23% of monochorionic pregnancies. Nuchal translucency measurements were not helpful in predicting TTTS.

Evidence level 2++

Unfortunately, common symptoms of twin pregnancy overlap with those associated with pathological conditions, such as TTTS. Many women with TTTS indicate that several weeks before presentation they note an increase in symptoms of breathlessness and abdominal distension. Pregnant women with monochorionic twins should have a low threshold for presenting to healthcare professionals with concerns. This should be discussed by healthcare professionals at their first booking visit.

The ultrasound diagnosis of TTTS is based on the following criteria (see Table 1):

- Significant amniotic fluid discordance. This is the key to the diagnosis: there must be oligohydramnios with DVP less than 2 cm in one sac (the donor) and polyhydramnios in the other sac (DVP more than 8 cm before 20 weeks of gestation and more than 10 cm after 20 weeks of gestation) (the recipient).[48–50]
- Discordant bladder appearances – with no urine in the 'donor' fetal bladder in severe TTTS (presenting before 26 weeks of gestation).
- Haemodynamic and cardiac compromise – both in the 'recipient' and/or 'donor' twins.

Evidence level 2–

In most centres, treatment for TTTS would not start until 16 weeks of gestation and therefore, first trimester screening was evaluated as having little benefit over initiating ultrasound scans at 16 weeks of gestation in apparently uncomplicated monochorionic twins.[1,6]

Evidence level 4

For ultrasound screening in the second trimester, several studies reported that inter-twin membrane folding (usually with less severe amniotic fluid discordance) predicted TTTS later in gestation.[19,44,48] Twins below 20 weeks of gestation with an amniotic fluid discordance (from DVP depth) of 3.1 cm or more had a risk of TTTS of 85.7%. Sensitivity for diagnosis of TTTS was 55%. An inter-twin EFW discordance of 25% or more had 63% sensitivity and 76% specificity for sGR without TTTS.[48] If there is liquor volume discordance in monochorionic twins that does not reach the 'threshold' for the diagnosis of TTTS, management should be individualised with a high degree of vigilance.

Evidence level 2–

No studies were identified in relation to using femur length, abdominal circumference, EFW, ultrasonography of placental anastomoses, tricuspid regurgitation or absent visualisation of a donor bladder to predict the development of TTTS.

6.4.2 Screening for TAPS

TAPS should be screened for following fetoscopic laser ablation for TTTS and in other complicated monochorionic pregnancies requiring referral to a fetal medicine centre (such as those complicated by sGR) by serial MCA PSV. ✓

TAPS is a form of TTTS characterised by a significant discordance in haemoglobin level between twins without significant amniotic fluid discordance.[16–18] This can be diagnosed by the presence of increased MCA PSV in the donor, suggestive of fetal anaemia (greater than 1.5 multiples of the normal median), and a decreased MCA PSV in the recipient twin, suggestive of polycythaemia (less than 1.0 multiples of the normal median), with the absence of significant oligohydramnios/polyhydramnios sequence.[18] TAPS may occur spontaneously in up to 2%[17,18] of monochorionic twins and in up to 13% following fetoscopic laser for TTTS.[15,51]

Evidence level 2–

The placentas in monochorionic pregnancies complicated by TAPS are characterised by the presence of only a few minuscule artery–vein vascular anastomoses. These small anastomoses allow a slow transfusion of blood from the donor to the recipient, leading progressively to a significant discordance in haemoglobin levels. The absence of severe amniotic fluid discordances in TAPS may be related to the very slow inter-twin blood transfusion, allowing more time for haemodynamic compensatory mechanisms to take place.[16–18]

Evidence level 3

Because TAPS mainly occurs in complicated cases and because there is little evidence to guide management (see section 7.3), screening of monochorionic twins for TAPS using serial MCA PSV measurements is not routine and should be confined to complicated monochorionic twin pregnancy where the risk of TAPS is high (those with TTTS or sGR). Further prospective research evaluating the role of undertaking MCA PSV screening in monochorionic twin pregnancies routinely to detect TAPS and to improve pregnancy outcome is required.

Postnatal diagnosis of TAPS is based on the presence of (chronic) anaemia in the donor (including reticulocytosis) and polycythaemia in the recipient. Postnatal haematological criteria include an inter-twin haemoglobin difference greater than 80 g/l and a reticulocyte count ratio greater than 1.7.[18,52]

Evidence level 3

6.4.3 Screening for sGR

At each scan from 20 weeks of gestation (at 2-weekly intervals) onwards, calculate EFW discordance using two or more biometric parameters. Calculate percentage EFW discordance using the following formula: ([larger twin EFW – smaller twin EFW]/larger twin EFW) x 100. Liquor volumes as DVP should be measured and recorded (to differentiate from TTTS).

C

An EFW discordance of greater than 20% is associated with an increase in perinatal risk. Such pregnancies should be referred for assessment and management in fetal medicine units with recognised relevant expertise.

B

Umbilical artery Doppler evaluation in monochorionic twins with sGR allows definition of prognosis and potential morbidity. In particular, those with absent or reversed end-diastolic velocities (AREDV) and 'cyclical' umbilical artery Doppler waveforms (intermittent AREDV [iAREDV]) are at increased risk of perinatal mortality and morbidity (Appendix IV).

C

Unequal placental sharing, and marginal or velamentous cord insertions are common in monochorionic twins and can result in discordant fetal growth, where one fetus is usually normal size and the other small for gestational age (defined as EFW less than the tenth centile). However, even if both fetuses have an EFW greater than the tenth centile there may be significant size discordance. This is termed sGR.[53–56]

Evidence level 2+

