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RCOG GREEN-TOP GUIDELINES

Management of Monochorionic Twin Pregnancy Green-Top Guideline No. 51 (2024 Partial Update)

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1 | Executive Summary

1.1 | Diagnosis of Monochorionic Twin Pregnancy

1.1.1 | How Is Monochorionicity Diagnosed Prenatally and What Is the Accuracy of Prenatal Ultrasound Chorionicity Allocation?

All women with a twin pregnancy should be offered an ultrasound examination between 11^{+2} and 14^{+1} weeks of gestation (crown–rump length 45–84 mm) to assess fetal viability, gestational age (i.e., dating of the pregnancy) and allocate chorionicity. It will also exclude major congenital malformations. [B]

Chorionicity should be determined at the time the twin pregnancy is detected/diagnosed by ultrasound. This is based upon the number of placental masses, the appearance of the intertwin membrane attachment to the placenta and the membrane thickness. This scan is best performed before 14 weeks of gestation. After this gestation, fetal sex determination may also help with the allocation of chorionicity. [D] ***Updated 2024***

An electronic ultrasound image record should be taken documenting the ultrasound appearance of the membrane attachment to the placenta and linked to the individualised patient records (Appendix 2). [GPP] ***Updated 2024***

If there is uncertainty about the diagnosis of chorionicity, a photographic record of the ultrasound appearance of the membrane attachment to the placenta should be retained and a second opinion should be sought. [GPP]

If there is still doubt in the diagnosis of chorionicity, the woman should be referred to a fetal medicine specialist without delay, as chorionicity is best determined before 14 weeks of gestation. [D]

On ultrasound, the fetuses in twin pregnancies should be assigned nomenclature (i.e., upper and lower, or left and right) and this should be clearly documented in the woman's case notes to ensure consistency throughout pregnancy. Fetus A should be with amniotic sac closest to the maternal cervix. [C]

1.2 | Outcome of Monochorionic Twin Pregnancy

1.2.1 | What Is the Outcome of Monochorionic Compared With Dichorionic Twin Pregnancies?

Clinicians and women should be aware that monochorionic twin pregnancies have higher fetal loss (miscarriage, stillbirth, and neonatal death) rates than dichorionic twin pregnancies, and overall may have a higher risk of associated neurodevelopmental morbidity. This should form part of the parental counselling. [GPP]

This is a partial update of the third edition of this guideline and should replace the previously published under the same title in September 2016 (second edition) and December 2008 (first edition).

1.3 | Optimal Screening for Chromosomal Abnormalities, Structural Abnormalities, and Other Fetal Complications in Monochorionic Twin Pregnancies

1.3.1 | What Is the Optimum Method of Screening for Chromosomal Anomalies in Monochorionic Twin Pregnancies?

Women with monochorionic twins who wish to have aneuploidy screening should be offered nuchal translucency measurements in conjunction with first-trimester serum markers (combined screening test) at 11^{+2}–$^{+1}$ weeks of gestation (crown–rump length 45–84 mm). [C]

In women with monochorionic twin pregnancies who 'miss' or who have unsuccessful first-trimester screening for aneuploidy, second-trimester screening by the quadruple test should be offered. [D]

Cell free fetal (cff) DNA testing (also known as NIPT), contingent on the results of the first-trimester combined test for major autosomal trisomies, in twin pregnancies, including monochorionic twins has been validated and is recommended by the UK National Screening Committee. [A] ***New 2024***

1.3.2 | 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^{+0} 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]

1.3.3 | 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 of gestation onwards until birth (Appendix 3). [D]

At every ultrasound examination (performed at 2 weekly intervals from 16^{+0} weeks of gestation until birth), liquor volume in each of the amniotic sacs should be assessed and the deepest vertical pocket (DVP) depth measured and recorded. In addition, the umbilical artery pulsatility index (UA-PI) should be measured at every scan from 16^{+0} weeks and middle cerebral artery peak systolic velocity (MCA PSV) should be measured at every scan from 20 weeks of gestation and recorded. Fetal bladders should also be visualised (Appendix 3). [GPP]

From 16^{+0} weeks of gestation, fetal biometry should be used to calculate an estimated fetal weight (EFW) and the difference in EFW calculated and documented. As the risk of selective growth restriction (sGR) extends to birth, this should be performed at 2-weekly intervals until birth. [D]

1.3.4 | What Are the Optimum Methods of Screening for Specific Complications of Monochorionic Twin Pregnancies?

1.3.4.1 | Screening for twin-to-twin transfusion syndrome (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 a subjective, sudden increases in abdominal size, reduced fetal movements and/or maternal breathlessness to healthcare professionals in their secondary or tertiary centres (as this may be a manifestation of TTTS). [GPP]

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

If there are concerns about differences between amniotic fluid levels (as denoted by a difference in DVP of each amniotic sac of 4 cm or more) in the second or third trimester, then an increase in the frequency of ultrasound diagnostic monitoring for feto-fetal transfusion syndrome to at least weekly should be instituted. [GPP] ***New 2024***

1.3.4.2 | Screening for Twin Anaemia polycythaemia Sequence (TAPS).

TAPS is a pathologic condition potentially associated with adverse outcomes requiring discussion with/and referral to a fetal medicine centre. This condition should be screened for using serial Doppler MCA PSV assessment, in all monochorionic twin pregnancies from 20^{+0} weeks of gestation at fortnightly intervals until birth. It is relatively rare in 'uncomplicated' monochorionic multiple pregnancies and is significantly more common following fetoscopic laser ablation for TTTS and in other complicated monochorionic pregnancies. [GPP]

1.3.4.3 | Screening for sGR.

At each scan from 16^{+0} 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) × 100. Liquor volumes as DVP should be measured and recorded (to differentiate from TTTS). [C]

An EFW discordance of greater than 20% (with the smaller fetus having an EFW or abdominal circumference (AC)

of less than 10th centile for gestational age) is associated with a small increase in perinatal risk. Such pregnancies should have weekly increased ultrasound surveillance (to at least weekly intervals) initiated. If the monochorionic twin pregnancy becomes complicated by sGR (EFW of one fetus less than 3rd centile OR 2 of the following 3 parameters—(i) EFW discordance of greater than 25%; (ii) EFW or AC of smaller fetus less than the 10th centile; (iii) UA Doppler of smaller fetus abnormal (umbilical cord pulsatility index [UA-PI] greater than the 95th centile or demonstrating absent or reversed end-diastolic flow [EDF]) then a referral should be made for assessment and management in fetal medicine units with recognised relevant expertise, to explore management options. [B]

Umbilical Artery Doppler velocimetry evaluation in monochorionic twins with sGR allows definition of prognosis and potential morbidity. 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 4). These MCDA twins are at increased risk of TAPS and serial MCA PSV measurement should be performed as discussed. [C]

1.4 | Management of Complex Pathologies Associated With a Monochorionic Twin Pregnancy

1.4.1 | The Management of TTTS

1.4.1.1 | How Useful Are Grading Systems for the Severity of TTTS in Establishing Prognosis?.

At ultrasound diagnosis, TTTS should be staged using the Quintero system. In addition, measurement of umbilical artery Doppler velocities, MCA PSV and Ductus Venosus Doppler studies should be performed and documented at each ultrasound scan. [D]

1.4.1.2 | What Is (Are) the Optimal Treatment(s) of TTTS and Their Outcomes?.

TTTS should be managed in conjunction with fetal medicine centres with recourse to specialist expertise and treatment in supraregional centres. [GPP]

TTTS presenting before 26^{+0} weeks of gestation should be treated by fetoscopic laser ablation rather than amnioreduction or septostomy. After 26^{+0} weeks of gestation care should be individualised. [A]

There is evidence that the fetoscopic laser ablative method should be by a serial, sequential technique followed by equatorial laser dichorionisation (the SOLOMON technique). [A] *New 2024*

Supraregional centres performing fetoscopic laser ablation should perform at least 15 procedures per year (rolling 3-year average). [GPP]

Weekly, detailed ultrasound assessment (including examination of the fetal brain, heart and limbs) and serial measurements of UA-PI, MCA PSV and Ductus Venosus Doppler velocities should be performed. After 2 weeks post-treatment, the ultrasound interval may be increased to every 2 weeks (noting UA-PI, MCA PSV, and DVP) with documentation of adequate fetal growth (by calculating EFW). [GPP]

In treated TTTS pregnancies, an ultrasound examination of the fetal heart should be performed by the fetal medicine specialist to exclude functional and acquired structural heart anomalies. [GPP]

1.4.1.3 | When Should the Birth of Monochorionic Twin Pregnancies Complicated by TTTS Take Place?

Birth of monochorionic twin pregnancies with treated TTTS should be at 36 completed weeks of gestation, unless there are complications noted. [D]

1.4.2 | The Management of sGR

sGR in monochorionic twins requires evaluation in a fetal medicine centre with expertise in the management of such pregnancies. [GPP]

In cases of early-onset sGR in association with poor fetal growth velocity and abnormal umbilical artery Doppler assessments, selective reduction, or fetoscopic laser ablation may be considered treatment options. These twin pregnancies require assessment in fetal medicine centres with appropriate expertise. [C]

In sGR, ultrasound surveillance of fetal growth should be undertaken at an interval of at least every 2 weeks with fetal Doppler assessment (by umbilical artery and middle cerebral artery pulsatility index, and peak systolic velocity from) weekly. Ultrasound surveillance and frequency should be individualised. If umbilical artery Doppler velocities are abnormal (type II or III), the Doppler assessments should be undertaken in line with national guidance, measuring Ductus Venosus Doppler waveforms. [D]

Clinicians should be aware that there is a longer 'latency period' between diagnosis and timing of birth in monochorionic twins complicated by sGR compared with growth restriction in dichorionic twin pregnancy or singleton pregnancy. [D]

Abnormal Ductus Venosus Doppler waveforms (reversed flow during atrial contraction) or computerised CTG short-term variation should be taken into consideration jointly, along with fetal biometric measurement and growth velocities when deciding upon timing of birth. [B]

In type I sGR, planned birth should be considered between 34^{+0}–35^{+6} weeks of gestation if there is satisfactory fetal growth velocity and normal umbilical artery Doppler waveforms. [GPP].

In type II and III sGR, birth should be planned by 32 weeks of gestation, unless fetal growth velocity is significantly abnormal or there is a worsening of the fetal Doppler assessment. [GPP]

It is important to prospectively inform parents that in sGR and TTTS (even after successful treatment) there can be acute and serious complications, including sudden transfusional events (which are neither predictable nor preventable), and therefore, despite regular monitoring, there may still be adverse perinatal outcomes. [GPP]

1.4.3 | Management of TAPS

Clinicians should be aware that the natural history, fetal and neonatal implications, and optimal treatment and/or surveillance of monochorionic pregnancies diagnosed with TAPS are poorly established. [D]

When TAPS is suspected or diagnosed the management should be agreed in discussion with woman, her partner and in conjunction with experts in a fetal medicine centre that has the expertise and experience in performing treatment, if appropriate. [D]

1.4.4 | The Management of Monochorionic Twin Pregnancies Complicated by Single Twin Demise

1.4.4.1 | What Are the Consequences for the Surviving Twin After Fetal Death of the Co-Twin in a Monochorionic Pregnancy and What Is Optimal Clinical Care?.

Clinicians should be aware that monochorionic pregnancies not complicated by TTTS, sGR or TAPS are still at risk of fetal death and neurological abnormality. [D]

After a single fetal death in a monochorionic pregnancy, clinicians should be aware that the risks to the surviving twin of death or neurological abnormality are of the order of up to 15% and 26%, respectively. [B]

After a single fetal death in a monochorionic pregnancy, the risk of co-twin demise, prematurity and neonatal death is significantly increased. The aim is to deliver the fetus by 36^{+6} weeks of gestation. Regular ultrasound surveillance of the surviving twin is mandatory and the timing and mode of birth should be individualised taking into account fetal size, growth velocity, the women's obstetric and medical history, and her preference. [B]

Single fetal death in a monochorionic pregnancy should be referred and assessed in a fetal medicine centre, with multidisciplinary expertise to manage these cases. [GPP].

Fetal magnetic resonance imaging of the brain may be performed up to 4 weeks after co-twin demise to aid in the detection of brain neurological morbidity. This information is of value in planning management. [D]

1.4.4.2 | How Should Fetal Anaemia Be Monitored After Single Twin Intrauterine Death?.

Fetal anaemia may be assessed by measurement of the fetal MCA PSV using Doppler ultrasonography. Parents should be informed that treatment may improve perinatal survival but may not alter the risk of the development of ischaemic brain injury. [D]

1.5 | Timing and Mode of Birth in Uncomplicated Monochorionic Pregnancies

1.5.1 | What Is the Optimal Timing and Mode of Birth for Otherwise Uncomplicated Monochorionic Pregnancies (Without TTTS, sGR or TAPS)?

Women with monochorionic, diamniotic twins should have timing of birth discussed and be offered planned birth from 36 completed weeks of pregnancy. [C]

If preterm birth of monochorionic twins is planned then if: (i) up to 34^{+6} weeks of gestation maternal steroids should be administered and (ii) if before 34^{+0} weeks of gestation maternal magnesium sulfate treatment should be given. [D]

It is appropriate to aim for vaginal birth of MCDA twins unless there are other specific clinical indications for caesarean section. [A]

A documented discussion with parents of the risks and benefits of planned vaginal versus caesarean birth for any monochorionic pregnancy should be undertaken. [D]

In the context of birth of monochorionic twins whether complicated or uncomplicated, the role of delayed umbilical cord clamping is controversial because of the theoretical risks of feto-fetal transfusion with 'intact' placental anastomoses. At present, there is not sufficient evidence to recommend for or against delayed cord clamping in monochorionic pregnancies. [D]

1.6 | Timing and Mode of Birth in Complicated Monochorionic Pregnancies, Including Those With 'Treated' TTTS

Timing for an optimal cut-off for planned preterm birth in laser operated TTTS appears not to have a strong evidence base. However, perinatal mortality after 32^{+0} weeks of gestation appears low (although perinatal morbidity may be unpredictable). In monochorionic twin pregnancies, post-fetoscopic laser ablation the twin pregnancy should be delivered by 36^{+6} weeks of gestation.

1.7 | MCMA Pregnancies

1.7.1 | What Are the Specific Problems of MCMA Pregnancies and How Should They Be Managed?

MCMA twins almost always have umbilical cord entanglement when visualised using colour flow Doppler. Such a finding has not consistently been demonstrated to contribute to overall morbidity and mortality. [D]

MCMA twin pregnancies have similar fetal mortality whether increased fetal surveillance is as an in-patient or as an outpatient. [C]

MCMA twins have a high risk of fetal demise and should be a planned caesarean birth between 32^{+0} and 34^{+0} weeks of gestation. [D]

1.8 | Higher Order Multiple Pregnancies With Reference to Monochorionicity

1.8.1 | What Is the Outcome of Monochorionic and Dichorionic Compared With Trichorionic Triplet Pregnancies?

Clinicians should be aware that monochorionic/dichorionic triplet pregnancies have higher fetal loss rates than trichorionic triplet pregnancies and may be complicated by TTTS, sGR and TAPS. [C]

Selective reduction should be discussed in all higher-order pregnancies including triplets. Parents should understand that in monochorionic or dichorionic triplet pregnancies procedures to induce selective reduction are complex and may be associated with fetal mortality and morbidity. [GPP]

Increased ultrasound surveillance is warranted in a fetal medicine centre with expertise to manage such cases. Such surveillance may be resource-intensive and complex. [GPP]

1.9 | Discordant Abnormalities in Monochorionic Pregnancies

1.9.1 | What Is the Incidence of and the Therapeutic Options for Discordant Abnormalities in Monochorionic Pregnancies, Including TRAP Sequence?

Monochorionic twins that are discordant for fetal anomaly must be referred promptly for assessment and counselling in a fetal medicine centre with consideration for treatment. [GPP]

Karyotyping of monochorionic twins should be cared for in a fetal medicine centre. [GPP]

Meticulous mapping of the position of the twins within the uterus should be performed both at the time of prenatal diagnostic tests and invasive treatments. [GPP]

During amniocentesis, both amniotic sacs should be sampled in monochorionic twin pregnancies, unless monochorionicity is confirmed before 14^{+0} weeks and the fetuses appear concordant for growth and anatomy. [GPP]

Prior to invasive testing or in the context of twins discordant for an abnormality, selective reduction should be discussed and made available to those requesting the procedure after appropriate counselling. [GPP]

Monitoring for disseminated intravascular coagulopathy is not indicated in monochorionic twin pregnancies undergoing selective reduction. [GPP]

Selective feticide by intravascular injection of an abortifacient is <u>not</u> an option in monochorionic pregnancies because of the presence of placental anastomoses. The potential risks of complex intrafetal/umbilical cord ablative procedures should be discussed prospectively, including the risk of co-twin loss and neurological morbidity. [GPP]

Documentation and discussion of heterokaryotypic monozygotic karyotypic abnormalities should take place prior to any invasive diagnostic testing. [GPP]

1.10 | Conjoined Twins

1.10.1 | How Are Conjoined Twins Diagnosed and What Are the Outcomes?

Conjoined twins are exceedingly rare and prenatal assessment is required in a tertiary fetal medicine centre so that diagnosis can be confirmed, and prognosis discussed in conjunction with a multidisciplinary team. [GPP]

1.11 | What Are the Training Competencies Required for Managing Monochorionic Pregnancies?

All ultrasonographers who undertake routine ultrasound scans during pregnancy must be trained to establish chorionicity and the correct labelling of twins. [GPP]

All ultrasonographers who undertake mid-trimester (18^{+0}–20^{+6} weeks of gestation) and fetal growth scans of monochorionic twins should be made aware of the appearances of TTTS, sGR and TAPS, and the need to refer women and pregnant people on to specialist centres if such features present. [GPP]

Fetal medicine centres undertaking fetal therapy for relatively rare complications of monochorionic twins should have a minimum of two experienced operators and more than 15 cases per year (rolling 3-year average) to maximise perinatal outcomes and minimise long-term morbidity. [D]

2 | Purpose and Scope

This guideline provides evidence-based recommendations and advice on best practices for the clinical care of monochorionic twin (and much rarer higher order) pregnancies. The use of ultrasound to determine chorionicity and amnionicity is key to the management of multiple pregnancies and the interpretation of potential risks to the fetuses. This guideline will outline the best evidence to guide clinical care, including fetal surveillance, the screening for, and treatment of complications associated with monochorionic multiple pregnancy. It is important to emphasise that this guideline is focused on the management of monochorionic multiple pregnancies rather than all multiple pregnancies.

It is also recognised that women carrying a monochorionic pregnancy (most commonly twins) may have concerns and anxieties surrounding their pregnancy. This requires accurate and evidence-based information given in a sensitive manner by healthcare professionals and supported by a multidisciplinary team, ideally within a multiple-pregnancy clinic [1, 2]. In the UK, support is also often given in conjunction with the Twins Trust (formally the Twins And Multiple Births Association [TAMBA]) and The Multiple Births Foundation.

The guideline has been updated by reviewing the whole document and adding additional referenced supporting evidence from the contemporary literature. The areas where there has been a change in management policy relate to:

- The use of cffDNA screening in monochorionic twins for major/common autosomal trisomies 21,18 and 13. The UK National Screening Committee indicates that cffDNA should be used in the 'contingent' test screening pathway in monochorionic twins. However, in the free text accompanying this recommendation, we acknowledge that in many parts of the world, cffDNA is used as a first-line screening test (as almost all monochorionic twins are monozygotic).
- The diagnostic classification of selective Growth restriction in monochorionic twins based upon new, published expert consensus data from a Delphi survey. This will help to focus increased surveillance and possible 'treatment' on monochorionic twins with a high probability of significant pathology. It is also recommended that all uncomplicated monochorionic twins/pregnancies have ultrasound scans at 2 weekly intervals beyond 26 weeks, to maximize prenatal detection of monochorionic twins with selective growth restriction.
- Additional recommendation that all uncomplicated monochorionic twins, as well as having an ultrasound scan to measure fetal biometry and umbilical artery Doppler velocimetry at 2 weekly intervals from 16 weeks throughout the pregnancy, in addition from 20 weeks gestation, middle cerebral artery Doppler velocimetry screening for twin anaemia polycythaemia sequence (TAPS) is added to each scan.
- A section discussing the timing of birth for complicated monochorionic twins as well as uncomplicated twin pregnancies.

3 | Introduction and Background Epidemiology

A monochorionic pregnancy is a multiple pregnancy, most commonly a twin pregnancy (99% of cases), in which babies are dependent on a single, shared placenta and where there are placental anastomoses conjoining the fetal circulations. Approximately 20% of twin pregnancies in the UK are monochorionic. Monochorionic placentation can also occur in rarer, higher-order multiples, especially triplets (i.e., dichorionic or monochorionic triplets).

There has been an increase in all types of multiple pregnancies with the use of assisted reproductive technology and the choice of individuals to defer pregnancy to a later maternal age (especially pronounced in high/middle-income countries). Although the rates of twining and higher order pregnancies are increased in people of Nigerian ethnicity, the rate of monochorioncity is not significantly increased in this group. Assisted reproductive technology increases the prevalence of both dichorionic and monochorionic twinning. However, using day 5 blastocyst transfers seems to be associated with a significantly higher rate of monozygotic twinning compared with cleavage stage day 3 transfers (adjusted OR 2.04, 95% CI 1.29–4.48) [3–5].

All multiple pregnancies have increased risks of preterm birth, fetal growth restriction (FGR), pre-eclampsia, postpartum haemorrhage, and additional postnatal potentially morbid complications, such as infant feeding difficulties and adverse puerperal mood change [1, 2, 6, 7]. These complications are not addressed further in this guideline as they are not specific to monochorionic placentation.

The challenges of monochorionic pregnancies arise from the single, shared placenta and placental vascular anastomoses that are almost universal and connect the fetal circulations of both twins, rather than monozygosity itself.

Specific complications associated with inter-twin vascular anastomoses are listed in Table 1. Please note that there may occasionally be some challenging diagnostic and clinical overlaps among the definition of these potentially pathologic conditions (e.g., twin-to-twin transfusion syndrome [TTTS] and selective growth restriction [sGR] with reduced liquor around the smaller twin—see section 6.4.3).

Single intrauterine death, although not exclusive to monochorionic twin pregnancy, is more common and has potentially significant morbid consequences for the co-twin, in the form of brain damage (if it survives).

In addition, the consequences of single fetal death and the management of discordant fetal anomalies (i.e., structural and chromosomal anomalies) in monochorionic twins and higher-order pregnancies are important (and are discussed in more detail later in this document).

Monochorionic diamniotic (MCDA) twin pregnancies carry a higher risk of overall fetal and perinatal loss compared with dichorionic pregnancies due to the conjoining of the fetal circulations within the single placenta. Monochorionic monoamniotic

TABLE 1 | Complications associated with inter-fetal placental vascular anastomoses.

Twin to twin Transfusion Syndrome (TTTS) (Quintero staging) Complicates up to 15%–20% of monochorionic twins (mostly monochorionic diamniotic twins).	I	A significant discordance in amniotic fluid volumes. This is defined as oligohydramnios with deepest vertical pocket (DVP) < 2 cm in donor sac and polyhydramnios in the recipient sac (DVP > 8 cm before 20^{+0} weeks of gestation and > 10 cm after 20^{+0} weeks of gestation). The Donor bladder is visible on ultrasound and the Umbilical Artery Doppler velocimetry is normal (in Quintero stages > 1, there is always polyhydramnios in the recipient fetal amniotic sac)
	II	The bladder is not visible on ultrasound and there is often severe oligohydramnios due to anuria, of the donor twin. Umbilical Artery Doppler studies are minimally abnormal
	III	Doppler studies are critically abnormal in either the donor or recipient fetus (or both), with typically abnormal (absent or reversed) umbilical arterial Doppler velocities and/or abnormal venous Doppler velocities in the recipient (reversed flow during atrial contraction within the Ductus Venosus and/or abnormal pulsatility of the Umbilical Vein velocities)
	IV	The presence of fetal effusions (ascites, pericardial or pleural effusions), with scalp oedema or overt hydrops fetalis present in either twin (but usually in the recipient)
	V	One or both babies have died (not amenable to therapy)
Twin Anaemia polycythaemia Sequence (TAPS) Up to 2% of uncomplicated monochorionic diamniotic (MCDA) and ~13% of monochorionic twins post-fetoscopic laser ablation		Signs of fetal anaemia in the donor and polycythaemia in the recipient **without** significant oligohydramnios/polyhydramnios (discordant amniotic fluid measurements) being present. The donor has increased middle cerebral artery peak systolic velocity (MCA PSV) and the recipient has decreased MCA PSV. The difference in MCA PSV is greater than 1.0 MoM
Selective Growth Restriction (sGR) (*Selective Growth Restriction [sGR] is where estimated fetal weight [EFW] of one is less than 3rd centile OR there are 2 of the following 3 parameters—(i) a growth discordance of greater than 25% difference in EFW between the fetuses (ii) the smaller fetus having an EFW or AC less than 10th centile for gestation); (iii) abnormal umbilical artery (UA) Doppler of the smaller fetus (UA-PI of greater than 95th centile or shows absent or reversed end-diastolic velocity). In up to 20% of monochorionic twins	I	*Growth discordance but positive diastolic velocities in both fetal umbilical arteries
	II	Growth discordance with absent or reversed end-diastolic velocities (AREDV) in one or both fetuses
	III	Growth discordance with "cyclical" umbilical artery diastolic waveforms (positive diastolic velocity in the umbilical artery Doppler velocimetry followed by absent, and then reversed end-diastolic velocimetry in a cyclical pattern over several cardiac cycles [intermittent AREDV; iAREDV])
Twin Reverse Arterial Perfusion (TRAP) Sequence Approximately 1% of monochorionic twins		An acardiac twin (with usually no cardiac tissue and often no fetal brain) is perfused by the anatomically 'normal' pump twin through a large artery–artery anastomosis on the monochorionic placental surface

(MCMA) pregnancies, where both twins are in a single amniotic *sac* (1% of monochorionic twins), are associated with an even higher risk of fetal/perinatal loss, most commonly before 24^{+0} weeks of gestation (due to discordant fetal anomalies or associated Twin Reverse Arterial Perfusion [TRAP] syndrome). These monochorionic twins though, carry a significant excess risk throughout a pregnancy (even compared to MCDA twins) [1, 2, 6, 8–11].

All monochorionic placentas contain vascular anastomoses running between the two fetal umbilical cords within and on the surface of the placenta. There are of three types: (i) arterial–arterial; (ii) arterial–venous; and (iii) venous–venous. In many cases, the anastomoses are bidirectional (which rarely lead to haemodynamic imbalance between the fetal circulations) but still conjoins the fetal circulations, a situation associated with excess, sudden fetal death (of one or both twins) [12–14].

In TTTS, which complicates between 15%–20% of monochorionic pregnancies [6, 11], the placenta has a predominance of unidirectional, arterial–venous anastomoses. This may predispose to, and cause, a haemodynamic imbalance within the fetal circulations, adversely affecting fetal cardiac function, fetoplacental perfusion and causing secondary, fetal endocrine dysfunction [15, 16].

Postnatal placental perfusion studies have noted unequal placental 'territories' shared by the fetuses with associated marginal or 'velamentous' cord insertions. Such findings are common both in TTTS and sGR (which is present in 60% of TTTS cases) complicated monochorionic twin pregnancies [13, 17–19].

Very rarely, TTTS complicates MCMA twin pregnancies, as well as dichorionic and monochorionic triplet pregnancies [17, 20].

Twin Anaemia Polycythaemia Sequence (TAPS) is an important and potentially morbid association in monochorionic pregnancies. Spontaneous TAPS is relatively uncommon (~2%) in apparently uncomplicated monochorionic pregnancies (most commonly MCDA twins). However, if it occurs it is associated with a high risk of perinatal morbidity and mortality with the donor fetus particularly at risk [21]. It may complicate TTTS, occurring in up to 13% of cases post-treatment by fetoscopic laser ablation (if the SOLOMON technique is not used) [22]. If TAPS is suspected, then discordance of liquor volumes (measured by ultrasound) in the fetal amniotic sacs must be excluded, as if present would indicate a recurrence of TTTS (most often due to treatment failure).

The pathogenesis of TAPS is evidenced through postnatal placental injection studies demonstrating 'minuscule' artery–vein anastomoses (less than 1 mm) allowing the relatively slow transfusion of blood from the donor to the recipient. This may be associated postnatally with highly discordant haemoglobin levels (80 g/L or greater) between fetuses, with a measured reticulocyte count ratio > 1.7 [22–25].

Significant intrauterine fetal size discordance in monochorionic twins (difference in estimated fetal weight [EFW] of greater than 20% and the smaller twin with EFW or abdominal circumference (AC) on ultrasound of < 10th centile for gestation) is associated with marginally increased perinatal risk but is an indication for increased antenatal surveillance, often with ultrasound scans and Doppler measurements more frequently than every 2 weeks [2].

When the selective fetal discordance is greater than 25%, it is termed 'selective growth restriction' (sGR)(see Table 1) [2], and complicates 20% of monochorionic twins, in the absence of TTTS. It is also present in up to 60% of monochorionic twins complicated by TTTS (with associated pathologic discordance in amniotic fluid volumes) [29]. sGR is recognised as a pathological entity associated with a significant rise in twin perinatal mortality, and a significantly differing inter-twin placental territory [18].

A Delphi consensus of expert opinion [26] has defined sGR in monochorionic twins and this is used in this document. It is defined as where the estimated EFW of one fetus is less than 3rd centile OR when two of the following three parameters exist: (i) a growth discordance of greater than 25% difference in EFW between the fetuses; (ii) the smaller fetus having an EFW or AC less than 10th centile for gestation; (iii) abnormal umbilical artery (UA) Doppler of the smaller fetus (UA-PI of greater than 95th centile or shows absent or reversed end-diastolic velocity).

The overall incidence of sGR is often greater than in dichorionic pregnancies. This is because it is often a co-pathology in TTTS [27]. The management of discordant growth and sGR requires experience and close fetal surveillance, by a fetal medicine centre. The ubiquitous placental anastomoses conjoining the fetal circulations make this condition associated with high risks of associated single or double miscarriage and stillbirth rates, if managed conservatively.

It is recognised that because of the aforementioned specific risks associated with monochorioncity, parents may have significant anxieties and concerns, even in uncomplicated pregnancies. Accurate information, presented sensitively, is important to allay unnecessary concerns while imparting to parents the importance of appropriate increased prenatal surveillance [1, 2, 9, 10].

4 | Identification and Assessment of Evidence

This guideline was developed in accordance with standard methodology for producing Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guidelines. The Cochrane Library (including the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects [DARE]), EMBASE, Trip, MEDLINE and PubMed (electronic databases) were searched for relevant randomised controlled trials, systematic reviews and meta-analyses. The search was restricted to articles published between 1966 and 2020. The databases were searched using the relevant Medical Subject Headings (MeSH) terms, including all subheadings, and were combined with a keyword search. Search words included 'monochorionic twin', 'TTTS', 'twin-twin transfusion syndrome', 'TRAP syndrome', 'amnioreduction', 'laser ablation', 'septostomy', and 'cord occlusion' and the search was limited to humans and the English language. The National Library for Health and the National Guideline Clearinghouse were also searched for relevant guidelines and reviews. The most important of these is the 2011 National Institute for Health and Care Excellence (NICE) clinical guideline 129 [1, 9], which was based upon an extensive review of the evidence for the antenatal management of twin and triplet pregnancies. This initial NICE guidance (published in 2011), focused on prenatal care. This was further updated and published in 2019 [2]. This provides additional recent, evidence-based clinical guidance on the management of complications in monochorionic twins and clinical guidance on the intrapartum management of both dichorionic and monochorionic twins.

In addition, qualitative information and lay representation have been provided by the Twins Trust (previously TAMBA) and the Multiple Births Foundation (who had representation on both versions of the NICE Guideline groups).

Where possible, recommendations are based on available evidence. In the absence of published evidence, these have been annotated as 'good practice points'. Further information about the assessment of evidence and the grading of recommendations may be found in Appendix 1.

5 | Diagnosis of Monochorionic Twin Pregnancy

5.1 | How Is Monochorionicity Diagnosed Prenatally and What Is the Accuracy of Prenatal Ultrasound Chorionicity Allocation?

All women with a twin pregnancy should be offered an ultrasound examination between 11^{+2} weeks and 14^{+1} weeks of gestation (crown–rump length 45–84 mm) to assess fetal viability, gestational age (i.e., dating of the pregnancy) and allocate chorionicity. It will also exclude major congenital malformations. [B]

Chorionicity should be determined at the time the twin pregnancy is detected/diagnosed by ultrasound. This is based upon the number of placental masses, the appearance of the intertwin membrane attachment to the placenta and the membrane thickness. This scan is best performed before 14^{+0} weeks of gestation. After this gestation, fetal sex determination may also help with the allocation of chorionicity. [D] ***Updated 2024***

An electronic ultrasound image record should be taken documenting the ultrasound appearance of the membrane attachment to the placenta and linked to the individualised patient records (Appendix 2). [GPP] ***Updated 2024***.

If there is uncertainty about the diagnosis of chorionicity, a photographic record of the ultrasound appearance of the membrane attachment to the placenta should be retained and a second opinion should be sought. [GPP]

If there is still doubt in the diagnosis of chorionicity, the woman should be referred to a fetal medicine specialist without delay, as chorionicity is best determined before 14^{+0} weeks of gestation. [D]

On ultrasound, the fetuses in twin pregnancies should be assigned nomenclature (i.e., upper and lower, or left and right) and this should be clearly documented in the woman's case notes to ensure consistency throughout pregnancy. Fetus A should be with amniotic sac closest to the maternal cervix. [C]

First trimester ultrasound scanning is important in multiple pregnancies as it confirms viability, determines gestational age, defines chorionicity (by denoting placental mass numbers and intertwin membrane thickness), determines the number of amniotic sacs and may identify major fetal anomalies (i.e., large cystic hygroma, anencephaly) [1, 2, 10, 28, 29]. In monochorionic twins, it is also important to exclude 'acardiac twinning', which is associated with a TRAP sequence. At this ultrasound examination, screening for fetal aneuploidy may also be offered to parents (see below). *[Evidence level 2++]*

In monochorionic twins and higher-order pregnancies, gestational age can be determined at the first-trimester scan by using the crown-rump length of the larger fetus to avoid the risk of estimating it from a baby with early growth pathology [1, 2, 27].

The accurate assessment of chorionicity is more sensitive and specific in the first trimester and it is important to assess and document chorionicity clearly at this gestational age. NICE guidance [1, 2, 9, 10] indicates that this should be performed at the time of the first-trimester scan to screen for fetal aneuploidy. There is a significant benefit in identifying women with monochorionic pregnancies early, as these pregnancies will require additional fetal surveillance. It also allows women to be fully counselled on the risks and appropriate management of monochorioncity to be implemented. Differentiating between monochorionic and dichorionic pregnancies will save time and emotional stress by avoiding unnecessary additional interventions in dichorionic pregnancies. *[Evidence level 4]*

Monochorionic twin pregnancies have a single placental mass and a thin inter-twin membrane that inserts into the placenta at a perpendicular plane (T-sign). In contrast, dichorionic twin pregnancies have two placental masses (or adjacent placental masses forming a 'lambda sign' as placental tissue is present where the thick inter-twin membrane inserts onto the placenta [Appendix 2]) [1, 2, 9, 10, 30]. *[Evidence level 2++]*

Clinicians should be aware that, although ultrasound assessment of chorionicity is very accurate, it is not 100% diagnostic. NICE Guideline NG137 *Twin and triplet pregnancy* identified 14 studies investigating diagnostic accuracy of the following characteristics (as determined by an ultrasound scan) for determining chorionicity: [1, 2, 9, 10]

- Number of placental sites and the characteristics of the inter-twin membrane placental insertion (so-called lambda/T-sign) in the first trimester. Approximately 3% of monochorionic placentas have two placental masses (bilobed placenta), so these are not necessarily dichorionic.
- Inter-twin membrane thickness using two-dimensional ultrasound: (i) with thickness usually subjectively defined, but in the literature, this is less than 1.8 mm for monochorionic twins; and (ii) 1.5–2.0 mm can be inconclusive for monochorionic twins, but when used with other factors, chorionicity can usually be defined in 99% of cases [30, 31].
- The number of membrane layers (subjectively noted) [32].
- Composite measures based on the above characteristics and others (number of placental masses, number of gestational sacs, concordant fetal sex [in monochorionic twins] and number of fetal poles) [1, 6, 9, 10]. *[Evidence level 1+]*

The strongest likelihood ratios were reported for a composite method involving the presence of a lambda or T-sign and noting the number of placental masses identified using ultrasound in the first trimester. Using such criteria, sensitivity and specificity was greater than 95% [30]. *[Evidence level 2+]*

This assessment should be followed up by noting concordant fetal sex at the second trimester ultrasound scans [6]. *[Evidence level 4]*

It is again necessary to review the assigned chorionicity of multiple pregnancies in the second trimester. An archived ultrasound electronic image record will allow this to be easily reviewed.

The sensitivity and specificity of ultrasound to define chorionicity is highest before 14^{+0} weeks of gestation [1, 30, 31]. If a trained sonographer, as part of routine first-trimester screening, cannot define with confidence the chorionicity of the pregnancy, then a second opinion must be sought from a senior sonographer or the woman should be offered referral to a healthcare professional (usually a fetal medicine specialist) who is competent in determining chorionicity by ultrasound scan as soon as possible [1, 2]. *[Evidence level 3]*

If it is difficult to determine chorionicity, even after referral (e.g., because the woman has booked late in pregnancy), then the pregnancy should be managed as monochorionic until proved otherwise [1, 2]. *[Evidence level 3]*

Accuracy in labelling monochorionic twins is important so that serial growth scan measurements can be consistently applied to the same twin throughout pregnancy, and that any intrauterine or neonatal management can be directed towards the correct twin [33]. It is also essential, prior to and during, prenatal invasive diagnostic testing in monochorionic (and dichorionic) twins. A retrospective study [32] found that ascribing labels based on lateral or vertical orientation was a reliable method of twin labelling. This study, based on 416 twin pregnancies, labelled the twin whose gestational sac was closest to the cervix at the 11–14-week scan as twin 1 and recorded the twins' orientation as lateral or vertical given their relative positions to each other (left/right or top/bottom, respectively). Approximately 90% of twins were oriented laterally and 10% vertically. The presenting order of 8.5% of the laterally oriented twins changed between the first and last scans; there were no such changes in the vertically oriented pregnancies. Based on a subset of mixed-sex twins ($n = 108$), the presenting order in a third-trimester scan was different from the subsequent birth order in 5.9% of pregnancies born vaginally and 20.3% of pregnancies by caesarean birth. *[Evidence level 2+]*

The authors concluded that recording the twins' relative position to each other was a reliable method of labelling twin pregnancies. The fetus whose amniotic sac is closest to the maternal cervix should be named fetus A and subsequent fetuses labelled with their uterine position [30, 33]. *[Evidence level 2+]*

6 | Outcome of Monochorionic Twin Pregnancy

6.1 | What Is the Outcome of Monochorionic Compared With Dichorionic Twin Pregnancies?

Clinicians and women should be aware that monochorionic twin pregnancies have higher fetal loss (miscarriage, stillbirth, and neonatal death) rates than dichorionic twin pregnancies, and overall may have a higher risk of associated neurodevelopmental morbidity. This should form part of the parental counselling. [GPP]

National data (from Denmark) based upon a prospectively collected population-based registry of twin pregnancies followed from the first trimester between 2008 and 2011 noted that, of 3621 twin pregnancies, 84.3% were dichorionic (DC) pregnancies and 15.7% monochorionic (MC) pregnancies (of which 15% were MCDA and 0.7% MCMA). Significantly more DC resulted in at least one live-born infant 98.2% versus 92.3% in MCDA ($p < 0.05$) and 66.7% in MCMA pregnancies ($p < 0.05$). The rates of spontaneous loss of both fetuses before week 22 were 0.9%, 2.4%, and 20.8% for DC, MCDA and MCMA twins, respectively ($p < 0.05$). The rate of intrauterine death of one fetus after week 22 was higher in MCDA twins than DC twins 1.7% versus 0.6% ($p < 0.05$) [34].

A retrospective study of 1407 twin pregnancies in the Netherlands over a 10-year period noted the perinatal mortality rate to be 11.6% in monochorionic twins compared with 5.0% in dichorionic twins. Monochorionic twins continued to be at greater risk (of mortality and morbidity) even after 32^{+0} weeks of gestation [35].

A retrospective study of all twin pregnancies of known chorionicity (from ultrasound assessment) with two live fetuses at 11–13 weeks' gestation from a large regional cohort of nine hospitals over a 17-year period in south London, indicated that in DC twins, the rate of loss at before 24^{+0} weeks' gestation in all fetuses was 2.3%; this rate was higher in MCDA twins (7.7%; relative risk (RR), 3.258; 95% CI 2.706–3.923) and increased further in MCMA twins (21.8%; RR, 9.289; 95% CI 6.377–13.530). In DC twins, the rate of perinatal death after 24 weeks in all twins (alive at 24 weeks) was 1.0%; this rate was higher in MCDA twins (2.5%; RR, 2.456; 95% CI 1.779–3.389) and more so in MCMA twins (9.3%; RR, 9.130; 95% CI 4.584–18.184). In DC twins, the rate of preterm birth before 37^{+0} weeks' gestation in pregnancies with at least one liveborn fetus was 48.6%; this rate was higher in MCDA twins (88.5%; RR, 1.824; 95% CI 1.760–1.890) and more so in MCMA twins (100%; RR, 2.060; 95% CI 2.000–2.121). In DC twins, the rate of preterm birth at before 32^{+0} weeks was 7.4%; this rate was higher in MCDA twins (14.2%; RR, 1.920; 95% CI 1.616–2.281) and more so in MCMA twins (26.8%; RR, 3.637; 95% CI 2.172–6.089). In DC twin pregnancies with at least one liveborn twin, the rate of a small-for-gestational-age neonate among all liveborn twins was 31.2% and in MCDA twins this rate was higher (37.8%; RR, 1.209; 95% CI 1.138–1.284); in MCMA twins, the rate was not significantly different (33.3%; RR, 1.067; 95% CI 0.783–1.455) [36–38]. These data concurs with other UK studies [27] and studies in different parts of the world [39]. *[Evidence level 2+]*

In addition, studies have documented that neurological morbidity may be up to seven-fold higher in preterm monochorionic infants compared with dichorionic infants due to associated complications of TTTS, sGR, TAPS, TRAP and single twin death in utero [40–44]. *[Evidence level 2+]*

7 | Optimal Screening for Chromosomal anomalies, Structural anomalies, and Other Fetal Complications in Monochorionic Twin Pregnancies

7.1 | What Is the Optimum Method of Screening for Chromosomal anomalies in Monochorionic Twin Pregnancies?

Women with monochorionic twins who wish to have aneuploidy screening should be offered nuchal translucency measurements in conjunction with first-trimester serum markers (combined screening test) at 11^{+2} weeks to 14^{+1} weeks of gestation (crown–rump length 45–84 mm). [C]

In women with monochorionic twin pregnancies who 'miss' or who have unsuccessful first-trimester screening for aneuploidy, second-trimester screening by the quadruple test should be offered. [D]

cff DNA testing (also known as NIPT), contingent on the results of the first-trimester combined test for major autosomal trisomies, in twin pregnancies, including monochorionic twins has been validated and is recommended by the UK National Screening Committee. [A] ***New 2024***

Monochorionic twins are not at increased risk of chromosomal anomalies over dichorionic twins, but the prevalence of aneuploidy is slightly increased overall in multiple pregnancies because of an indirect association with increased maternal age [1, 2]. *[Evidence level 3]*

First-trimester combined screening using nuchal translucency and the serum analytes of free beta-human chorionic gonadotrophin and pregnancy-associated plasma protein A (combined test screening) should be offered to pregnant women with monochorionic twins at a crown–rump length of between 45 and 84 mm [1, 45]. This screening test has good sensitivity for detecting aneuploidy (90%), but the false-positive rate (up to 10%) is higher than in singletons (2.5%) and dichorionic twins (5%) [1, 45, 46]. *[Evidence level 2+]*

When screening is performed by nuchal translucency, first-trimester serum screening and maternal age, a pregnancy-specific risk is calculated in monochorionic twins. This contrasts with dichorionic twins in whom a fetus-specific risk is calculated [1, 2, 45, 46]. *[Evidence level 2+]*

Approximately 10% of pregnant women do not have their first antenatal booking appointment in the first trimester. If the gestation at the first visit is after 14^{+0} weeks, then second-trimester serum screening should be offered using the quadruple screen test (with an 80% detection rate and a false-positive rate of 3%) to not disadvantage these women. This screening test in monochorionic twins provides a pregnancy-specific risk [1, 2, 47]. *[Evidence level 3]*

NIPT for fetal trisomy 21, 18 and 13 screening 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) [48–50]. In 2021, an updated cohort study at 10–14 weeks and meta-analysis was published in twin pregnancies. The weighted pooled detection rate (DR) for trisomy 21 in twin pregnancies was 99% for a false-positive rate (FPR) of 0.02% [51]. For trisomy 18 the detection rate was 92.8% and the false positive rate 0.01%. In the combined total of 11 cases of trisomy 13 and 6290 non-trisomy-13 pregnancies, the pooled weighted DR and FPR were 94.7% and 0.10%, respectively [49]. A subsequent publication by the Fetal Medicine Foundation, demonstrated the feasibility of introducing NIPT testing, contingent on the results of the first-trimester combined test for major trisomies, in a routine population of twin pregnancies [45]. This has subsequently been funded as routine contingent screening of twin pregnancies in England [50]. *[Evidence level 1+]*

In settings where NIPT is offered as the "first-choice" screening method in singleton pregnancies routinely or for high-risk cases (e.g., advanced maternal age or previous history of aneuploidy in pregnancy), it can also be offered in monochorionic twin pregnancy (Please see section 11 for invasive diagnostic testing in twin pregnancy).

7.2 | What Is the Optimum Method of Screening for Structural anomalies 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 anomalies, particularly cardiac anomalies, are more common in twin and higher order pregnancies than in singleton pregnancies [28]. This is mainly because of the higher incidence of anomalies in monozygotic twins (owing to the unusual nature of the cleavage of the conceptus) compared with dizygotic twins [52]. Monozygotic twins are monochorionic in 70% of cases; hence the higher rates of anomaly in monochorionic twins. Anomalies specific to monozygotic twins are often midline (such as holoprosencephaly, neural tube defects and cardiac abnormalities) [52]. 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, 2, 10]. *[Evidence level 4]*

In a Scandinavian study of twin pregnancies [53] where women had a "package of scans" (comprising a first-trimester, nuchal translucency scan, an anomaly scan at 19^{+0} weeks of gestation, fetal echocardiography at 21^{+0} weeks of gestation and a cervical length scan at 23^{+0} weeks of gestation) it was noted 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). The study concluded that formal fetal echocardiography by a cardiologist was not justified.

From the UK, a retrospective analysis of prospectively collected data of 6366 twin pregnancies with two live fetuses at 11–13 weeks gestation at the Fetal Medicine Foundation, included 4979 (78.2%) DC and 1387 (21.8%) MC twin pregnancies. The main findings were: (i) the overall incidence of fetal anomalies was higher in MC than in DC twins (2.8% versus 1.3%); (ii) the proportion of anomalies diagnosed in the first trimester was higher in MC than in DC twins (52.6% versus 27.1%); (iii) the pattern of anomalies in relation to detectability at the 11–13-week scan (always detectable, sometimes detectable and never detectable) was similar to that reported previously in singleton pregnancies; (iv) always-detectable anomalies included acrania, alobar holoprosencephaly, encephalocele, pentalogy of Cantrell, exomphalos, body-stalk anomaly, twin reversed arterial perfusion sequence and conjoined twins; (v) the incidence of fetal NT ≥ 95th percentile was higher in those with an anomaly than in those without (16.5% versus 4.5% in DC twins and 19.2% versus 5.9% in MC twins) and this was also true for NT ≥ 99th percentile (8.3% versus 1.0% in DC twins and 15.4% versus 2.0% in MC

twins); and finally (vi) the incidence of CRL discordance ≥ 10% was higher in those with than in those without an anomaly (20.2% versus 7.9% in DC twins and 33.8% versus 9.3% in MC twins) and this was also true for CRL discordance ≥ 15% (10.1% versus 1.9% in DC twins and 28.2% versus 2.8% in MC twins) [14, 28, 38]. *[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 [53–57]. A systematic review of first-trimester ultrasound in the detection of congenital anomalies in twin pregnancies indicates a specificity of less than 30% [58]. Therefore, routine anomaly screening by a trained screening sonographer between 18^{+0} and 20^{+6} weeks of gestation is appropriate (even though a first-trimester ultrasound scan may have been performed) [1, 2, 57] and should include extended cardiac views as per the NHS Fetal Anomaly Screening Programme's current screening protocols [57]. *[Evidence level 4]*

The management of monochorionic pregnancies where one fetus has a congenital anomaly is complex. 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 procedures. Because of placental anastomoses "conjoining" the fetal circulations highly specialised procedures using vascular ablative techniques are required to minimise fetal loss or morbidity in the surviving co-twin. 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.

7.3 | 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 birth (Appendix 3). [D]

At every ultrasound examination (performed at 2 weekly intervals from 16 weeks until birth), liquor volume in each of the amniotic sacs should be assessed and the deepest vertical pocket (DVP) depth measured and recorded. In addition, the umbilical artery pulsatility index (UA-PI) should be measured at every scan from 16^{+0} weeks and middle cerebral artery peak systolic velocity (MCA PSV) should be measured at every scan from 20^{+0} weeks and recorded. Fetal bladders should also be visualised (Appendix 3). [GPP]

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

Several serious pathologies in monochorionic twin pregnancy 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^{+0} and 26^{+0} weeks of gestation, at 2 weekly intervals, focus primarily on detecting TTTS [1, 2]. After 26^{+0} weeks, when the presentation of TTTS is more uncommon, the main purpose of the ultrasound surveillance is to detect sGR or concordant growth restriction. Twin Anaemia Polycythaemia sequence may occur spontaneously and should be screened for by performing MCA PSV measurements from 20^{+0} weeks gestation at each ultrasound scan. One of the prime reasons for performing serial ultrasound scans at two weekly intervals in monochorionic twins between 16^{+0} and 26^{+0} weeks is to detect TTTS. Thus, the development of discordance in liquor volumes within the amniotic sacs is pivotal to the detection and diagnosis of this pathologic process (see Table 1) [59]. However, after 26^{+0} weeks, TTTS may still occur and in addition, sGR is more prevalent and may also be associated with discordant liquor volumes (with oligohydramnios in the smaller fetal amniotic sac) (Table 1). For this reason, the 2016 Green-top Guideline (and the updated 2019 NICE guideline) was modified to include the recommendation that ultrasound surveillance is performed from 16^{+0} weeks until birth at 2-weekly intervals. *[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^{+0} weeks). Few twin pregnancies were included in the randomised trials of umbilical artery Doppler velocimetry to detect FGR and these were not specifically monochorionic [60, 61]. *[Evidence level 2–]*

Ultrasound screening from 16^{+0} weeks gestation, should include, as a minimum, documentation of fetal biometry measurements (head, abdominal, and femur measurements), measurement and recording of DVP depth of both amniotic sacs, and evaluation of fetal bladders (i.e., size and visibility). From 16^{+0} weeks of gestation, EFW should be calculated and documented (Appendix 3).

In all monochorionic twins (even if apparently uncomplicated), 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 16 weeks of gestation, umbilical artery Doppler velocimetry PI should be recorded and plotted on standard charts. In addition (and new to this updated document), serial MCA PSV should also be performed from 20 weeks of gestation, as a screening test for TAPS (as discussed below). This should be performed in conjunction with a multiple-pregnancy clinic.

If at any point in time, there is evidence of significant growth discordance or suspicion of TTTS then, in addition to umbilical artery and middle cerebral artery Doppler velocimetry, Ductus Venosus Doppler velocimetry should be performed.

The STORK population-based data set analysed and evaluated fetal biometry in the second and third trimesters of 323 monochorionic

twin pregnancies. These data noted 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." [62] 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 the calculation of EFW that include a combination of head, abdomen and femur measurements perform best in both singleton and twin pregnancies (Hadlock 2 formula) [63]. *[Evidence level 2+]*

7.4 | What Are the Optimum Methods of Screening for Specific Complications of Monochorionic Twin Pregnancies?

7.4.1 | 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 a subjective, sudden increases in abdominal size, reduced fetal movements and/or maternal breathlessness to healthcare professionals in their secondary or tertiary centres (as this may be a manifestation of TTTS). [GPP]

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 and their presence documented. [GPP]

If there are concerns about differences between amniotic fluid levels (as denoted by a difference in DVP of each amniotic sac of 4 cm or more) in the second or third trimester, then an increase in the frequency of ultrasound diagnostic monitoring for feto-fetal transfusion syndrome to at least weekly should be instituted. [GPP] ***New 2024***

It is not currently possible to prospectively predict adverse outcomes in monochorionic twin pregnancies using first-trimester pregnancy-related factors with high accuracy (ultrasound measurements, maternal characteristics, biomarkers) [64]. A large retrospective series of prospectively collected twin pregnancies with two living fetuses in the first trimester noted that in MCDA twin pregnancies with no major fetal anomalies, measurement of NT at the 11–13-week scan is a poor screening test for adverse pregnancy outcome. Discordance of fetal crown-rump lengths of more than 20% in monochorionic twins was associated with a trend towards adverse pregnancy outcome and a high rate of treatment by endoscopic laser surgery of the placenta [11, 38, 64, 65].

A large, prospective, Scandinavian, five-centre study that reported on 74 monochorionic pregnancies diagnosed before 15 weeks of gestation [53] 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 birth. TTTS was diagnosed in 23% of monochorionic pregnancies. Nuchal translucency measurements were not helpful in predicting the risk of the onset of 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, reduced fetal movements and abdominal distension. Pregnant women with twin pregnancies must be encouraged to seek clinical advice if concerned. This should be discussed by healthcare professionals with parents at their first booking visit and should be taken seriously by the obstetric and midwifery teams, especially when assessing a monochorionic twin pregnancy with an emergency presentation [66].

The ultrasound diagnosis of TTTS is based on the following criteria. Simply put, it is defined by the presence of polyhydramnios in one monochorionic amniotic sac and oligohydramnios in the other fetal sac (the majority of twins complicated by TTTS being MCDA). It may be formally staged (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^{+0} weeks of gestation and more than 10 cm after 20^{+0} weeks of gestation) (the recipient) [67–69]. NICE Guidance 2019 indicated that an increased frequency of diagnostic monitoring for feto-fetal transfusion syndrome in the women's second or third trimester should be instituted at least weekly intervals if there are any concerns relating to differences between the baby's amniotic fluid levels (with a difference in DVP measurement of 4 cm or more) [2].
- Discordant bladder appearances—with no urine in the 'donor' fetal bladder in severe TTTS.
- Haemodynamic and cardiac compromise (as measured by abnormalities of umbilical artery (absent or reversed end-diastolic velocimetry), Ductus Venosus (DV) Doppler velocimetry (reversed velocimetry in the DV during atrial contraction) and or tricuspid regurgitation) – both in the 'recipient' and/or 'donor' twins. *[Evidence level 2–]*

In most centres, treatment for TTTS would not start until 16^{+0} weeks of gestation of gestation and therefore, first-trimester screening has been noted as having little benefit over initiating ultrasound scans at 16 weeks of gestation in apparently uncomplicated monochorionic twins [1, 2, 10]. *[Evidence level 4]*

A retrospective study of 675 MCDA twin pregnancies followed with a fortnightly ultrasound scan protocol from 16^{+0} weeks of gestation onward noted that this surveillance detected nine out of 10 (90%) TTTS pregnancies [70]. 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 [29, 39, 59, 69]. Twins below 20^{+0} 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%. The 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 [69]. If there is liquor volume discordance in monochorionic twins that does not reach the 'threshold' for the diagnosis of TTTS, care should be individualised with a high degree of vigilance and ultrasound surveillance of, at least, weekly intervals. *[Evidence level 2–]*

7.4.2 | Screening for TAPS

TAPS is a pathologic condition potentially associated with adverse outcomes requiring discussion with/and referral to a fetal medicine centre. This condition should be screened for using serial Doppler MCA PSV assessment, in all monochorionic twin pregnancies from 20^{+0} weeks of gestation at fortnightly intervals until birth. It is relatively rare in 'uncomplicated' monochorionic multiple pregnancies and is significantly more common following fetoscopic laser ablation for TTTS and in other complicated monochorionic pregnancies. [GPP]

TAPS is characterised by a significant discordance in haemoglobin level between twins without significant amniotic fluid discordance [23, 24, 71]. Prenatally, this can be diagnosed by the presence of increased MCA PSV in the donor fetus, suggestive of fetal anaemia (greater than 1.5 multiples of the normal median), and a relative decreased in MCA PSV of the recipient fetus, suggestive of polycythaemia, in the absence of significant oligohydramnios/polyhydramnios sequence [25]. TAPS may occur spontaneously in up to 2% [21, 24, 25] of monochorionic twins and in up to 13% following fetoscopic laser for TTTS, especially if the SOLOMON technique of vascular ablation is not used [22, 71]. A recent consensus document, analysing data from 132 international experts and using Delphi methodology, agreed the antenatal diagnosis of TAPS, as the combination of MCA PSV $\geq$ 1.5 MoM in the anaemic twin and $\leq$ 0.8 MoM in the polycythaemia twin. A high sensitivity and specificity was obtained when MCA PSV discordance $\geq$ 1 MoM was used to diagnose TAPS [72]. *[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 micro-anastomoses allow a slow blood transfusion from the donor to the recipient, progressively leading 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 [21, 23–25]. *[Evidence level 3]*

TAPS occurs more frequently in complicated monochorionic cases (i.e., those with selective growth restriction or treated TTTS), but also spontaneously in previously uncomplicated MCDA pregnancies. It is acknowledged that there is currently no robust evidence base to guide the optimal and superior treatment of TAPS but detailed evaluation and expert advice about how to monitor the pregnancy and timing of birth is required, as this complication is potentially serious and morbid.

Such screening will allow individualised twin pregnancy care, discussion, and joint decision-making between the parents and the fetal medicine experts. Care options may include: (i) conservative management with close observation and surveillance, (ii) in utero transfusion [of the anaemic twin] with or without exchange transfusion [of the polycythaemic fetus], (iii) treatment by fetoscopic laser ablation, and (iv) in some circumstances a discussion of selective termination of pregnancy [73].

Therefore, it is recommended that such cases should be referred to, or at least there should be a consultation with, the regional maternal–fetal medicine program or fetal therapy centre. In many cases, the chosen management type is dependent upon the gestational age at diagnosis of TAPS, the severity, monochorionic twin characteristics (i.e., placental site) and parental wishes.

Postnatal diagnosis of TAPS is based on the presence of (usually chronic) anaemia in the donor and polycythaemia in the recipient. Postnatal haematological diagnostic criteria include an inter-twin haemoglobin difference of greater than 80 g/L with an associated reticulocyte count ratio greater than 1.7 [24, 25, 73]. *[Evidence level 3]*

7.4.3 | Screening for sGR

At each scan from 16^{+0} 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) × 100. Liquor volumes as DVP should be measured and recorded (to differentiate from TTTS). [C]

An EFW discordance of greater than 20% (with the smaller fetus having an EFW or AC of less than 10^{th} centile for gestational age) is associated with a small increase in perinatal risk. Such pregnancies should have weekly increased ultrasound surveillance (to at least weekly intervals) initiated. If the monochorionic twin pregnancy becomes complicated by sGR (EFW of one fetus less than 3rd centile OR two of the following three parameters—(i) EFW discordance of greater than 25%; (ii) EFW or AC of smaller fetus less than the 10th centile; (iii) UA Doppler of smaller fetus abnormal (UA-PI greater than the 95th centile or demonstrating absent or reversed EDF) then a referral should be made for assessment and management in fetal medicine units with recognised relevant expertise, to explore care options. [B]

Umbilical Artery Doppler velocimetry evaluation in monochorionic twins with sGR allows definition of prognosis and potential morbidity. 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 4). These MCDA twins are at increased risk of TAPS and serial MCA PSV measurement should be performed as discussed. [C]

Unequal feto-placental 'territory' 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. However, even if both fetuses have an EFW greater than the tenth centile there may be significant size discordance. This is termed sGR [74–80].*[Evidence level 2+]*

sGR is encountered in approximately 20% of all monochorionic multiple pregnancies. It is defined as one fetus with EFW less than the 3rd centile or where there are two of the three following parameters—(i) an EFW discordance of greater than 25%; with (ii) the smaller fetus having an EFW or AC of less than 10th centile for gestation; (iii) abnormal UA Doppler of the smaller fetus (UA-PI of greater than 95th centile or shows absent or reversed EDF) [26]. This condition's pathophysiology and natural history are different from growth discordance in dichorionic multiple pregnancies. The prospective diagnosis initially may be difficult as there may be a diagnostic 'overlap' between mild TTTS and sGR. Amniotic liquor (DVP) in TTTS may differ between the fetuses because of polyhydramnios in one of the amniotic sacs and oligohydramnios in the other amniotic sac (but sGR may also be present). However, in isolated sGR, this will differ as there is commonly oligohydramnios in one of the amniotic sacs and normal liquor in the other amniotic sac [2, 74–80]. *[Evidence level 3]*

Poor in utero growth of both twins may reflect multifactorial causes, such as maternal factors resulting in global uteroplacental dysfunction. Whereas discordant twin growth may be attributed to differences in genetic potential between co-twins, placental dysfunction confined to one placenta only or one placental territory within a shared placenta [74, 79]. In addition, TTTS represents a distinct entity of which discordant growth is a common feature [74, 75, 79]. *[Evidence level 2+]*

Discordant growth is recognised as an independent risk factor for adverse perinatal outcomes in monochorionic twins [74–80]. Clinical evolution depends on the combination of the effects of placental insufficiency in the growth-restricted twin with intertwin blood transfer through placental anastomoses [74, 79].

A calculated difference in EFW is a sensitive method of defining sGR, and appears to be linked with adverse outcomes when this is significantly different and associated with the smaller fetus having an EFW below the 10th centile for gestation (see below). The ultrasonic methods used to estimate fetal weight appear to be equally accurate [37, 63, 76], but one study favoured formulas that include a combination of head, abdomen, and femur measurements [76]. *[Evidence level 2+]*

A prospective study from Ireland noted that perinatal mortality, individual morbidity, and composite perinatal morbidity are all seen to increase with birthweight discordance exceeding 18% for monochorionic twins without TTTS (hazard ratio 2.6, 95% CI 1.6–4.3; $p < 0.001$); a minimum two-fold increase in risk of perinatal morbidity exists even when both twin birthweights are appropriate for gestational age [77]. However, others have studied monochorionic and dichorionic twins and noted that prenatal risk does not increase until the difference in EFW is greater than 25% [1, 2, 37]. *[Evidence level 2+]*

Umbilical artery Doppler velocity waveforms in monochorionic twins with sGR may reflect adverse prognosis for the pregnancy [26, 60, 79]. For this reason, it is recommended that UA-PI measurements are taken from 20^{+0} weeks of gestation and plotted on gestational nomogram charts (with umbilical artery Doppler velocities noted to have positive or AREDV from 16 weeks). Doppler waveforms may demonstrate positive diastolic velocities (type I), AREDV (type II), or cyclical diastolic waveforms (type III), with an attendant worsening of prognosis for perinatal mortality and morbidity. So called 'Cyclical' iAREDV on umbilical artery Doppler velocity assessment is more common in MCDA sGR (45%) than uncomplicated (5%) pregnancies or those complicated by severe TTTS (2%) [75]. This condition appears to result from a large artery–artery anastomoses. *[Evidence level 2+]*

sGR type I (Table 1) is associated with a relatively good outcome (more than 90% perinatal survival). Type II sGR is associated with a high risk (up to 29%) of intrauterine demise of the growth-restricted twin and/or preterm birth. Type III sGR is associated with a 10%–20% risk of the unexpected fetal demise of the smaller twin (even if stable ultrasound features and/or normal computerised cardiotocography [CTG] hours or days before) and a 10%–20% risk of neurological injury in the larger twin [79]. *[Evidence level 2+]*

8 | Management of Complex Pathologies Associated With a Monochorionic Twin Pregnancy

8.1 | The Management of TTTS

8.1.1 | How Useful Are Grading Systems for the Severity of TTTS in Establishing Prognosis?

At ultrasound diagnosis, TTTS should be staged using the Quintero system. In addition, measurement of umbilical artery Doppler velocities, MCA PSV and Ductus Venosus Doppler studies should be performed and documented at each ultrasound scan. [D]

The Quintero system of staging TTTS (Table 1) has some prognostic value, but the course of the condition is unpredictable and may involve improvement or rapid deterioration within a short period [81–83]. [*Evidence level 2+*]

In a series of 173 pregnancies complicated by TTTS from three centres in the USA and Australia, where treatment was either by amnioreduction or selective laser ablation, the outcome of at least one neonatal survivor was 91% (stage I), 88% (stage II), 67% (stage III) and 50% (stage IV) [68, 82]. Similar findings were reported from Germany in a series of 200 TTTS pregnancies treated by laser ablation: at least one neonatal survivor in 93% (stage I), 83% (stage II), 83% (stage III), and 70% (stage IV) [84, 85]. [*Evidence level 2+*]

Many reports of TTTS are difficult to interpret because of referral bias. A study from Western Australia is valuable because it is population-based, coming from the sole perinatal tertiary service in this Australian Territory [82]. A prospective cohort of 71 women with TTTS was treated with amnioreduction or septostomy. There was a relationship between Quintero stage at diagnosis and mean gestational age at birth and perinatal

survival: stage I, 32 weeks of gestation, 77% survival; stage II, 31 weeks of gestation, 70% survival; stage III, 28 weeks of gestation, 54% survival; and stage IV, 27 weeks of gestation, 44% survival. However, disease progression was often unpredictable, with 28% of pregnancies improving, 35% worsening and 37% remaining in the same grade throughout gestation. Pregnancies appeared, for example, to progress from stage I to stage III without obviously passing through stage II. Very similar findings came from a smaller cohort study in the USA ($n = 18$) [83]. There were similar rates of regression and progression. Another study found a change of stage with time to be of greater prognostic significance than the stage itself [81] and others in a research setting have found recipient cardiac diastolic function to be important in long-term prognosis [86, 87]. *[Evidence level 2+]*

Amniotic fluid discordance, without fulfilling the 8 cm/2 cm criteria (i.e., within the 'normal range'), together with normal umbilical artery Doppler velocimetry is associated with good outcome (93% overall survival) and low risks of progression to severe TTTS (14%) [69, 85, 88]. In addition, an evidence-based assessment of the literature indicated that an increased frequency of diagnostic monitoring for feto-fetal transfusion syndrome in the woman's second and third trimester to at least weekly if there is a difference in amniotic fluid DVP depth of 4 cm or more [2]. *[Evidence level 2+]*

There is controversy about the Quintero staging of TTTS, since stage I disease may not necessarily be associated with the best outcome and indeed recipient twins within stage I TTTS may have evidence of cardiac dysfunction [89]. *[Evidence level 2+]*

To emphasise this, a cross-sectional study from a single centre in the USA has indicated that monochorionic twin pregnancies complicated by TTTS as mild as Quintero stages I and II have a significant proportion of recipient twins with ventricular hypertrophy (17/28; 61%), atrioventricular valve regurgitation (6/28; 21%) and objective abnormalities in either right (12/24; 50%) or left (14/24; 58%) ventricular function [87] at fetal echocardiography. The suggestion that structural and/or functional assessment of the fetal heart (especially in the recipient) by echocardiography of monochorionic pregnancies at risk of or with TTTS may be useful in defining the prognostic risk of severe TTTS and treatment modalities, such as fetoscopic laser ablation [86, 87], are of interest. Specific focus upon the management of Stage I TTTS is discussed below in section 7.1.2 *[Evidence level 2+]*

8.1.2 | What Is (Are) the Optimal Treatment(s) of TTTS and Their Outcomes?

TTTS should be managed in conjunction with fetal medicine centres with recourse to specialist expertise and treatment in supraregional centres. [GPP]

TTTS presenting before 26^{+0} weeks of gestation should be treated by fetoscopic laser ablation rather than amnioreduction or septostomy. After 26^{+0} weeks care should be individualised. [A]

There is evidence that the fetoscopic laser ablative method should be by a serial, sequential technique followed by equatorial laser dichorionisation (the SOLOMON technique). [A] ***New 2024***

Supraregional centres performing fetoscopic laser ablation should perform at least 15 procedures per year (rolling 3-year average). [GPP]

Weekly, detailed ultrasound assessment (including examination of the fetal brain, heart and limbs) and serial measurements of UA-PI, MCA PSV and Ductus Venosus Doppler velocities should be performed. After 2 weeks post-treatment, the ultrasound interval may be increased to every 2 weeks (noting UA-PI, MCA PSV, and DVP) with documentation of adequate fetal growth (by calculating EFW). [GPP]

In treated TTTS pregnancies, an ultrasound examination of the fetal heart should be performed by the fetal medicine specialist to exclude functional and acquired structural heart anomalies. [GPP]

TTTS is a morbid complication of monochorionic twin pregnancies [9]. Once there is a suspicion of the disease or the diagnosis has been prospectively made using ultrasound, the pregnancy should be managed in conjunction with a fetal medicine centre, with specialists that perform treatment of the condition, including fetoscopic laser ablation. This is in concordance with the national commissioning guidance for the management of this condition in England [90]. *[Evidence level 4]*

There are supraregional centres in the UK (and internationally) that will offer fetoscopic laser ablation for TTTS. Each case should be managed on an individual basis, but commonly, this treatment is for Quintero stage II or more and many will treat this condition if there is Quintero stage I with significant polyhydramnios (8 cm or more) or cervical shortening (less than 25 mm) [9]. *[Evidence level 4]*

The Euro-fetus consortium trial randomised women with TTTS to either laser ablation or amnioreduction [91]. The planned sample size of 172 women aimed to demonstrate a 15% difference in survival. Most women had Quintero stage II or III TTTS. Three women in the laser group did not undergo the procedure. Two women in the amnioreduction group did not undergo the procedure and seven underwent laser ablation, with associated amnioreduction in 86% (6/7). As compared with the amnioreduction group, the laser group had a significantly greater likelihood of the survival of at least one twin to 28 days of age and 6 months of age. Infants in the laser group also had a lower incidence of cystic periventricular leukomalacia and were more likely to be free of neurological complications at 6 months of age. The authors' conclusion was that fetoscopic laser coagulation of anastomoses is a more effective first-line treatment than serial amnioreduction for severe TTTS diagnosed before 26^{+0} weeks of gestation. *[Evidence level 1+]*

Another randomised trial compared amnioreduction with septostomy (the deliberate creation of a hole in the dividing septum

with the intention of improving amniotic fluid volume in the donor sac) [92]. The trial included 73 women with TTTS (of all stages). The primary outcome was at least one infant surviving until hospital discharge. The trial was stopped after an interim analysis because no significant differences were seen in the primary outcome. *[Evidence level 1+]*

The results of a third randomised controlled study, the National Institute of Child Health, and Human Development trial of amnioreduction versus laser ablation [93], have been added to the Cochrane review on the topic [94]. In this randomised controlled trial, pregnancies with severe TTTS were only entered into the study after a 'test' amnioreduction. This may have produced bias in the study. This trial noted that there was no statistically significant difference in 30-day postnatal survival between laser ablation and amnioreduction treatment for donors at 55% (11/20) versus 55% (11/20) ($p=1.0$; OR 1, 95% CI 0.242–4.14) or recipients at 30% (6/20) versus 45% (9/20) ($p=0.51$; OR 1.88, 95% CI 0.44–8.64). There was no difference in 30-day survival of one or both twins on a per-pregnancy basis between amnioreduction at 75% (15/20) and laser ablation at 65% (13/20) ($p=0.73$; OR 1.62, 95% CI 0.34–8.09). Overall survival (newborns divided by the number of fetuses treated) was not statistically significant for amnioreduction at 60% (24/40) versus laser ablation at 45% (18/40) ($p=0.18$; OR 2.01, 95% CI 0.76–5.44). There was a statistically significant increase in fetal recipient mortality in the laser ablation arm at 70% (14/20) versus the amnioreduction arm at 35% (7/20) ($p=0.25$; OR 5.31, 95% CI 1.19–27.6). This was offset by an increased recipient neonatal mortality of 30% (6/20) in the amnioreduction arm. *[Evidence level 1+]*

The results of the three studies have been re-analysed in a Cochrane review, adjusting where possible for clustering, and recognising the non-independence of twin fetuses within a pair [94]. *[Evidence level 1+]*

The Cochrane review concluded that endoscopic laser coagulation of anastomotic vessels should continue to be considered in the treatment of all stages of TTTS to improve neurodevelopmental outcomes in the child. When compared with amnioreduction, treatment with laser coagulation does not appear to increase or reduce the risk of overall death (stillbirth, neonatal and postneonatal) in this condition, but it appears to result in more children being alive without neurological abnormality. *[Evidence level 1+]*

Since this time, a further RCT, a large cohort case study, and one systematic review have reinforced that fetoscopic laser ablation increases fetal survival while reducing long-term neurologic morbidity in survivors [22, 85, 95].

Amnioreduction can be retained as a treatment option for those situations where the expertise and facilities for laser coagulation is not available, pending transfer to a unit where such treatment can be obtained or when the condition is diagnosed after 26 weeks of pregnancy. However, this may complicate future treatment if associated with inadvertent septostomy [94, 95]. *[Evidence level 1+]*

Randomised evaluation of interventions, such as septostomy, serial amniocentesis, and placental laser ablation, about their respective effect on relatively mild forms of TTTS (Quintero stage I) and more severe forms (Quintero stage IV) are required [94, 95].

An international randomised trial of intrauterine fetoscopic laser surgery versus expectant management in stage 1 TTTS indicated survival in 84 of 109 (77%) expectant cases and in 89 of 114 (78%) ($p=0.88$) immediate surgery cases. Severe neurologic morbidity occurred in 5 of 109 (4.6%) and 3 of 114 (2.6%) ($p=0.49$) cases in the expectant and immediate surgery groups, respectively. In women followed expectantly, 24 of 58 (41%) cases remained stable with dual survival in 36 of 44 (86%). Survival was lower following surgery than for the non-progressive cases, although not significantly (78% and 71% following immediate and rescue surgery, respectively). The authors concluded that it is unlikely that early fetal surgery is of benefit for stage 1 TTTS in pregnant women with a long cervix. Although expectant management is reasonable for these cases, 60% of the cases will progress and require consideration of surgery [96]. *[Evidence level 1+]*

However, there is some evidence that fetoscopic laser ablation is the best treatment of TTTS in early-onset (less than 17 weeks) and late-onset (after 26 weeks) disease [97, 98]. However, management of these cases (especially at gestational age above 26 weeks) should be individualised. *[Evidence level 3]*

Anastomoses may be unseen at fetoscopic laser ablation, and this is the most common cause of recurrence and morbidity [22, 94]. Recurrent discordant amniotic/liquor volumes herald a recurrence of TTTS and can occur in up to 14% of pregnancies treated with fetoscopic laser ablation (and be associated with or without TAPS) [22]. Such outcomes are associated with a worsening of neonatal morbidity. There is randomised controlled trial evidence that modification of the primary fetoscopic laser technique by 'equatorial laser dichorionisation' (or the SOLOMON technique) significantly reduces these complications of recurrent TTTS and TAPS [22]. *[Evidence level 1+]*

Fetoscopic laser ablation can be performed in monochorionic and dichorionic (triamniotic) triplet pregnancies, but the placental angioarchitecture is usually more complex and the perinatal outcomes are in general poorer than in the treatment of twins [99, 100]. *[Evidence level 3]*

Some women request termination of pregnancy when severe TTTS is diagnosed, and this should be discussed as an option. Another option is to offer selective termination of pregnancy using bipolar diathermy of one of the umbilical cords or using radiofrequency ablation, with the inevitable demise of that baby [101, 102]. This may be appropriate, for example, if there is evidence of cerebral damage in either twin [103]. *[Evidence level 2+]*

There are little data to inform how frequently ultrasound surveillance is required after fetoscopic laser ablation (or amnioreduction). Following laser treatment, the recurrence rate is up to 13%, likely to be secondary to unseen anastomoses at the time of initial laser treatment [22]. However, most experts advocate that ultrasound examination (with brain imaging, fetal measurement, and Doppler assessment, especially of the MCA PSV) should be performed every week for the first 2–4 weeks and then every other week following clinical resolution. TAPS may complicate post fetoscopic laser ablation in up to 13% of cases (the most common complication after fetal demise). Therefore, at these ultrasound examinations, MCA

PSV should be performed, and the result recorded. *[Evidence level 2+]*

However, some have indicated that functional cardiac studies may add to the prognosis of MCDA twins complicated by TTTS [86, 87, 89]. In a case series of 89 survivors from 73 pregnancies treated by laser ablation for severe TTTS, 11% of fetuses had secondary, structural heart disease, primarily right-sided cardiac lesions, predominantly pulmonary stenosis [88]. *[Evidence level 2–]*

8.1.3 | When Should the Birth of Monochorionic Twin Pregnancies Complicated by TTTS Take Place?

Birth of monochorionic twin pregnancies with treated TTTS should be at 36 completed weeks of gestation, unless there are complications noted. [D]

International expert opinion has indicated that, even after successful treatment, regular ultrasound surveillance should be routinely performed and is good clinical practice [29, 104]. Consideration should be given to the birth of the surviving twin(s) between 34^{+0} and 35^{+6} weeks of gestation [9, 104, 105], or earlier if there are clinical concerns. As with previous RCOG and NICE guidance, prophylactic maternal steroids should be given up to 34^{+6} weeks. Mode of birth can be individualised, but often this is by caesarean section (guided by the clinician and patient preference) [106]. *[Evidence level 2–]*

8.2 | The Management of sGR

sGR in monochorionic twins requires evaluation in a fetal medicine centre with expertise in the management of such pregnancies. [GPP]

In cases of early-onset sGR in association with poor fetal growth velocity and abnormal umbilical artery Doppler assessments, selective reduction, or fetoscopic laser ablation may be considered treatment options. These twin pregnancies require assessment in fetal medicine centres with appropriate expertise. [C]

In sGR, ultrasound surveillance of fetal growth should be undertaken at an interval of at least every 2 weeks with fetal Doppler assessment (by umbilical artery and middle cerebral artery pulsatility index, and peak systolic velocity from) weekly. Ultrasound surveillance and frequency should be individualised. If umbilical artery Doppler velocities are abnormal (type II or III), the Doppler assessments should be undertaken in line with national guidance, measuring Ductus Venosus Doppler waveforms. [D]

Clinicians should be aware that there is a longer 'latency period' between diagnosis and timing of birth in monochorionic twins complicated by sGR compared with growth restriction in dichorionic twin pregnancy or singleton pregnancy. [D]

Abnormal Ductus Venosus Doppler waveforms (reversed flow during atrial contraction) or computerised CTG short-term variation should be taken into consideration jointly, along with fetal biometric measurement and growth velocities when deciding upon timing of birth. [B]

In type I sGR, planned birth should be considered between 34^{+0}–35^{+6} weeks of gestation if there is satisfactory fetal growth velocity and normal umbilical artery Doppler waveforms. [GPP]

In type II and III sGR, birth should be planned by 32 weeks of gestation, unless fetal growth velocity is significantly abnormal or there is a worsening of the fetal Doppler assessment. [GPP]

It is important to prospectively inform parents that in sGR and TTTS (even after successful treatment) there can be acute and serious complications, including sudden transfusional events (which are neither predictable nor preventable), and therefore, despite regular monitoring, there may still be adverse perinatal outcomes. [GPP]

Once there is a suspicion of sGR or the diagnosis has been prospectively made using ultrasound, the pregnancy should be managed in conjunction with a regional fetal medicine centre with specialist expertise in managing this condition. There is a need to measure amniotic sac liquor volumes and to assess Doppler velocities within the fetal arterial and venous circulations [74, 75, 79]. *[Evidence level 4]*

Umbilical artery Doppler velocimetry evaluation in monochorionic twins with sGR allows the prospective definition of three subtypes (see Table 1) and the consequences are dependent upon this evaluation and gestational age [107]. *[Evidence level 3]*

When sGR is diagnosed then reduced fetal growth velocity, fetal and perinatal loss is increased [29, 77]. Prior to viability (24 weeks), if the small twin has a significantly reduced fetal growth velocity (change in measured abdominal circumference of less than 1 SD over 14 days) in the presence of umbilical artery Doppler abnormalities, there is a significant risk of single fetal demise [79, 107]. *[Evidence level 2+]*

In such circumstances, to protect the appropriately grown co-twin, selective termination of pregnancy using vaso-occlusive techniques, such as bipolar cord occlusion or radiofrequency ablation may be considered [103, 108]. This should be assessed and performed in a tertiary centre with expertise. An informed but sensitive discussion with women is essential. In addition, fetoscopic laser surgery may be considered in selected cases. The evidence base does not conclusively identify a care plan that is consistently optimal in these complex monochorionic twins [61]. Therefore, care is often individualised and based upon the gestation of diagnosis, peripheral and intracardiac arterial and venous Doppler velocimetry, the percentage of discordance in EFW, growth velocity of twins, and parental wishes. *[Evidence level 2+]*

There is limited evidence to guide clinical care in these complex cases. However, there is international consensus that such monochorionic twin pregnancies require regular review with interval ultrasound biometry to monitor fetal growth velocity, and placental

and fetal circulation assessment by umbilical artery, middle cerebral artery, and ductus venosus Doppler waveform measurements [74, 75, 79]. The aim is to prolong pregnancy to at least viability and to achieve appropriate gestation for birth (optimally 32–34 weeks), but to avoid the complication of single fetal death and the consequences for the surviving fetus [79]. *[Evidence level 2–]*

It should be noted that sGR may progress from type I to the potentially more pathological type II/III sGR.

Timing of birth is dependent upon fetal growth velocities, fetal Doppler measurements and the presence of any co-morbidities (either fetal or maternal). If preterm birth between 26^{+0} and 32^{+0} weeks of gestation is considered (most likely in type II and III sGR) them the timing of birth is dependent upon assessment by Ductus Venosus waveform velocimetry and cCTG may be used between ultrasound to monitor fetal wellbeing [109]. However, reliance upon specific 'thresholds' prompting birth should be guarded against and a trend and cluster of investigations used to time birth. This is because fetal mortality is not primarily secondary to hypoxaemia with more variable, unpredictable pathologies making individualised care advisable.

When there is type II or type III sGR (with AREDFV), then birth should be undertaken at 32 weeks (in line with singleton FGR with AREDV) [109].*[Evidence level 2++]*

The placental anastomoses in monochorionic twins paradoxically may be beneficial for the smaller twin as a transfusion from the larger twin may compensate for the placental insufficiency, thus interfering with the natural history in comparison with singleton and dichorionic twin pregnancies. This is also associated with the presence of artery–artery anastomoses. This prolongs survival in the growth-restricted fetus, resulting in a longer (than in singletons) latency period to deterioration and birth (up to 10 weeks versus 3–4 weeks from diagnosis of Fetal Growth Restriction) [12]. *[Evidence level 3].*

In monochorionic twins, where the placental vascular anastomoses remain intact, there is a risk of acute 'inter-twin' transfusional events causing fetal death and morbidity in the form of neurological morbidity. This is true of apparently uncomplicated monochorionic twins, but more prevalent in monochorionic twins complicated by sGR and even treated TTTS [1, 2]. *[Evidence level 3]*

8.3 | Management of TAPS

Clinicians should be aware that the natural history, fetal and neonatal implications, and optimal treatment and/or surveillance of monochorionic pregnancies diagnosed with TAPS are poorly established. [D]

When TAPS is suspected or diagnosed the management should be agreed in discussion with woman, her partner and in conjunction with experts in a fetal medicine centre that has the expertise and experience in performing treatment, if appropriate. [D]

Fetoscopic laser ablation for the treatment of TTTS, using the SOLOMON technique, significantly reduces the risk of recurrent disease and TAPS [22]. There are several treatment options available for the management of TAPS. It is not clear from the literature which treatment type is superior and the choice is likely to be dependent upon the gestational age of diagnosis, the severity of the TAPS (as well as clinician and parent views). Options include expectant management, planned twin birth, intrauterine blood transfusion (intravenous and/or intraperitoneal, with or without partial exchange transfusion), selective feticide, or fetoscopic laser surgery [73, 110].

Fetoscopic laser surgery is the only therapy coagulating the minuscule anastomoses responsible for the pathology. This therapy may be more technically challenging (due to the absence of polyhydramnios) than in TTTS but is associated with reduced rates of long-term morbidity but high rates of fetal demise [22, 73]. If TAPS is suspected prenatally, management options therefore need to be individualised, in discussion with supraregional fetal medicine expertise, and any uncertainty discussed with the parents. *[Evidence level 3]*

Perinatal outcome in TAPS is not well described (with or without treatment) and appears to vary according to the severity, the gestational age at diagnosis, and the presence of co-morbidities. The outcome may range from double intrauterine fetal demise to the birth of two healthy neonates with a significant inter-twin haemoglobin discordance. Knowledge of the neonatal and long-term morbidity in TAPS is scarce and based on case reports and small series [110, 111].

A retrospective international registry documenting the treatment and outcome of 370 cases with spontaneous or post-laser TAPS has been published, outlining experience from 17 centres. Three hundred seventy monochorionic twin pregnancies with TAPS were included in the study. Of these, 31% ($n=113$) were managed expectantly, 30% ($n=110$) with laser surgery, 19% ($n=70$) with in utero transfusion (±exchange transfusion), 12% ($n=43$) with birth, 8% ($n=30$) with selective termination and 1% ($n=4$) underwent termination of the whole twin pregnancy. Perinatal mortality was relatively high occurring in 17% (39/225) of pregnancies in the expectant-management group, 18% (38/215) in the fetoscopic laser group, 18% (25/140) in the in utero transfusion group, 10% (9/86) in the birth group and in 7% (2/30) of the co-twins in the selective-feticide group. The incidence of severe neonatal morbidity was 49% (41/84) in the birth group, 46% (56/122) in the in-utero transfusion (± partial exchange transfusion) group, 31% (60/193) in the expectant management group, 31% (57/182) in the laser-surgery group and 25% (7/28) in the selective termination group. The median diagnosis-to-birth interval was longest after selective termination (10.5 [IQR 4.2–14.9] weeks), followed by laser surgery (9.7 [IQR 6.6–12.7] weeks), expectant management (7.8 [IQR 3.8–14.4] weeks), transfusion (4.0 [IQR 2.0–6.9] weeks) and birth (0.3 [IQR 0.0–0.5] weeks). Treatment choices for TAPS varied greatly within and between the 17 fetal therapy centres and in some respect reflects the heterogeneity of TAPS severity in this cohort [73].

Neonatal morbidity in TAPS appears to be mainly limited to haematological problems at birth but there may be long-term morbidities (i.e., physical and mental handicap). Donor twins may be severely anaemic and require blood transfusions, whereas recipient twins may be severely polycythaemic and require partial

exchange transfusion [24, 25, 73]. There have been cases of severe cerebral injury in TAPS described and some evidence of neurosensory hearing loss in TAPS 'donors' [73, 111]. *[Evidence level 3]*

8.4 | The Management of Monochorionic Twin Pregnancies Complicated by Single Twin Demise

8.4.1 | What Are the Consequences for the Surviving Twin After Fetal Death of the Co-Twin in a Monochorionic Pregnancy and What Is Optimal Clinical Care?

Clinicians should be aware that monochorionic pregnancies not complicated by TTTS, sGR or TAPS are still at risk of fetal death and neurological anomaly. [D]

After a single fetal death in a monochorionic pregnancy, clinicians should be aware that the risks to the surviving twin of death or neurological anomaly are of the order of up to 15% and 26%, respectively. [B]

After a single fetal death in a monochorionic pregnancy, the risk of co-twin demise, prematurity and neonatal death is significantly increased. The aim is birth of the fetus by 36^{+6} weeks gestation. Regular ultrasound surveillance of the surviving twin is mandatory and the timing and mode of birth should be individualised taking into account fetal size, growth velocity, the women's obstetric and medical history, and her preference. [B]

Single fetal death in a monochorionic pregnancy should be referred and assessed in a fetal medicine centre, with multidisciplinary expertise to manage these cases. [GPP]

Fetal magnetic resonance imaging of the brain may be performed up to 4 weeks after co-twin demise to aid in the detection of brain neurological morbidity. This information is of value in planning care. [D]

In monochorionic pregnancies, where the placental vascular anastomoses remain intact, there is a risk of acute 'inter-twin' transfusional events causing fetal death and neurological morbidity (usually because of associated ischaemic brain injury or haemorrhage) [42–44]. This is true of apparently uncomplicated monochorionic twins, but more prevalent in monochorionic twins complicated by sGR and TTTS (even after fetoscopic laser ablation) [1, 2]. *[Evidence level 3]*

Damage to the surviving monochorionic twin after the death of its co-twin is believed to be caused by acute haemodynamic changes around the time of death, with associated ischaemia in the surviving fetus that often loses part of its circulating volume into the circulation of the dying twin. This may cause transient or persistent hypotension and low perfusion, leading to the risk of ischaemic organ damage, notably but not exclusively, to the watershed areas of the brain [42–44, 112]. *[Evidence level 3]*

Systematic reviews [113, 114] have identified 22 full manuscripts considered of high enough quality of evidence to include in the review and meta-analysis. Twenty manuscripts were used to calculate overall summary statistics for monochorionic and dichorionic twins showing rates of co-twin death after single fetal death (15% compared with 3%), rates of preterm birth after single fetal death (68% compared with 54%), the rate of abnormal postnatal cranial imaging after single fetal death (34% compared with 16%) and the rate of neurodevelopmental impairment after single fetal death (26% compared with 2%). Odds ratios were calculated from 16 manuscripts. There was no significant difference reported between the preterm birth of monochorionic and dichorionic twins (OR 1.1, 95% CI 0.34–3.51; $p = 0.9$). After single fetal death, monochorionic twins had higher odds of abnormal cranial imaging after birth, although, this was not significant (OR 3.25, 95% CI 0.66–16.1; $p = 0.12$). After a single fetal death, monochorionic twins were 4.81 times more likely to have neurodevelopmental morbidity (95% CI 1.39–16.6; $p < 0.05$). *[Evidence level 1–]*

In the second and third trimesters particularly, the risk of death of the surviving fetus is increased [115]. This is at least two-fold higher if the single intrauterine demise occurs before 28^{+0} weeks; with a five-fold increase in premature birth and an almost three-fold increase in neonatal death [115].

Clinical management is complex and should be overseen by fetal medicine experts with the knowledge and experience to advise parents about the advantages and disadvantages of different approaches [113–115]. Rapid birth is usually unwise, unless gestational age is close to 36 weeks, as fetal brain injury of the surviving twin occurs at the time of the demise of the co-twin. Therefore, immediate birth only adds prematurity to the possible hypotensive cerebral injury the surviving twin may have already sustained. Serious compromise of the surviving fetus may be anticipated, and this should be discussed with parents, including the significant risk of long-term morbidity. Evidence of fetal compromise (such as significant cardiotocographic abnormality and/or evidence of anaemia in the survivor if single fetal death occurs late in pregnancy) could represent continuing and/or established damage to the brain. Fetal anaemia in the surviving twin may be associated with the future development of neurological morbidity [42–44, 113–115]. *[Evidence level 4]*

A conservative management policy is often appropriate, with serial fetal brain ultrasound imaging and a fetal cranial magnetic resonance imaging (MRI) scan planned, commonly 4 weeks after the 'sentinel event' [114]. The appearances of intracranial neurological morbidity on ultrasound are variable and may take up to 4 weeks to develop. Fetal MRI provides earlier and more detailed information about brain lesions (haemorrhagic or ischaemic) in the surviving fetus than ultrasound and its use should be considered [42–44, 116, 117]. *[Evidence level 3]*

In cases of single intrauterine demise with MRI or ultrasound findings of neurological morbidity, late termination of pregnancy would be an option. The gestational age at the time of diagnosis is relevant and the views of the parents will be of paramount importance.

8.4.2 | How Should Fetal Anaemia Be Monitored After Single Twin Intrauterine Death?

Fetal anaemia may be assessed by measurement of the fetal MCA PSV using Doppler ultrasonography. Parents

should be informed that treatment may improve perinatal survival but may not alter the risk of the development of ischaemic brain injury. [D]

In a prospective series of 20 monochorionic pregnancies complicated by single fetal death, there was a strong correlation between fetal anaemia (assessed by fetal blood sampling) and fetal MCA PSV [118, 119]. *[Evidence level 3]*

In a small series ($n=26$) of pregnancies complicated by TTTS and single fetal death, the prognosis was worse for donor twins following the death of the recipient twin than vice versa. This is in keeping with the concept of increased blood loss through a unidirectional anastomosis [119]. There are a few reports of intrauterine transfusion of anaemic surviving co-twins, but the value of this intervention is not established within the context of preventing perinatal and long-term neurological morbidity [120, 121]. *[Evidence level 3]*

The presence of an increased MCA PSV in the surviving twin would suggest fetal anaemia and therefore, a significant inter-twin transfusion. This is most common within a week of single twin demise. This would increase the risk of neurological injury and therefore, would be helpful information in the counselling of parents and timing of fetal brain MRI. Treatment by intrauterine transfusion is controversial, as this may improve fetal survival without reducing the long-term risks of neurological morbidity.

9 | Timing and Mode of Birth in Uncomplicated Monochorionic Pregnancies

9.1 | What Is the Optimal Timing and Mode of Birth for Otherwise Uncomplicated Monochorionic Pregnancies (Without TTTS, sGR or TAPS)?

Women with monochorionic, diamniotic twins should have timing of birth discussed and be offered planned birth from 36 completed weeks of pregnancy. [C]

If preterm birth of monochorionic twins is planned then if: (i) up to 34^{+6} weeks maternal steroids should be administered and (ii) if before 34^{+0} weeks maternal magnesium sulfate treatment should be given. [D]

It is appropriate to aim for vaginal birth of MCDA twins unless there are other specific clinical indications for caesarean section. [A]

A documented discussion with parents of the risks and benefits of planned vaginal versus caesarean birth for any monochorionic pregnancy should be undertaken. [D]

In the context of birth of monochorionic twins whether complicated or uncomplicated, the role of delayed umbilical cord clamping is controversial because of the theoretical risks of feto-fetal transfusion with 'intact' placental anastomoses. At present, there is not sufficient evidence to recommend for or against delayed cord clamping in monochorionic pregnancies. [D]

For uncomplicated monochorionic pregnancies, there may be a higher risk of unexplained fetal demise despite intensive fetal surveillance [122]. The 2011 and 2019 NICE guidelines examined this topic [1, 2]. The gestational age profile for spontaneous birth in twin and triplet pregnancies has been assessed in one cross-sectional study which suggested that the majority (58%) of women with uncomplicated twin pregnancies give birth spontaneously before 37^{+0} weeks [2]. *[Evidence level 2–]*

Furthermore, two systematic reviews concluded that even uncomplicated monochorionic, diamniotic twin pregnancies are at risk of stillbirth throughout the third trimester, which is higher than in dichorionic twin pregnancies. The largest of these reviews [123] noted that in monochorionic, diamniotic twin pregnancies beyond 34 weeks (13 studies, 2149 pregnancies), there was a trend towards an increase in stillbirths compared with neonatal deaths after 36 weeks, with an additional 2.5 per 1000 perinatal deaths, which was not significant (−12.4 to 17.4/1000).

Given the risk of fetal death to the co-twin, these data should inform decisions around the timing of birth in seemingly normal monochorionic diamniotic twin pregnancies; women with monochorionic twins should be offered planned birth from 36 completed weeks [2, 122, 123]. *[Evidence level 2+]*

The Twin Birth Study [124], a multicentre, international randomised controlled trial of planned vaginal birth versus planned caesarean birth of twins, included a sub-cohort of uncomplicated MCDA twins (600 of 1398 randomised). The study concluded that in twin pregnancies between 32^{+0} and 38^{+6} weeks of gestation (when the first twin is a cephalic presentation), planned caesarean birth did not significantly decrease (or increase) the risks of fetal or neonatal death, or serious new-born morbidity as compared with vaginal birth. Furthermore, post hoc subgroup analysis demonstrated no significant interaction of chorionicity with the primary outcomes. It was concluded that there was no significant benefit from planned caesarean birth for any subgroup, including monochorionic twins. *[Evidence level 1+]*

As with all pregnancies, parental views will also be important in concluding the best, individualised method of monochorionic twin birth, including opting for a caesarean section.

In addition to the complexities of twin birth (i.e., malpresentation) there is a small risk of acute feto–fetal transfusional events during labour and this is one of the reasons why continuous electronic fetal monitoring during labour is recommended [2]. In the context of birth of monochorionic twins whether complicated or uncomplicated, the role of delayed umbilical cord clamping is controversial because of the theoretical risks of feto-fetal transfusion with 'intact' placental anastomoses. At present, there is not sufficient evidence to recommend for or against delayed cord clamping in monochorionic pregnancies.

10 | Timing and Mode of Birth in Complicated Monochorionic Pregnancies, Including Those With 'Treated' TTTS

Timing for an optimal cut-off for planned preterm birth in laser operated TTTS appears not to have a strong

evidence base. However, perinatal mortality after 32^{+0} appears low (although perinatal morbidity may be unpredictable). In monochorionic twin pregnancies, post-fetoscopic laser ablation the twin pregnancy should be delivered by 36 weeks gestation.

Despite significant improvements in the overall prognosis, fetoscopic laser coagulation for TTTS carries a high risk of postoperative complications such as fetal demise, miscarriage, TAPS and/or recurrence. In most cases, these complications occur shortly after surgery and are therefore expected, if not predictable. The consequence of these complications is an overall reduced survival rate compared to uncomplicated monochorionic pregnancies.

In uncomplicated monochorionic pregnancies, high rates of late stillbirths have prompted a policy of elective preterm birth as early as 32 weeks but in the majority by 36 weeks gestation. Following laser surgery for TTTS, the management and timing of birth may consider two opposite options: (i) that these pregnancies are still at high risk up until late gestation because of possible late unpredictable complications; or (ii) that surgery has reduced the likelihood of such late events and that they could be managed as dichorionic pregnancies.

Optimal management, therefore, involves a balance between the risk of intrauterine adverse events and the consequences of planned preterm birth. Moreover, newborns following TTTS have been shown to carry a higher rate of neurological impairment. Therefore, in the absence of relevant decision-making results, one may favour the reduction of unnecessary preterm births or favour the prevention of potential late unpredictable complications. A retrospective study of 602 consecutive monochorionic twin pregnancies complicated by TTTS who underwent laser ablation therapy in Paris were examined using a cumulative risk model analysis. The results did not identify an optimal cut-off for planned preterm birth in laser-operated TTTS. Perinatal mortality was low after 32 completed weeks of gestation but the study concluded that medical history, clinical findings on ultrasound, parental demand, and clinical expert assessment should fashion the timing of birth between 32^{+0} and 36^{+0} weeks of gestation [125]. In the UK, most fetal medicine subspecialists would attempt prolongation of gestation until 36^{+6} weeks of gestation and manage the pregnancies individually.

In monochorionic twin pregnancies complicated or previously complicated by TAPS, selective growth restriction or single fetal demise, the risk of fetal mortality, prematurity and neonatal death are significantly increased. The aim is to prolong gestation until 36^{+6} weeks of gestation. However, the timing and mode of birth are to be individualised taking into account the prospective ultrasound findings (including peripheral and central arterial and venous Doppler velocimetry), fetal growth velocity, and the women's obstetric, medical history and preferences. Again, in the context of birth of monochorionic twins, the role of delayed umbilical cord clamping is controversial because of the theoretical risks of feto-fetal transfusion with 'intact' placental anastomoses. At present, there is not sufficient evidence to recommend for or against delayed cord clamping in monochorionic pregnancies.

11 | MCMA Pregnancies

11.1 | What Are the Specific Problems of MCMA Pregnancies and How Should They Be Managed?

MCMA twins almost always have umbilical cord entanglement when visualised using colour flow Doppler. Such a finding has not consistently been demonstrated to contribute to overall morbidity and mortality. [D]

MCMA twin pregnancies have similar fetal mortality whether increased fetal surveillance is as an in-patient or as an outpatient. [C]

MCMA twins have a high risk of fetal demise and should be a planned caesarean birth between 32^{+0} and 34^{+0} weeks. [D]

MCMA twins have classically been thought to be at risk from cord entanglement (almost always visualised during ultrasound examination) and fetal demise. A retrospective study of 30 MCMA twin pairs reported a total survival of 60% [8]. Two pairs died after 32 weeks of gestation. Of the 10 twin pairs that died in utero, cord entanglement was documented in eight. The authors recommended planned birth at 32 weeks of gestation. *[Evidence level 3]*

However, a study of 32 MCMA twin pregnancies has suggested that cord entanglement is a feature of all MCMA twin pregnancies, and most deaths occur before 20 weeks of gestation due to other complications (i.e., TRAP, discordant fetal anomaly or fetal conjoining) [126]. MCMA twins are, therefore, probably not as dangerous as previously thought, although, surveillance and care should always be individualised [127]. Management by using maternal administration of sulindac to reduce amniotic fluid volumes has been advocated, but the evidence-base for this treatment is scanty. The authors, therefore, recommended re-evaluating the very early timing of birth for MCMA twins, but is usually between 32 and 34 weeks of gestation [126, 127]. *[Evidence level 2–]*

A retrospective multicentre cohort study of 193 MCMA twin sets found that fetal deaths occurred in 18.1% of fetuses. The prospective risk of a non-respiratory neonatal complication was significantly lower than the prospective risk of fetal death after 32^{+4} weeks of gestation. This consortium's recommendation was to give birth to MCMA twins at approximately 33 weeks of gestation. All such cases should be managed in fetal medicine centres with specialist expertise and decisions on birth made on an individual basis [128]. A recent cohort studying MCMA twin pregnancies noted in-patient surveillance was associated with similar fetal complications and mortality as outpatient management [129]. *[Evidence level 2–]*

12 | Higher Order Multiple Pregnancies With Reference to Monochorionicity

12.1 | What Is the Outcome of Monochorionic and Dichorionic Compared With Trichorionic Triplet Pregnancies?

Clinicians should be aware that monochorionic/dichorionic triplet pregnancies have higher fetal loss rates than trichorionic triplet pregnancies and may be complicated by TTTS, sGR and TAPS. [C]

Selective reduction should be discussed in all higher-order pregnancies including triplets. Parents should understand that in monochorionic or dichorionic triplet pregnancies procedures to induce selective reduction are complex and may be associated with fetal mortality and morbidity. [GPP]

Increased ultrasound surveillance is warranted in a fetal medicine centre with expertise to manage such cases. Such surveillance may be resource-intensive and complex. [GPP]

A retrospective study of 88 naturally conceived triplet pregnancies cared for in three tertiary referral units in the UK found a 5.5-fold increased risk of perinatal death in dichorionic triamniotic pregnancies (i.e., containing monochorionic twins) than trichorionic triamniotic pregnancies (OR 5.5, 95% CI 2.5–12.2) [130]. Referral bias may have influenced the findings. A similar retrospective study from two tertiary centres in Germany described 84% survival in fetuses of monochorionic and dichorionic triplet pregnancies combined compared with 92% in fetuses of trichorionic triplet pregnancies [131]. This difference did not reach statistical significance. *[Evidence level 3]*

The consensus views arising from the 50th RCOG Study Group [9] recommend that selective reduction should be discussed in all higher-order pregnancies. A systematic review provides information on the risks of this procedure in trichorionic triplets and on the alternative option of conservative management (from six cohort studies) [132]. In the reduction group ($n = 482$ pregnancies) compared with the expectantly managed group ($n = 411$), the rate of miscarriage (before 24^{+0} weeks of gestation) was higher (8.1% vs. 4.4%; relative risk [RR] 1.83, 95% CI 1.08–3.16; $p = 0.036$) and the rate of early preterm birth was lower (10.4% vs. 26.7%; RR 0.37, 95% CI 0.27–0.51; $p < 0.0001$). It was calculated that seven (95% CI 5–9) reductions needed to be performed to prevent one early preterm birth, while the number of reductions that would cause one miscarriage was 26 (95% CI 14–193) [132]. *[Evidence level 2+]*

In monochorionic or dichorionic triamniotic triplets (because of shared placental vasculature), this would mean either a procedure to reduce the fetal numbers to one or to consider intrafetal ablative therapy to reduce dichorionic triplets to dichorionic twins [133]. Such options are associated with an increase in total pregnancy loss. *[Evidence level 3]*

If TTTS does occur, then it is most appropriately treated by laser ablation and the overall prognosis is better for dichorionic versus monochorionic triamniotic triplet pregnancies [94]. *[Evidence level 3]*

13 | Discordant Anomalies in Monochorionic Pregnancies

13.1 | What Is the Incidence of and the Therapeutic Options for Discordant Anomalies in Monochorionic Pregnancies, Including TRAP Sequence?

Monochorionic twins that are discordant for fetal anomaly must be referred promptly for assessment and counselling in a fetal medicine centre with consideration for treatment. [GPP]

Karyotyping of monochorionic twins should be managed in a fetal medicine centre. [GPP]

Meticulous mapping of the position of the twins within the uterus should be performed both at the time of prenatal diagnostic tests and invasive treatments. [GPP]

During amniocentesis, both amniotic sacs should be sampled in monochorionic twin pregnancies, unless monochorionicity is confirmed before 14^{+0} weeks of gestation and the fetuses appear concordant for growth and anatomy. [GPP]

Prior to invasive testing or in the context of twins discordant for an anomaly, selective reduction should be discussed and made available to those requesting the procedure after appropriate counselling. [GPP]

Monitoring for disseminated intravascular coagulopathy is not indicated in monochorionic twin pregnancies undergoing selective reduction. [GPP]

Selective feticide by intravascular injection of an abortifacient is <u>not</u> an option in monochorionic pregnancies because of the presence of placental anastomoses. The potential risks of complex intrafetal/umbilical cord ablative procedures should be discussed prospectively, including the risk of co-twin loss and neurological morbidity. [GPP]

Documentation and discussion of heterokaryotypic monozygotic karyotypic anomalies should take place prior to any invasive diagnostic testing. [GPP]

A higher rate of structural anomalies is observed in twins compared with singletons [28, 52, 53]. Approximately 1%–2% of twin pregnancies face the dilemma of expectant management versus selective termination following diagnosis of an anomaly affecting only one fetus. *[Evidence level 4]*

In a structurally or size discordant monochorionic pair, discordant aneuploidy is rare, although, not impossible. Structural anomalies in monochorionic pregnancies are twice that expected in dichorionic pairs, given the monozygosity [52]. Detailed ultrasound assessment, fetal karyotyping, and a discussion of

prognosis are required with reference both to the abnormal and normal twin. *[Evidence level 4]*

Selective termination in a monochorionic pregnancy is an option for parents [102, 103], but as the fetal circulations are not independent, it cannot be performed with injection of medical therapeutics because of the effect on the co-twin. More invasive and higher-risk procedures, such as cord coagulation, and intrafetal ablative procedures, such as radiofrequency ablation or laser ablation are necessary to cause the demise of one twin without causing morbidity or death in its co-twin [102, 103]. *[Evidence level 4]*

It is essential that at the time of prenatal diagnostic tests, the pregnancy is mapped carefully, noting the position and placenta in relation to the fetuses/amniotic sacs, and this should be formally documented. This is ideally performed by the operator who would perform the technique of selective termination of pregnancy, if required. It is mandatory to discuss selective termination of pregnancy and complicating factors in monochorionic twins, including the potential risk to the normal twin [1, 2]. *[Evidence level 4]*

Twin and triplet pregnancies in which the abnormal fetus underwent umbilical cord coagulation by bipolar diathermy or intrafetal laser ablation for complex pathologies have been well described [134, 135]. Overall, up to 82% of co-twins survived. Preterm rupture of membranes (10%–15%) and chorioamnionitis remains a significant complication. Fetal loss rates are 15%–18% and some series have recorded transfusional neurological sequelae in up to 15%. Similar experience is reported using radiofrequency ablation [134, 136, 137]. *[Evidence level 3]*

Monochorionic twins complicated by the presence of an acardiac twin and TRAP sequence do not always require invasive treatment. Selection for treatment appears to be dependent on:

a. the relative size of the 'acardiac' twin to the 'pump' twin (the larger the acardiac twin, the greater the risk and need for therapy) and
b. the presence of any cardiovascular impairment in the 'pump' twin [138]. *[Evidence level 3]*

If treatment is considered in a TRAP twin pregnancy, then there is some evidence that treatment should take place before 16 weeks of gestation, and it should be performed in centres with expertise in such treatment modalities. Careful monitoring and ultrasound surveillance are required [137]. Further research evidence as to the timing of any intervention is required. *[Evidence level 3]*

Rarely, monozygous twins can have different chromosome make-ups. This is known as *heterokaryotypic monozygous* twinning. When anomalies are identified in the first or early second trimester in one of a monochorionic twin pair which may be markers of aneuploidy, a discussion should take place as to the merits and risks of chorionic villus sampling versus waiting for a double amniocentesis at 15–16 weeks of gestation when both sacs are sampled, and the individual karyotype of each twin can be determined with certainty [49]. *[Evidence level 4]*

14 | Conjoined Twins

14.1 | How Are Conjoined Twins Diagnosed and What Are the Outcomes?

Conjoined twins are exceedingly rare and prenatal assessment is required in a tertiary fetal medicine centre so that diagnosis can be confirmed, and prognosis discussed in conjunction with a multidisciplinary team. [GPP]

Conjoined twins are very rare and are MCMA twin pregnancies. The prevalence is up to 1 in 100 000 pregnancies. The underlying pathogenic mechanism remains uncertain. Such MCMA twins are complex and require careful detailed expert ultrasound imaging (and usually MRI) and multidisciplinary discussion. In one series of 14 cases of prenatally diagnosed conjoined twins at a single referral centre, 20% of parents opted for termination of pregnancy, 10% of fetuses died in utero and the overall individual survival rate to discharge of pregnancy continuation was about 25%, the majority of whom have significant morbidity [139]. Most cases are now prenatally diagnosed and born by planned caesarean birth, but vaginal birth of conjoined twins is reported [140]. Risk of dystocia and uterine rupture has been reported in association with cases undiagnosed prenatally. In the United Kingdom, postnatal care is performed in a single centre (University College London). *[Evidence level 2–]*

Prenatal diagnosis of conjoined twins with ultrasound is now well reported from the first trimester, with a detailed assessment of the fetal morphological and cardiovascular anatomy being important for determining prognosis and planning care.

15 | What Are the Training Competencies Required for Managing Monochorionic Pregnancies?

All ultrasonographers who undertake routine ultrasound scans during pregnancy must be trained to establish chorionicity and the correct labelling of twins. [GPP]

All ultrasonographers who undertake mid-trimester (18^{+0}–20^{+6} weeks of gestation) and fetal growth scans of monochorionic twins should be made aware of the appearances of TTTS, sGR and TAPS, and the need to refer women on to specialist centres if such features present. [GPP]

Fetal medicine centres undertaking fetal therapy for relatively rare complications of monochorionic twins should have a minimum of two experienced operators and more than 15 cases per year (rolling 3-year average) to maximise perinatal outcomes and minimise long-term morbidity. [D]

Fetal medicine centres should follow the NHS England Specialised Services Clinical Reference Group for Fetal Medicine recommendations for experience [90]. *[Evidence level 4]*

16 | Recommendations for Future Research

- The use of serial MCA PSV in screening for TAPS in women with monochorionic twins and its evaluation in a diagnostic accuracy study, with relevance to pregnancy outcomes.
- Research evaluating early versus late treatment for monochorionic twins complicated by TRAP sequence and its assessment in terms of pregnancy outcomes.
- STOPPIT-3 study is a RCT that this ongoing in the UK evaluating the role of Antenatal Corticosteroids for Planned Birth in Twins.
- To examine the impact and effects of ethnicity and socioeconomic deprivation upon the diagnosis and outcomes in monochorionic twins.

17 | Auditable Topics

- Prospective outcome (primary outcomes: perinatal mortality and long-term paediatric morbidity) after fetoscopic laser ablation for TTTS corrected for stage, the experience of operators and severity of disease at presentation. At least one survivor in 85% of twins.
- Offer women who present in the first trimester with monochorionic twins screening for fetal aneuploidy (100%).
- The proportion of neurological morbidity post laser ablation for the treatment of TTTS in each fetus (less than 10%).
- Labelling of twins undertaken at first scan and followed consistently with serial scans (100%).
- The proportion of monochorionic twins who have extended fetal heart views undertaken at the mid-trimester anomaly scan (more than 85%).
- The proportion of monochorionic twins who have 2-weekly ultrasound from 16 weeks of gestation (more than 95%).

18 | Useful Links and Support Groups

- National Institute for Health and Clinical Excellence. *Multiple pregnancy. The management of twin and triplet pregnancies in the antenatal period*. NICE clinical guideline 129. Manchester: NICE; 2011 [https://www.nice.org.uk/guidance/cg129].
- Royal College of Obstetricians and Gynaecologists. *Monochorionic twins. [insert web address]*.
- The Multiple Births Foundation [http://www.multiplebirths.org.uk/].
- Twins And Multiple Births Association, now the Twins Trust (since 2019) [https://twinstrust.org/].
- Antenatal Results and Choices [ARC] (www.arc-uk.org).
- International Council of Multiple Birth Organisations [iCOMBO] (https://icombo.org).

Conflicts of Interest

MK receives royalties for book sales from Cambridge University Press and Taylor and Francis Publishing; payment for medicolegal expert opinions; and travel and accomodation expenses covered to attend the RCOG Genomics Committee meeting as Chair and biannually for the Fetal Medicine Foundation Congress; he is also a member of the Fetal Committee of the British Society of Genetic Medicine; he also received payment from Illumina-Genomics while working with them from. LB receives royalties for book sales from Cambridge University Press.

References

1. National Institute for Health and Clinical Excellence, *Multiple Pregnancy. The Management of Twin and Triplet Pregnancies in the Antenatal Period. NICE Clinical Guideline 129* (Manchester, UK: NICE, 2011).

2. National Institute for Health and Clinical Excellence, "Twin and Triplet Pregnancy. NICE Guideline [NG137]," Published: 04 September 2019, accessed January 19, 2022, https://www.nice.org.uk/guidance/ng137.

3. S. Kawachiya, D. Bodri, N. Shimada, K. Kato, Y. Takehara, and O. Kato, "Blastocyst Culture Is Associated With an Elevated Incidence of Monozygotic Twinning After Single Embryo Transfer," *Fertility and Sterility* 95 (2011): 2140–2142.

4. T. Nakasuji, H. Saito, R. Araki, et al., "The Incidence of Monozygotic Twinning in Assisted Reproductive Technology: Analysis Based on Results From the 2010 Japanese ART National Registry," *Journal of Assisted Reproduction and Genetics* 31 (2014): 803–807.

5. M. Dziadosz and M. I. Evans, "Re-Thinking Elective Single Embryo Transfer: Increased Risk of Monochorionic Twinning—A Systematic Review," *Fetal Diagnosis and Therapy* 42, no. 2 (2017): 81–91.

6. M. D. Kilby, P. N. Baker, H. O. Critchley, and D. J. Field, eds., "Consensus Views Arising From the 50th Study Group: Multiple Pregnancy," in *Multiple Pregnancy. In: Multiple Pregnancy* (London, UK: RCOG Press, 2006), 283–286.

7. C. Francisco, D. Wright, Z. Benkő, A. Syngelaki, and K. H. Nicolaides, "Competing-Risks Model in Screening for Pre-Eclampsia in Twin Pregnancy by Maternal Characteristics and Medical History," *Ultrasound in Obstetrics & Gynecology* 50, no. 4 (2017): 501–506.

8. Y. Ezra, D. Shveiky, E. Ophir, et al., "Intensive Management and Early Delivery Reduce Antenatal Mortality in Monoamniotic Twin Pregnancies," *Acta Obstetricia et Gynecologica Scandinavica* 84 (2005): 432–435.

9. C. Visintin, M. A. Mugglestone, D. James, M. D. Kilby, and Guideline Development Group, "Antenatal Care for Twin and Triplet Pregnancies: Summary of NICE Guidance," *British Medical Journal* 343 (2011): d5714.

10. NHS Evidence, "Multiple Pregnancy: Evidence Update March 2013. A Summary of Selected New Evidence Relevant to NICE Clinical Guideline 129 'The Management of Twin and Triplet Pregnancies in the Antenatal Period' (2011)," Evidence Update 37. Manchester: NICE; 2013.

11. E. Litwinska, A. Syngelaki, B. Cimpoca, L. Frei, and K. H. Nicolaides, "Outcome of Twin Pregnancy With Two Live Fetuses at 11-13 Weeks' Gestation," *Ultrasound in Obstetrics & Gynecology* 55, no. 1 (2020): 32–38.

12. M. L. Denbow, P. Cox, M. Taylor, D. M. Hammal, and N. M. Fisk, "Placental Angioarchitecture in Monochorionic Twin Pregnancies: Relationship to Fetal Growth, Fetofetal Transfusion Syndrome, and Pregnancy Outcome," *American Journal of Obstetrics and Gynecology* 182 (2000): 417–426.

13. S. F. de Villiers, F. Slaghekke, J. M. Middeldorp, F. J. Walther, D. Oepkes, and E. Lopriore, "Arterio-Arterial Vascular Anastomoses in

Monochorionic Placentas With and Without Twin–Twin Transfusion Syndrome," *Placenta* 33 (2012): 652–654.

14. B. Cimpoca, A. Syngelaki, M. A. Chi, E. Savvoulidou, and K. H. Nicolaides, "Twin Pregnancy With Two Live Fetuses at 11-13 Weeks: Effect of One Fetal Death on Pregnancy Outcome," *Ultrasound in Obstetrics & Gynecology* 55, no. 4 (2020): 482–488.

15. M. D. Kilby, C. Platt, M. J. Whittle, J. Oxley, and G. B. Lindop, "Renin Gene Expression in Fetal Kidneys of Pregnancies Complicated by Twin-Twin Transfusion Syndrome," *Pediatric and Developmental Pathology* 4 (2001): 175–179.

16. D. Mahieu-Caputo, A. Meulemans, J. Martinovic, et al., "Paradoxic Activation of the Renin-Angiotensin System in Twin-Twin Transfusion Syndrome: An Explanation for Cardiovascular Disturbances in the Recipient," *Pediatric Research* 58, no. 4 (2005): 685–688.

17. A. Umur, M. J. van Gemert, and P. G. Nikkels, "Monoamniotic-Versus Diamniotic-Monochorionic Twin Placentas: Anastomoses and Twin-Twin Transfusion Syndrome," *American Journal of Obstetrics and Gynecology* 189 (2003): 1325–1329.

18. Y. L. Chang, S. D. Chang, A. S. Chao, P. C. Hsieh, C. N. Wang, and T. H. Wang, "Clinical Outcome and Placental Territory Ratio of Monochorionic Twin Pregnancies and Selective Intrauterine Growth Restriction With Different Types of Umbilical Artery Doppler," *Prenatal Diagnosis* 29 (2009): 253–256.

19. D. P. Zhao, S. F. de Villiers, F. Slaghekke, et al., "Prevalence, Size, Number and Localization of Vascular Anastomoses in Monochorionic Placentas," *Placenta* 34 (2013): 589–593.

20. D. Gallot, J. P. Saulnier, D. Savary, H. Laurichesse-Delmas, and D. Lemery, "Ultrasonographic Signs of Twin-Twin Transfusion Syndrome in a Monoamniotic Twin Pregnancy," *Ultrasound in Obstetrics & Gynecology* 25 (2005): 308–309.

21. L. S. A. Tollenaar, F. Slaghekke, L. Lewi, et al., "Spontaneous Twin Anemia Polycythemia Sequence: Diagnosis, Management, and Outcome in an International Cohort of 249 Cases," *American Journal of Obstetrics and Gynecology* 224, no. 2 (2021): 213.e1–213.e11.

22. F. Slaghekke, E. Lopriore, L. Lewi, et al., "Fetoscopic Laser Coagulation of the Vascular Equator Versus Selective Coagulation for Twin-To-Twin Transfusion Syndrome: An Open-Label Randomised Controlled Trial," *Lancet* 383 (2014): 2144–2151.

23. E. Lopriore, J. Deprest, F. Slaghekke, et al., "Placental Characteristics in Monochorionic Twins With and Without Twin Anemia-Polycythemia Sequence," *Obstetrics and Gynecology* 112 (2008): 753–758.

24. E. Lopriore, F. Slaghekke, D. Oepkes, J. M. Middeldorp, F. P. Vandenbussche, and F. J. Walther, "Hematological Characteristics in Neonates With Twin anemia–Polycythemia Sequence (TAPS)," *Prenatal Diagnosis* 30 (2010): 251–255.

25. F. Slaghekke, W. J. Kist, D. Oepkes, et al., "Twin Anemia-Polycythemia Sequence: Diagnostic Criteria, Classification, Perinatal Management and Outcome," *Fetal Diagnosis and Therapy* 27 (2010): 181–190.

26. A. Khalil, I. Beune, K. Hecher, et al., "Consensus Definition and Essential Reporting Parameters of Selective Fetal Growth Restriction in Twin Pregnancy: A Delphi Procedure," *Ultrasound in Obstetrics & Gynecology* 53, no. 1 (2019): 47–54, Erratum in: Ultrasound Obstet Gynecol 2020;56(6):967.

27. N. J. Sebire, C. D'Ercole, W. Soares, R. Nayar, and K. H. Nicolaides, "Intertwin Disparity in Fetal Size in Monochorionic and Dichorionic Pregnancies," *Obstetrics and Gynecology* 91 (1998): 82–85.

28. A. Syngelaki, B. Cimpoca, E. Litwinska, R. Akolekar, and K. H. Nicolaides, "Diagnosis of Fetal Defects in Twin Pregnancies at Routine 11-13-Week Ultrasound Examination," *Ultrasound in Obstetrics & Gynecology* 55, no. 4 (2020): 474–481.

29. L. Lewi and J. Deprest, "Management of Twin Pregnancies: Where Do We Go From Here?," *Ultrasound in Obstetrics & Gynecology* 41 (2013): 601–604.

30. S. G. Carroll, P. W. Soothill, S. A. Abdel-Fattah, H. Porter, I. Montague, and P. M. Kyle, "Prediction of Chorionicity in Twin Pregnancies at 10–14 Weeks of Gestation," *British Journal of Obstetrics and Gynaecology* 109 (2002): 182–186.

31. M. V. Senat, E. Quarello, J. M. Levaillant, A. Buonumano, M. Boulvain, and R. Frydman, "Determining Chorionicity in Twin Gestations: Three-Dimensional (3D) Multiplanar Sonographic Measurement of Intra-Amniotic Membrane Thickness," *Ultrasound in Obstetrics & Gynecology* 28 (2006): 665–669.

32. M. E. D'Alton and D. K. Dudley, "The Ultrasonographic Prediction of Chorionicity in Twin Gestation," *American Journal of Obstetrics and Gynecology* 160 (1989): 557–561.

33. T. Dias, S. Ladd, S. Mahsud-Dornan, A. Bhide, A. T. Papageorghiou, and B. Thilaganathan, "Systematic Labeling of Twin Pregnancies on Ultrasound," *Ultrasound in Obstetrics & Gynecology* 38, no. 2 (2011): 130–133.

34. M. K. Kristiansen, B. S. Joensen, C. K. Ekelund, O. B. Petersen, P. Sandager, and Danish Fetal Medicine Study Group, "Perinatal Outcome After First-Trimester Risk Assessment in Monochorionic and Dichorionic Twin Pregnancies: A Population-Based Register Study," *British Journal of Obstetrics and Gynaecology* 122, no. 10 (2015): 1362–1369.

35. K. E. Hack, J. B. Derks, S. G. Elias, et al., "Increased Perinatal Mortality and Morbidity in Monochorionic Versus Dichorionic Twin Pregnancies: Clinical Implications of a Large Dutch Cohort Study," *British Journal of Obstetrics and Gynaecology* 115 (2008): 58–67.

36. Southwest Thames Obstetric Research Collaborative (STORK), "Prospective Risk of Late Stillbirth in Monochorionic Twins: A Regional Cohort Study," *Ultrasound in Obstetrics & Gynecology* 39 (2012): 500–504.

37. F. D'Antonio, A. Khalil, T. Dias, B. Thilaganathan, and Southwest Thames Obstetric Research Collaborative (STORK), "Crown–Rump Length Discordance and Adverse Perinatal Outcome in Twins: Analysis of the Southwest Thames Obstetric Research Collaborative (STORK) Multiple Pregnancy Cohort," *Ultrasound in Obstetrics & Gynecology* 41 (2013): 621–626.

38. E. Litwinska, A. Syngelaki, B. Cimpoca, I. Sapantzoglou, and K. H. Nicolaides, "Intertwin Discordance in Fetal Size at 11-13 Weeks' Gestation and Pregnancy Outcome," *Ultrasound in Obstetrics & Gynecology* 55, no. 2 (2020): 189–197.

39. L. Lewi, J. Jani, I. Blickstein, et al., "The Outcome of Monochorionic Diamniotic Twin Gestations in the Era of Invasive Fetal Therapy: A Prospective Cohort Study," *American Journal of Obstetrics and Gynecology* 199, no. 514 (2008): e1–e8.

40. A. L. Adegbite, S. Castille, S. Ward, and R. Bajoria, "Neuromorbidity in Preterm Twins in Relation to Chorionicity and Discordant Birth Weight," *American Journal of Obstetrics and Gynecology* 190 (2004): 156–163.

41. O. Barigye, L. Pasquini, P. Galea, H. Chambers, L. Chappell, and N. M. Fisk, "High Risk of Unexpected Late Fetal Death in Monochorionic Twins Despite Intensive Ultrasound Surveillance: A Cohort Study," *PLoS Medicine* 2 (2005): e172.

42. P. D. Griffiths, S. Sharrack, K. L. Chan, J. Bamfo, F. Williams, and M. D. Kilby, "Fetal Brain Injury in Survivors of Twin Pregnancies Complicated by Demise of One Twin as Assessed by In Utero MR Imaging," *Prenatal Diagnosis* 35, no. 6 (2015): 583–591.

43. G. Conte, A. Righini, P. D. Griffiths, et al., "Brain-Injured Survivors of Monochorionic Twin Pregnancies Complicated by Single Intrauterine Death: MR Findings in a Multicenter Study," *Radiology* 288, no. 2 (2018): 582–590.

44. S. Shinar, K. Harris, T. Van Mieghem, et al., "Early Imaging Predictors of Cerebral Ischemic Injury in Monochorionic Pregnancies Complicated by Spontaneous Single Intrauterine Death," *Ultrasound in Obstetrics & Gynecology* 59, no. 4 (2021): 497–505, https://doi.org/10.1002/uog.24844.

45. S. Galeva, L. Konstantinidou, M. M. Gil, R. Akolekar, and K. H. Nicolaides, "Routine First-Trimester Screening for Fetal Trisomies in Twin Pregnancy: Cell-Free Fetal DNA Test Contingent on Results From Combined Test," *Ultrasound in Obstetrics & Gynecology* 53, no. 2 (2019): 208–213.

46. F. Audibert, A. Gagnon, and Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada; Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists, "Prenatal Screening for and Diagnosis of Aneuploidy in Twin Pregnancies," *Journal of Obstetrics and Gynaecology Canada* 33 (2011): 754–767.

47. A. Garchet-Beaudron, S. Dreux, N. Leporrier, J. F. Oury, F. Muller, and ABA Study Group; Clinical Study Group, "Second-Trimester Down Syndrome Maternal Serum Marker Screening: A Prospective Study of 11 040 Twin Pregnancies," *Prenatal Diagnosis* 28 (2008): 1105–1109.

48. A. Khalil, R. Archer, V. Hutchinson, et al., "Noninvasive Prenatal Screening in Twin Pregnancies With Cell-Free DNA Using the IONA Test: A Prospective Multicenter Study," *American Journal of Obstetrics and Gynecology* 225, no. 1 (2021): 79.e1–79.e13.

49. H. Judah, M. M. Gil, A. Syngelaki, et al., "Cell-Free DNA Testing of Maternal Blood in Screening for Trisomies in Twin Pregnancy: Updated Cohort Study at 10-14 Weeks and Meta-Analysis," *Ultrasound in Obstetrics & Gynecology* 58, no. 2 (2021): 178–189.

50. "Screening for Down's Syndrome, Edwards' Syndrome and Patau's Syndrome: NIPT Updated 23 September 2021. NHS Fetal Anomaly Screening Programme (FASP)," Public Health England. Gov.UK, accessed January 20, 2022, https://www.gov.uk/government/publications/screening-for-downs-syndrome-edwards-syndrome-and-pataus-syndrome-non-invasive-prenatal-testing-nipt/screening-for-downs-syndrome-edwards-syndrome-and-pataus-syndrome-nipt.

51. M. M. Gil, R. Akolekar, M. S. Quezada, B. Bregant, and K. H. Nicolaides, "Analysis of Cell-Free DNA in Maternal Blood in Screening for Aneuploidies: Meta-Analysis," *Fetal Diagnosis and Therapy* 35 (2014): 156–173.

52. J. G. Hall, "Twinning," *Lancet* 362 (2003): 735–743.

53. L. Sperling, C. Kiil, L. U. Larsen, et al., "Detection of Chromosomal Abnormalities, Congenital Abnormalities and Transfusion Syndrome in Twins," *Ultrasound in Obstetrics & Gynecology* 29 (2007): 517–526.

54. Y. L. Chang, A. S. Chao, P. J. Cheng, et al., "Presence of a Single Fetal Major Anomaly in a Twin Pregnancy Does Not Increase the Preterm Rate," *Australian & New Zealand Journal of Obstetrics & Gynaecology* 44, no. 4 (2004): 332–336.

55. B. L. Anderson, F. S. Sherman, F. Mancini, and H. N. Simhan, "Fetal Echocardiographic Findings Are Not Predictive of Death in Twin-Twin Transfusion Syndrome," *Journal of Ultrasound in Medicine* 25 (2006): 455–459.

56. H. Li, T. Meng, T. Shang, et al., "Fetal Echocardiographic Screening in Twins for Congenital Heart Diseases," *Chinese Medical Journal* 120 (2007): 1391–1394.

57. "NHS Fetal Anomaly Screening Programme (FASP)," accessed November 5, 2015, https://www.gov.uk/topic/population-screening-programmes/fetal-anomaly.

58. F. D'Antonio, A. Familiari, B. Thilaganathan, et al., "Sensitivity of First-Trimester Ultrasound in the Detection of Congenital Anomalies in Twin Pregnancies: Population Study and Systematic Review," *Acta Obstetricia et Gynecologica Scandinavica* 95, no. 12 (2016): 1359–1367.

59. L. Lewi, P. Lewi, A. Diemert, et al., "The Role of Ultrasound Examination in the First Trimester and at 16 Weeks' Gestation to Predict Fetal Complications in Monochorionic Diamniotic Twin Pregnancies," *American Journal of Obstetrics and Gynecology* 199, no. 493 (2008): e1–e7.

60. W. B. Giles, "Doppler Ultrasound in Multiple Pregnancies," *Baillière's Clinical Obstetrics and Gynaecology* 12 (1998): 77–89.

61. R. Townsend, J. M. N. Duffy, F. Sileo, et al., "Core Outcome Set for Studies Investigating Management of Selective Fetal Growth Restriction in Twins," *Ultrasound in Obstetrics & Gynecology* 55, no. 5 (2020): 652–660.

62. O. T. Stirrup, A. Khalil, F. D'Antonio, B. Thilaganathan, and Southwest Thames Obstetric Research Collaborative (STORK), "Fetal Growth Reference Ranges in Twin Pregnancy: Analysis of the Southwest Thames Obstetric Research Collaborative (STORK) Multiple Pregnancy Cohort," *Ultrasound in Obstetrics & Gynecology* 45 (2015): 301–307.

63. A. Khalil, F. D'Antonio, T. Dias, D. Cooper, B. Thilaganathan, and Southwest Thames Obstetric Research Collaborative (STORK), "Ultrasound Estimation of Birth Weight in Twin Pregnancy: Comparison of Biometry Algorithms in the STORK Multiple Pregnancy Cohort," *Ultrasound in Obstetrics & Gynecology* 44 (2014): 210–220.

64. F. L. Mackie, M. J. Hall, R. K. Morris, and M. D. Kilby, "Early Prognostic Factors of Outcomes in Monochorionic Twin Pregnancy: Systematic Review and Meta-Analysis," *American Journal of Obstetrics and Gynecology* 219, no. 5 (2018): 436–446.

65. B. Cimpoca, A. Syngelaki, E. Litwinska, A. Muzaferovic, and K. H. Nicolaides, "Increased Nuchal Translucency at 11-13 Weeks' Gestation and Outcome in Twin Pregnancy," *Ultrasound in Obstetrics & Gynecology* 55, no. 3 (2020): 318–325.

66. MBRRACE-UK, "Perinatal Confidential Enquiry. Stillbirths and Neonatal Deaths in Twin Pregnancies," 2021, accessed January 20, 2022, https://www.google.co.uk/url?esrc=s&q=&rct=j&sa=U&url=https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/perinatal-report-2020-twins/MBRRACE-UK_Twin_Pregnancies_Confidential_Enquiry.pdf&ved=2ahUKEwjP9aqh1b31AhVynVwKHSTRAwYQFnoECAoQAg&usg=AOvVaw0CIaUZubZyEzUxY7-lQXEK.

67. R. A. Quintero, W. J. Morales, M. H. Allen, P. W. Bornick, P. K. Johnson, and M. Kruger, "Staging of Twin-Twin Transfusion Syndrome," *Journal of Perinatology* 19 (1999): 550–555.

68. R. A. Quintero, J. E. Dickinson, W. J. Morales, et al., "Stage-Based Treatment of Twin-Twin Transfusion Syndrome," *American Journal of Obstetrics and Gynecology* 188 (2003): 1333–1340.

69. T. Van Mieghem, E. Eixarch, L. Gucciardo, et al., "Outcome Prediction in Monochorionic Diamniotic Twin Pregnancies With Moderately Discordant Amniotic Fluid," *Ultrasound in Obstetrics & Gynecology* 37 (2011): 15–21.

70. I. Couck, S. Ponnet, L. Thewissen, et al., "The Detection, Outcome, and Presentation of Twin-Twin Transfusion Syndrome in Monochorionic Diamniotic Twin Pregnancies Followed With a Protocol of Fortnightly Ultrasound Examination," *Fetal Diagnosis and Therapy* 48, no. 5 (2021): 353–360.

71. R. Robyr, L. Lewi, L. J. Salomon, et al., "Prevalence and Management of Late Fetal Complications Following Successful Selective Laser Coagulation of Chorionic Plate Anastomoses in Twin-To-Twin Transfusion Syndrome," *American Journal of Obstetrics and Gynecology* 194 (2006): 796–803.

72. A. Khalil, S. Gordijn, W. Ganzevoort, et al., "Consensus Diagnostic Criteria and Monitoring of Twin Anemia-Polycythemia Sequence: Delphi Procedure," *Ultrasound in Obstetrics & Gynecology* 56, no. 3 (2020): 388–394.

73. L. S. A. Tollenaar, F. Slaghekke, L. Lewi, et al., "Treatment and Outcome of 370 Cases With Spontaneous or Post-Laser Twin Anemia-Polycythemia Sequence Managed in 17 Fetal Therapy Centers," *Ultrasound in Obstetrics & Gynecology* 56, no. 3 (2020): 378–387.

74. E. Gratacós, L. Lewi, E. Carreras, et al., "Incidence and Characteristics of Umbilical Artery Intermittent Absent and/or Reversed End-Diastolic Flow in Complicated and Uncomplicated Monochorionic Twin Pregnancies," *Ultrasound in Obstetrics & Gynecology* 23 (2004): 456–460.

75. E. Gratacós, L. Lewi, B. Muñoz, et al., "A Classification System for Selective Intrauterine Growth Restriction in Monochorionic

Pregnancies According to Umbilical Artery Doppler Flow in the Smaller Twin," *Ultrasound in Obstetrics & Gynecology* 30 (2007): 28–34.

76. L. M. Harper, K. A. Roehl, M. G. Tuuli, A. O. Odibo, and A. G. Cahill, "Sonographic Accuracy of Estimated Fetal Weight in Twins," *Journal of Ultrasound in Medicine* 32 (2013): 625–630.

77. F. M. Breathnach, F. M. McAuliffe, M. Geary, et al., "Definition of Intertwin Birth Weight Discordance," *Obstetrics and Gynecology* 118 (2011): 94–103.

78. F. D'Antonio, A. Khalil, B. Thilaganathan, and Southwest Thames Obstetric Research Collaborative (STORK), "Second-Trimester Discordance and Adverse Perinatal Outcome in Twins: The STORK Multiple Pregnancy Cohort," *British Journal of Obstetrics and Gynaecology* 121 (2014): 422–429.

79. D. V. Valsky, E. Eixarch, J. M. Martinez, F. Crispi, and E. Gratacós, "Selective Intrauterine Growth Restriction in Monochorionic Twins: Pathophysiology, Diagnostic Approach and Management Dilemmas," *Seminars in Fetal & Neonatal Medicine* 15 (2010): 342–348.

80. F. D'Antonio, A. Khalil, T. Dias, B. Thilaganathan, and Southwest Thames Obstetric Research Collaborative (STORK), "Weight Discordance and Perinatal Mortality in Twins: Analysis of the Southwest Thames Obstetric Research Collaborative (STORK) Multiple Pregnancy Cohort," *Ultrasound in Obstetrics & Gynecology* 41 (2013): 643–648.

81. M. J. Taylor, L. Govender, M. Jolly, L. Wee, and N. M. Fisk, "Validation of the Quintero Staging System for Twin-Twin Transfusion Syndrome," *Obstetrics and Gynecology* 100 (2002): 1257–1265.

82. J. E. Dickinson and S. F. Evans, "The Progression of Disease Stage in Twin-Twin Transfusion Syndrome," *Journal of Maternal-Fetal & Neonatal Medicine* 16 (2004): 95–101.

83. F. I. Luks, S. R. Carr, M. Plevyak, et al., "Limited Prognostic Value of a Staging System for Twin-To-Twin Transfusion Syndrome," *Fetal Diagnosis and Therapy* 19 (2004): 301–304.

84. A. Huber, W. Diehl, T. Bregenzer, B. J. Hackelöer, and K. Hecher, "Stage-Related Outcome in Twin–Twin Transfusion Syndrome Treated by Fetoscopic Laser Coagulation," *Obstetrics and Gynecology* 108 (2006): 333–337.

85. C. Bamberg, W. Diehl, A. Diemert, S. Sehner, and K. Hecher, "Differentiation Between TTTS Stages I vs II and III vs IV Does Not Affect Probability of Double Survival After Laser Therapy," *Ultrasound in Obstetrics & Gynecology* 58, no. 2 (2021): 201–206.

86. M. J. Raboisson, J. C. Fouron, J. Lamoureux, et al., "Early Intertwin Differences in Myocardial Performance During the Twin-To-Twin Transfusion Syndrome," *Circulation* 110 (2004): 3043–3048.

87. E. Michelfelder, W. Gottliebson, W. Border, et al., "Early Manifestations and Spectrum of Recipient Twin Cardiomyopathy in Twin–Twin Transfusion Syndrome: Relation to Quintero Stage," *Ultrasound in Obstetrics & Gynecology* 30 (2007): 965–971.

88. A. Huber, W. Diehl, L. Zikulnig, T. Bregenzer, B. J. Hackelöer, and K. Hecher, "Perinatal Outcome in Monochorionic Twin Pregnancies Complicated by Amniotic Fluid Discordance Without Severe Twin–Twin Transfusion Syndrome," *Ultrasound in Obstetrics & Gynecology* 27 (2006): 48–52.

89. Y. Ville, "Twin-To-Twin Transfusion Syndrome: Time to Forget the Quintero Staging System?," *Ultrasound in Obstetrics & Gynecology* 30 (2007): 924–927.

90. NHS England Specialised Services Clinical Reference Group for Fetal Medicine, "Clinical Commissioning Policy: Management of Twin to Twin Syndrome by Fetoscopic Laser Ablation," 2015 NHS England E12/P/b, London: NHS England, accessed November 5, 2015, https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/e12-mgmnt-twin-twin.pdf.

91. M. V. Senat, J. Deprest, M. Boulvain, A. Paupe, N. Winer, and Y. Ville, "Endoscopic Laser Surgery Versus Serial Amnioreduction for Severe Twin-To-Twin Transfusion Syndrome," *New England Journal of Medicine* 351 (2004): 136–144.

92. K. J. Moise, Jr., K. Dorman, G. Lamvu, et al., "A Randomized Trial of Amnioreduction Versus Septostomy in the Treatment of Twin-Twin Transfusion Syndrome," *American Journal of Obstetrics and Gynecology* 193 (2005): 701–707.

93. T. M. Crombleholme, D. Shera, H. Lee, et al., "A Prospective, Randomized, Multicenter Trial of Amnioreduction vs Selective Fetoscopic Laser Photocoagulation for the Treatment of Severe Twin-Twin Transfusion Syndrome," *American Journal of Obstetrics and Gynecology* 197, no. 396 (2007): e1–e9.

94. D. Roberts, J. P. Neilson, M. D. Kilby, and S. Gates, "Interventions for the Treatment of Twin-Twin Transfusion Syndrome," *Cochrane Database of Systematic Reviews* 2014, no. 1 (2014): CD002073.

95. D. Murgano, A. Khalil, F. Prefumo, et al., "Outcome of Twin-To-Twin Transfusion Syndrome in Monochorionic Monoamniotic Twin Pregnancy: Systematic Review and Meta-Analysis," *Ultrasound in Obstetrics & Gynecology* 55, no. 3 (2020): 310–317.

96. J. Stirnemann, F. Slaghekke, N. Khalek, et al., "Intrauterine Fetoscopic Laser Surgery Versus Expectant Management in Stage 1 Twin-To-Twin Transfusion Syndrome: An International Randomized Trial," *American Journal of Obstetrics and Gynecology* 224, no. 5 (2021): 528.e1–528.e12.

97. J. M. Middeldorp, E. Lopriore, M. Sueters, et al., "Twin-To-Twin Transfusion Syndrome After 26 Weeks of Gestation: Is There a Role for Fetoscopic Laser Surgery?," *British Journal of Obstetrics and Gynaecology* 114 (2007): 694–698.

98. D. Baud, R. Windrim, J. Keunen, et al., "Fetoscopic Laser Therapy for Twin-Twin Transfusion Syndrome Before 17 and After 26 Weeks' Gestation," *American Journal of Obstetrics and Gynecology* 208, no. 197 (2013): e1–e7.

99. D. Van Schoubroeck, L. Lewi, G. Ryan, et al., "Fetoscopic Surgery in Triplet Pregnancies: A Multicenter Case Series," *American Journal of Obstetrics and Gynecology* 191 (2004): 1529–1532.

100. W. Sepulveda, E. Surerus, H. Vandecruys, and K. H. Nicolaides, "Fetofetal Transfusion Syndrome in Triplet Pregnancies: Outcome After Endoscopic Laser Surgery," *American Journal of Obstetrics and Gynecology* 192 (2005): 161–164.

101. M. J. Taylor, E. Shalev, S. Tanawattanacharoen, et al., "Ultrasound-Guided Umbilical Cord Occlusion Using Bipolar Diathermy for Stage III/IV Twin-Twin Transfusion Syndrome," *Prenatal Diagnosis* 22 (2002): 70–76.

102. G. Paramasivam, R. Wimalasundera, M. Wiechec, E. Zhang, F. Saeed, and S. Kumar, "Radiofrequency Ablation for Selective Reduction in Complex Monochorionic Pregnancies," *British Journal of Obstetrics and Gynaecology* 117 (2010): 1294–1298.

103. R. C. Wimalasundera, "Selective Reduction and Termination of Multiple Pregnancies," *Seminars in Fetal & Neonatal Medicine* 15 (2010): 327–335.

104. O. Cavicchioni, M. Yamamoto, R. Robyr, Y. Takahashi, and Y. Ville, "Intrauterine Fetal Demise Following Laser Treatment in Twin-To-Twin Transfusion Syndrome," *British Journal of Obstetrics and Gynaecology* 113 (2006): 590–594.

105. I. Blickstein, B. Arabin, F. A. Chervenak, et al., "The Istanbul International Consensus Statement on the Perinatal Care of Multiple Pregnancy," *Journal of Perinatal Medicine* 35 (2007): 465–467.

106. National Institute for Health and Care Excellence. *NICE Guideline NG 25. Preterm Labour and Birth*. (London: NICE, 2015). Updated 2019.

107. E. Gratacós, E. Carreras, J. Becker, et al., "Prevalence of Neurological Damage in Monochorionic Twins With Selective Intrauterine Growth Restriction and Intermittent Absent or Reversed End-Diastolic Umbilical Artery Flow," *Ultrasound in Obstetrics & Gynecology* 24 (2004): 159–163.

108. S. Kumar, G. Paramasivam, E. Zhang, et al., "Perinatal- and Procedure-Related Outcomes Following Radiofrequency Ablation in Monochorionic Pregnancy," *American Journal of Obstetrics and Gynecology* 210, no. 454 (2014): e1–e6.

109. Royal College of Obstetricians and Gynaecologists, "The Investigation and Management of the Small-For-Gestational-Age Fetus," 2013 Green-top Guideline No. 31, London, UK, RCOG.

110. L. Genova, F. Slaghekke, F. J. Klumper, et al., "Management of Twin anemia-Polycythemia Sequence Using Intrauterine Blood Transfusion for the Donor and Partial Exchange Transfusion for the Recipient," *Fetal Diagnosis and Therapy* 34 (2013): 121–126.

111. E. Lopriore, F. Slaghekke, K. J. Kersbergen, et al., "Severe Cerebral Injury in a Recipient With Twin Anemia—Polycythemia Sequence," *Ultrasound in Obstetrics & Gynecology* 41 (2013): 702–706.

112. T. Simões, N. Amaral, R. Lerman, F. Ribeiro, E. Dias, and I. Blickstein, "Prospective Risk of Intrauterine Death of Monochorionic-Diamniotic Twins," *American Journal of Obstetrics and Gynecology* 195 (2006): 134–139.

113. S. S. Ong, J. Zamora, K. S. Khan, and M. D. Kilby, "Prognosis for the Co-Twin Following Single-Twin Death: A Systematic Review," *British Journal of Obstetrics and Gynaecology* 113 (2006): 992–998.

114. S. C. Hillman, R. K. Morris, and M. D. Kilby, "Co-Twin Prognosis After Single Fetal Death: A Systematic Review and Meta-Analysis," *Obstetrics and Gynecology* 118 (2011): 928–940.

115. F. L. Mackie, A. Rigby, R. K. Morris, and M. D. Kilby, "Prognosis of the Co-Twin Following Spontaneous Single Intrauterine Fetal Death in Twin Pregnancies: A Systematic Review and Meta-Analysis," *British Journal of Obstetrics and Gynaecology* 126, no. 5 (2019): 569–578.

116. A. Righini, S. Salmona, E. Bianchini, et al., "Prenatal Magnetic Resonance Imaging Evaluation of Ischemic Brain Lesions in the Survivors of Monochorionic Twin Pregnancies: Report of 3 Cases," *Journal of Computer Assisted Tomography* 28 (2004): 87–92.

117. B. Weisz, C. Hoffmann, S. Ben-Baruch, et al., "Early Detection by Diffusion-Weighted Sequence Magnetic Resonance Imaging of Severe Brain Lesions After Fetoscopic Laser Coagulation for Twin–Twin Transfusion Syndrome," *Ultrasound in Obstetrics & Gynecology* 44 (2014): 44–49.

118. M. V. Senat, S. Loizeau, S. Couderc, J. P. Bernard, and Y. Ville, "The Value of Middle Cerebral Artery Peak Systolic Velocity in the Diagnosis of Fetal Anemia After Intrauterine Death of One Monochorionic Twin," *American Journal of Obstetrics and Gynecology* 189 (2003): 1320–1324.

119. U. Nicolini, M. P. Pisoni, E. Cela, and A. Roberts, "Fetal Blood Sampling Immediately Before and Within 24 Hours of Death in Monochorionic Twin Pregnancies Complicated by Single Intrauterine Death," *American Journal of Obstetrics and Gynecology* 179 (1998): 800–803.

120. M. V. Senat, J. P. Bernard, S. Loizeau, and Y. Ville, "Management of Single Fetal Death in Twin-To-Twin Transfusion Syndrome: A Role for Fetal Blood Sampling," *Ultrasound in Obstetrics & Gynecology* 20 (2002): 360–363.

121. M. Nakata, M. Sumie, S. Murata, I. Miwa, E. Kusaka, and N. Sugino, "A Case of Monochorionic Twin Pregnancy Complicated With Intrauterine Single Fetal Death With Successful Treatment of Intrauterine Blood Transfusion in the Surviving Fetus," *Fetal Diagnosis and Therapy* 22 (2007): 7–9.

122. D. Danon, R. Sekar, K. E. Hack, and N. M. Fisk, "Increased Stillbirth in Uncomplicated Monochorionic Twin Pregnancies: A Systematic Review and Meta-Analysis," *Obstetrics and Gynecology* 121 (2013): 1318–1326.

123. F. Cheong-See, E. Schuit, D. Arroyo-Manzano, et al., "Prospective Risk of Stillbirth and Neonatal Complications in Twin Pregnancies: Systematic Review and Meta-Analysis," *British Medical Journal* 6, no. 354 (2016): i4353.

124. J. F. Barrett, M. E. Hannah, E. K. Hutton, et al., "A Randomized Trial of Planned Cesarean or Vaginal Delivery for Twin Pregnancy," *New England Journal of Medicine* 369 (2013): 1295–1305.

125. J. J. Stirnemann, T. Quibel, M. Essaoui, L. J. Salomon, L. Bussieres, and Y. Ville, "Timing of Delivery Following Selective Laser Photocoagulation for Twin-To-Twin Transfusion Syndrome," *American Journal of Obstetrics and Gynecology* 207, no. 2 (2012): 127. e1–127.e6.

126. T. Dias, S. Mahsud-Dornan, A. Bhide, A. T. Papageorghiou, and B. Thilaganathan, "Cord Entanglement and Perinatal Outcome in Monoamniotic Twin Pregnancies," *Ultrasound in Obstetrics & Gynecology* 35 (2010): 201–204.

127. K. E. Hack, J. B. Derks, A. H. Schaap, et al., "Perinatal Outcome of Monoamniotic Twin Pregnancies," *Obstetrics and Gynecology* 113 (2009): 353–360.

128. T. Van Mieghem, R. De Heus, L. Lewi, et al., "Prenatal Management of Monoamniotic Twin Pregnancies," *Obstetrics and Gynecology* 124 (2014): 498–506.

129. MONOMONO Working Group, "Inpatient vs Outpatient Management and Timing of Delivery of Uncomplicated Monochorionic Monoamniotic Twin Pregnancy: The MONOMONO Study," *Ultrasound in Obstetrics & Gynecology* 53, no. 2 (2019): 175–183.

130. A. L. Adegbite, S. B. Ward, and R. Bajoria, "Perinatal Outcome of Spontaneously Conceived Triplet Pregnancies in Relation to Chorionicity," *American Journal of Obstetrics and Gynecology* 193 (2005): 1463–1471.

131. A. Geipel, C. Berg, A. Katalinic, et al., "Prenatal Diagnosis and Obstetric Outcomes in Triplet Pregnancies in Relation to Chorionicity," *British Journal of Obstetrics and Gynaecology* 112 (2005): 554–558.

132. A. T. Papageorghiou, K. Avgidou, V. Bakoulas, N. J. Sebire, and K. H. Nicolaides, "Risks of Miscarriage and Early Preterm Birth in Trichorionic Triplet Pregnancies With Embryo Reduction Versus Expectant Management: New Data and Systematic Review," *Human Reproduction* 21 (2006): 1912–1917.

133. P. Chaveeva, P. Kosinski, C. Birdir, L. Orosz, and K. H. Nicolaides, "Embryo Reduction in Dichorionic Triplets to Dichorionic Twins by Intrafetal Laser," *Fetal Diagnosis and Therapy* 35 (2014): 83–86.

134. L. Lewi, E. Gratacos, E. Ortibus, et al., "Pregnancy and Infant Outcome of 80 Consecutive Cord Coagulations in Complicated Monochorionic Multiple Pregnancies," *American Journal of Obstetrics and Gynecology* 194 (2006): 782–789.

135. G. Pagani, F. D'Antonio, A. Khalil, A. Papageorghiou, A. Bhide, and B. Thilaganathan, "Intrafetal Laser Treatment for Twin Reversed Arterial Perfusion Sequence: Cohort Study and Meta-Analysis," *Ultrasound in Obstetrics & Gynecology* 42 (2013): 6–14.

136. A. Roman, R. Papanna, A. Johnson, et al., "Selective Reduction in Complicated Monochorionic Pregnancies: Radiofrequency Ablation vs. Bipolar Cord Coagulation," *Ultrasound in Obstetrics & Gynecology* 36 (2010): 37–41.

137. K. Gaerty, R. M. Greer, and S. Kumar, "Systematic Review and Metaanalysis of Perinatal Outcomes After Radiofrequency Ablation and Bipolar Cord Occlusion in Monochorionic Pregnancies," *American Journal of Obstetrics and Gynecology* 213, no. 5 (2015): 637–643.

138. B. Weisz, R. Peltz, B. Chayen, et al., "Tailored Management of Twin Reversed Arterial Perfusion (TRAP) Sequence," *Ultrasound in Obstetrics & Gynecology* 23 (2004): 451–455.

139. T. C. Mackenzie, T. M. Crombleholme, M. P. Johnson, et al., "The Natural History of Prenatally Diagnosed Conjoined Twins," *Journal of Pediatric Surgery* 37 (2002): 303–309.

140. U. Agarwal, P. Dahiya, and A. Khosla, "Vaginal Birth of Conjoined Thoracopagus – A Rare Event," *Archives of Gynecology and Obstetrics* 269 (2003): 66–67.

Appendix 1

Explanation of Grades and Evidence Levels

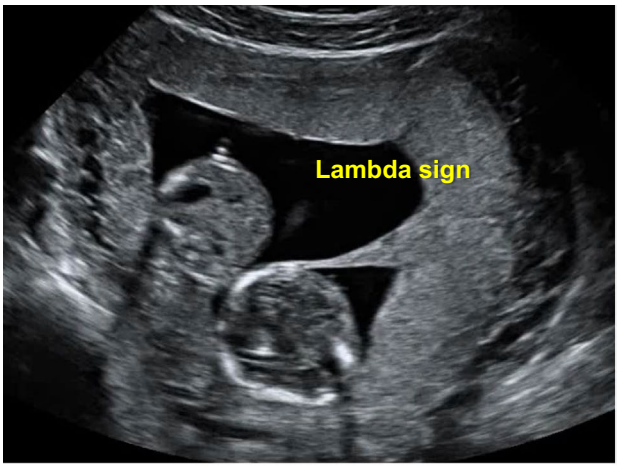
Classification of evidence levels

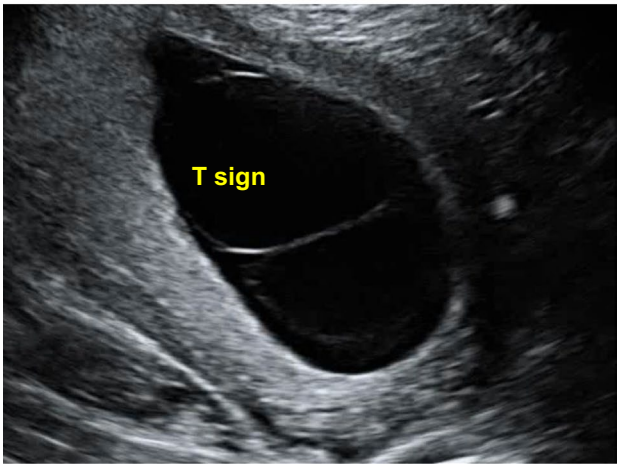
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias
1−	Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2−	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies, e.g. case reports, case series
4	Expert opinion
Grades of Recommendation	
A	At least one meta-analysis, systematic reviews or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+ directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
Good Practice Points	
GPP	Recommended best practice based on the clinical experience of the guideline development group*

*On the occasion when the guideline development group finds there is an important practical point that they wish to emphasise but for which there is not, nor is there likely to be any research evidence. This will typically be where some aspect of treatment is regarded as a such sound clinical practice that nobody is likely to question it; these are marked in the guideline. It must be emphasised that these are NOT an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

Appendix 2

Ultrasound Appearance of the Membrane Attachment to the Placenta

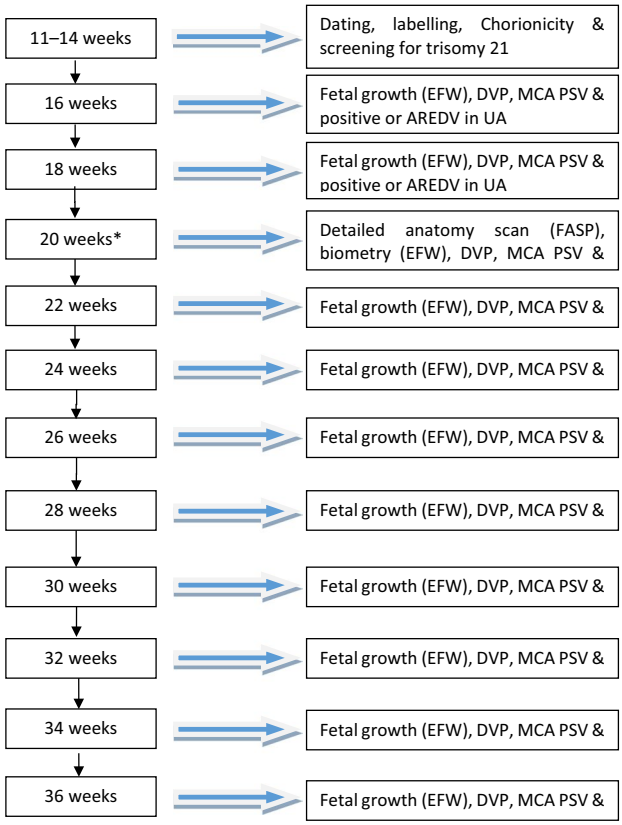




Reference: A. Khalil, M. Rodgers, et al., ISUOG Practice Guidelines: Role of Ultrasound in Twin Pregnancy, *Ultrasound in Obstetrics and Gynecology* 47 (2016): 247–263.

Appendix 3

Assessment in Uncomplicated Monochorionic Twin Pregnancy



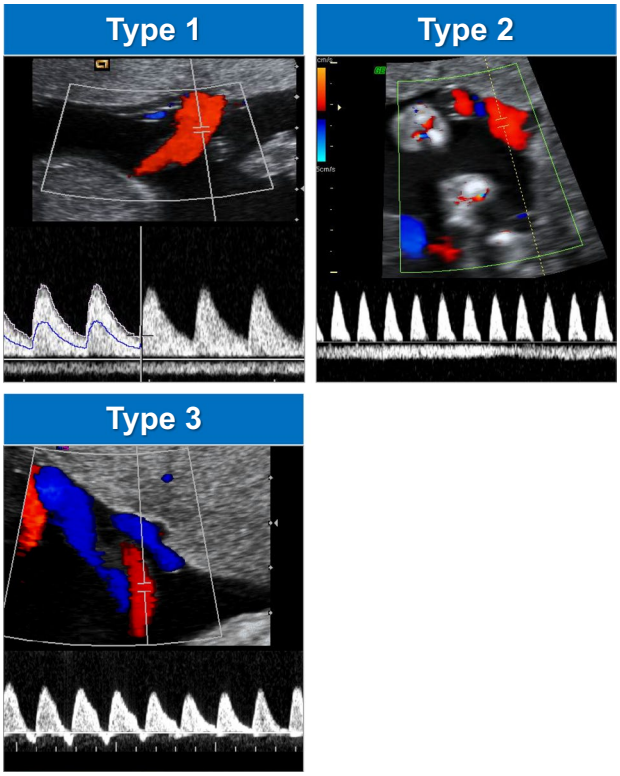
All routine antenatal assessment as in the NICE NGC 129 *Multiple Pregnancy. The Management of Twin and Triplet Pregnancies in the Antenatal Period* (2011) should be followed.

*At the 20–24-week scan, routine cervical length measurement is not advocated (NICE, 2011) outside a randomised controlled trial.

Abbreviations: AREDV, absent or reversed end-diastolic velocities; **DVP**, deepest vertical pocket; **EFW**, estimated fetal weight; **FASP**, fetal Anomaly Screening Programme; **UA**, umbilical artery; **UA-PI**, umbilical artery pulsatility index.

Appendix 4

Types of Selective Growth Restriction



Reference: A. Khalil, M. Rodgers, et al., ISUOG Practice Guidelines: Role of Ultrasound in Twin Pregnancy, *Ultrasound in Obstetrics and Gynecology* 47 (2016): 247–263.

Appendix 5

Consideration for Delivery Criteria for Twins Between 26 + 0 and 34 Weeks Onwards With sGR[†].

- Static growth of the IUGR fetus.
- Abnormal DV Doppler of the IUGR fetus (absent or reversed 'a' wave).
- Abnormal computerised CTG as defined by:
  - Spontaneous repeated persistent unprovoked fetal heart rate decelerations (greater than one deceleration).
  - 26 + 0 to 28 + 6 weeks: STV less than 2.6 ms.
  - 29 + 0 to 31 + 6 weeks: STV less than 3.0 ms.
  - 32 + 0 to 33 + 6 weeks: STV less than 3.5 ms.
  - 34 weeks onward: STV less than 4.5 ms.

([†]As indicated. The authors/developers have a consensus view that in the management of monochorionic twin pregnancies (either apparently uncomplicated or complicated), it is unwise to be over-prescriptive about the reliance upon any one method of surveillance in timing birth. Utilising several surveillance modalities (i.e., biometric and Doppler ultrasound +/− cCTG) is probably optimal, whilst realising that MC twin pregnancies have the propensity to behave unpredictably).

Appendix 6

Glossary of Terms

Monochorionic; MC	Multiple pregnancy with single placenta
Dichorionic; DC	Multiple pregnancy with two placentas
Monoamniotic; MA	Single amniotic sac
Diamniotic; DA	Two amniotic sacs
Triamniotic; TA	Three amniotic sacs (in triplets)
Twin-to-twin transfusion syndrome; TTTS	A morbid condition affecting monochorionic twin pregnancies where there is significant discordance in inter-twin liquor volumes and cardiovascular measurements
Twin Anaemia-Polycythaemia sequence; TAPS	An antenatal or postnatal diagnosis of significant haemoglobin difference between monochorionic twins (see text)
Middle Cerebral Artery Peak Systolic velocity; MCA PSV	The peak systolic velocity measured using Doppler insonation of the middle cerebral artery. The higher the MCA PSV, the lower the fetal haemoglobin
Selective Growth Restriction; sGR	A difference of estimated fetal weight of more than 20% between twins
Twin Reversed Arterial Perfusion (TRAP) Sequence	This is a monochorionic twin pregnancy where one twin, the 'pump' twin, is perfusing its co-twin, which has no cardiac activity and often is associated with major and lethal fetal anomalies

This guideline was produced on behalf of the Royal College of Obstetricians and Gynaecologists by: **Professor MD Kilby FRCOG, Birmingham and Dr L Bricker FRCOG, Abu Dhabi, United Arab Emirates**.

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