Twin pregnancies

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Abstract

Twin pregnancies occur in approximately 12 per 1,000 pregnancies worldwide, and are associated with substantially increased maternal, fetal and neonatal morbidity and mortality compared with singleton pregnancies. Although zygosity describes whether twins arise from one fertilised egg (monozygotic) or two separately fertilised ova (dizygotic), clinical risk is primarily determined by chorionicity (whether twins share a placenta) and amnionicity (whether twins share an amniotic sac). Accurate early determination of chorionicity and amnionicity is therefore fundamental to counselling, risk stratification, surveillance and clinical management, and should be established and documented consistently throughout pregnancy. Monochorionic twins are uniquely susceptible to complications arising from shared placental vascular anastomoses, including twin–twin transfusion syndrome (TTTS) and twin anaemia–polycythaemia sequence (TAPS). Preterm birth remains the leading cause of perinatal morbidity and mortality in twin pregnancies, with the risk of extreme preterm birth markedly higher than in singleton gestations. Contemporary surveillance strategies aim to identify evolving complications sufficiently early to enable timely intervention and optimise outcomes. This Primer reviews the epidemiology, mechanisms, and pathophysiology of twin pregnancy, as well as approaches to diagnosing, screening, preventing, and managing major maternal and fetal complications. We also discuss long-term outcomes, quality-of-life considerations, and emerging research priorities that are likely to shape future care.

Introduction

Multiple pregnancies account for approximately 1–3% of births worldwide, with twins comprising more than 95% of these pregnancies.[1,2] Global twinning rates have risen substantially in recent decades, largely driven by delayed childbearing and the widespread use of medically assisted reproduction (MAR), including ovulation induction and in vitro fertilisation.[3] Despite advances in antenatal surveillance and neonatal care, twin pregnancies remain associated with substantially increased maternal, fetal and neonatal morbidity and mortality compared with singleton gestations.[1] These risks are particularly pronounced in low-resource settings, where limited access to specialised obstetric and neonatal care disproportionately contributes to adverse outcomes.[3]

Twin pregnancy represents a unique biological and clinical model in human development. Although twins are commonly classified according to zygosity as monozygotic (MZ) or dizygotic (DZ), clinical outcomes are influenced primarily by chorionicity and amnionicity, that is, whether fetuses share a placenta and/or amniotic sac.[4] Monochorionic (MC) twins, which share a single placenta, are uniquely vulnerable to complications arising from placental vascular anastomoses, including twin–twin transfusion syndrome (TTTS), twin anaemia–polycythaemia sequence (TAPS), selective fetal growth restriction (sFGR), and acute intertwin transfusion events.[1] In addition, twins experience markedly increased rates of spontaneous and medically indicated preterm birth, which remains the principal driver of neonatal morbidity and long-term neurodevelopmental impairment.[1]

The pathophysiology of twin pregnancy reflects the interaction between plurality-associated maternal adaptation, placental architecture and fetal developmental biology. Twin gestations are associated with substantial cardiovascular, metabolic and haemodynamic adaptations, contributing to increased risks of hypertensive disorders, gestational diabetes mellitus and severe maternal morbidity.[5] At the same time, MC placentation introduces unique fetal circulatory dynamics that have no parallel in singleton pregnancy.[1] Advances in fetal imaging, placental biology, fetal therapy and neonatal care have transformed the management of complicated twin pregnancies, particularly MC disease, yet important uncertainties remain regarding screening strategies, optimal surveillance, long-term outcomes and equitable access to specialised care.[1,6]

Twin pregnancy also occupies a unique position in biomedical research. Twin studies have contributed fundamentally to understanding the relative contributions of genetic, epigenetic and environmental factors to human developmental variations and disease.[7] At the same time, twins themselves and their mothers have historically been underrepresented in obstetric and neonatal research, resulting in important gaps in evidence-based management.[8] Many diagnostic thresholds, growth standards and therapeutic interventions continue to be extrapolated from singleton populations despite important physiological differences between singleton and twin gestations.[1]

This Primer reviews the epidemiology, developmental biology, placentation, pathophysiology, diagnosis, screening and management of twin pregnancy, with emphasis on the complications that contribute most substantially to maternal and perinatal morbidity. We discuss advances in fetal therapy, neonatal and long-term outcomes, quality of life, ethical considerations and future research directions, highlighting the need for twin-specific evidence, multidisciplinary care pathways and equitable global access to specialised services.

Epidemiology

Incidence and global distribution

Twin births account for the overwhelming majority (>98%) of multiple pregnancies worldwide, whereas triplets and higher-order multiples are relatively rare, particularly in spontaneous conception.[3] Natural twinning rates vary markedly across populations and geographic regions (Fig 1). During the 2010s, approximately 1.6 million twin pairs were born annually worldwide, corresponding to a global twinning rate of approximately 12 per 1,000 births.[3] The highest natural twinning rates occur in sub-Saharan Africa, particularly within parts of Central Africa, where rates may exceed 18 per 1,000 births.[3,9] By contrast, twinning rates are substantially lower in East and Southeast Asia, where rates of 6–9 per 1,000 births are typical.[3] Intermediate rates are observed across Europe, North America and South Asia.[3]

Geographic variation in twinning rates is driven almost entirely by differences in DZ twinning, whereas MZ twinning occurs at a relatively stable rate of approximately 3–4 per 1,000 births across populations.[10,11] Population differences in DZ twinning reflect complex interactions between genetic predisposition, maternal age, parity, ancestry and use of MAR.[9, 12-15] Although genome-wide association studies have begun to identify genetic loci associated with DZ twinning in populations of European ancestry[15], the genetic determinants of twinning in African and Asian populations remain poorly characterised.

Temporal trends and medically assisted reproduction

Twinning rates increased substantially across most high-income countries between the 1980s and early 2010s (Fig 2).[3] In many regions, rates approximately doubled during this period, largely owing to delayed childbearing and widespread use of MAR, including ovulation induction, in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI).[3,13,16,17] The rise was particularly marked during the 1990s and 2000s, when transfer of multiple embryos during IVF was common practice. More recently, implementation of single embryo transfer policies and improvements in

embryo selection have contributed to declining or plateauing twinning rates in several high-income settings.[3,13,18]

In contrast to dizygotic twinning, MZ twinning rates were historically considered relatively constant across populations and over time.[10,11] However, recent studies suggest a modest increase in MZ twinning associated with ART, particularly following blastocyst transfer and embryo micromanipulation techniques.[16,17] These observations have challenged classical concepts of MZ twinning and stimulated renewed interest in the developmental biology of early embryonic divergence.

Mortality, morbidity and global inequities

Twin pregnancies are associated with substantially increased maternal, fetal and neonatal morbidity and mortality compared with singleton pregnancies.[1] Preterm birth, FGR and complications related to MC placentation contribute disproportionately to adverse outcomes. The burden of mortality is particularly high in low- and middle-income countries (LMICs), where access to specialised antenatal surveillance, fetal therapy and neonatal intensive care remains limited. In sub-Saharan Africa, twins account for a disproportionately large proportion of neonatal deaths despite representing a small minority of births.[19]

Maternal morbidity is also increased in twin pregnancy, including higher rates of hypertensive disorders, haemorrhage, gestational diabetes mellitus and severe maternal complications.[5] Twin pregnancy in LMIC settings has been associated with approximately two- to four-fold higher maternal mortality compared with singleton gestations, although absolute risk estimates vary considerably according to healthcare access and study setting. These disparities highlight the growing importance of twin pregnancy as a global public health challenge, particularly as twinning rates continue to rise in regions undergoing demographic and epidemiological transition.[3]

Mechanisms and Pathophysiology

Twin pregnancy arises through distinct biological pathways that differ fundamentally in embryonic origin, placental architecture and fetal physiology. DZ twins result from fertilisation of two separate oocytes and typically develop as dichorionic pregnancies with independent placental circulations. By contrast, MZ twins originate from a single fertilised oocyte and may share placental and amniotic structures, depending on early embryonic organisation and placental differentiation. Chorionicity is therefore the principal determinant of clinical outcome in twin pregnancy, linking early developmental biology to placental vascular architecture, fetal haemodynamics and risk of pregnancy complications.

Genetic variation

Research conducted during the past decade has revealed that MZ twins are not strictly genetically identical. This finding is variously explained by co-twin discordance for pre-twinning mutations (gene changes)[20], post-twinning mutations[21], differential X chromosome inactivation in female twins[22], mosaicism (coexistence of different cell lines)[23], and/or epigenetic processes[24]. On rare occasions, MZ twins and triplets differ in sex due to chromosomal nondisjunction[25]. DZ twins also show considerable variation, in that some twins have different fathers (heteropaternal twinning, due to superfecundation) or are conceived several weeks apart (superfetation)[26] or derived from two separate cell lines (chimerism). These and other types of MZ and DZ twins are examined in detail in other sources[27].

The cause of MZ Twinning

MZ twinning arises from a single fertilised oocyte and results in two genetically near-identical individuals (Fig 3)[28]. Traditional models of MZ twinning link inferred timing of embryonic division to chorionicity and amnionicity[28]; division before differentiation of the trophoblast is thought to produce dichorionic diamniotic twins, whereas division after formation of the inner cell mass is associated with MC placentation[28]. Very late or incomplete separation is proposed to bring about monoamniotic or conjoined twinning[28]. While this schema is heuristic and can be used as “a rule of thumb”, it is not based on direct observation, does not capture the biological processes driving embryonic divergence, and does not explain why MZ twinning occurs in only a small subset of pregnancies[29]. Despite these limitations, timing-based frameworks remain clinically useful as pragmatic tools for counselling, risk stratification and antenatal surveillance.

Evidence from IVF has highlighted the limitations of timing-based models. MZ twinning has been documented following elective single-embryo transfer at both cleavage and blastocyst stages,[30] and discordance between chorionicity and zygosity has been observed, including rare cases of MC DZ twins[31]. These findings indicate that placental configuration alone is insufficient to infer embryonic origin and suggest that multiple developmental pathways may lead to MZ twin formation.

Increasingly, MZ twinning is viewed as an outcome of early developmental plasticity rather than a discrete, deterministic splitting event[32]. Experimental and clinical observations indicate that the early mammalian embryo exhibits considerable flexibility in cell fate allocation, spatial organisation and lineage commitment[29]. MZ twinning may arise when early developmental trajectories diverge sufficiently to permit the establishment of two embryonic axes within a single conceptus[32]. Several non-mutually exclusive mechanisms have been proposed for the development/origin of MZ twinning, including early divergence within the inner cell mass, altered cell–cell adhesion or polarity cues during compaction, and mechanical or spatial constraints during blastocyst expansion and hatching[32]. Rather than a genetically encoded “twinning programme”[29], these findings are consistent with probabilistic-based models in which random fluctuation interacts with embryonic context to produce twin

formation.[32] MAR may act as a perturbation model that increases the likelihood of such divergence, without representing a primary cause of MZ twinning.

Time-lapse imaging studies in the context of IVF have provided rare, direct observations of early embryonic events relevant to MZ twinning[33]. Retrospective cohort studies combining single blastocyst transfer with blinded time-lapse annotation have documented patterns consistent with inner cell mass splitting or duplication during early blastocyst development[33]. These observations support the concept that MZ twinning can arise after implantation-competent stages and that early embryonic organisation is dynamic rather than fixed.

Although MZ twins share a common genome, molecular studies demonstrate that divergence can occur very early in development[34]. Long after birth, epigenomic analyses have detected persistent DNA methylation signatures in MZ twins that are consistent with early embryonic programming events[34]. These findings provide independent support for early developmental divergence and plasticity, without implying a specific timing or mechanism of twin formation. The common wisdom has been that separate fetal membranes and placenta reflect early zygotic splitting; however, this understanding, while plausible, has not been scientifically confirmed[27].

Rare and atypical twinning phenotypes, such as MC DZ twins, chimerism, and conjoined twins, suggest that early human development permits a spectrum of organisational outcomes involving partial separation, duplication or sustained tissue continuity[29]. Together, these observations support a continuum model of early embryonic organisation, of which MZ twinning represents one outcome rather than a well-described developmental anomaly[35].

Pathophysiology of fetal complications in twin pregnancies

The pathophysiology of twin pregnancy reflects the interaction between embryonic developmental processes, placental sharing, vascular anastomoses and maternal physiological adaptation. MC placentation introduces unique circulatory dynamics that have no equivalent in singleton pregnancy, predisposing to haemodynamic instability, unequal placental sharing and chronic or acute intertwin transfusion. At the same time, all twin pregnancies are associated with increased metabolic, cardiovascular and mechanical demands that contribute to maternal complications and preterm birth.

In twin pregnancies, outcomes depend on chorionicity and amnionicity[4]. DC twins have separate circulations, whereas MC twins have a shared circulation. The later the cleavage, the more structures these MZ twins allegedly share[36], and the higher the risk of complications and structural anomalies[37,38]. All DC twins and 95% of MC twins are diamniotic (DA); 5% of MC pairs are MC monoamniotic (MCMA), sharing a single amniotic cavity. MC pregnancies are at risk of transfusion imbalances, which largely explain their three times higher loss rate (11%) as compared to DC twins

(3%)[37]; MCMA pregnancies are at high risk of cord entanglement. The ideal MC placenta is equally divided with both cords inserting similarly within the placental disk (either both marginal, eccentric or velamentous), with a bidirectional artery-to-artery (AA) connection that balances the unidirectional flow across any artery-to-vein (AV) anastomoses (Fig 4)[39-41].

Fetal complications unique to MC twins

In about 15% of MCDA twin pregnancies, the shared circulation leads to chronic and acute transfusion imbalances, including TTTS, TAPS, and acute perimortem or peripartum transfusion (Fig 5). Chronic TTTS occurs in 10% of MCDA twins, usually before 26 weeks[42]. TTTS is a sonographic diagnosis based on a major amniotic fluid discordance with an oligouric hypovolemic (with reduced plasma volume and reduced urinary output) donor having little or no fluid, and a polyuric hypervolemic (with increased plasma volume and increased urinary output) recipient with severe polyhydramnios. Although there is no unique placental pattern, the typical TTTS placenta in up to two-thirds of cases lacks the bidirectional AA anastomosis (vascular connections)[40,41,43], and may contain a velamentous cord insertion (into the fetal membranes rather than directly into the placental mass) or vein-to-vein connections[41,43].

TAPS is marked by a major intertwin haemoglobin discordance, unlike the fluid discordance seen in TTTS. TAPS occurs in up to 5% of MCDA twins and typically presents after 26 weeks[42]. TAPS placentas contain only minuscule (< 1mm) anastomoses and usually lack the bidirectional AA anastomosis[44] (Fig 6). TAPS develops when red blood cells slowly transfer through these hair-thin anastomoses, causing gradual anaemia in one twin and polycythemia in the other. In TTTS, any haemoglobin discordance may be masked by volume shifts; volume contraction with oliguria and oligohydramnios hides donor anaemia, whereas volume expansion with polyuria and polyhydramnios dilutes recipient polycythemia[45]. However, 5-10% of TTTS cases exhibit features of both syndromes[46], when few intermediate-size anastomoses are present and volume compensation fails[47]. Furthermore, post-laser TAPS can occur after incomplete surgery for TTTS, if coagulation is incomplete and small anastomoses are missed.[48,49]

While TTTS and TAPS develop over days or weeks, acute imbalances within minutes are associated with a large AA or VV connection[50]. In acute perimortem transfusion, the surviving twin exsanguinates into its demised co-twin, causing double demise in 50-60% of cases and a 20%-30% risk of antenatal brain damage in the surviving co-twin[51,52]. During vaginal birth, acute peripartum transfusion affects less than 5% of MC twins, often triggered by fetal heart rate decelerations or delayed cord clamping[53]. MCMA placentas usually have side-by-side cord insertions with a large AA or VV connection (Fig 7)[54], making them less prone to TTTS and TAPS but more vulnerable to acute imbalances, resulting in double demise[55].

Twin-reversed arterial perfusion (TRAP) and conjoined twins are rare anomalies unique to MC twins. TRAP occurs in about 2.5% of MC pairs[56] when an early embryonic demise leads the surviving “pump” twin to supply its demised “acardiac” twin through a large AA anastomosis[57]. Conjoined twins are MCMA twins who also share body parts. Comprising 1% of MC twins[58], they result from a late splitting after the embryonic disk starts to form.

Fetal complications not unique to MC twins

Compared with singletons, both MC and DC twins are more vulnerable to impaired growth. As the pregnancy enters the third trimester, twin growth velocity starts to lag behind that of singletons, particularly in MC pairs[59]. Whether this slower growth is a benign adaptation or a pathological process remains a subject of debate.

A phenomenon unique to twins is sFGR, in which one twin is smaller than its co-twin. Since DC twins have separate placental circulations and 90% are DZ, size discordance likely reflects differences in placental function, genetic factors, and/or discordant congenital infections, as in singletons. MC twins share the same genetic growth potential, so theoretically, they should grow concordantly. Besides placental function, their nutrient and oxygen supply is determined by how evenly the placenta is divided and the blood flow across the placental anastomoses[39]. Growth discordance in MC pairs strongly correlates with an unevenly divided placenta, which is often reflected by a discordant cord insertion (Fig 8). Typically, the normally growing twin’s cord inserts centrally in the placenta, and the smaller twin has a marginal or velamentous cord insertion[41,60]. However, the vascular anastomoses may both alleviate or aggravate growth discordance in MC pregnancies[39,44,61,62].

Another unique complication in twin pregnancies is the intrauterine demise (IUD) of one fetus. After the first trimester, this occurs in about 2% of dichorionic (DC) twins and 10% of MC twins[37,52]. In MC pregnancies, approximately half of these losses are iatrogenic, typically following fetal therapy that separates the shared circulation in cases such as TTTS, sFGR, or fetal anomalies and 80% of co-twins survive[42,63]. In contrast, spontaneous IUD in MC twins presents as double IUD in 50–60% of cases, and surviving co-twins face a 20–30% risk of antenatal brain injury due to acute transfusion through placental vascular connections[51,52]. Because DC twins have separate circulations, the surviving fetus is not directly affected by the co-twin’s death. However, in both MC and DC pregnancies, single IUD increases the likelihood of preterm birth, with the risk increasing when the demise occurs later in gestation[64].

A structural anomaly without chromosomal abnormality is present in about 1 in 50 singleton pregnancies[38]. In DC twins, because of the presence of two fetuses, the rate of anomalies rises to 1 in 20 DC pairs[38]. The risk of cardiac anomalies may be slightly higher, as 10% of DC twins are MZ and many result from fertility treatment. In MCDA pairs, the rate of structural anomalies is approximately 1 in 10 pairs, with one twin typically affected[38], while in MCMA, the rate is 1 in 5 pregnancies[65]. The higher anomaly rate in MC twins likely stems from both the developmental consequences

intrinsic to monozygotic twinning, which predispose to midline and laterality defects, and from acquired lesions caused by transfusion imbalances, which can result in cardiac dysfunction or vascular disruptions affecting the brain, bowel, kidneys, or limbs [66]. When adjusted for maternal age, aneuploidy is less common in twins than in singletons, probably because these pregnancies are less likely to survive in a twin setting[65]. A comparison of DC, MCDA, and MCMA twin pregnancies is illustrated in Fig 9.

Preterm Birth

Twin gestations frequently result in preterm birth: approximately 55–60% deliver preterm (<37 weeks), and 10–12% very preterm (<32 weeks)[67]. Preterm birth in twin gestations arises through overlapping obstetrical pathways. Spontaneous preterm labor with intact membranes accounts for 45–50% of cases. Preterm prelabor rupture of membranes contributes 20–25%, while medically indicated preterm delivery represents 20–25%, most often related to hypertensive disorders, FGR, or fetal compromise related to complications of MC twins[68]. Cervical insufficiency is associated with delivery at very early gestational ages[69,70].

Gestational age (GA) at delivery, rather than twin status itself, is the dominant determinant of prognosis[71,72]; the risk of adverse short- and long-term outcomes increases in a dose–response manner with decreasing GA, irrespective of plurality[72]. When analyses adjust for GA and birthweight, differences in long-term health, neurodevelopmental, and functional outcomes are attenuated or disappear[71]; the excess burden of adverse outcomes observed in twins is largely mediated by their increased likelihood of being born preterm.

Pre-eclampsia

Individuals with multiple pregnancies have a substantially increased risk of pre-eclampsia, with earlier onset and greater severity compared with singleton gestations[73]. Crude pre-eclampsia rates in twins are three to fourfold higher than those of singletons, but these figures can be misleading since twins are often delivered earlier[73,74]. When GA is considered, in ongoing pregnancies the cumulative incidence of preterm pre-eclampsia (<37 weeks) is approximately eight to ninefold higher in twins compared to singletons[73,75].

Gestational diabetes

Gestational diabetes mellitus (GDM) is a common pregnancy complication[76-78], affecting 6-10% of all pregnancies in North America[79,80]. Twin pregnancies are associated with a higher incidence of GDM managed with diet alone than singleton pregnancies[81], which is believed to result from the greater transient increase in insulin resistance rather than reflecting a maternal predisposition to type-2 diabetes due to underlying beta-cell dysfunction, as is the case in singleton pregnancies[82-83]. In support of this hypothesis, women who had GDM in a twin pregnancy were 25%

less likely to develop future type-2 diabetes compared to those with GDM in a singleton pregnancy[84].

While mild GDM is more common in twin pregnancies, it is less likely to be associated with adverse outcomes and accelerated fetal growth than in singleton pregnancies, and may even reduce the risk of FGR[85]. In a recent meta-analysis, the association of GDM with cesarean delivery and neonatal intensive care unit (NICU) admission was weaker in twin than singleton pregnancies[86]. In addition, GDM was associated with reduced risk of having a small for gestational age (SGA) newborn (RR 0.89, 95% CI 0.81-0.97) and of neonatal death (RR 0.50, 95% CI 0.39-0.65) in twin but not singleton pregnancies. Similarly, a recent large population-based study found that GDM was less likely to be associated with hypertensive disorders of pregnancy, cesarean delivery, preterm birth, NICU admission, respiratory morbidity, jaundice requiring phototherapy, and neonatal hypoglycemia in twins compared with singletons[87].

Overall, these findings support the hypothesis that the greater transient increase in insulin resistance observed in twin pregnancies, often diagnosed as mild GDM based on standard diagnostic criteria, is merely a physiologic exaggeration of the normal increase in insulin resistance seen in singleton pregnancies rather than a pathology requiring treatment. This hypothesis aligns with the observation that most physiologic changes of pregnancy are exaggerated in twin pregnancies, including greater increases in cardiac output and blood volume[88].

Diagnosis, Screening and Prevention

The management of twin pregnancy depends fundamentally on accurate early classification of chorionicity and amnionicity, which determine subsequent risks, surveillance pathways and management strategies. Advances in ultrasound imaging, fetal Doppler assessment, placental biomarkers and non-invasive prenatal testing have transformed the diagnosis and monitoring of twin pregnancies. However, many screening algorithms and diagnostic thresholds continue to be extrapolated from singleton populations despite important physiological differences between singleton and twin gestations.[1]

First-trimester assessment

First-trimester ultrasound forms the cornerstone of assessment in twin pregnancy. Its principal aims are to establish GA, determine chorionicity and amnionicity, label fetuses consistently, and provide screening for chromosomal and structural abnormalities.[1] Accurate determination of chorionicity is the single most important component of early twin assessment, as chorionicity predicts the likelihood of placental vascular complications, guides surveillance frequency and influences counselling, fetal therapy and timing of delivery.[1,4] Diagnostic accuracy is highest

during the first trimester, before fusion of the amnion and chorion reduces the sonographic distinction between dichorionic and MC placentation[89].

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines recommend that spontaneous twin pregnancies should be dated before 13^{+6} weeks' gestation using the crown–rump length (CRL) of the larger twin.[1] In pregnancies presenting after 14 weeks, dating should be based on head circumference.[1] Although alternative approaches using the smaller or mean CRL have been explored[90,91], evidence remains insufficient to support their routine clinical use.

Before 10 weeks' gestation, chorionicity can be inferred from the number of gestational sacs: two separate sacs suggest dichorionic placentation, whereas a single gestational sac containing two embryos suggests monochorionicity[92]. Later in the first trimester, dichorionic pregnancies are characterised sonographically by the "lambda" or "twin peak" sign, reflecting chorionic tissue extending between the intertwin membranes, whereas MC diamniotic pregnancies demonstrate the thinner "T-sign" (Fig 10).[1,93] Combining membrane appearance with placental number provides very high diagnostic accuracy for chorionicity determination during the first trimester.[93] In MC pregnancies, assessment of amnionicity is particularly important because monoamniotic twins are at substantially increased risk of cord entanglement and acute fetal compromise.[1]

Consistent fetal labelling throughout pregnancy is essential to ensure accurate longitudinal assessment and safe clinical management. Labelling should ideally incorporate multiple anatomical landmarks, including placental location, cord insertion sites and fetal orientation, because fetal position relative to the cervix may change during gestation.[1]

Screening for chromosomal abnormalities

Screening for fetal aneuploidy should be offered to all twin pregnancies.[1] However, screening in twin pregnancy presents unique challenges, including uncertain zygosity in DC twin pairs, differing fetal fraction contributions, vanishing twin phenomena and the need to estimate risk either per fetus or per pregnancy according to chorionicity.

Cell-free DNA (cfDNA)-based non-invasive prenatal testing (NIPT) currently provides the highest screening performance for trisomy 21 in twin pregnancies. A meta-analysis of prospective studies reported a detection rate of 98.2% and false-positive rate of 0.05% for trisomy 21, with slightly lower performance for trisomies 18 and 13[94]. Subsequent studies have confirmed the high accuracy of cfDNA screening in twin gestations[95,96]. ISUOG guidelines therefore recommend cfDNA screening as the preferred approach for trisomy 21 screening in twin pregnancy where available.[1] Combined first-trimester screening using maternal age, nuchal translucency thickness, free β-human chorionic gonadotrophin and pregnancy-associated plasma protein-A remains an alternative when cfDNA testing is unavailable or declined.[97]

Vanishing twin syndrome is defined in the case of early demise of one twin, and it complicates the interpretation of both biochemical and cfDNA screening because residual placental DNA from the demised fetus may persist for several weeks.[1,98,99] Although recent data from the TRIDENT-2 study suggest acceptable performance of cfDNA screening for trisomy 21 following vanishing twin pregnancy, particularly after 15 weeks' gestation,[100] uncertainty remains regarding optimal screening strategies in this setting.

Ultrasound surveillance

Surveillance strategies in twin pregnancy differ fundamentally according to chorionicity. MC pregnancies require intensive longitudinal monitoring because placental vascular anastomoses permit rapid development of haemodynamic complications, whereas surveillance in dichorionic pregnancies focuses primarily on fetal growth, preterm birth and maternal complications.

In uncomplicated dichorionic twin pregnancies, ultrasound surveillance of fetal growth, amniotic fluid volume and Doppler studies is generally performed every four weeks after the second-trimester anomaly scan.[1,101] In MC pregnancies, surveillance is recommended every two weeks from 16 weeks' gestation onwards to facilitate early detection of TTTS, TAPS, sFGR and other complications associated with shared placental circulation.[1,102]

Doppler surveillance in twin pregnancy typically includes assessment of the umbilical artery pulsatility index (UA-PI), middle cerebral artery pulsatility index (MCA-PI) and ductus venosus pulsatility index (DV-PI). In MC pregnancies, middle cerebral artery peak systolic velocity (MCA-PSV) is additionally used to screen for fetal anaemia and TAPS.[1,101] The ultrasound surveillance and recommended delivery in twin pregnancy according to chorionicity and amnionicity are shown in Fig 11.

Diagnosis of complications unique to MC twins

TTTS reflects progressive haemodynamic imbalance arising from unidirectional placental vascular anastomoses and discordant amniotic fluid regulation between twins. The diagnosis is established sonographically by the presence of oligohydramnios in the donor twin and polyhydramnios in the recipient twin after 16 weeks' gestation.[1] Severity is commonly classified according to the Quintero staging system, although alternative systems incorporating cardiovascular assessment have also been proposed.[103]

TAPS differs pathophysiologically from TTTS in that it reflects chronic slow transfusion of erythrocytes across minuscule placental vascular anastomoses rather than major haemodynamic volume shifts. Prenatal diagnosis relies primarily on discordance in MCA-PSV between twins. ISUOG guidelines define TAPS by an MCA-PSV >1.5 multiples of the median (MoM) in the donor twin and <1.0 MoM in the recipient twin.[1] A recent Delphi consensus suggested alternative criteria incorporating delta MCA-PSV values between twins.[104] Additional sonographic

features may include discordant placental echogenicity and the “starry sky” appearance of the recipient liver.[1]

Twin reversed arterial perfusion (TRAP) sequence may be diagnosed during the first trimester by identification of an acardiac twin receiving retrograde perfusion from a structurally normal “pump” twin through abnormal placental vascular connections.[1,105]

Selective fetal growth restriction

Selective fetal growth restriction represents one of the most challenging complications in twin pregnancy. Importantly, sFGR in dichorionic and MC pregnancies likely represents biologically distinct disorders. In dichorionic twins, discordant growth largely reflects differences in placental function, fetal genetics or environmental exposures, analogous to singleton FGR. By contrast, MC sFGR arises within a shared genetic and placental environment and is strongly influenced by unequal placental sharing and vascular intertwin communication[1].

Diagnostic criteria for sFGR remain controversial. ISUOG guidelines define sFGR by the presence of one fetus with estimated fetal weight (EFW) below the 10th centile together with intertwin discordance exceeding 25%.[1] Alternative Delphi consensus criteria additionally incorporate fetal Doppler parameters because of their prognostic relevance.[106-109]

Whether growth standards in twins should reflect physiological adaptation or pathological growth restriction remains a major unresolved question in perinatal medicine. Twin pregnancies demonstrate reduced growth velocity from the late second trimester onwards,[110] and the use of singleton growth charts may substantially overestimate the prevalence of SGA fetuses.[111] Twin-specific charts appear to identify fetuses at genuinely increased risk of adverse neonatal outcome more accurately than singleton standards.[111]

Prediction of spontaneous preterm birth

Spontaneous preterm birth in twin pregnancy has multiple etiologies, including mechanical uterine distension, inflammatory activation, cervical remodelling, and placental dysfunction. Transvaginal cervical length measurement between 20 and 24 weeks' gestation currently represents the most informative screening tool for predicting spontaneous preterm birth in twin gestations.[67,112] The risk of spontaneous preterm birth before 32 weeks is approximately 30–40% among patients with a cervical length ≤25 mm, compared with 8–12% among those with a longer cervix.[67] Biochemical markers such as cervicovaginal fetal fibronectin provide only limited additional predictive value in asymptomatic twin pregnancies.[113] These observations support a precision-based approach to prevention in which cervical phenotype identifies the subgroup most likely to benefit from intervention.

Prediction and prevention of preeclampsia

Twin pregnancies are associated with a markedly increased risk of preeclampsia compared with singleton gestations.[73,74] The pathophysiology of preeclampsia in twin pregnancy may differ partly from singleton disease because of greater placental mass, altered angiogenic signalling and more pronounced maternal haemodynamic adaptation.[74,114]

First-trimester prediction models incorporating maternal characteristics, mean arterial pressure, uterine artery Doppler pulsatility index and placental biomarkers have demonstrated good predictive performance in twin pregnancies.[115,116] Although uterine artery Doppler indices are generally lower in twins because of increased placental mass, elevated values remain associated with early-onset disease.[74,117,118] Placental growth factor concentrations are also altered in twin pregnancy, necessitating twin-specific reference ranges.[119-121]

Low-dose aspirin is currently recommended by many professional societies for the prevention of preeclampsia in twin pregnancy because of the high baseline risk and favourable safety profile, although robust twin-specific randomised evidence remains limited.[122-126] Ongoing trials, including ASPRE-Twins, are expected to clarify the effectiveness of aspirin prophylaxis in this population.

Gestational diabetes mellitus

Twin pregnancies are associated with greater physiological insulin resistance and higher rates of GDM than singleton pregnancies.[5,81-84] Emerging evidence suggests that mild hyperglycaemia in twin pregnancy may partly reflect physiological exaggeration of normal metabolic adaptation rather than pathological dysglycaemia. Consistent with this hypothesis, GDM in twin pregnancy appears less strongly associated with adverse neonatal outcomes than in singleton gestations.[85-87]

While data on twin-specific screening and diagnostic criteria are presently scarce, preliminary findings suggest that the optimal screening and diagnostic criteria in twin pregnancies may be higher than those currently used for singleton pregnancies[127-130]. Until these findings are validated in prospective studies, we recommend that screening and diagnosis of GDM in twin pregnancies follow the same approach currently used for singleton pregnancies.

Management of complications in twin pregnancies

Management strategies in twin pregnancy are determined primarily by chorionicity, GA and the balance between risks of fetal compromise and iatrogenic prematurity. Advances in fetal imaging, fetoscopic surgery, neonatal care and multidisciplinary management have transformed outcomes in complicated twin pregnancies, particularly in MC disease. Nevertheless, many interventions continue to rely on observational evidence or extrapolation from singleton pregnancies, highlighting the need for twin-specific trials and long-term outcome data.

Management of complications unique to MC twins

Twin–twin transfusion syndrome

Untreated severe second-trimester TTTS is associated with very high rates of fetal loss and extreme preterm birth.[133] The introduction of fetoscopic laser photocoagulation (FLP) has fundamentally altered the prognosis of TTTS by directly targeting the underlying placental vascular pathology.[48,134,135] FLP selectively coagulates placental vascular anastomoses to separate the fetal circulations and eliminate chronic intertwin transfusion. Compared with serial amnioreduction, FLP substantially improves survival and reduces neurological morbidity.[136-140]

Following contemporary laser therapy, survival of at least one twin occurs in approximately 85–90% of pregnancies, while dual survival is achieved in approximately 60–70%.[140] Outcomes are generally more favourable in earlier Quintero stages than in advanced disease.[141] However, even after successful treatment, pregnancies remain at increased risk of miscarriage, preterm birth and fetal neurological injury.[142] Incomplete coagulation of placental anastomoses may result in fetal demise, recurrent TTTS or post-laser TAPS.[48,49,143–145] Long-term complications may include acquired cardiac abnormalities, cerebral injury and rare vascular disruption syndromes affecting the limbs or gastrointestinal tract.[146–149]

Centralisation of fetal therapy services has improved procedural expertise and appears to be associated with better survival and neurodevelopmental outcomes.[150] TTTS management, therefore, exemplifies the importance of specialised multidisciplinary care pathways in complex twin pregnancy.

Twin anaemia–polycythaemia sequence

Management of spontaneous TAPS remains challenging because robust randomised evidence is lacking and disease severity may evolve unpredictably. Current management strategies are individualised according to GA, severity of anaemia and polycythaemia, technical feasibility of intervention and parental preference. FLP may arrest intertwin transfusion by coagulating residual placental anastomoses, although the procedure is technically more demanding in TAPS than in TTTS because of the absence of polyhydramnios and the extremely small connections.[49]

Intrauterine transfusion (IUT) may temporarily correct donor anaemia but does not address the underlying placental transfusion imbalance and may exacerbate recipient polycythaemia.[151] Consequently, repeated procedures are often required. Before fetal viability, expectant management may be appropriate in selected stable cases to minimise iatrogenic risks. In later gestation, progressive severe disease may prompt either fetal intervention or delivery, depending on GA and anticipated neonatal outcomes.[151]

Postnatal management frequently requires neonatal transfusion support. Donor twins commonly require red blood cell transfusion because of severe anaemia, whereas

recipient twins may require partial exchange transfusion for symptomatic polycythaemia and hyperviscosity.[152]

Selective fetal growth restriction

Management of sFGR requires balancing the competing risks of fetal deterioration, intrauterine demise and iatrogenic prematurity. These challenges are particularly complex in MC pregnancies because deterioration or demise of one fetus may precipitate acute haemodynamic injury to the co-twin through shared placental vascular connections.[51,52]

In dichorionic pregnancies, management of sFGR broadly follows principles used in singleton FGR, with surveillance focused on fetal growth velocity, Doppler abnormalities and timing of delivery.[153-155] In MC pregnancies, however, the pathophysiology and clinical implications differ fundamentally because of unequal placental sharing and vascular interdependence between twins.

Management strategies for MC sFGR depend in part on the Doppler phenotype and disease severity. Expectant management with intensive surveillance may be appropriate in stable cases, whereas severe deterioration may prompt delivery or fetal intervention. The role of FLP in isolated MC sFGR remains controversial because interruption of placental vascular connections may not substantially improve outcomes for the larger twin and is associated with risk of fetal loss and preterm birth.[156,157] In selected severe cases, particularly when sFGR coexists with TTTS or when imminent demise of the smaller twin threatens the co-twin, FLP or selective fetal reduction may be considered.

Fetal anomalies and selective reduction

Management of fetal anomalies in twin pregnancy depends on chorionicity, severity of the anomaly, GA and parental preferences. Counselling should involve multidisciplinary input from fetal medicine specialists, neonatologists, paediatric subspecialists and, when appropriate, clinical geneticists.

In dichorionic pregnancies discordant for severe anomalies, management options include expectant management, selective reduction or palliative neonatal care. Selective reduction in dichorionic twins is generally performed by ultrasound-guided intracardiac injection. Procedure-related pregnancy loss and preterm birth risks increase with advancing gestation, emphasising the importance of early fetal anatomical assessment and aneuploidy screening.[38,158,159]

In MC pregnancies, selective reduction is technically more complex because direct fetal vascular connections create the risk of acute co-twin exsanguination following the demise of the affected fetus. Consequently, vascular occlusive techniques such as cord coagulation or intrafetal ablation are required to isolate the fetal circulation.[48] These procedures are associated with higher rates of pregnancy loss and preterm birth than selective reduction in dichorionic pregnancies because they are performed later in gestation in twins with a shared circulation and require larger fetoscopic

access.[48] In monoamniotic pregnancies, cord transection may additionally be required to prevent fatal cord entanglement following fetal demise.[160]

Management of complications not unique to MC twins

Prevention and management of preterm birth

Preterm birth is the principal determinant of neonatal morbidity and mortality in twin pregnancy.[67] Despite extensive investigation, no intervention has been shown to reduce preterm birth in unselected twin gestations. Activity restriction and bed rest are ineffective and may increase maternal morbidity.[161-163]

Current evidence supports a targeted rather than universal prevention strategy. In twin pregnancies with a short cervix, vaginal progesterone reduces the risk of spontaneous preterm birth and neonatal morbidity. Administration of vaginal progesterone is associated with an approximately 30–35% reduction in spontaneous preterm birth before 32 weeks and reduced neonatal morbidity in twin gestations with a short cervix.[164–166] Consequently, some professional guidelines recommend progesterone treatment in twin pregnancies with cervical shortening while discouraging routine use in twins with normal cervical length.[167]

Cervical cerclage has not demonstrated benefit in unselected twin pregnancies and may increase adverse outcomes in women without cervical dilation.[69,70,168,169] However, emergency cerclage in the presence of painless cervical dilation may prolong pregnancy in selected cases of cervical insufficiency, although supporting evidence remains limited.[69,170] Cervical pessary has not consistently reduced preterm birth in twin gestations.[170]

When preterm birth is anticipated, antenatal corticosteroids reduce neonatal respiratory morbidity in twin pregnancies similarly to singleton pregnancies, particularly when administered within seven days before delivery.[171-174] Antenatal magnesium sulphate administered before very preterm birth provides fetal neuroprotection and reduces the risk of cerebral palsy.[175,176]

Prevention and management of preeclampsia

Twin pregnancies are associated with a substantially increased risk of preeclampsia and related maternal complications.[73,74] Low-dose aspirin is currently the only preventive intervention with strong evidence in singleton pregnancy, although definitive twin-specific evidence remains limited.[122-124] Nevertheless, many professional societies recommend aspirin prophylaxis for twin pregnancies because of the high baseline risk and favourable safety profile.[125,126] Ongoing randomised studies are expected to clarify the magnitude of benefit in twin gestations.

Management of established preeclampsia in twin pregnancy generally follows singleton principles but is complicated by earlier GA at presentation, increased rates of FGR and higher likelihood of preterm delivery. Decisions regarding the timing of

delivery require careful balancing of maternal disease severity against risks of prematurity.

Gestational diabetes mellitus

Management of GDM in twin pregnancy remains controversial because the metabolic adaptations of twin gestation differ substantially from singleton physiology. Twin pregnancies exhibit greater physiological insulin resistance and lower average birth weights than singleton pregnancies, raising uncertainty regarding optimal glycaemic targets and treatment thresholds.[5,129,130,177-180]

Although treatment of GDM improves outcomes in singleton pregnancies, robust evidence for benefit in twin gestations is lacking. Preliminary data suggest that overly strict glycaemic control in mild twin GDM may increase rates of FGR and SGA birth without reducing neonatal morbidity.[131,132] Until twin-specific evidence becomes available, most clinical guidelines continue to recommend management in accordance with singleton protocols. However, clinicians should remain attentive to maternal nutritional status and fetal growth, particularly when one or both fetuses demonstrate impaired growth velocity.

Timing and mode of delivery

The timing of delivery in a twin pregnancy depends primarily on chorionicity and the presence of maternal or fetal complications. Even in otherwise uncomplicated pregnancies, the risk of stillbirth increases with advancing gestation, particularly in MC twins. Consequently, elective delivery is generally recommended earlier than in a singleton pregnancy.[1]

The mode of delivery depends on chorionicity, fetal presentation, GA, estimated fetal weight, and clinician expertise. Vaginal birth is feasible for many twin pregnancies when the presenting twin is cephalic, although intrapartum management requires experienced multidisciplinary teams and immediate access to operative delivery if required. Twin pregnancies overall have substantially higher caesarean delivery rates than singleton pregnancies because of fetal malpresentation, intrapartum complications and clinician or parental preference.

Neonatal and long-term outcomes

Twins have less favourable neonatal and long-term neurodevelopmental outcomes than singletons, largely because they are more likely to be born preterm and with lower birthweight. In MC twins, this background risk is compounded by complications of a shared placenta, including TTTS, TAPS, sFGR and acute intertwin transfusion. These pregnancies therefore carry a “double-hit” risk: injury related to the underlying MC disorder and injury related to iatrogenic or spontaneous preterm birth.[152,181]

Twin–twin transfusion syndrome

FLP has substantially improved survival after TTTS, and most survivors have favourable childhood outcomes. Nevertheless, TTTS survivors remain at increased risk of neonatal and long-term morbidity, including cardiovascular dysfunction, renal impairment, haematological complications, cerebral injury and rare vascular disruption syndromes.[152,181,182] Brain injury is the complication most strongly associated with long-term disability and occurs in approximately 10% of survivors.[139,183-185] The risk is higher after serial amnioreduction than after laser treatment and may be increased further by recurrent TTTS or post-laser TAPS.[139,183,186]

Long-term neurodevelopmental impairment, including cerebral palsy, intellectual disability, autism, occurs in approximately 10% of TTTS survivors, although estimates vary according to GA at birth, birthweight, disease stage, treatment modality, neonatal brain imaging findings and duration of follow-up.[150,186,187] Centralisation of fetal therapy services appears to improve not only survival but also long-term outcomes.[150] These data support structured neurodevelopmental follow-up for TTTS survivors, ideally extending to school age, even when neonatal imaging is reassuring.[187]

Twin anaemia–polycythaemia sequence

TAPS is associated with a distinct pattern of neonatal and long-term morbidity. Donor twins are particularly vulnerable to anaemia-related complications and auditory neuropathy spectrum disorder, a severe form of sensorineural hearing loss that may occur in up to 15% of survivors after spontaneous TAPS.[188,189] Standard otoacoustic emission screening may fail to detect this condition; therefore, automated auditory brainstem response testing should be considered in TAPS survivors to enable early detection and intervention.[188,189]

Emerging MRI data suggest that cerebral injury at birth may be more common in TAPS survivors than previously recognised.[190,191] Unlike TTTS, in which impairment risk is broadly similar between twins, neurodevelopmental impairment after TAPS appears more frequent in donor twins than in recipients.[188] These findings reinforce the need for syndrome-specific neonatal assessment and long-term follow-up pathways after complicated MC pregnancy.

Selective fetal growth restriction

sFGR is associated with important neonatal and long-term consequences. Growth-restricted twins may have a lower immediate risk of respiratory distress syndrome than their larger co-twins, possibly reflecting accelerated lung maturation following chronic intrauterine stress.[192] However, they have an increased risk of bronchopulmonary dysplasia, suggesting that chronic fetal hypoxia and impaired intrauterine growth may adversely affect pulmonary development.[192]

Neurodevelopmental outcomes are also less favourable in growth-restricted twins than in their appropriately grown co-twins. In the LEMON study, growth-restricted

twins had an almost fivefold increase in the risk of mild neurodevelopmental impairment and lower intelligence quotient scores across domains of intelligence.[193] These findings support the concept that chronic placental insufficiency and fetal hypoxia leave lasting effects on brain development. Longitudinal MRI and functional follow-up studies are needed to clarify how altered fetal growth affects brain maturation, connectivity and later cognitive outcomes.

Co-twin loss and psychological outcomes

Single intrauterine death in a twin pregnancy has consequences that extend beyond immediate obstetric risk. In MC pregnancies, acute haemodynamic transfusion through placental vascular anastomoses can result in co-twin death or antenatal brain injury in the surviving co-twin.[51,52] In both MC and DC pregnancies, co-twin loss may also have profound psychological consequences for parents and, when survival occurs, for the surviving twin. The emotional significance of twinship should therefore be recognised in counselling, bereavement care and long-term family support.

The twinship experience

Twinship is also a distinctive social and developmental experience. MZ twins often report particularly close social relationships, including a higher likelihood of identifying their co-twin as their closest friend, lower negativity within the relationship and greater grief after co-twin loss compared with dizygotic twins.[26] Population data suggest that twins may have lower suicide rates than non-twins despite a slightly higher frequency of mental illness, although findings are not consistently stratified by zygosity.[194-196] These observations highlight the practice that outcomes after twin pregnancy should be assessed not solely by mortality and morbidity metrics but also by psychosocial development, family experience, and quality of life.

Implications for follow-up

Long-term follow-up after twin pregnancy should be risk-stratified according to chorionicity, GA at birth, birthweight, neonatal course and antenatal complications. Children surviving TTTS, TAPS, sFGR, single intrauterine demise or very preterm birth require particular attention to neurodevelopment, hearing, vision, cardiovascular health, respiratory outcomes and family wellbeing. Harmonised outcome reporting, linkage between fetal therapy and childhood follow-up registries, and inclusion of parent- and child-reported outcomes are needed to capture the full impact of twin pregnancy and its complications.

Future directions in management

Management of twin pregnancy is increasingly moving toward precision-based care integrating chorionicity, fetal growth trajectories, placental imaging, Doppler haemodynamics and biochemical biomarkers. Advances in fetal surgery, neonatal intensive care, and longitudinal neurodevelopmental follow-up have substantially improved outcomes, particularly in MC disease. However, major evidence gaps remain regarding optimal screening strategies, prevention of spontaneous preterm

birth, management of mild metabolic disease and long-term outcomes after fetal intervention. Future research should prioritise twin-specific randomised trials, harmonised outcome reporting and equitable access to specialised multidisciplinary care.

Outlook and future directions

Advances in fetal imaging, placental biology, fetal therapy and neonatal intensive care have transformed the management and survival of twin pregnancies over recent decades. Nevertheless, major challenges remain in understanding the biological mechanisms underlying twin development, improving prediction and prevention of complications, and reducing the substantial global burden of maternal and perinatal morbidity associated with multiple pregnancy. Future progress will require integration of developmental biology, precision medicine, placental science, data science and equitable models of specialised care.

Understanding the biology of twinning

Despite centuries of observation, the biological mechanisms underlying MZ twinning remain incompletely understood. Classical models proposing simple mechanical splitting of the embryo at defined developmental stages are increasingly challenged by observations from ART, discordance between chorionicity and zygosity, and emerging insights into early embryonic plasticity.[29,32] Future research integrating embryology, stem cell biology, single-cell transcriptomics and epigenetic profiling may provide a new understanding of how developmental trajectories diverge to permit the formation of two embryonic axes within a single conceptus.

Improved understanding of the molecular determinants of dizygotic twinning is also needed. Genome-wide association studies have identified several loci associated with ovulation and follicular development,[15] but the genetic architecture of twinning across diverse populations remains poorly characterised. This limitation is particularly important given the marked geographic variation in dizygotic twinning rates and the underrepresentation of African populations in genetic studies.

Precision placental medicine

Increasing evidence suggests that many complications of twin pregnancy reflect complex interactions between placental architecture, vascular communication and fetal adaptive responses. Future approaches are therefore likely to move beyond static anatomical classification toward functional assessment of placental physiology. Advances in placental imaging, fetal cardiovascular assessment, angiogenic biomarkers, and computational modelling may improve prediction of complications such as TTTS, TAPS, sFGR, and preeclampsia before overt clinical disease develops.

The MC placenta represents a unique natural model of shared human circulation and vascular adaptation. High-resolution placental mapping, three-dimensional vascular reconstruction, and the integration of placental pathology with fetal imaging and neonatal outcomes may provide a deeper understanding of how placental architecture affects disease phenotype and long-term outcomes.

Artificial intelligence and digital health

Artificial intelligence (AI) and machine learning are increasingly being explored in fetal ultrasound, risk prediction and longitudinal pregnancy surveillance. In twin pregnancy, AI-assisted approaches have the potential to improve the automated determination of chorionicity, fetal biometry, Doppler interpretation, and the prediction of complications using integrated multimodal datasets. However, most current algorithms have been trained predominantly on singleton pregnancies, and twin-specific validation remains limited.

Remote monitoring and digitally supported antenatal pathways may also improve access to specialised care, particularly in geographically dispersed or resource-limited settings. Home blood pressure monitoring, wearable technologies and telemedicine-based fetal assessment could reduce healthcare burden while facilitating earlier detection of maternal and fetal deterioration. However, careful evaluation is required to ensure that digital innovation reduces rather than exacerbates existing healthcare inequities.

Fetal therapy and minimally invasive intervention

Fetal therapy for MC complications has evolved rapidly, particularly following the introduction of FLP for TTTS. Future developments are likely to focus on improving procedural precision, reducing iatrogenic preterm birth and optimising long-term neurodevelopmental outcomes. Innovations in fetoscopic instrumentation, image guidance and robotic-assisted fetal surgery may facilitate safer and more selective intervention.

There is also increasing interest in earlier intervention before the development of advanced disease. Improved understanding of placental haemodynamics and biomarkers may eventually permit pre-symptomatic identification of pregnancies at highest risk of severe MC complications, enabling more individualised surveillance and treatment strategies.

Long-term follow-up and life-course outcomes

As neonatal survival improves globally, long-term health and developmental outcomes are becoming increasingly important. Future studies should move beyond short-term survival metrics to evaluate neurodevelopment, cardiovascular health, metabolic disease, mental health, educational attainment and quality of life across the life course.

The developmental origins of health and disease framework may be particularly relevant to twin pregnancy due to altered fetal growth trajectories, placental physiology, and intrauterine adaptation. Longitudinal cohort studies integrating fetal imaging, placental phenotyping, genomics and adult outcomes may provide important insights into how early intrauterine exposures influence lifelong health.

Twin-specific evidence and harmonised outcomes

Many areas of twin pregnancy management continue to rely on extrapolation from singleton populations despite important physiological differences between singleton and twin gestations. Twin-specific evidence is particularly lacking in areas such as screening and diagnostic thresholds, fetal growth standards, preeclampsia prevention, gestational diabetes management, preterm birth prevention and long-term follow-up strategies

Future research should prioritise adequately powered twin-specific randomised trials and internationally harmonised outcome reporting. The development of core outcome sets for twin pregnancy and fetal therapy studies facilitates comparison across studies and improves evidence synthesis.[197,198]

Global health and equitable access to care

Twin pregnancy represents a growing global health challenge. Although twinning rates have increased substantially in high-income countries owing to delayed childbearing and ART, the greatest burden of mortality and morbidity remains concentrated in LMICs, particularly in sub-Saharan Africa.[3] Limited access to antenatal ultrasound, specialised fetal medicine services, neonatal intensive care and timely delivery contributes substantially to adverse outcomes.

Reducing global disparities in outcomes will require investment not only in specialised fetal therapy centres but also in scalable systems for early diagnosis, referral and risk stratification. Training programmes, international collaborations, telemedicine networks, and context-specific care pathways may help expand access to high-quality care for twin pregnancies in resource-limited settings.

Conclusions

Twin pregnancy represents a unique intersection of developmental biology, placental physiology, maternal adaptation and fetal medicine. Chorionicity links early embryonic development to placental architecture, haemodynamic interaction and clinical outcome, making it the central biological determinant of risk in twin gestation. Although advances in imaging, fetal therapy and neonatal care have improved outcomes substantially, twin pregnancies continue to contribute disproportionately to maternal and perinatal morbidity worldwide.

Future progress will depend on integrating mechanistic biology with precision clinical care, generating twin-specific evidence, and ensuring equitable global access to specialised services. As understanding of placental function, fetal development and

long-term health continues to evolve, twin pregnancy will remain not only a major clinical challenge but also a uniquely informative model of human development and disease.

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