

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Kulkarni AD, Jamieson DJ, Jones HW, Jr., et al. Fertility treatments and multiple births in the United States. <i>N Engl J Med.</i> 2013;369(23):2218-2225.	Review/Other-Dx	N/A	To conduct a longitudinal analysis to determine the trends in and magnitude of the contribution of fertility treatments to multiple births.	We estimated that by 2011, a total of 36% of twin births and 77% of triplet and higher-order births resulted from conception assisted by fertility treatments. The observed incidence of twin births increased by a factor of 1.9 from 1971 to 2009. The incidence of triplet and higher-order births increased by a factor of 6.7 from 1971 to 1998 and decreased by 29% from 1998 to 2011. This decrease coincided with a 70% reduction in the transfer of 3 or more embryos during in vitro fertilization ( $P<0.001$ ) and a 33% decrease in the proportion of triplet and higher-order births attributable to in vitro fertilization ( $P<0.001$ ).	4
2. ACOG Practice Bulletin No. 144: Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. <i>Obstet Gynecol.</i> 2014;123(5):1118-1132.	Review/Other-Dx	N/A	To discuss the incidence of multifetal gestations in the U.S. over the past several decades.	No results stated in abstract.	4
3. DeJesus Allison SO, Javitt MC, Glanc P, et al. ACR Appropriateness Criteria(R) Multiple gestations. <i>Ultrasound Q.</i> 2012;28(2):149-155.	Review/Other-Dx	N/A	To recommend imaging for high risk multiple gestations.	N/A	4
4. Ghai V, Vidyasagar D. Morbidity and mortality factors in twins. An epidemiologic approach. <i>Clin Perinatol.</i> 1988;15(1):123-140.	Review/Other-Dx	N/A	To review the epidemiologic characteristics of twin pregnancies and twin infants.	We found that twins are prone to be born prematurely and have lower birth weights than their singleton counterparts after 30 to 34 weeks of gestation. Twins are also more prone to birth asphyxia, hyaline membrane disease, respiratory disorders, and seizures. Congenital anomalies and nonrespiratory morbidity were not found to be increased in twins. Twins have a 6 times higher perinatal mortality rate than do singletons. This is accounted for by prematurity in the main. A part of the excess mortality in twins is accounted for by a higher mortality in larger, near-term twins.	4

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5. Morin L, Lim K. Ultrasound in twin pregnancies. <i>J Obstet Gynaecol Can.</i> 2011;33(6):643-656.	Review/Other-Dx		To review the literature with respect to the use of diagnostic US in the management of twin pregnancies. To make recommendations for the best use of US in twin pregnancies.	1. There are insufficient data to make recommendations on repeat anatomical assessments in twin pregnancies. Therefore, a complete anatomical survey at each scan may not be needed following a complete and normal assessment. 2. There are insufficient data to recommend a routine preterm labor surveillance protocol in terms of frequency, timing, and optimal cervical length thresholds. 3. Singleton growth curves currently provide the best predictors of adverse outcome in twins and may be used for evaluating growth abnormalities. 4. It is suggested that growth discordance be defined using either a difference (20 mm) in absolute measurement in abdominal circumference or a difference of 20% in US-derived EFW. 5. Although there is insufficient evidence to recommend a specific schedule for US assessment of twin gestation, most experts recommend serial US assessment every 2 to 3 weeks, starting at 16 weeks of gestation for monochorionic pregnancies and every 3 to 4 weeks, starting from the anatomy scan (18 to 22 weeks) for dichorionic pregnancies. 6. Umbilical artery Doppler may be useful in the surveillance of twin gestations when there are complications involving the placental circulation or fetal hemodynamic physiology. 7. Although many methods of evaluating the level of amniotic fluid in twins have been described, there is not enough evidence to suggest that 1 method is more predictive than the others of adverse pregnancy outcome. 8. Referral to an appropriate high-risk pregnancy center is indicated when complications unique to twins are suspected on US. These complications include: 1. TTTS 2. Monoamniotic twins gestation 3. Conjoined twins 4. Twin reversed arterial perfusion sequence 5. Single fetal death in the second or third trimester 6. Growth discordance in monochorionic twins.	4

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6. Simpson LL. Ultrasound in twins: dichorionic and monochorionic. <i>Semin Perinatol.</i> 2013;37(5):348-358.	Review/Other-Dx	N/A	To assess the evidence that supports the use of US in twin pregnancies.	The reasons for US in twins include pregnancy dating, determination of chorionicity, NT assessment, anatomical survey, placental evaluation, cervical length assessment, routine fetal growth, and serial surveillance of pregnancies complicated by anomalies, cervical shortening, fetal growth disturbances, and amniotic fluid abnormalities. Twins with monochorionic placentation require heightened scrutiny for monoamniocity, conjoined twins, TRAP syndrome, TTTS, unequal placental sharing with discordant twin growth or selective IUGR, TAPS, and single fetal demise.	4
7. Bajoria R, Kingdom J. The case for routine determination of chorionicity and zygosity in multiple pregnancy. <i>Prenat Diagn.</i> 1997;17(13):1207-1225.	Review/Other-Dx	N/A	To provide supporting evidence for routine determination of chorionicity and zygosity in multiple pregnancy.	No results stated in abstract.	4
8. Dube J, Dodds L, Armson BA. Does chorionicity or zygosity predict adverse perinatal outcomes in twins? <i>Am J Obstet Gynecol.</i> 2002;186(3):579-583.	Observational-Dx	1008 twin pregnancies	To evaluate chorionicity and zygosity as risk factors for adverse perinatal outcomes in twins.	Outcomes from 1008 twin pregnancies were analyzed. Monochorionic/monozygotic twins had lower mean birth weights compared with dichorionic/dizygotic twins. Rates of perinatal mortality of at least 1 twin were significantly higher among monochorionic/monozygotic twins relative to dichorionic/dizygotic twins (RR, 2.5; 95% CI, 1.1–2.5). Dichorionic/majority monozygotic twins had similar perinatal outcomes compared with dichorionic/dizygotic twins.	3
9. Finberg HJ. The “twin peak” sign: reliable evidence of dichorionic twinning. <i>J Ultrasound Med.</i> 1992;11(11):571-577.	Review/Other-Dx	15 twin pregnancies	To describe an observation, dubbed the “twin peak” sign, which, when present, confirms that the twin pregnancy is dichorionic.	This observation, dubbed the “twin peak” sign, was identified in 15 twin pregnancies, all proven to be dichorionic at birth, and in 5 triplet pregnancies, all proven to be trichorionic. This finding is produced by proliferating chorionic villi growing into the potential space between the 2 layers of chorion in the intertwin membrane. The single chorion of a monoplacental twin pregnancy serves as an intact barrier, preventing villi from growing between the 2 amniotic layers.	4

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10. Menon DK. A retrospective study of the accuracy of sonographic chorionicity determination in twin pregnancies. <i>Twin Res Hum Genet.</i> 2005;8(3):259-261.	Observational-Dx	463 twin pregnancies	To determine the accuracy of US chorionicity determination in the largest sample of twin pregnancies to date.	Out of 436 twin pregnancies, 428 were correctly diagnosed for chorionicity as confirmed by pathology reports. US as a screening tool for monochorionic twin pregnancies has a sensitivity of 100%, a specificity of 97.9% and a predictive value positive of 88.2%. Transvaginal scanning in the first trimester determined twin chorionicity with a sensitivity and a specificity of 100%.	4
11. Monteagudo A, Timor-Tritsch IE, Sharma S. Early and simple determination of chorionic and amniotic type in multifetal gestations in the first fourteen weeks by high-frequency transvaginal ultrasonography. <i>Am J Obstet Gynecol.</i> 1994;170(3):824-829.	Review/Other-Dx	54 pregnancies	To determine the chorionic and amniotic types in multifetal pregnancies with transvaginal US at $\geq 14$ weeks' gestation.	US evaluation of the 212 pregnancies demonstrated 64 twin, 87 triplet, 41 quadruplet, 18 quintuplet, 1 sextuplet, and 1 septuplet gestation. 9 of the twin pregnancies were MCDA; 2 of the triplets were dichorionic-triamniotic, and 4 of the quadruplets were trichorionic-quadrarniomatic. In the 43 patients with both US and pathologic assessment, there were 40 twins, 5 of which were monochorionic diamniotic type. All 3 triplets were trichorionic-triamniotic type. In all 43 transvaginal US correctly predicted the chorionic and amniotic type as determined by the pathologic findings.	4
12. Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. <i>Obstet Gynecol.</i> 2006;107(4):927-941.	Review/Other-Dx	N/A	Review risk factors and management of placenta previa, placenta accrete and vasa previa.	Placenta previa; diagnostic modality of choice is transvaginal US. Women with a complete placenta previa should be delivered by cesarean. Placenta accrete; prenatal diagnosis by imaging, followed by planning of peripartum management by a multidisciplinary team. Hysterectomy required for women with placenta accreta. Vasa previa; diagnosed prenatally by US examination.	4
13. Winn HN, Gabrielli S, Reece EA, Roberts JA, Salafia C, Hobbins JC. Ultrasonographic criteria for the prenatal diagnosis of placental chorionicity in twin gestations. <i>Am J Obstet Gynecol.</i> 1989;161(6 Pt 1):1540-1542.	Observational-Dx	103 twin pregnancies	To quantitatively establish the US criteria for the prenatal diagnosis of chorion status in twin gestations.	With a thickness of 2 mm used as a cutoff point, the accuracy in predicting monochorionic or dichorionic twinning was 82% and 95%, respectively.	4

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14. Benirschke K. The biology of the twinning process: how placentation influences outcome. <i>Semin Perinatol.</i> 1995;19(5):342-350.	Review/Other-Dx	N/A	To discuss how placentation influences outcome of twinning process.	No results stated in abstract.	4
15. Fichera A, Prefumo F, Stagnati V, Marella D, Valcamonico A, Frusca T. Outcome of monochorionic diamniotic twin pregnancies followed at a single center. <i>Prenat Diagn.</i> 2015;35(11):1057-1064.	Observational-Dx	300 MCDA twin pregnancies	To review our experience and to report the pregnancy and neonatal outcome of a cohort of MCDA twin pregnancies followed from the first trimester onwards at a single center over an 11-year period	There were 2 surviving infants in 259/300 (86.4%) pregnancies, 1 survivor in 22/300 (7.3%) and no survivors in 19/300 (6.3%) with an overall mortality of 60/600 (10%). TTTS was diagnosed in 33 cases (11%), isolated intertwin weight discordance $\geq 25\%$ in 35 (11.6%) and major congenital structural anomalies in 10 (3.3%). After 32 weeks, the prospective risk of spontaneous fetal intrauterine death was 1 in 248 (0.4%) per pregnancy.	4
16. Dias T, Mahsud-Dornan S, Bhide A, Papageorghiou AT, Thilaganathan B. Cord entanglement and perinatal outcome in monoamniotic twin pregnancies. <i>Ultrasound Obstet Gynecol.</i> 2010;35(2):201-204.	Review/Other-Dx	32 monoamniotic pregnancies	To assess the prevalence of cord entanglement and perinatal outcome in a large series of monoamniotic twin pregnancies and to review the recent literature on similar published large series.	A total of 32 monoamniotic pregnancies were diagnosed during the study period, including 3 conjoined twins, 7 pregnancies with TRAP syndrome, 3 surgical pregnancy interruptions for discordant fetal abnormality and 1 miscarriage before 16 weeks' gestation. The remaining 18 monoamniotic pregnancies were included in the study analysis. All monoamniotic pregnancies were complicated with antenatal cord entanglement diagnosed by B-mode and color Doppler US. There were 34 live births and a double intrauterine death diagnosed at 19 + 2 weeks' gestation. There were 2 late neonatal deaths, 1 from congenital complete heart block and the other after surgery for transposition of the great arteries. The overall perinatal loss rate was 11.1% after 16 weeks and 5.9% after 20 weeks' gestation. The cumulative rates of cord entanglement and perinatal mortality in the reviewed literature were 74% and 21%, respectively.	4

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17. Cordero L, Franco A, Joy SD. Monochorionic monoamniotic twins: neonatal outcome. <i>J Perinatol.</i> 2006;26(3):170–175.	Review/Other-Dx	36 sets of twins	To report our experience with 36 sets of monochorionic monoamniotic twins (1990 to 2005) and to provide updated information for counseling.	Cord entanglement was observed in 15 pregnancies, but only 1 twin with entanglement and a true knot, experienced related morbidity. 4 of 71 live births were IUGR. Malformations were diagnosed prenatally (1 hypoplastic left heart and 1 body stalk) and postnatally (1 vertebral anomalies-anal atresia-tracheoesophageal fistula-renal defect and 2 lung hypoplasias). TTTS affected 3 sets of twins. 5 twin sets delivered before 31, 19 sets at 31 to 32 and 12 sets at 33 to 34 weeks. 6 of 71 (8%) twins died (4 malformations, 1 TTTS and 1 26 weeks premature). Head USs in 59 of 65 survivors showed 2 (3%) periventricular leukomalacia, 5 (9%) Grade I-II intraventricular hemorrhage and 52 (88%) normal.	4
18. Rodis JF, Vintzileos AM, Campbell WA, Nochimson DJ. Intrauterine fetal growth in discordant twin gestations. <i>J Ultrasound Med.</i> 1990;9(8):443-448.	Observational-Dx	25 twin pairs	To assess longitudinal growth of twins who were ultimately discordant at birth and to see how they differ from the concordant group.	25 discordant twin pairs were assessed by US in a longitudinal fashion and were compared with a group of 60 concordant twin pairs. The growth parameters of the larger fetus of the discordant pair did not differ significantly from the concordant twins, while the smaller of the discordant pair exhibited a slower rate of intrauterine growth as early as 23 to 24 weeks.	3
19. Kagan KO, Gazzoni A, Sepulveda-Gonzalez G, Sotiriadis A, Nicolaides KH. Discordance in nuchal translucency thickness in the prediction of severe twin-to-twin transfusion syndrome. <i>Ultrasound Obstet Gynecol.</i> 2007;29(5):527-532.	Observational-Dx	512 monochorionic twin pregnancies	To examine in monochorionic pregnancies the possible value of intertwin discordance in NT thickness in the prediction of early fetal death or severe TTTS.	In 412 (80.5%) pregnancies there was a normal outcome, in 58 (11.3%) there was severe TTTS requiring endoscopic laser surgery at 18–24 weeks, in 19 (3.7%) there was death of 1 or both fetuses at 13–18 weeks and in 23 (4.5%) there was fetal death at 21–38 weeks. In the 4 outcome groups the median discordance in NT was 11%, 22%, 35% and 7%, respectively. Significant prediction of early fetal death and severe TTTS was provided by the discordance in fetal NT, which was not significantly improved by including the discordance in CRL. If the discordance in NT was 20% or more, the false positive rate was 20%, the detection rate of early fetal death was 63% and the detection rate of severe TTTS was 52%.	3

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20. D'Antonio F, Khalil A, Pagani G, Papageorghiou AT, Bhide A, Thilaganathan B. Crown-rump length discordance and adverse perinatal outcome in twin pregnancies: systematic review and meta-analysis. <i>Ultrasound Obstet Gynecol.</i> 2014;44(2):138-146.	Review/Other-Dx	17 studies	To explore the relationship between CRL discordance detected at 11–14 weeks of gestation and adverse outcome in twin pregnancy and to assess its predictive accuracy.	A total of 2008 articles were identified and 17 studies were included in the systematic review. Twin pregnancies with CRL discordance $\geq 10\%$ were at significantly higher risk of perinatal loss (RR, 2.80; 95% CI, 1.25–6.27; $P=0.012$ ), fetal loss at $\geq 24$ weeks (RR, 4.07; 95% CI, 1.47–11.23; $P=0.006$ ), BWD (RR, 2.24; 95% CI, 1.89–2.64; $P<0.001$ ) and preterm delivery at $<34$ weeks (RR, 1.49; 95% CI, 1.23–1.80; $P<0.001$ ) but not of fetal loss at $<24$ weeks ( $P=0.130$ ). A meta-analysis of fetal anomalies was not possible because fewer than 2 studies explored this outcome. However, when used alone to screen for adverse pregnancy outcome, the predictive accuracy of CRL discordance was low for each of the outcomes explored.	4
21. Kalish RB, Gupta M, Perni SC, Berman S, Chasen ST. Clinical significance of first trimester crown-rump length disparity in dichorionic twin gestations. <i>Am J Obstet Gynecol.</i> 2004;191(4):1437-1440.	Observational-Dx	159 twin pregnancies	To determine the clinical significance of first trimester crown-rump disparity in dichorionic twin gestations.	Of 159 twin pregnancies, there were 7 fetal structural anomalies, 2 fetal chromosomal anomalies, 5 second-trimester spontaneous abortions, 3 second-trimester fetal deaths, and 1 third-trimester fetal death. Pregnancies that were complicated by fetal structural or chromosomal anomalies had significantly greater median CRL discordance than pregnancies without fetal anomalies (4.0 mm vs 2.0 mm; $P=0.02$ ). CRL discordance $>10\%$ , which is the 90th percentile for intertwin CRL disparity in our population, was associated with a significantly higher incidence of fetal anomalies (22.2% vs 2.8%; $P=0.02$ ).	3

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22. Baxi LV, Walsh CA. Monoamniotic twins in contemporary practice: a single-center study of perinatal outcomes. <i>J Matern Fetal Neonatal Med.</i> 2010;23(6):506-510.	Review/Other-Dx	25 monochorionic-monoamniotic pregnancies	To assess perinatal mortality rates of monochorionic monoamniotic twins.	Of the 25 monochorionic-monoamniotic pregnancies delivered, 98% (49/50) of twins were live-born. All women were delivered by cesarean section. There was 1 IUFD, which was secondary to anencephaly. There were 3 neonatal deaths, 2 in association with complex congenital heart disease. 1 twin died outside the neonatal period following cardiac surgery. In total, 28% (7/25) of pregnancies were complicated by major congenital anomalies. There was 1 case of mild transient TTTS. The overall perinatal mortality rate for nonanomalous twins was 2.4% (95% CI = 0.06%–13.59%).	4
23. Lewi L, Jani J, Blickstein I, et al. The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study. <i>Am J Obstet Gynecol.</i> 2008;199(5):514 e511-518.	Observational-Dx	202 twin pairs	To document pregnancy and neonatal outcome of MCDA twin pregnancies.	Of the 202 included twin pairs, 172 (85%) resulted in 2 survivors, 15 (7.5%) in 1 survivor, and 15 (7.5%) in no survivors. The mortality was 45/404 (11%), and 36/45 (80%) were fetal losses of 24 weeks or less, 5/45 (11%) between 24 weeks and birth, and 4/45 (9%) were neonatal deaths. TTTS occurred in 18/202 (9%). The mortality of TTTS was 20/36 (55%), which accounted for 20/45 (44%) of all losses. Severe discordant growth without TTTS occurred in 29/202 (14%). Its mortality was 5/58 (9%), which accounted for 5/45 (11%) of all losses. Major discordant congenital anomalies occurred in 12/202 (6%). Of the 178 pairs that continued after 24 weeks, 10 (6%) had severe hemoglobin differences at birth. After 32 weeks, the prospective risk of intrauterine demise was 2 in 161 pregnancies (1.2%; 95% CI, 0.3–4.6).	3

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24. Fuchs F, Senat MV. Multiple gestations and preterm birth. <i>Semin Fetal Neonatal Med.</i> 2016;21(2):113-120.	Review/Other-Dx	N/A	To review the existing literature regarding the prediction and prevention of preterm birth in both symptomatic and asymptomatic twin pregnancies.	In asymptomatic twin pregnancies, the best 2 predictive tests were cervical length measurement and cervicovaginal fetal fibronectin testing. A single measurement of transvaginal cervical length at 20-24 weeks of gestation <20 mm or <25 mm is a good predictor of spontaneous preterm birth at <28, <32, and <34 weeks of gestation. A cervical length beyond 25 mm is associated with a 2% risk for birth before 28 weeks and with a 65% chance for a term pregnancy. Cervicovaginal fetal fibronectin may be slightly less accurate than cervical length; however, it has a high negative predictive value in women presenting with threatened preterm labor, as <2% of these women will deliver within 1 week if the fetal fibronectin is negative. In symptomatic twin pregnancies, no tests have proven accurate in predicting the risk of preterm birth. For the prevention of preterm birth in asymptomatic twins, regardless of cervical length, no treatment including bed rest, limitation of home activities, prophylactic tocolysis, progesterone, or cerclage has been shown to reduce the rate of preterm birth.	4
25. Hubinont C, Lewi L, Bernard P, Marbaix E, Debieve F, Jauniaux E. Anomalies of the placenta and umbilical cord in twin gestations. <i>Am J Obstet Gynecol.</i> 2015;213(4 Suppl):S91-S102.	Review/Other-Dx	N/A	To review the anomalies of the placenta and umbilical cord in twin gestations.	No results stated in abstract.	4
26. Quintero RA. Twin-twin transfusion syndrome. <i>Clin Perinatol.</i> 2003;30(3):591-600.	Review/Other-Dx	N/A	To discuss and review TTTS.	No results stated in abstract.	4
27. Bahtiyar MO, Emery SP, Dashe JS, et al. The North American Fetal Therapy Network consensus statement: prenatal surveillance of uncomplicated monochorionic gestations. <i>Obstet Gynecol.</i> 2015;125(1):118-123.	Review/Other-Dx	N/A	To briefly describe complications of monochorionic gestations and to provide multidisciplinary, evidence-based, and consensus-driven recommendations for surveillance of uncomplicated monochorionic gestations.	No results stated in abstract.	4

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28. Lopriore E, Bokenkamp R, Rijlaarsdam M, Sueters M, Vandenbussche FP, Walther FJ. Congenital heart disease in twin-to-twin transfusion syndrome treated with fetoscopic laser surgery. <i>Congenit Heart Dis.</i> 2007;2(1):38-43.	Review/Other-Tx	101 twin pairs	To determine the incidence of congenital heart disease and RVOTO in TTTS treated with fetoscopic laser surgery and evaluate the role of increased afterload by determining the difference in blood pressure and endothelin-1 at birth between donor and recipient twins.	The incidence of congenital heart disease in the TTTS group and non-TTTS group was 5.4% (4/74) and 2.3% (2/87) ( $P=.42$ ), respectively. RVOTO was diagnosed in 1 recipient twin delivered at our center and 2 recipient twins delivered elsewhere. The incidence of RVOTO in recipients was 4% (3/75). Mean systolic blood pressure at birth was similar in donor and recipient twins, respectively, 53 mm Hg vs 56 mm Hg ( $P=.42$ ). Mean endothelin-1 level at birth was also similar between donors and recipients, respectively, 14.3 ng/L and 13.2 ng/L ( $P=.64$ ).	4
29. Pettit KE, Merchant M, Machin GA, Tacy TA, Norton ME. Congenital heart defects in a large, unselected cohort of monozygotic twins. <i>J Perinatol.</i> 2013;33(6):457-461.	Review/Other-Dx	926 monozygotic twins	To determine the prevalence of congenital heart defects in a large, unselected cohort of monozygotic twins.	A total of 926 liveborn monozygotic twins met inclusion criteria. The prevalence of congenital heart defects was 7.5%, 11.6 times the general population rate (CI 9.2 to 14.5). Septal defects were most common. 20% of infants with heart defects had TTTS vs 8% of infants without defects ( $P<0.01$ ); this association remained significant when controlling for potential confounders.	4
30. Panagiotopoulou O, Fouzas S, Sinopidis X, Mantagos SP, Dimitriou G, Karatza AA. Congenital heart disease in twins: The contribution of type of conception and chorionicity. <i>Int J Cardiol.</i> 2016;218:144-149.	Observational-Dx	874 twins	To study the incidence of congenital heart disease in a cohort of twins to clarify the contribution of type of conception and chorionicity.	In the assisted reproductive technology group 32/389 (8.2%) had congenital heart disease compared to 21/485 (4.3%) infants conceived naturally (OR 1.90, 95% CI, 1.08-3.34, $P=0.024$ ). Spontaneous-conception gestations had higher incidence of monozygotic placentation (47/245 vs 4/197, $P<0.001$ ), and included younger mothers (29.1+/-5.2 vs 33.9+/-5.5 years, $P<0.001$ ) who had higher parity (median 2 [range 1-7] vs 1 Pinborg (2005), Blondel and Kaminski (2002), Knopman et al. (2014), Kyvik and Derom (2006); $P<0.001$ ). Multivariable logistic regression analysis showed that assisted reproductive technology (OR 2.60, 95% CI, 1.24-5.45) and monozygoticity (OR 3.49, 95% CI, 1.57-7.77) were significant determinants of congenital heart disease, independently of maternal age, parity, and the gender of the offspring.	3

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31. Zanardini C, Prefumo F, Fichera A, Botteri E, Frusca T. Fetal cardiac parameters for prediction of twin-to-twin transfusion syndrome. <i>Ultrasound Obstet Gynecol.</i> 2014;44(4):434-440.	Observational-Dx	100 pregnancies	To assess myocardial performance index measured by conventional Doppler (MPI) and by tissue Doppler imaging (MPI) at 18 weeks' gestation in MCDA twins for the prediction of TTTS.	Of the 100 pregnancies, 88 were controls (84 uncomplicated and 4 developed sIUGR) and 12 developed TTTS. Right ventricle-conventional Doppler and left ventricle-conventional Doppler, and left ventricle-tissue Doppler imaging were significantly higher in future TTTS recipients than in controls, while right ventricle-tissue Doppler imaging was significantly lower in donors. Right ventricle-conventional Doppler and left ventricle-conventional Doppler were found to be predictive indicators in pregnancies that had not yet developed TTTS. Their negative predictive values were >90%, and their specificities >80%. The best performing index left ventricle-tissue Doppler imaging, with a sensitivity of 91.7% and specificity of 88.6%.	3
32. Eschbach SJ, Boons LS, van Zwet E, et al. Right ventricular outflow tract obstruction in complicated monochorionic twin pregnancies. <i>Ultrasound Obstet Gynecol.</i> 2016:[Epub ahead of print].	Observational-Dx	485 pregnancies	To evaluate pregnancy characteristics of neonates with RVOTO in complicated monochorionic twin pregnancies.	A total of 485 twin pregnancies received laser therapy for TTTS. RVOTO was diagnosed in 3.0% (11/385) of the live born TTTS-recipients. 2 of them showed a mild Ebstein anomaly additionally. Before laser therapy, pericardial effusion was seen in 45% (5/11) of RVOTO cases ( $P<0.01$ ), abnormal A-wave in ductus venosus was seen in 73% (8/11) ( $P=0.03$ ) and gestational age at time of laser therapy was 17w3d compared to 20w3d in controls ( $P=0.03$ ). A prediction model was constructed. 1 donor had RVOTO after development of transient hydrops after laser therapy. 3 larger twins in pregnancies complicated by sIUGR developed RVOTO, in all 3 cases onset of RVOTO was visible in early second trimester.	3

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33. Sassoon DA, Castro LC, Davis JL, Hobel CJ. Perinatal outcome in triplet versus twin gestations. <i>Obstet Gynecol.</i> 1990;75(5):817-820.	Observational-Dx	15 triplet and twin pregnancies	To determine whether triplet pregnancies are associated with a significantly worse perinatal outcome than twin pregnancies.	Maternal and neonatal outcome was evaluated in 15 triplet and twin pregnancies that were matched for maternal age, race, type of medical insurance, delivery mode, parity, and history of previous preterm delivery. Preterm labor occurred significantly more often in triplet than in twin gestations (80% vs 40%), as did preterm delivery (87% vs 26.7%). Triplets had a significantly lower mean birth weight (1720 vs 2475 g) and gestational age at delivery (33 vs 36.6 weeks). In addition, 53.3% of triplet pregnancies but only 6.7% of twin pregnancies had 1 or more neonates with intrauterine growth retardation. Discordancy also occurred more frequently in triplets than in twins (66.7 vs 13.3%). The mean averaged neonatal hospital stay was significantly higher in triplets (29 vs 8.5 days), and triplets had a fivefold increased risk of requiring neonatal intensive care as compared with twins. However, there were no significant differences between the groups in maternal morbidity or major neonatal complications such as respiratory distress syndrome or intraventricular hemorrhage.	3
34. Bora SA, Papageorgiou AT, Bottomley C, Kirk E, Bourne T. Reliability of transvaginal ultrasonography at 7-9 weeks' gestation in the determination of chorionicity and amnionicity in twin pregnancies. <i>Ultrasound Obstet Gynecol.</i> 2008;32(5):618-621.	Observational-Dx	67 twin pregnancies	To assess the agreement in the diagnosis of chorionicity and amnionicity between transvaginal US examination at 7-9 weeks' gestation and at the 11-14-week transabdominal scan.	Chorionicity and amnionicity were documented in 67 viable twin pregnancies at both 7-9 and 11-14 weeks' gestation. There was agreement in the chorionicity and amnionicity reported at each of the 2 scans in 65 out of 67 (97%) cases. Of the dichorionic-diamniotic pregnancies reported at 7-9 weeks, 53 out of 54 (98%) were confirmed at the 11-14-week scan and 1 (2%) was found to be MCDA. However, at birth these twins were of different sex, confirming dichorionic-diamniotic twins as initially diagnosed at 7-9 weeks. Of the 12 pregnancies diagnosed as MCDA at 7-9 weeks, all were found to be MCDA at the 11-14-week scan. There was 1 monochorionic-monoamniotic pregnancy diagnosed at 7-9 weeks that was subsequently found to be MCDA at the 11-14-week scan.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Lee YM, Cleary-Goldman J, Thaker HM, Simpson LL. Antenatal sonographic prediction of twin chorionicity. <i>Am J Obstet Gynecol.</i> 2006;195(3):863-867.	Observational-Dx	410 twins	To determine the accuracy of antenatal diagnosis of twin chorionicity at a single tertiary care center and assess the consequences of incorrect diagnoses.	Chorionicity was correctly assigned antenatally in 392/410 (95.6%) twins. The sensitivity, specificity, and positive and negative predictive values of monozygosity assessed $\leq 14$ weeks were 89.8%, 99.5%, 97.8%, and 97.5%. Corresponding statistical values for the second trimester were 88.0%, 94.7%, 88.0%, and 94.7%. 2 cases of inaccurate antenatal diagnoses affected patient counseling or were associated with adverse clinical outcomes.	3
36. Vayssiere C, Benoist G, Blondel B, et al. Twin pregnancies: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). <i>Eur J Obstet Gynecol Reprod Biol.</i> 2011;156(1):12-17.	Review/Other-Dx	N/A	To provide a guideline for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF) for twin pregnancies.	No results stated in abstract.	4
37. Carroll SGM, Soothill PW, Abdel-Fattah SA, Porter H, Montague I, Kyle PM. Prediction of chorionicity in twin pregnancies at 10–14 weeks of gestation. <i>BJOG: An International Journal of Obstetrics &amp; Gynaecology.</i> 2002;109(2):182-186.	Observational-Dx	150 women	To examine the accuracy of US determination of chorionicity in twin pregnancies at 10–14 weeks of gestation.	In 150 cases with confirmation of chorionicity following delivery, 116 were postnatally classified as dichorionic and 34 monozygotic. Prenatal US examination correctly identified chorionicity in 149 (99.3%) cases. The most reliable indicator for dichorionicity was a combination using the $\lambda$ sign or 2 separate placentae with a sensitivity and specificity of 97.4% and 100%, respectively. The most useful test in predicting monozygosity was the T sign with a sensitivity of 100% and specificity of 98.2%. Measurement of the inter-twin membrane thickness was a less reliable indicator where the sensitivity for dichorionicity and specificity for monozygosity was only 92.6%.	2

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Bromley B, Benacerraf B. Using the number of yolk sacs to determine amnionicity in early first trimester monochorionic twins. <i>J Ultrasound Med.</i> 1995;14(6):415-419.	Review/Other-Dx	22 pregnancies	To evaluate the relationship between the number of yolk sacs and amnionicity in monochorionic twin pregnancies scanned early in the first trimester.	20 MCDA pregnancies and 2 monochorionic-monoamniotic pregnancies met the criteria for inclusion in the study. In diamniotic pregnancies scanned at <8 weeks' gestation, only the yolk sacs were identified; none of the dividing amniotic membranes were detected. 2 yolk sacs were identified in all but 1 case. In this case, although 1 yolk sac was seen at 6 weeks, follow-up scanning at 8 weeks revealed 2 yolk sacs. In each of the monochorionic-monoamniotic twin pregnancies, 1 yolk sac was seen at 9 weeks and a single amnion encircled both embryos.	4
39. Corbett SL, Shmorgun D. Yolk sac number does not predict reliably amnionicity in monochorionic twin pregnancies: a case of a monochorionic monoamniotic twin pregnancy with two distinct yolk sacs on early first-trimester ultrasound. <i>Ultrasound Obstet Gynecol.</i> 2012;39(5):607-608.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4
40. Shen O, Samueloff A, Beller U, Rabinowitz R. Number of yolk sacs does not predict amnionicity in early first-trimester monochorionic multiple gestations. <i>Ultrasound Obstet Gynecol.</i> 2006;27(1):53-55.	Review/Other-Dx	22 pregnancies	To determine the relationship between amnionicity and number of yolk sacs before 11 weeks of gestation.	In 17/20 (85%) cases of MCDA twins, 2 yolk sacs were seen. In 3/20 (15%) cases of MCDA twins, a single yolk sac was seen. In the 1 case of MCDA triplets, 2 yolk sacs were visualized. In 1 case of monoamniotic twins, a single yolk sac was observed.	4
41. Dias T, Arcangeli T, Bhide A, Napolitano R, Mahsud-Dornan S, Thilaganathan B. First-trimester ultrasound determination of chorionicity in twin pregnancy. <i>Ultrasound Obstet Gynecol.</i> 2011;38(5):530-532.	Observational-Dx	648 pregnancies	To determine the accuracy of US at 11–14 weeks' gestation in the diagnosis of chorionicity in twin pregnancy.	A total of 648 pregnancies were assigned chorionicity by first-trimester US during the study period. Chorionicity was ascertained in 613 cases, either by histology (n = 340) or discordant sex (n = 273). Chorionicity was correctly assigned by US at 11–14 weeks in 612/613 pregnancies (accuracy 99.8%). Sensitivity and specificity for determining monochorionicity were 100% and 99.8%, respectively.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Senat MV, Quarello E, Levailant JM, Buonumano A, Boulvain M, Frydman R. Determining chorionicity in twin gestations: three-dimensional (3D) multiplanar sonographic measurement of intra-amniotic membrane thickness. <i>Ultrasound Obstet Gynecol.</i> 2006;28(5):665-669.	Observational-Dx	84 twin pregnancies	To determine whether chorionicity in twin pregnancies during the second and third trimesters can be diagnosed by measuring the thickness of the intra-amniotic membranes with 3D multiplanar US.	In monochorionic and dichorionic pregnancies, respectively, the mean thickness was 1.42 (SD, 0.31) mm and 2.48 (SD, 0.47) mm. With 3D US, the intraclass correlation coefficient was 0.99 in all cases. The 95% limits of agreement were all within +/-0.2 mm. The best cut-off for membrane thickness for discriminating monochorionic from dichorionic twinning was 1.8 mm. Using this cut-off, there were 1 false-negative (sensitivity, 97%; 95% CI, 83%–99%) and 3 false-positive (specificity, 94%; 95% CI, 85%–99%) diagnoses of monochorionic twins. Kappa indices for intra- and interoperator variability were all above 90%, suggesting almost perfect agreement. Measurements with 2D US were less accurate (sensitivity and specificity, 83%).	3
43. Sepulveda W, Sebire NJ, Hughes K, Odibo A, Nicolaides KH. The lambda sign at 10–14 weeks of gestation as a predictor of chorionicity in twin pregnancies. <i>Ultrasound Obstet Gynecol.</i> 1996;7(6):421-423.	Observational-Dx	369 twin pregnancies	To examine the value of the lambda sign at 10–14 weeks of gestation in determining chorionicity in twin pregnancies.	Chorionicity was prospectively determined in 369 twin pregnancies by US at 10–14 weeks of gestation. Pregnancies were classified as monochorionic if there was a single placental mass in the absence of the lambda sign at the inter-twin membrane-placental junction, and dichorionic if there was a single placental mass but the lambda sign was present, or the placentas were not adjacent to each other. In 81 (22%) cases, the pregnancies were classified as monochorionic and in 288 (78%) as dichorionic. Pregnancy outcome was available in 279 cases and all 63 of these pregnancies classified as monochorionic resulted in the delivery of same-sex twins. Similarly, all 100 different-sex pairs were correctly classified as dichorionic.	3
44. Stenhouse E, Hardwick C, Maharaj S, Webb J, Kelly T, Mackenzie FM. Chorionicity determination in twin pregnancies: how accurate are we? <i>Ultrasound Obstet Gynecol.</i> 2002;19(4):350-352.	Observational-Dx	131 pregnancies	To determine the accuracy of antenatal prediction of chorionicity in twin pregnancies in our institution.	Chorionicity was correctly determined in 95% of cases (n = 131); 91% of the monochorionic and 96% of the dichorionic pregnancies were correctly determined. If chorionicity was assessed prior to 14 weeks' gestation (n = 96) the correct diagnosis was made in all except 1 case.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Chaudhuri K, Su LL, Wong PC, et al. Determination of gestational age in twin pregnancy: Which fetal crown-rump length should be used? <i>J Obstet Gynaecol Res.</i> 2013;39(4):761-765.	Observational-Dx	52 pairs of twins	To determine whether the larger, smaller or the mean CRL is more accurate in determining the gestational age in the first trimester of pregnancy.	A total of 52 pairs of twins were included in the study. According to Robinson's chart, the proportion of larger, smaller and mean CRL values that were closest to the reference value was found in 11.5%, 75.0% and 5.8% of cases respectively. The larger, smaller and the mean CRLs were closest to the reference CRL in the Hadlock chart for 28.9%, 44.2% and 19.2% of cases, respectively, and closest to the reference CRL in the Chitty chart for 17.3%, 59.6% and 15.4% of cases, respectively.	3
46. D'Antonio F, Khalil A, Dias T, Thilaganathan B. Crown-rump length discordance and adverse perinatal outcome in twins: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. <i>Ultrasound Obstet Gynecol.</i> 2013;41(6):621-626.	Observational-Dx	2155 twin pregnancies	To determine the association between CRL discordance and adverse perinatal outcome in twin pregnancies.	A total of 2155 twin pregnancies were analyzed, of which 420 were monochorionic and 1735 dichorionic. There were 42 fetal losses before 24 weeks' gestation and 23 perinatal deaths. CRL discordance was poorly predictive for fetal loss at <24 weeks (AUC, 0.54 (95% CI, 0.46–0.62)), perinatal loss (AUC, 0.52 (95% CI, 0.41–0.64)), BWD (AUC, 0.61 (95% CI, 0.56–0.65)), birthweight <5(th) centile (AUC, 0.56 (95% CI, 0.53–0.59)), EFW discordance (AUC, 0.55 (95% CI, 0.51–0.60)) and preterm birth at <34 weeks (AUC, 0.50 (95% CI, 0.47–0.54)). Overall mortality was significantly higher in monochorionic (5.0%) than in dichorionic (2.6%) twins ( $P=0.016$ ). Logistic regression analysis demonstrated that chorionicity (OR 2.09 (95% CI, 1.06–4.10); $P=0.033$ ) independently contributed to determining mortality, while CRL discordance ( $P=0.201$ ) did not. Adjusting for chorionicity did not improve the detection of adverse outcomes using CRL discordance.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Ewigman BG, Crane JP, Frigoletto FD, LeFevre ML, Bain RP, McNellis D. Effect of prenatal ultrasound screening on perinatal outcome. RADIUS Study Group. <i>N Engl J Med.</i> 1993;329(12):821-827.	Observational-Dx	15,151 pregnant women	To test the hypothesis that routine screening with standardized US on 2 occasions would reduce perinatal morbidity and mortality.	The mean numbers of USs obtained per woman in the US-screening and control groups were 2.2 and 0.6, respectively. The rate of adverse perinatal outcome was 5.0% among the infants of the women in the US-screening group and 4.9% among the infants of the women in the control group (RR, 1.0; 95% CI, 0.9 to 1.2; $P=0.85$ ). The rates of preterm delivery and the distribution of birth weights were nearly identical in the 2 groups. The US detection of congenital anomalies had no effect on perinatal outcome. There were no significant differences between the groups in perinatal outcome in the subgroups of women with post-date pregnancies, multiple-gestation pregnancies, or infants who were small for gestational age.	3
48. Weissmann-Brenner A, Weisz B, Achiron R, Shrim A. Can discordance in CRL at the first trimester predict birth weight discordance in twin pregnancies? <i>J Perinat Med.</i> 2012;40(5):489-493.	Observational-Dx	792 fetuses	To examine the correlation between measurements of CRL, NT, and birth weight in dichorionic and monochorionic twin pregnancies.	The study population comprised 792 fetuses: 94 MCDA and 698 dichorionic/diamniotic. Maternal age, gestational age at delivery, birth weight, and birth length were all significantly higher for the dichorionic group. Male fetuses had significantly higher NT and higher birth weight than female fetuses. Discordance in CRL was found to correlate with discordance in birth weight in the entire study population ( $P<0.0001$ , $R=0.25$ ), in the dichorionic twins ( $P<0.0001$ , $R=0.275$ ), but not in monochorionic twins ( $R=0.10$ , $P=0.33$ ). CRL discordance above the 90th percentile (>12%) predicted 14/40 pregnancies with BWD above the 90th percentile (>24%) [ $P<0.001$ , likelihood ratio =4.1 (2.6–6.2)]. CRL discordance above the 95th percentile (>16%) predicted 5/21 pregnancies with BWD above the 95th percentile (>30%) [ $P<0.001$ , likelihood ratio =5.5 (2.6–10.4)]. NT discordance was correlated with CRL discordance ( $R=0.15$ , $P<0.0001$ ), but not with birth weight, regardless of chorionicity or gender.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Memmo A, Dias T, Mahsud-Dornan S, Papageorgiou AT, Bhide A, Thilaganathan B. Prediction of selective fetal growth restriction and twin-to-twin transfusion syndrome in monochorionic twins. <i>Bjog</i> . 2012;119(4):417-421.	Observational-Dx	242 twin pregnancies	To study the correlation of discrepancy between CRL and NT in monochorionic twins at 11–14 weeks of gestation and subsequent development of TTTS and selective fetal growth restriction.	A total of 242 monochorionic twin pregnancies were studied (102 TTTS, 36 selective fetal growth restriction and 104 controls). The median CRL discrepancy in the selective fetal growth restriction group (11.9%) was significantly higher ( $P<0.001$ ) than in the TTTS group (3.8%) and control group (3.5%). Median inter-twin NT discrepancies were not significantly different ( $P=0.869$ ) between selective fetal growth restriction and both TTTS and control groups (15.6%, 16.7% and 14.8%, respectively). Discrepancy in CRL performs well as a screening test for selective fetal growth restriction (AUC = 0.89), but not for TTTS (AUC = 0.58).	3
50. Salomon LJ, Cavicchioni O, Bernard JP, Duyme M, Ville Y. Growth discrepancy in twins in the first trimester of pregnancy. <i>Ultrasound Obstet Gynecol</i> . 2005;26(5):512-516.	Review/Other-Dx	182 twin pregnancies	To refine the incidence and outcome of this discrepancy in relation to dating of the pregnancy and other biometric parameters.	A total of 182 twin pregnancies was included. The mean+/-SD discrepancy in CRL was 3.4+/-3.18 mm or 5.1+/-4.69% and the 95th centile was 9.8 mm or 14.3%. There was no influence of chorionicity ( $P=0.44$ ), mode of conception ( $P=0.18$ ) and no relation with outcome ( $P=0.54$ ). In conceptions resulting from assisted technology, the measured CRL of the smaller twin was closer to the actual gestational age. Cephalic and abdominal biometric measurements were significantly greater in the twin with the smaller CRL ( $P<0.05$ ). The 2 cases with a discrepancy >15 mm were affected by trisomy 18 and triploidy, respectively.	4

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Sebire NJ, Snijders RJ, Hughes K, Sepulveda W, Nicolaides KH. Screening for trisomy 21 in twin pregnancies by maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation. <i>Br J Obstet Gynaecol.</i> 1996;103(10):999-1003.	Review/Other-Dx	22,518 pregnant women	To determine the prevalence of increased fetal NT thickness in twin pregnancies and to evaluate screening for trisomy 21 by a combination of translucency thickness and maternal age.	In the 448 twin pregnancies the NT thickness was above the 95th centile of the normal range (for CRL in singletons) in 65/896 fetuses (7.3%), including 7/8 (88%) with trisomy 21. Increased translucency was also present in 4 fetuses with other chromosomal abnormalities. In the chromosomally normal twin pregnancies the prevalence of increased NT was higher in fetuses from monochorionic (8.4%; 16/190) than in those with dichorionic pregnancies (5.4%; 37/688). The minimum estimated risk for trisomy 21, based on maternal age and fetal NT thickness, was 1 in 300 in 19.5% (175/896) of the twins including all 8 of those with trisomy 21.	4
52. Spencer K, Nicolaides KH. Screening for trisomy 21 in twins using first trimester ultrasound and maternal serum biochemistry in a one-stop clinic: a review of three years experience. <i>Bjog.</i> 2003;110(3):276-280.	Observational-Dx	230 twin pregnancies	To evaluate the performance of screening for fetal trisomy 21 in the first trimester of twin pregnancies by a combination of maternal serum biochemistry and US.	Overall, 97.4% of the women with twins (224/230) accepted first trimester screening. The rate of detection of trisomy 21 was 75% (3/4). Fetal death at presentation was found in 3.4% of fetuses (16/460). Of women who accepted screening, 4.3% (10/230) presented too late for fetal NT measurement and 10.0% of women (23/230) presented too early. A risk for trisomy 21 was calculated for each fetus based on the individual fetal NT thickness and the maternal biochemistry. The false positive rate among those eligible for first trimester screening was 9.0% (19/206) of pregnancies and 6.9% of fetuses (28/412). Uptake of invasive testing was 59% (10/17) with chorionic villus sampling in 8 cases and amniocentesis in 2. No fetal loss occurred within 28 days of chorionic villus sampling and no loss occurred after amniocentesis. 1 case of trisomy 21 was identified for every 3 invasive procedures.	3

**Multiple Gestations  
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Sperling L, Kiil C, Larsen LU, et al. Detection of chromosomal abnormalities, congenital abnormalities and transfusion syndrome in twins. <i>Ultrasound Obstet Gynecol.</i> 2007;29(5):517-526.	Observational-Dx	495 pregnancies	To evaluate the outcome of screening for structural malformations in twins and the outcome of screening for TTTS among monochorionic twins through a number of US scans from 12 weeks' gestation.	Among the 495 pregnancies the prenatal detection rate for severe structural abnormalities including chromosomal aneuploidies was 83% by the combination of a first-trimester NT scan and the anomaly scan in week 19. The incidence of severe structural abnormalities was 2.6% and two-thirds of these anomalies were cardiac. There was no significant difference between the incidence in monozygotic and dizygotic twins, nor between twins conceived naturally or those conceived by assisted reproduction. The incidence of TTTS was 23% from 12 weeks until delivery, and all those monochorionic twin pregnancies that miscarried had signs of TTTS.	3
54. Vandecruys H, Faiola S, Auer M, Sebire N, Nicolaides KH. Screening for trisomy 21 in monochorionic twins by measurement of fetal nuchal translucency thickness. <i>Ultrasound Obstet Gynecol.</i> 2005;25(6):551-553.	Observational-Dx	769 twin pregnancies	To determine whether in screening for trisomy 21 by measurement of fetal NT thickness in monochorionic twin pregnancies it is preferable to use the higher, smaller or average NT.	The median maternal age was 33 (range, 16–45) years, the CRL was 62 (range, 45–84) mm and gestational age was 12 (range, 11 to 13 + 6) weeks. Either the fetal karyotype was normal, or phenotypically normal babies were born, in 761 cases. The karyotype was abnormal in 8 cases, including 6 with trisomy 21. The estimated risk using the higher, smaller and average NT was 1 in 300 or more in 6 (100%), 4 (66.7%) and 6 (100%) of the trisomy 21 pregnancies and in 148 (19.4%), 57 (7.5%) and 106 (13.9%) of the normal pregnancies. For a detection rate of 100%, the false positive rates using the higher, smaller and average NT would be 5.1%, 45.9% and 4.2%, respectively.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Wald NJ, Rish S, Hackshaw AK. Combining nuchal translucency and serum markers in prenatal screening for Down syndrome in twin pregnancies. <i>Prenat Diagn.</i> 2003;23(7):588-592.	Review/Other-Dx	N/A	To combine the US marker NT with serum markers so that they can be used together in prenatal screening for Down syndrome in twin pregnancies.	For monochorionic twin pregnancies (taken as monozygous), the 2 fetus-specific NT measurements are averaged before risk is calculated and before the contribution of the serum markers is incorporated. For dichorionic twin pregnancies (taken as dizygous), the risk for each fetus based on the individual NT measurements is calculated, the 2 fetus-specific risks are added together, and then the contribution of the serum markers is incorporated. In this way, all the screening markers can be used in combination to produce a pregnancy-specific “pseudo-risk”, rather than a fetus-specific pseudo-risk. We refer to pseudo-risk because in the absence of sufficient data on the screening markers in affected twin pregnancies, a true risk estimate cannot be calculated. Tentative estimates are given of screening performance in twins using NT, the combined test (NT with first-trimester serum markers), and the integrated test (NT with first- and second-trimester serum markers), all interpreted with maternal age.	4
56. Sebire NJ, D'Ercole C, Hughes K, Carvalho M, Nicolaides KH. Increased nuchal translucency thickness at 10–14 weeks of gestation as a predictor of severe twin-to-twin transfusion syndrome. <i>Ultrasound Obstet Gynecol.</i> 1997;10(2):86-89.	Observational-Dx	132 twin pregnancies	To examine a possible association between increased NT thickness at 10–14 weeks of gestation in monochorionic twin pregnancies and the subsequent development of severe TTTS.	In 132 monochorionic twin pregnancies, including 16 that developed severe TTTS at 15–22 weeks of gestation and 116 that did not develop TTTS, CRL, NT thickness and fetal heart rate were measured at 10–14 weeks. In those that developed severe TTTS, the prevalence of NT thickness above the 95th centile of the normal range and the intertwin difference in NT thickness and fetal heart rate were significantly higher than in the non-TTTS group; there were no significant differences between the groups in the intertwin difference in CRL. For fetal NT above the 95th centile, the positive and negative predictive values for the development of TTTS were 38% and 91%, respectively; the likelihood ratios of NT above or below the 95th centile for the development of severe TTTS were 4.4 (1.8–9.7) and 0.7 (0.4–0.9), respectively.	3

\* See Last Page for Key

**Multiple Gestations  
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Sebire NJ, Souka A, Skentou H, Geerts L, Nicolaides KH. Early prediction of severe twin-to-twin transfusion syndrome. <i>Hum Reprod.</i> 2000;15(9):2008-2010.	Observational-Dx	303 pregnancies	To explore the possible association of increased fetal NT thickness in the early prediction of severe TTTS.	Of 303 pregnancies, there were 16 in which at least 1 fetus was structurally or chromosomally abnormal and in the remaining 287 ongoing pregnancies there were 43 (15%) which developed severe TTTS. The median fetal NT was 1.0 multiples of the median and NT was >95th centile in 47 (8.2%) fetuses and in at least 1 fetus in 37 (12.9%) pregnancies. The prevalence of increased NT in the pregnancies that developed TTTS [17.4% (n = 15) of fetuses and 28% (n = 12) of pregnancies] was significantly higher than in the non-TTTS group [6.6% (n = 32) and 10.2% (n = 25) respectively; Z: = -3.4, P<0.001 and Z: = 3.2, P<0.001 respectively], likelihood ratio of increased fetal NT for prediction of TTTS = 3.5 [95% CI, 1.9–6.2]. In 153 of the pregnancies, an US examination was also performed at 15–17 weeks gestation and intertwin membrane folding was seen in 49 (32%) cases; 21 of these (43%) subsequently developed TTTS compared to 2 (1.9%) of the 104 pregnancies without membrane folding (Z: = 6.6, P<0.001), likelihood ratio of membrane folding for prediction of TTTS = 4.2 (95% CI, 3.0–6.0).	3
58. Sueters M, Middeldorp JM, Oepkes D, Lopriore E, Vandenbussche FP. Twin-to-twin transfusion syndrome at 11 weeks of gestation. <i>Am J Obstet Gynecol.</i> 2005;193(3 Pt 1):887-888.	Review/Other-Dx	N/A	To present the case of a monochorionic twin at 11+0 weeks of gestation with single increased NT and normal karyotypes.	At 12+5 weeks of gestation, double intrauterine death was diagnosed, followed by delivery of a strikingly red and white fetus.	4
59. Edlow AG, Reiss R, Benson CB, Gerrol P, Wilkins-Haug L. Monochorionic diamniotic twin gestations discordant for markedly enlarged nuchal translucency. <i>Prenat Diagn.</i> 2011;31(3):299-306.	Review/Other-Dx	162 twin pairs	To assess karyotypes and outcomes of MCDA twin pregnancies discordant for markedly enlarged NT in the first trimester.	Of 162 MCDA twin pairs, 11 were discordant for NT $\geq 3.5$ . Chromosomal abnormalities were present in 3 cases: 1 twin pair was concordant for trisomy 18; 1 pair discordant for mosaic trisomy 2; and 1 pair discordant for confined placental mosaicism (high frequency tetraploidy). Adverse outcomes for twins with euploid or unknown karyotypes included TRAP sequence, growth discordance, and esophageal atresia with tracheoesophageal fistula.	4

**Multiple Gestations  
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Allaf MB, Vintzileos AM, Chavez MR, et al. First-trimester sonographic prediction of obstetric and neonatal outcomes in monochorionic diamniotic twin pregnancies. <i>J Ultrasound Med.</i> 2014;33(1):135-140.	Observational-Dx	177 pregnancies	To investigate whether discordant NT and CRL measurements in MCDA twins are predictive of adverse obstetric and neonatal outcomes.	54 of the 177 pregnancies included (31%) had an adverse composite obstetric outcome, with TTTS in 19 (11%), IUGR in 21 (12%), discordant growth in 14 (8%), IUFD in 14 (8%), and preterm birth before 28 weeks in 10 (6%). Of the 254 neonates included in the study, 69 (27%) were complicated by adverse composite neonatal outcomes, with respiratory distress syndrome being the most common (n = 59 [23%]). The AUCs for the combined discordances to predict composite obstetric and neonatal outcomes were 0.62 (95% CI, 0.52–0.72), and 0.54 (95% CI, 0.46–0.61), respectively.	3
61. Chauhan SP, Scardo JA, Hayes E, Abuhamad AZ, Berghella V. Twins: prevalence, problems, and preterm births. <i>Am J Obstet Gynecol.</i> 2010;203(4):305-315.	Review/Other-Dx	N/A	To discuss the prevalence, problems and preterm births of twins.	No results stated in abstract.	4
62. Wenstrom KD, Gall SA. Incidence, morbidity and mortality, and diagnosis of twin gestations. <i>Clin Perinatol.</i> 1988;15(1):1-11.	Review/Other-Dx	N/A	To discuss the incidence, morbidity and mortality, and diagnosis of twin gestations.	No results listed in abstract.	4
63. Weis MA, Harper LM, Roehl KA, Odibo AO, Cahill AG. Natural history of placenta previa in twins. <i>Obstet Gynecol.</i> 2012;120(4):753-758.	Review/Other-Dx	67,895 pregnancies	To estimate the incidence of placenta previa in twin pregnancies compared with singletons and to estimate the rate and gestational age of previa resolution in twin pregnancies.	Of 67,895 pregnancies included, 2.1% (1,381/65,701) of singleton and 2.5% (56/2,194) of twin pregnancies had previa diagnosed ( $P=.15$ ). Dichorionic twins had an increased risk of placenta previa compared with singletons (adjusted OR 1.54, 95% CI, 1.15–2.06) or monochorionic twin pregnancies (RR 3.29, 95% CI, 1.32–8.21). Of the 1,738 twin pregnancies with serial US examinations, 51 (2.9%) were noted to have previa. 69% of the previa resolved by 32 weeks, at between 32 and 36 weeks an additional 47% of the remaining previa resolved, and no previa resolved after 36 weeks.	4

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Manning N, Archer N. A study to determine the incidence of structural congenital heart disease in mono chorionic twins. <i>Prenat Diagn.</i> 2006;26(11):1062-1064.	Review/Other-Dx	165 sets of twins	To determine the incidence of structural heart disease in at least 1 of a mono chorionic twin pair excluding any cardiac effects of TTTS.	The overall risk of at least 1 of a mono chorionic twin pair having a structural congenital cardiac anomaly was 9.1% (15/165); for MCDA twins, this figure was 7.0% (11/158) but for mono chorionic-monoamniotic twins the risk for at least 1 affected twin was 57.1% (4/7). If 1 of a pair of mono chorionic twins was affected, the risk to the other twin for a structural cardiac anomaly was 26.7% (4/15).	4
65. Vink J, Wapner R, D'Alton ME. Prenatal diagnosis in twin gestations. <i>Semin Perinatol.</i> 2012;36(3):169-174.	Review/Other-Dx	N/A	To discuss prenatal diagnosis in twin gestations.	No results stated in abstract.	4
66. Gul A, Cebeci A, Aslan H, Polat I, Sozen I, Ceylan Y. Perinatal outcomes of twin pregnancies discordant for major fetal anomalies. <i>Fetal Diagn Ther.</i> 2005;20(4):244-248.	Observational-Dx	267 twin pregnancies	To determine perinatal outcomes of twin pregnancies discordant for a major fetal anomaly and to compare with twins without anomaly.	There were 48 cases of MCDA, 2 cases of mono chorionic monoamniotic and 217 twins with dichorionic placentation. Out of 267 twin pregnancies, there were 17 (6.3%) twins with fetal anomaly. Twins discordant for a major fetal anomaly were diagnosed in 13 cases (4.8%). We observed 3 cases with MCDA and 10 cases with dichorionic placentation and the incidence of discordance for a major fetal anomaly as 4.6% (10/217) in dichorionic and 6.0% (3/50) in mono chorionic twin pregnancies. We identified 8 cases (62%) with craniospinal, 2 (15%) with gastrointestinal, 2 (15%) with urinary system, and 1 case (8%) with both craniospinal and gastrointestinal anomalies. There were significant differences between the normal co-twin of the major anomaly group (n = 13) and twins without anomaly group (n = 235) in mean gestational age at delivery (32 vs 34 weeks; $P=0.029$ ), mean birth weight (1,640 vs 2,030 g; $P=0.022$ ) and perinatal survival rate (69.2 vs 91.1%; $P=0.018$ ), respectively.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Yonetani N, Ishii K, Kawamura H, Mabuchi A, Hayashi S, Mitsuda N. Significance of Velamentous Cord Insertion for Twin-Twin Transfusion Syndrome. <i>Fetal Diagn Ther.</i> 2015;38(4):276-281.	Review/Other-Dx	357 twin pregnancies	To evaluate the actual association between VCI and TTTS in the native cohort concerning the natural history of monochorionic twin pregnancies.	A total of 357 MCDA twin pregnancies were analyzed. VCI in both twins was noted in 2.5% of cases and VCI in at least 1 twin was noted in 22.1% of cases. The incidence of TTTS was 8.4%; the incidence of a composite of adverse outcomes in at least 1 twin was 9.8%. There was no correlation between VCI and TTTS as well as a composite of adverse outcomes.	4
68. Costa-Castro T, De Villiers S, Montenegro N, et al. Velamentous cord insertion in monochorionic twins with or without twin-twin transfusion syndrome: Does it matter? <i>Placenta.</i> 2013;34(11):1053-1058.	Observational-Dx	630 placentas	To study the association between VCI and different outcomes in monochorionic twins with and without TTTS.	A total of 630 monochorionic placentas with TTTS (n = 304) and without TTTS (n = 326) were studied. The incidence of VCI in the TTTS and non-TTTS group was 36.8% and 35.9%, respectively (P=0.886). The presence of VCI in 1 twin was significantly associated with small for gestational age status (OR [OR] 1.45, 95% CI 1.13, 1.87) and severe BWD (OR 3.09, 95% CI 1.93, 4.96). Our results also showed significant interaction between TTTS and VCI when we considered IUFD and gestational age at birth. The prevalence of IUFD in monochorionic pregnancies without TTTS increased from 4.6% to 14.1% in the presence of VCI (P=0.027). In the TTTS group, the prevalence of IUFD was comparable in the absence or presence of VCI. Similarly, gestational age at birth was significantly lower in the presence of VCI only in the non-TTTS group.	3
69. Papathanasiou D, Witlox R, Oepkes D, Walther FJ, Bloemenkamp KW, Lopriore E. Monochorionic twins with ruptured vasa previa: double trouble! <i>Fetal Diagn Ther.</i> 2010;28(1):48-50.	Review/Other-Dx	N/A	To present a case of acute fetal distress in 2 fetuses in a monochorionic twin pregnancy caused by ruptured vasa previa that was not detected antenatally.	No results stated in abstract.	4
70. Finberg H, Mendelson E, Bohm-Velez M, et al. Evaluation of multiple gestations. American College of Radiology. ACR Appropriateness Criteria. <i>Radiology.</i> 2000;215 Suppl:903-914.	Review/Other-Dx	N/A	To evaluate multiple gestations and provide clinical practice guidelines.	No abstract available.	4

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Vayssiere C, Favre R, Audibert F, et al. Cervical length and funneling at 22 and 27 weeks to predict spontaneous birth before 32 weeks in twin pregnancies: a French prospective multicenter study. <i>Am J Obstet Gynecol.</i> 2002;187(6):1596-1604.	Observational-Dx	466 pregnant women	To determine the accuracy of cervical length and funneling of the internal os in the prediction of the spontaneous very preterm birth of twin pregnancies.	The median gestational age at delivery was 36 weeks in both populations. Of the population that was included at 22 weeks of gestation, 5.2% (13 women) gave birth spontaneously before 32 weeks of gestation, and 13.2% (33 women) gave birth spontaneously before 35 weeks of gestation; the median cervical length was 40 mm. The receiver operating characteristic curve showed no clear best cutoff point for cervical length. For spontaneous delivery before 32 and 35 weeks of gestation, the sensitivity of cervical length $\leq 30$ mm was 46% and 27%, respectively; the specificity was 89% and 90%, respectively. The sensitivity of funneling was 54% and 33%, and its specificity 89% and 91%, respectively. After multivariate analysis, only funneling remained significant for delivery before both 32 and 35 weeks of gestation. Of the population that was included at 27 weeks, 3.3% (7 women) gave birth spontaneously before 32 weeks of gestation, and 12.4% (26 women) gave birth spontaneously before 35 weeks of gestation; the median cervical length was 35 mm. The receiver operating characteristic curve showed 25 mm to be the best cutoff point for cervical length. For spontaneous delivery before 32 and 35 weeks of gestation, the sensitivity of cervical length $\leq 25$ mm was 100% and 54%, respectively, and the specificity was 84% and 87%, respectively. The sensitivity of funneling was 86% and 54%, and the specificity 78% and 82%, respectively. After multivariate analysis, both indicators remained significant for delivery before 35 weeks of gestation. Funneling after transfundal pressure at 22 or 27 weeks did not predict very preterm delivery.	3
72. Modena AB, Berghella V. Antepartum management of multifetal pregnancies. <i>Clin Perinatol.</i> 2005;32(2):443-454, vii.	Review/Other-Dx	N/A	To review important issues surrounding these complicated pregnancies while discussing current management options and recommendations.	No results stated in abstract.	4

\* See Last Page for Key

**Multiple Gestations  
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Lodeiro JG, Vintzileos AM, Feinstein SJ, Campbell WA, Nochimson DJ. Fetal biophysical profile in twin gestations. <i>Obstet Gynecol.</i> 1986;67(6):824-827.	Observational-Dx	49 patients	To assess the fetal biophysical profile in the antenatal fetal surveillance of twin gestations and to determine if such fetal evaluation would prove a reliable means of follow-up of nonreactive nonstress testing in this group of patients.	The fetal biophysical profile (nonstress test, fetal breathing movements, fetal movements, fetal tone, amniotic fluid volume, placental grading) was assessed in 49 consecutive referred high-risk patients with twin gestations. The relationship between the last fetal biophysical profile score before delivery was compared with the pregnancy outcome--as reflected by the presence of fetal distress and perinatal death. These data suggest that the fetal biophysical profile is a useful tool for observing fetal status in patients with twin gestations, and could be reliably used as a means of follow-up of nonreactive nonstress testing in these patients.	3
74. Lewi L, Van Schoubroeck D, Gratacos E, Witters I, Timmerman D, Deprest J. Monochorionic diamniotic twins: complications and management options. <i>Curr Opin Obstet Gynecol.</i> 2003;15(2):177-194.	Review/Other-Dx	N/A	To review the unpredictable vascular anastomoses and the often asymmetrical distribution of the single placenta between both twins that leads to disproportionately high fetal loss rates in monochorionic compared to dichorionic twins.	No results stated in abstract.	4
75. Sueters M, Oepkes D. Diagnosis of twin-to-twin transfusion syndrome, selective fetal growth restriction, twin anaemia-polycythaemia sequence, and twin reversed arterial perfusion sequence. <i>Best Pract Res Clin Obstet Gynaecol.</i> 2014;28(2):215-226.	Review/Other-Dx	N/A	To discuss the definitions and symptoms of TTTS, selective fetal growth restriction, TAPS, and TRAP sequence, to be able to recognize each disease and take the required action.	No results stated in abstract.	4
76. Weisz B, Hogen L, Yinon Y, et al. Perinatal outcome of monochorionic twins with selective IUGR compared with uncomplicated monochorionic twins. <i>Twin Res Hum Genet.</i> 2011;14(5):457-462.	Observational-Dx	128 twin pregnancies	To evaluate the perinatal outcome of monochorionic twins with selective IUGR.	Neonatal outcome of fetuses complicated with selective IUGR and normal Doppler was similar to controls. Neonates born to pregnancies complicated by selective IUGR and abnormal Doppler had significantly increased incidence of central nervous system findings, respiratory distress syndrome, necrotizing enterocolitis, sepsis, and neonatal death compared to controls. Adverse outcome in this group was independently associated only with gestational age at birth.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
77. Ishii K, Murakoshi T, Hayashi S, et al. Ultrasound predictors of mortality in monozygotic twins with selective intrauterine growth restriction. <i>Ultrasound Obstet Gynecol.</i> 2011;37(1):22-26.	Observational-Dx	101 twin pregnancies	To evaluate the use of US assessment to predict risk of mortality in expectantly managed monozygotic twin fetuses with selective IUGR.	Of 101 selective IUGR twins, 22 (21.8%) fetuses suffered intrauterine demise and 9 (8.9%) suffered neonatal death; 70 (69.3%) survived the neonatal period. Multiple logistic regression analysis revealed that the stuck twin phenomenon (OR (OR): 14.5; 95% CI: 2.2–93.2; <i>P</i> =0.006) and constantly absent diastolic flow in the umbilical artery (OR: 29.4; 95% CI: 3.3–264.0; <i>P</i> =0.003) were significant risk factors for mortality.	3
78. De Paepe ME, Luks FI. What-and why-the pathologist should know about twin-to-twin transfusion syndrome. <i>Pediatr Dev Pathol.</i> 2013;16(4):237-251.	Review/Other-Dx	N/A	To summarize the current knowledge of the placental contributions to TTTS and other complications of monozygotic twinning and describe the strengths and limitations of placental examination in these settings.	No results stated in abstract.	4
79. Abdel-Sattar M, Platt LD, DeVore G, Porto M, Benirschke K, Chmait RH. Treatment of Complicated Spontaneous Twin Anemia-Polycythemia Sequence via Fetoscopic Laser Ablation of the Vascular Communications. <i>Fetal Diagn Ther.</i> 2015;38(3):233-237.	Review/Other-Dx	3 cases	To describe 3 complicated cases of spontaneously TAPS successfully treated with selective laser photocoagulation of communicating vessels.	In 2 of the cases, placental pathology identified thrombosed fetal vessels of the polycythemic twin.	4
80. Slaghekke F, Kist WJ, Oepkes D, et al. Twin anemia-polycythemia sequence: diagnostic criteria, classification, perinatal management and outcome. <i>Fetal Diagn Ther.</i> 2010;27(4):181-190.	Review/Other-Dx	N/A	To focus on the pathogenesis, incidence, diagnostic criteria, management options and outcome in TAPS and to propose a classification system for antenatal and postnatal TAPS.	No results stated in abstract.	4
81. Oepkes D, Seaward PG, Vandenbussche FP, et al. Doppler ultrasonography versus amniocentesis to predict fetal anemia. <i>N Engl J Med.</i> 2006;355(2):156-164.	Observational-Dx	165 fetuses	To test the hypothesis that Doppler US of the middle cerebral artery is not inferior to measurement of amniotic-fluid DeltaOD450 for the prediction of fetal anemia.	Of 165 fetuses, 74 had severe anemia. For the detection of severe fetal anemia, Doppler US of the middle cerebral artery had a sensitivity of 88% (95% CI, 78% to 93%), a specificity of 82% (95% CI, 73% to 89%), and an accuracy of 85% (95% CI, 79% to 90%). Amniotic-fluid DeltaOD450 had a sensitivity of 76% (95% CI, 65% to 84%), a specificity of 77% (95% CI, 67% to 84%), and an accuracy of 76% (95% CI, 69% to 82%). Doppler US was more sensitive, by 12 percentage points (95% CI, 0.3 to 24.0), and more accurate, by 9 percentage points (95% CI, 1.1 to 15.9), than measurement of amniotic-fluid DeltaOD450.	2

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
82. Hecher K, Lewi L, Gratacos E, Huber A, Ville Y, Deprest J. Twin reversed arterial perfusion: fetoscopic laser coagulation of placental anastomoses or the umbilical cord. <i>Ultrasound Obstet Gynecol.</i> 2006;28(5):688-691.	Observational-Tx	60 pregnancies	To assess the feasibility and outcome of fetoscopic laser coagulation in pregnancies with TRAP sequence.	Vascular coagulation with arrest of blood flow was achieved in 82% (49/60) of cases by laser alone and in a further 15% (9/60) by laser coagulation in combination with bipolar forceps. The overall survival rate of the pump twin was 80% (48/60). Median gestational age at delivery was 37.4 (range, 23.7–41.4) weeks and the median interval between the procedure and delivery was 18.2 (range, 1.1–25.7) weeks. Median birth weight was 2720 (range, 540–3840) g. Preterm premature rupture of membranes before 34 weeks' gestation occurred in 18% (11/60) at a median of 62 (range, 1–102) days after the procedure. However, only 2 (3%) women delivered within 28 days of the procedure.	2
83. Lee H, Wagner AJ, Sy E, et al. Efficacy of radiofrequency ablation for twin-reversed arterial perfusion sequence. <i>Am J Obstet Gynecol.</i> 2007;196(5):459 e451-454.	Review/Other-Dx	29 patients	To report our experience in the treatment of patients with TRAP sequence using radiofrequency ablation to stop perfusion to the acardiac twin and protect the pump twin.	The outcomes of all 29 of the patients treated with radiofrequency ablation are known. 26 of the patients had MCDA pregnancies, whereas 2 had monochorionic-monoamniotic pregnancies. 1 patient had a triplet pregnancy with a MCDA pair with TRAP sequence. Overall, 25/29 pump twins survived (86%), delivering at a mean gestational age of 34.6 weeks. Survival was 24/26 (92%) in MCDA pregnancies with a mean gestational age of 35.6 weeks. 2 women in our early experience sustained thermal injuries from the site of grounding pads.	4

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
84. Chaveeva P, Poon LC, Sotiriadis A, Kosinski P, Nicolaides KH. Optimal method and timing of intrauterine intervention in twin reversed arterial perfusion sequence: case study and meta-analysis. <i>Fetal Diagn Ther.</i> 2014;35(4):267-279.	Meta-analysis	N/A	To define the optimal method and timing of intervention in TRAP sequence.	A variety of techniques were used to interrupt the blood supply to the acardiac twin. Most procedures were performed at or after 16 weeks, and with most methods the survival rate of the pump twin was about 80%. Good results were also obtained for triplet pregnancies. In 18/30 cases (60%) diagnosed at 11–14 weeks, there was spontaneous cessation of flow in the acardiac twin before planned intervention at 16–18 weeks, and in 11 of these (61.1%) the pump twin died or suffered brain damage. In 103 pregnancies treated by intrafetal laser at 12–27 weeks, there was no correlation between gestational age at treatment and survival rate, but there was an inverse association between gestational age at treatment and gestational age at birth.	M
85. Kilby MD, Govind A, O'Brien PM. Outcome of twin pregnancies complicated by a single intrauterine death: a comparison with viable twin pregnancies. <i>Obstet Gynecol.</i> 1994;84(1):107-109.	Observational-Dx	342 twin births	To examine the perinatal and maternal outcomes in twin pregnancies when a single intrauterine death occurs.	Of a total 34,804 live deliveries, 342 were documented as twin births at a gestation of <20 weeks (incidence 0.98%). Of the twin pregnancies over this period, 20 (5.85%) were complicated by a single intrauterine death. There was an increase in the incidence of congenital structural abnormalities among those twins dying in utero as compared to uneventful twin pregnancies (25% vs 0.3%; $P<.001$ ). A significant proportion of these twin pregnancies had monochorionic placentas (35% vs 9%; $P<.001$ ) and were admitted to special care units (70% vs 5.6%; $P<.001$ ) as compared to the normal twin sample. Maternal morbidity has previously been described as being increased. Although there was an increased risk of nonproteinuric and mild pregnancy-induced hypertension, no adverse maternal effects of conservative management were noted in this study.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
86. Ong SS, Zamora J, Khan KS, Kilby MD. Prognosis for the co-twin following single-twin death: a systematic review. <i>Bjog</i> . 2006;113(9):992-998.	Review/Other-Dx	28 studies	To determine the incidence of a) co-twin death, b) neurological abnormality and c) preterm delivery for the surviving co-twin following single-twin death after 14 weeks of gestation.	The search strategy yielded 632 potentially relevant citations. Full manuscripts were retrieved for 54 citations and 28 studies were finally included in the review. Following the death of 1 twin, the risk of monochorionic and dichorionic co-twin demise was 12% (95% CI, 7–11) and 4% (95% CI, 2–7), respectively. The risk of neurological abnormality in the surviving monochorionic and dichorionic co-twin was 18% (95% CI, 11–26) and 1% (95% CI, 0–7), respectively. The risk of preterm delivery was 68% (95% CI, 56–78) and 57% (95% CI, 34–77), respectively. Where there was comparative data within studies, the odds of monochorionic co-twin intrauterine death was 6 times that of dichorionic twins (OR 6.04 [95% CI, 1.84–19.87]). Neurological abnormality was also higher in monochorionic compared with dichorionic pregnancies (OR 4.07 [95% CI, 1.32–12.51]).	4
87. Almog B, Levin I, Wagman I, et al. Adverse obstetric outcome for the vanishing twin syndrome. <i>Reprod Biomed Online</i> . 2010;20(2):256-260.	Observational-Dx	399 patients	To compare obstetric outcomes of in vitro fertilization singleton pregnancies diagnosed with vanishing twin syndrome with those pregnancies originating as singleton pregnancies and with twin pregnancies.	Mean gestational age was 35.1+/-3.7 vs 38.2+/-2.6 weeks ( $P=0.001$ ) for patients and singleton controls respectively. Birth weights were 2834.4+/-821.2 vs 3036+/-489.3g ( $P=0.02$ ), proportion of low birth weight (<2500 g) was 33.3% vs 11.7% ( $P=0.0001$ ) and very low birth weight (<1500 g) 3.5 vs 0.6% for patients and singleton controls respectively. The proportion of deliveries before 28 weeks of gestation was 7.0% vs 1.2% ( $P=0.01$ ) for patients and singleton controls respectively. When comparing the study group to twin control pregnancies, a similar gestational age at delivery (35 weeks) and rate of preterm birth (23%) were found.	4

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
88. Evron E, Sheiner E, Friger M, Sergienko R, Harlev A. Vanishing twin syndrome: is it associated with adverse perinatal outcome? <i>Fertil Steril</i> . 2015;103(5):1209-1214.	Observational-Dx	252,994 deliveries	To evaluate whether vanishing twin syndrome is associated with adverse perinatal outcome.	During the study period, 278 pregnancies with vanishing twin syndrome were compared with 1,801 pregnancies of dichorionic twins and 252,994 pregnancies of singletons. A significant linear association was documented among the 3 groups and various adverse outcomes, including gestational diabetes mellitus, IUGR, very low birth weight, and perinatal mortality. The higher risk was noted in the vanishing twin syndrome group, and the lowest in singletons. Using multivariable logistic regression models, while controlling for confounders such as fertility treatment and maternal age, vanishing twin syndrome (as compared with singletons) was found to be an independent risk factor for several adverse perinatal outcomes including gestational diabetes mellitus, IUGR, very low birth weight, low Apgar scores, and perinatal mortality (adjusted ORs with their respective 95% CIs, 1.4 [1.01–2.0], 2.7 [1.7–4.3], 6.9 [4.7–10.2], 1.9 [1.1–3.3], 2.4 [1.2–4.5]).	4
89. Branum AM, Schoendorf KC. The effect of birth weight discordance on twin neonatal mortality. <i>Obstet Gynecol</i> . 2003;101(3):570–574.	Observational-Dx	128,168 twin sets	To estimate the association between BWD and neonatal mortality controlling for the effects of fetal growth, and to understand the differences in the incidence of mortality between larger and smaller infants.	Mortality was 11 times higher among highly discordant smaller twins (30% or more) compared with nondiscordant smaller twins (43.4 and 3.8 per 1000, respectively). Risk estimates ranged from 1.08 (95% CI, 0.85, 1.38) among 15%–19% discordant twins to 2.05 (95% CI, 1.66, 2.51) among 30% or more discordant twins. Larger twins had similar risk estimates. After accounting for the association between fetal growth and discordance, mortality risk was substantially higher among smaller and larger twins who were highly discordant (30% or more). In addition, there was little difference in the magnitude of risk estimates between highly discordant smaller and larger twins.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. Kato N, Matsuda T. Estimation of optimal birth weights and gestational ages for twin births in Japan. <i>BMC Public Health</i> . 2006;6:45.	Review/Other-Dx	10,302,465 pregnancies	To estimate the birth weight and gestational age associated with the lowest perinatal death rate in contemporary Japan.	The overall perinatal mortality rates per 1,000 births for singletons was 6.9, and the lowest perinatal mortality rates was 1.1 for birth weight (3.5–4.0 kg) and gestational age (40–weeks). For twins, the overall perinatal mortality rates per 1,000 births was 36.8, and the lowest perinatal mortality rates was 3.9 for birth weight (2.5–3.0 kg) and gestational age (36–39 weeks). At optimal birth weight and gestational age, the perinatal mortality rates were reduced to 15.9% for singletons, and 10.6% for twins, compared to the overall perinatal mortality rates. The risk of perinatal mortality was greater in twins than in singleton sat the same deviation from the ideal category of each plurality.	4
91. Banks CL, Nelson SM, Owen P. First and third trimester ultrasound in the prediction of birthweight discordance in dichorionic twins. <i>Eur J Obstet Gynecol Reprod Biol</i> . 2008;138(1):34-38.	Observational-Dx	135 gestations	To assess the efficacy of routine third trimester US fetal biometry, third trimester fetal growth velocity and first trimester differences in size in the prediction of subsequent birthweight discordance.	135 dichorionic gestations were identified over a consecutive 3–year-period. 108 twin gestations had both CRL and sufficient US measurements in the third trimester to calculate fetal growth velocity. 26 pregnancies (24%) had discordant birthweight. Only EFW Z score difference was correlated with birthweight disparity ( $r=0.36$ , $P\leq 0.001$ ). An EFW Z score difference of 0.6 had an AUC of 0.70 (95% CI, 0.59–0.79) but this did not differ significantly from first trimester prediction of growth discordance which had an area of 0.55 (95% CI, 0.44–0.66). The likelihood ratio for first and third trimester prediction of discordance were low.	3
92. Chang YL, Chang TC, Chang SD, et al. Sonographic prediction of significant intertwin birth weight discordance. <i>Eur J Obstet Gynecol Reprod Biol</i> . 2006;127(1):35-40.	Observational-Dx	575 twin pregnancies	To evaluate the usefulness of US prediction of significant BWD in twin pregnancies.	A total of 575 twin pregnancies were included in the study. The estimated discordance by US examination proved to be an effective predictor of discordant twin growth. The BWD estimated by US tended to underestimate the degree of discordant twins.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
93. Danon D, Melamed N, Bardin R, Meizner I. Accuracy of ultrasonographic fetal weight estimation in twin pregnancies. <i>Obstet Gynecol.</i> 2008;112(4):759-764.	Observational-Dx	1112 pregnancies	To compare the accuracy of fetal weight estimations between normal and growth-restricted twin and singleton pregnancies in a single tertiary center.	The study groups included 278 twins and 834 singleton pregnancies. The twins group was characterized by a higher mean absolute percentage error compared with the singleton group (8.9% compared with 6.8%). Accuracy was lower for the second twins than for the first twins. When comparing the subgroup of fetal growth restriction, differences in sensitivity and specificity were small for singleton compared with overall twins (47.5% compared with 48.9% and 97.7% compared with 95.7%, respectively). Overall accuracy was better in the singleton group (95% compared with 88%), mainly due to relatively low accuracy in the second twin (86%). For detection of discordancy, EFW had a sensitivity of 52%, specificity of 88%, and overall accuracy of 81%.	3
94. Diaz-Garcia C, Bernard JP, Ville Y, Salomon LJ. Validity of sonographic prediction of fetal weight and weight discordance in twin pregnancies. <i>Prenat Diagn.</i> 2010;30(4):361-367.	Observational-Dx	283 twin pregnancies	To assess the accuracy of EFW in twins and to assess the accuracy of US examination to predict BWD.	283 twin pregnancies were included. Mean and SD (%) of the standardized errors were 1.54 +/- 12.19, 0.19 +/- 11.87, 10.93 +/- 15.55, - 1.91 +/- 14.93 and 5.37 +/- 14.91 for Hadlock1, Hadlock2, Shepard, Ong and Warsof formulas, respectively. Hadlock2's formula allowed for the highest proportion of newborns with birthweight within 10% of EFW and it also performed best to predict discordance of more than 25% as assessed by AUC.	3
95. Gonzalez-Quintero VH, Luke B, O'Sullivan M J, et al. Antenatal factors associated with significant birth weight discordancy in twin gestations. <i>Am J Obstet Gynecol.</i> 2003;189(3):813-817.	Observational-Dx	3910 twin gestations	To evaluate factors that are associated with significant BWD.	Severe BWD was associated with fetal growth deceleration by 20 to 28 weeks (adjusted OR, 4.90; 95% CI, 3.15–7.64) and between 28 weeks to birth (adjusted OR, 3.48; 95% CI, 1.72–7.06). Antenatal bleeding (adjusted OR, 1.86; 95% CI, 1.08–3.21), preeclampsia (adjusted OR, 1.70, 95% CI, 1.21–2.41), and monochorionicity (adjusted OR, 2.35, 95% CI, 1.71–3.23) were also associated with BWD.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
96. Hartley RS, Hitti J, Emanuel I. Size-discordant twin pairs have higher perinatal mortality rates than nondiscordant pairs. <i>Am J Obstet Gynecol.</i> 2002;187(5):1173-1178.	Observational-Dx	9590 twin pairs	To determine whether size-discordant twin pairs have worse perinatal mortality and neonatal morbidity rates than nondiscordant pairs and whether the smaller twins of discordant pairs have worse perinatal outcomes than the larger twins.	Discordant twin pairs had higher rates of perinatal mortality, neonatal mortality, and 5-minute Apgar scores of <7, even after stratification by gestational age. Discordant pairs had lower pair weights at each gestational age and were more likely to include small-for-gestational-age infants. Compared with the larger twins, the smaller twins of discordant pairs had higher rates of perinatal mortality.	3
97. Klam SL, Rinfret D, Leduc L. Prediction of growth discordance in twins with the use of abdominal circumference ratios. <i>Am J Obstet Gynecol.</i> 2005;192(1):247-251.	Observational-Dx	503 twin pregnancies	To assess the accuracy of US prediction of twin BWD using the abdominal circumference ratio.	Of 503 diamniotic twin pregnancies, 64 pregnancies (12.7%) had discordant fetal growth. The abdominal circumference ratio could be measured consistently throughout gestation in 100% of twin pairs. Receiver operating curve analysis showed that the abdominal circumference ratio was a good predictor of BWD (AUC = 0.80). An abdominal circumference ratio cutoff of 0.93 yielded a sensitivity and specificity of 61% and 84%, respectively.	3
98. Van Mieghem T, Deprest J, Klaritsch P, et al. Ultrasound prediction of intertwin birth weight discordance in monochorionic diamniotic twin pregnancies. <i>Prenat Diagn.</i> 2009;29(3):240-244.	Observational-Dx	60 pregnancies	To estimate the accuracy of US to predict birth weight (BW) and BWD in MCDA twin pregnancies.	60 pregnancies were included. Median Delta birthweight was 9.98%. 10(16,7%), 8(13,3%) and 5(8,3%) twin pairs had a Delta birthweight >20%, >25% and >30%, respectively. BW and EFW (r = 0.96; P<0.001) as well as Delta birthweight and DeltaEFW were well correlated with each other (r = 0.75; P<0.001). Bland-Altman analysis showed that US evaluation overestimated Delta birthweight if >20%. Negative predictive value of US for Delta birthweight >25% was 98%. The AUC to predict a Delta birthweight >25% at 16, 20, and 26 weeks and <2 weeks before birth was 0.79, 0.87, 0.93, and 0.95, respectively.	3

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
99. O'Connor C, McAuliffe FM, Breathnach FM, et al. Prediction of outcome in twin pregnancy with first and early second trimester ultrasound. <i>J Matern Fetal Neonatal Med.</i> 2013;26(10):1030–1035.	Observational-Dx	1028 twin pregnancies	To establish if first or second trimester biometry is a useful adjunct in the prediction of adverse perinatal outcome in twin pregnancy.	Differences in CRL were not predictive of adverse perinatal outcome. Between 14 and 22 weeks, a difference in abdominal circumference of more than 10% was the most useful predictor of adverse outcome, preterm delivery and 18% or more BWD in all twins. Overall the strongest correlation was observed for intertwin differences in biometry between 18 and 22 weeks.	3
100. Ayres A, Johnson TR. Management of multiple pregnancy: prenatal care-part I. <i>Obstet Gynecol Surv.</i> 2005;60(8):527-537.	Review/Other-Dx	N/A	To describe the effects of the rising rate of multiple pregnancies on perinatal morbidity and mortality, to recall the complications of diagnosing and treating abnormalities of multiple pregnancies, and to list the many changes that occur in both the mother and the fetuses in multiple pregnancies.	No results stated in abstract.	4
101. American College of Radiology. ACR Appropriateness Criteria®: Assessment of Fetal Well Being. Available at: <a href="https://acsearch.acr.org/docs/3094108/Narrative/">https://acsearch.acr.org/docs/3094108/Narrative/</a> .	Review/Other-Dx	N/A	To assess fetal well-being.	N/A	4
102. Pan M, Chen M, Leung TY, Sahota DS, Ting YH, Lau TK. Outcome of monochorionic twin pregnancies with abnormal umbilical artery Doppler between 16 and 20 weeks of gestation. <i>J Matern Fetal Neonatal Med.</i> 2012;25(3):277-280.	Review/Other-Dx	84 twin pregnancies	To study the perinatal outcome among MCDA twin pregnancies with absent or reversed end-diastolic flow of the umbilical artery absent or reversed end-diastolic flow at 16–20 weeks of gestation.	Absent or reversed end-diastolic flow was present in 56.7% of the 30 monochorionic twins with complications at recruitment. The mortality was significantly higher among those with absent or reversed end-diastolic flow. Among the 54 uncomplicated cases at recruitment, only 7.41% had absent or reversed end-diastolic flow. The presence of isolated absent or reversed end-diastolic flow was associated with significantly higher incidence of growth discordance (25.0% vs 2%). The incidence of perinatal mortality and TTTS was almost doubled (25.0% vs 9% and 25.0% vs 14%).	4
103. Newman RB, Ellings JM. Antepartum management of the multiple gestation: the case for specialized care. <i>Semin Perinatol.</i> 1995;19(5):387-403.	Review/Other-Dx	N/A	To discuss the antepartum management of multiple gestations and conclude that specialized care can improve both perinatal morbidity and mortality in these pregnancies.	No results stated in abstract.	4

**Multiple Gestations  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
104. American College of Radiology. ACR-SPR Practice Parameter for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation. Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/Pregnant_Patients.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/Pregnant_Patients.pdf</a> .	Review/Other-Dx	N/A	To provide current practical information to radiologists, other physicians, and medical practitioners implementing policies for imaging pregnant and potentially pregnant patients.	N/A	4
105. American College of Radiology. ACR-ACOG-AIUM-SRU Practice Parameter for the Performance of Obstetrical Ultrasound. Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/US_Obstetrical.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/US_Obstetrical.pdf</a> .	Review/Other-Dx	N/A	To assist practitioners in providing appropriate radiologic care for patients.	N/A	4
106. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. <i>J Magn Reson Imaging</i> . 2013;37(3):501-530.	Review/Other-Dx	N/A	Guidance document on MR safety practices to help guide MR practitioners regarding MR safety issues and provide a basis for them to develop and implement their own MR policies and practices.	N/A	4
107. American College of Radiology. <i>Manual on Contrast Media</i> . Available at: <a href="http://www.acr.org/Quality-Safety/Resources/Contrast-Manual">http://www.acr.org/Quality-Safety/Resources/Contrast-Manual</a> .	Review/Other-Dx	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	4
108. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: <a href="http://www.acr.org/~media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf">http://www.acr.org/~media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf</a> .	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	N/A	4

## Evidence Table Key

### Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
  - *Category 2* The study is moderately well-designed and accounts for most common biases.
  - *Category 3* There are important study design limitations.
  - *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
    - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
    - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
    - c) the study is an expert opinion or consensus document.
  - M = Meta-analysis
- 

Dx = Diagnostic

Tx = Treatment