Guidelines & Protocols in OBGY

A Ready Reckoner

Medical disorders in pregnancy - II

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From The President's Desk ...

Dear Members,

It gives me immense pleasure to release the fourth volume our **'READY RECKONER - The Guidelines and Protocols in Ob-Gy'**.

In this era of evidence based medicine, it is expected that all treatment modalities be guidelines based. To have a quick access to the standard guidelines and have them well sorted out, we will be releasing this ready reckoner on various essential topics every month.

This **first of its kind and unique attempt** is our small effort to simplify protocols.

With great pleasure we announce the release of its fourth volume : **'Medical disorders in pregnancy - Volume II'**. I am sure, this release will be valuable in your daily clinical practice and help in quick amending.

I will fail in my duty if, I don't acknowledge the tremendous efforts and contributions from the Clinical Secretary, Dr. Sumeet Baheti and the Coordinators, Dr. Jayshree Upadhay, Dr. Divya Assudani, Dr. Soumya Rathi. They have toiled very hard to compile these guidelines for your benefit .

Happy reading ... Wishing you all Safe and Ethical Clinical Practice ...

Academically yours,
Dr. Vaidehi Marathe
President NOGS - 2020-21

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Table of Contents

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Indications for Antepartum Fetal Surveillance?

- In general, antepartum fetal surveillance has been used in pregnancies in which the risk of antepartum fetal demise is increased.
- Antepartum fetal surveillance results have not been definitively demonstrated to improve perinatal outcome, so all indications for antepartum testing must be considered somewhat relative.
- Accordingly, some of the conditions for which testing may be indicated include, but are not limited to, those listed in Box 1

Box 1. Indications for Antepartum Fetal Surveillance Testing

Maternal conditions

- Pregestational diabetes mellitus
- Hypertension
- Systemic lupus erythematosus
- Chronic renal disease
- Antiphospholipid syndrome
- Hyperthyroidism (poorly controlled)
- Hemoglobinopathies (sickle cell, sickle cell– hemoglobin C, or sickle cell–thalassemia disease)
- Cyanotic heart disease

Pregnancy-related conditions

- Gestational hypertension
- Preeclampsia
- Decreased fetal movement
- Gestational diabetes mellitus (poorly controlled or medically treated)
- Oligohydramnios
- Fetal growth restriction
- Late term or postterm pregnancy
- Isoimmunization
- Previous fetal demise (unexplained or recurrent risk)
- Monochorionic multiple gestation (with significant growth discrepancy)

Initiating Antepartum Fetal Surveillance

- Choosing the appropriate point in gestation to begin antepartum fetal testing depends on several considerations, including
  - o Prognosis for neonatal survival,
  - o Risk of fetal death,
  - o Severity of maternal disease,
  - o Potential for iatrogenic prematurity complications resulting from false-positive test results.
- Both theoretic models and large clinical studies suggest that initiating antepartum fetal testing no earlier than 32 0/7 weeks of gestation is appropriate for most at-risk patients .
- In pregnancies with multiple or particularly worrisome high-risk conditions (eg, chronic hypertension with suspected fetal growth restriction), testing might begin at a gestational age when delivery would be considered for perinatal benefit .

Recommended frequency of testing

- There are no large clinical trials to guide the frequency of testing, and thus, the optimal frequency remains unknown; it depends on several factors and should be individualized and based on clinical judgment.
- If the indication for testing is not persistent (eg, a single episode of decreased fetal movement followed by reassuring testing in an otherwise uncomplicated pregnancy), testing need not be repeated.
- When the clinical condition that prompted testing persists, the test should be repeated periodically to monitor for continued fetal well-being until delivery.
- If the maternal medical condition is stable and test results are reassuring, tests of fetal well-being (NST, BPP, modified BPP, or CST) are typically repeated at weekly intervals
- In pregnancies complicated by fetal growth restriction, the optimal interval for fetal growth assessment and the optimal surveillance regimen have not been established.
- Most growth-restricted fetuses can be adequately evaluated with serial ultrasonography every 3–4 weeks; ultrasonographic assessment of growth should not be performed more frequently than every 2 weeks because the inherent error associated with ultrasonographic measurements can preclude an accurate assessment of interval growth.
- Any significant change in maternal or fetal status requires further reevaluation.

Antepartum Fetal Surveillance Techniques

Several antepartum fetal surveillance techniques (tests) are in clinical use. These include maternal perception of fetal movement, contraction stress test (CST), nonstress test (NST), biophysical profile (BPP), modified BPP, and umbilical artery Doppler velocimetry.

Maternal–Fetal Movement Assessment

- A decrease in the maternal perception of fetal movement may precede fetal death, in some cases by several days.
- This observation provides the rationale for fetal movement assessment by the mother ("kick counts") as a means of antepartum fetal surveillance.
- Although several counting protocols have been used, neither the optimal number of movements nor the ideal duration for counting movements has been defined. Thus, numerous protocols have been reported and appear to be acceptable
- In one approach, the woman was instructed to lie on her side and count distinct fetal movements. Perception of 10 distinct movements in a period of up to 2 hours was considered reassuring. The count was discontinued once 10 movements were perceived.
- In another approach, women were instructed to count fetal movements for 1 hour three times per week. The count was considered reassuring if it equaled or exceeded the woman's previously established baseline count. Thus, regardless of the fetal movement approach used, in the absence of a reassuring count, further fetal assessment is recommended
- Should all women perform daily fetal movement assessment ?
  Multiple studies have demonstrated that women who report decreased fetal movement are at an increased risk of adverse perinatal outcomes. Although not all women need to perform a daily fetal movement assessment, if a woman notices a decrease in fetal activity, she should be encouraged to contact her health care provider, and further assessment should be performed

Contraction Stress Test

- The CST is based on the response of the FHR to uterine contractions. It relies on the premise that fetal oxygenation will be transiently worsened by uterine contractions.
- In the suboptimally oxygenated fetus, the resultant intermittent worsening in oxygenation will, in turn, lead to the FHR pattern of late decelerations. Uterine contractions also may produce a pattern of variable decelerations caused by fetal umbilical cord compression, which in some cases is associated with oligohydramnios
- The results of the CST are categorized as follows:
  - Negative: no late or significant variable decelera- tions
  - Positive: late decelerations after 50% or more of contractions (even if the contraction frequency is fewer than three in 10 minutes)
  - Equivocal–suspicious: intermittent late decelera- tions or significant variable decelerations
  - Equivocal: FHR decelerations that occur in the pres- ence of contractions more frequent than every 2 min- utes or lasting longer than 90 seconds

- o Unsatisfactory: fewer than three contractions in 10 minutes or an uninterpretable tracing
- The CST is a safe and effective method of inves- tigating FHR nonreactivity in preterm gestations (16).
- Relative contraindications to the CST generally include conditions that also are contraindications to labor or vaginal delivery (17).

Nonstress Test

- The NST is based on the premise that the heart rate of a fetus that is not acidotic or neurologically depressed will temporarily accelerate with fetal movement.
- Heart rate reactivity is thought to be a good indicator of normal fetal autonomic function.
- Loss of reactivity is most commonly associated with a fetal sleep cycle but may result from any cause of central nervous system depression, including fetal acidemia.

Biophysical Profile

- The BPP consists of an NST combined with four obser- vations made by real-time ultrasonography.
- BPP comprises five components:
  1. Nonstress test—may be omitted without compro- mising test validity if the results of all four ultra- sound components of the BPP are normal
  2. Fetal breathing movements—one or more episodes of rhythmic fetal breathing movements of 30 seconds or more within 30 minutes
  3. Fetal movement—three or more discrete body or limb movements within 30 minutes
  4. Fetal tone—one or more episodes of extension of a fetal extremity with return to flexion, or opening or closing of a hand
  5. Determination of the amniotic fluid volume—a single deepest vertical pocket greater than 2 cm is considered evidence of adequate amniotic fluid
- Each of the five components is assigned a score of either 2 (present, as previously defined) or 0 (not present).
- A composite score of 8 or 10 is normal, a score of 6 is considered equivocal, and a score of 4 or less is abnormal.
- Regardless of the composite score, oligohydramnios (defined as an amniotic fluid volume of 2 cm or less in the single deepest vertical pocket) should prompt further evaluation

The Modified BPP

- It combines the NST, as a short-term indicator of fetal acid–base status, with an amniotic fluid volume assessment, as an indicator of long-term placental function.
- The results of the modified BPP are considered
  - Normal if the NST is reactive and the amniotic fluid volume is greater than 2 cm in the deepest vertical pocket
  - Abnormal if either the NST is nonreactive or amniotic fluid volume in the deepest vertical pocket is 2 cm or less (i.e. oligohydramnios is present).

Umbilical Artery Doppler Velocimetry

- Doppler ultrasonography is a noninvasive technique used to assess the hemodynamic components of vascular resistance in pregnancies complicated by fetal growth restriction.
- Specifically, the umbilical flow velocity waveform of normally growing fetuses is characterized by high-velocity diastolic flow, whereas in growth-restricted fetuses, there is decreased umbilical artery diastolic flow
- Abnormal flow velocity waveforms have been correlated histopathologically with small-artery obliteration in placental tertiary villi and functionally with fetal hypoxemia and acidemia as well as with perinatal morbidity and mortality.
- Commonly measured flow indices, based on the characteristics of peak systolic velocity and frequency shift (S), end-diastolic frequency shift (D), and mean peak frequency shift over the cardiac cycle (A), include the following:
  - Systolic to diastolic ratio (S/D)
  - Resistance index (S-D/S)
  - Pulsatility index (S-D/A)

What is the recommended management of an abnormal antepartum fetal test result?

- An abnormal antepartum fetal test result should always be considered in the context of the overall clinical picture.
  - Certain acute maternal conditions (eg, diabetic ketoacidosis or pneumonia with hypoxemia) can result in abnormal test results, which generally will normalize as the maternal condition improves.
  - In these circumstances, correcting the maternal condition and retesting the fetus may be appropriate.
  - In cases in which an abnormal test result is not associated with any clinical evidence of acute and potentially reversible worsening in the maternal status, a stepwise approach to the investigation of the fetal condition should be undertaken.

- Because antepartum fetal surveillance tests have high false-positive rates and low positive predictive values, abnormal test results are usually followed by another test or delivery based on consideration of test results, maternal and fetal condition, and gestational age .
- Such an approach takes advantage of the high negative predictive value generally exhibited by all commonly used antepartum tests and minimizes the potential for unnecessary delivery based on a single false-positive test result.
- Therefore, the response to an abnormal test result should be tailored to the clinical situation.
    - Maternal reports of decreased fetal movement should be evaluated by an NST, CST, BPP, or modified BPP.
    - Abnormal results from an NST or from a modified BPP generally should be followed by additional testing with either a CST or a BPP.
    - A BPP score of 6 out of 10 is considered equivocal and should prompt further evaluation or delivery based on gestational age.
    - In a fetus at or beyond 37 0/7 weeks of gestation, this score generally should prompt further evaluation and consideration of delivery, whereas in the fetus at less than 37 0/7 weeks of gestation, it should result in a repeat BPP in 24 hours .
    - A BPP score of 4 usually indicates that delivery is warranted, although in pregnancies at less than 32 0/7 weeks of gestation, management should be individualized, and extended monitoring may be appropriate. In most circumstances, a BPP score of less than 4 should result in delivery. If delivery is not planned (eg, given early gestational age), then antenatal surveillance should not be performed because the results will not change managment.
    - Guidelines from the Society for Maternal-Fetal Medicine suggest that with absent end-diastolic flow, delivery should be considered at or beyond 34 0/7 weeks of gestation, and with reversed end-diastolic flow, delivery should be considered at or beyond 32 0/7 weeks of gestation (after corticosteroid administration, if the maternal and fetal condition permit)
    - When the S/D ratio is elevated (i.e. greater than the 95th percentile) but diastolic flow is still present, delivery should be considered at or beyond 37 0/7 weeks of gestation.
    - In the absence of obstetric contraindications, delivery of the fetus with an abnormal test result often may be attempted by induction of labor, with continuous intrapartum monitoring of the FHR and uterine contractions.

Role of umbilical artery and other Doppler velocimetry studies

- In growth-restricted fetuses, umbilical artery Doppler velocimetry used in conjunction with standard fetal surveillance, such as NSTs or BPPs, or both, is associated with improved outcomes
- Umbilical artery Doppler velocimetry has not been shown to be predictive of outcomes in fetuses without growth restriction.
- Investigation of other fetal blood vessels with umbilical artery Doppler velocimetry, including assessments of the middle cerebral artery and the precordial venous system, has been explored in the setting of fetal growth restriction.
- However, these flow measurements have not been shown to improve perinatal outcome, and the role of these measures in clinical practice remains uncertain.

Conclusions based on good and consistent scientific evidence (Level A):

- The use of the deepest vertical pocket measurement, as opposed to the amniotic fluid index, to diagnose oligohydramnios is associated with a reduction in unnecessary interventions without an increase in adverse perinatal outcomes.
- In growth-restricted fetuses, umbilical artery Doppler velocimetry used in conjunction with standard fetal surveillance, such as NSTs, or BPPs, or both, is associated with improved outcomes.

Recommendation based on limited or inconsistent scientific evidence (Level B):

- Abnormal results from an NST or from a modified BPP generally should be followed by additional testing with either a CST or a BPP.

Recommendations based primarily on consensus and expert opinion (Level C):

- Initiating antepartum fetal testing no earlier than 32 0/7 weeks of gestation is appropriate for most at- risk patients. However, in pregnancies with multiple or particularly worrisome high-risk conditions (eg, chronic hypertension with suspected fetal growth restriction), testing might begin at a gestational age when delivery would be considered for perinatal benefit.
- When the clinical condition that prompted testing persists, the test should be repeated periodically to monitor for continued fetal well-being until delivery. If the maternal medical condition is stable and test results are reassuring, tests of fetal well-being (NST, BPP, modified BPP, or CST) are typically repeated at weekly intervals; however, in the presence of certain high-risk conditions, some investigators have performed more frequent testing, although the optimal regimen has not been established.

- In the absence of obstetric contraindications, delivery of the fetus with an abnormal test result often may be attempted by induction of labor, with continuous intrapartum monitoring of the FHR and uterine contractions.
- Based on expert opinion, in the setting of otherwise uncomplicated isolated and persistent oligohydramnios (deepest vertical pocket measurement less than 2 cm), delivery at 36–37 weeks of gestation is recommended.
- In pregnancies at less than 36 0/7 weeks of gestation with intact membranes and oligohydramnios, the decision to proceed with expectant management or delivery should be individualized based on gestational age and the maternal and fetal condition.

RCOG Green-top Guideline

Prepregnancy counselling

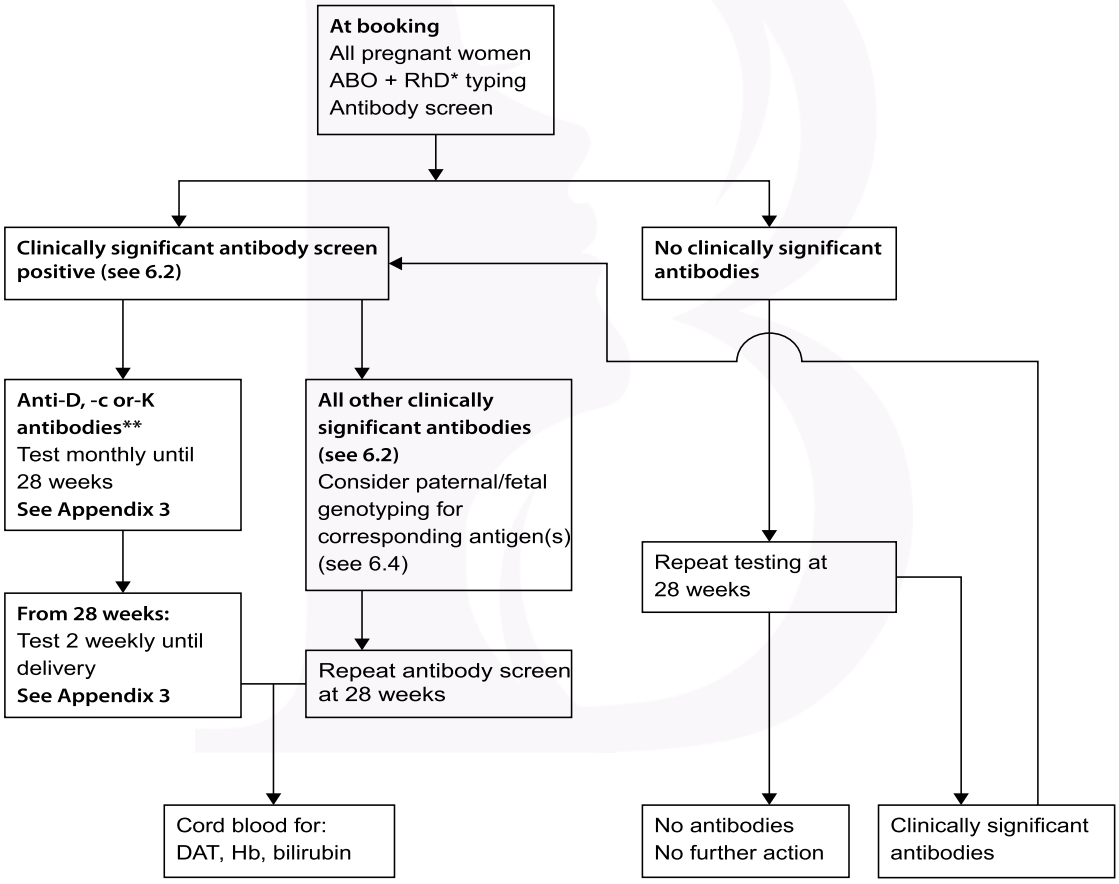
- Women with red cell antibodies, particularly if there is a risk of fetal anaemia or if compatible donor red cells for transfusion may be difficult to obtain, should attend for prepregnancy counselling

Red cell antibodies in pregnancy

- All women should have their blood group and antibody status determined at booking and at 28 weeks of gestation
- Severe fetal anaemia can result in hydrops which significantly worsens the perinatal outcome.
- Non-invasive fetal genotyping using maternal blood is now possible for D, C, c, E, e and K antigens. This should be performed in the first instance for the relevant antigen when maternal red cell antibodies are present.
- For other antigens, invasive testing (chorionic villus sampling [CVS] or amniocentesis) may be considered if fetal anaemia is a concern or if invasive testing is performed for another reason (e.g. karyotyping).
- Invasive testing is not contraindicated if alloimmunisation has occurred. Anti-D prophylaxis should be given to cover invasive testing if the mother is rhesus D (RhD) negative and is not sensitised.
- Referral to a fetal medicine specialist
  - o when there are rising antibody levels/titres, a level/titre above a specific threshold or ultrasound features suggestive of fetal anaemia
- An anti-D level - > 4 iu/ml.
  - o > 4 iu/ml but < 15 iu/ml - moderate risk of HDFN
  - o > 15 iu/ml - severe HDFN.
- An anti-c level - > 7.5 iu/ml
  - o > 7.5 iu/ml but < 20 iu/ml - moderate risk of HDFN
  - o > 20 iu/ml - high risk of HDFN
- For anti-K antibodies, referral should take place once detected, as severe fetal anaemia can occur even with low titres.
- The presence of anti-E potentiates the severity of fetal anaemia due to anti-c antibodies so that referral at lower levels/titres is indicated (unless the fetus has only one of these antigens).

- If there is a history of unexplained severe neonatal jaundice, neonatal anaemia requiring transfusion or exchange transfusion, in order to exclude haemolytic disease of the fetus and newborn (HDFN) as the cause.
- For antibodies other than anti-D, anti-c and anti-K,
  - History of previous significant HDFN or intrauterine transfusion (IUT),
  - Titre of 32 or above, especially if the titre is rising as rising titres correlate with increasing risk and severity of anaemia.

Appendix II: Timing and frequency of antibody screening in pregnancy

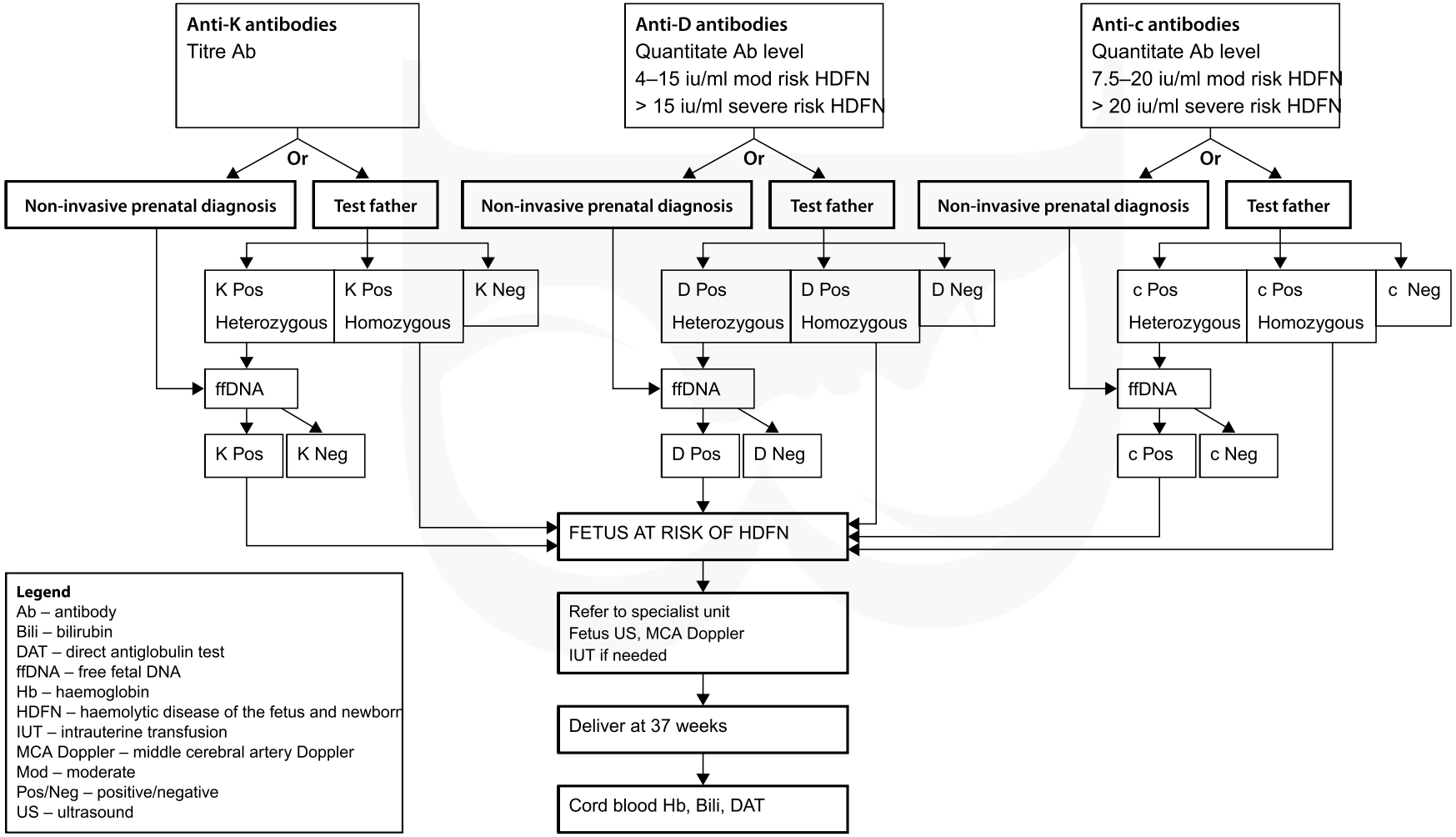


* If RhD-negative mother with no immune anti-D antibodies then advise anti-D prophylaxis for any potentially sensitising events in pregnancy and give routine antenatal anti-D prophylaxis either RAADP single dose or two doses (see RCOG anti-D guidelines); after delivery check cord sample for RhD type and maternal sample for fetomaternal haemorrhage (e.g. Kleihauer) testing to check if further anti-D needed in addition to the standard dose which should be given in the first instance after delivery.

** Pregnancies with immune anti-D, -K or -c are at particular risk of severe fetal HDFN so further early assessment and referral to fetal medicine specialist is indicated (see 6.7).

Legend
DAT – direct antiglobulin test; Hb – haemoglobin; RAADP – routine antenatal anti-D prophylaxis

Appendix III: Management algorithm for pregnancies complicated with anti-D, anti-K or anti-c alloimmunisation



Fetal transfusion

- Red cell preparations for IUT should be group O (low titre haemolysin) or ABO identical with the fetus (if known) and negative for the antigen(s) corresponding to maternal red cell antibodies.
- Blood for intrauterine transfusion (IUT) has the same requirements as blood for neonatal exchange except that plasma is removed by the blood centre to increase the haematocrit to 0.70–0.85 and it is always irradiated. Blood should be ABO compatible with the neonate and mother (to avoid ABO HDFN from the woman's anti-A or -B antibodies present), RhD negative (or RhD identical with neonate), K negative, negative for the corresponding antigen to which the woman has an antibody and cross-match compatible with the woman's blood sample. Blood should be less than 5 days old (to ensure low supernatant potassium levels), CMV negative and irradiated unless the risk to the baby of delaying exchange transfusion while obtaining irradiated blood outweighs this. It should be plasma reduced (rather than in saline-adenine-glucose-mannitol [SAGM] additive solution), with a haematocrit of 0.50–0.60.

Birth

- Timing of delivery for women with red cell antibodies that can cause fetal anaemia will depend on the antibody levels/titres, rate of rise as well as if any fetal therapy has been required. The mode, timing and place of delivery are otherwise dependent on standard obstetric grounds
- As these are 'high-risk' pregnancies, continuous electronic fetal heart monitoring is advised during labour.

Cord blood investigations

- If a woman has clinically significant antibodies, then cord samples should be taken for a direct antiglobulin test (DAT), haemoglobin and bilirubin levels.

Management of the neonate

- This depends on the risk of haemolysis or anaemia conferred by the relevant red cell antibody.
- The neonate should have regular clinical assessment of its neurobehavioural state and be observed for the development of jaundice and/or anaemia.
- Regular assessment of bilirubin and haemoglobin levels should be made and early discharge is not advisable.

- The mother should be encouraged to feed the baby regularly to guard against dehydration, since dehydration can increase the severity of jaundice.
- If bilirubin levels rise rapidly or above the interventional threshold, phototherapy and/or exchange transfusion may be required.
- Pregnancies complicated by red cell alloimmunisation with a minimal or no risk of fetal or neonatal anaemia require no specific treatment.

Future Risks

- Risk of recurrence in a future pregnancy - A woman with a history of a pregnancy or infant affected by HDFN should be referred for early assessment to a fetal medicine specialist in all further pregnancies.

Long-term consequences of red cell antibodies to women and their offspring

- Women can be advised that there are no long-term adverse health consequences associated with the presence of red cell antibodies.
- Some infants may experience anaemia persisting for a few weeks following birth. Some infants may develop late anaemia which is usually due to hyporegenerative anaemia.

BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn

- Following potentially sensitising events, anti-D Ig should be administered as soon as possible and always within 72 h of the event. If, exceptionally, this deadline has not been met some protection may be offered if anti-D Ig is given up to 10 days after the sensitising event
- In pregnancies < 12 weeks gestation, anti-D Ig prophylaxis is only indicated following ectopic pregnancy, molar pregnancy, therapeutic termination of pregnancy and in cases of uterine bleeding where this is repeated, heavy or associated with abdominal pain. The minimum dose should be 250 IU. A test for fetomaternal haemorrhage (FMH) is not required
- For potentially sensitising events between 12 and 20 weeks gestation, a minimum dose of 250 IU should be administered within 72 h of the event. A test for FMH is not required
- For potentially sensitising events after 20 weeks gestation, a minimum anti-D Ig dose of 500 IU should be administered within 72 h of the event. A test for FMH is required
- Appropriate tests for FMH should be carried out for all D negative, previously non-sensitised, pregnant women who have had a potentially sensitising event after 20 weeks of gestation, and additional dose(s) of anti-D Ig should be administered as necessary

- All D negative pregnant women who have not been previously sensitised should be offered routine antenatal prophylaxis with anti-D Ig (RAADP) either with a single dose regimen at around 28 weeks, or two-dose regimen given at 28 and 34 weeks
- It is important that the 28-week sample for blood group and antibody screen is taken prior to the first routine prophylactic anti-D Ig injection being given. This forms the second screen required in pregnancy
- Routine Antenatal Anti-D Ig Prophylaxis (RAADP) should be regarded as a separate entity and administered regardless of, and in addition to, any anti-D Ig that may have been given for a potentially sensitising event
- Following birth, ABO and Rh D typing should be performed on cord blood and if the baby is confirmed to be D positive, all D negative, previously non-sensitised, women should be offered at least 500 IU of anti-D Ig within 72 h following delivery. Maternal samples should be tested for FMH and additional dose(s) given as guided by FMH tests
- In the event of an intrauterine death (IUD), where no sample can be obtained from the baby, an appropriate dose of prophylactic anti-D Ig should be administered to D negative, previously non-sensitised women within 72 h of the diagnosis of IUD, irrespective of the time of subsequent delivery
- Where intra-operative cell salvage (ICS) is used during Caesarean section in D negative, previously nonsensitised women, and where cord blood group is confirmed as D positive (or unknown), a minimum dose of 1500 IU anti-D Ig should be administered following the re-infusion of salvaged red cells, and a maternal sample should be taken for

NICE Guidelines

Preconception planning and care

- Women with diabetes who are planning to become pregnant,
  - o Explain, establishing good blood glucose control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. It is important to explain that risks can be reduced but not eliminated.
    - § the risks associated with pregnancy in women with diabetes increase with how long the woman has had diabetes
    - § to use contraception until good blood glucose control has been established.
    - § that blood glucose targets, glucose monitoring, medicines for treating diabetes (including insulin regimens for insulin-treated diabetes) and medicines for complications of diabetes will need to be reviewed before and during pregnancy
  - o Offer individualised dietary advice & who have a BMI above 27 kg/m2 advice on how to lose weight.
  - o Advise to take folic acid (5 mg/day) until 12 weeks of gestation to reduce the risk of having a baby with a neural tube defect.
  - o Offer monthly measurement of their HbA1c level.
  - o Offer a meter for self-monitoring of blood glucose.
  - o Advise to aim for the same capillary plasma glucose target ranges as recommended for all people with type 1 diabetes:
  - o fasting plasma glucose level of 5–7 mmol/litre
  - o plasma glucose level of 4–7 mmol/litre before meals at other times of the day.
  - o Advise to aim to keep their HbA1c level below 48 mmol/mol (6.5%), if this is achievable without causing problematic hypoglycaemia.
  - o Strongly advise women with diabetes whose HbA1c level is above 86 mmol/mol (10%) not to get pregnant because of the associated risks.
  - o Women with diabetes may be advised to use metformin as an adjunct or alternative to insulin in the preconception period and during pregnancy, when the likely benefits from improved blood glucose control outweigh the potential for harm. All other oral blood glucose-lowering agents should be discontinued before pregnancy and insulin substituted.
  - o Use isophane insulin (also known as NPH insulin) as the first choice for long-acting insulin during pregnancy. Consider continuing treatment with long-acting insulin analogues (insulin detemir or insulin glargine) in women with diabetes who have established good blood glucose control before pregnancy.

- Offer **retinal assessment** to women with diabetes seeking preconception care at their first appointment (unless they have had an annual retinal assessment in the last 6 months) and then annually if no diabetic retinopathy is found.
- Offer women with diabetes a **renal assessment**, including a measure of albuminuria, before discontinuing contraception. If serum creatinine is abnormal (120 micromol/litre or more), the urinary albumin:creatinine ratio is greater than 30 mg/mmol or the estimated glomerular filtration rate (eGFR) is less than 45 ml/minute/1.73 m2, referral to a nephrologist should be considered before discontinuing contraception.

Risk assessment for gestational diabetes mellitus

- Assess risk of gestational diabetes using risk factors in a healthy population. At the booking appointment, determine the following risk factors for gestational diabetes:
  - Offer women with diabetes a **renal assessment**,
  - BMI above 30 kg/m2
  - previous macrosomic baby weighing 4.5 kg or above
  - previous gestational diabetes
  - family history of diabetes (first-degree relative with diabetes)
  - minority ethnic family origin with a high prevalence of diabetes.
- Do not use fasting plasma glucose, random blood glucose, HbA1c, glucose challenge test or urinalysis for glucose to assess risk of developing gestational diabetes.
- Be aware that glycosuria of 2+ or above on 1 occasion or of 1+ or above on 2 or more occasions detected by reagent strip testing during routine antenatal care may indicate undiagnosed gestational diabetes. If this is observed, consider further testing to exclude gestational diabetes.
- Use the 2-hour 75 g oral glucose tolerance test (OGTT) to test for gestational diabetes in women with risk factors.
- Offer women who have had gestational diabetes in a previous pregnancy:
  - early self-monitoring of blood glucose or
  - a 75 g 2-hour OGTT as soon as possible after booking (whether in the first or second trimester), and a further 75 g 2-hour OGTT at 24–28 weeks if the results of the first OGTT are normal.
- Offer women with any of the other risk factors for gestational diabetes - 75 g 2-hour OGTT at 24–28 weeks.
- Diagnose gestational diabetes if the woman has either:
  - fasting plasma glucose level of 5.6 mmol/litre or above **or**
  - 2-hour plasma glucose level of 7.8 mmol/litre or above.

- about the implications (both short and long term) of the diagnosis for her and her baby
- that good blood glucose control throughout pregnancy will reduce the risk of fetal macrosomia, trauma during birth (for her and her baby), induction of labour and/or caesarean section, neonatal hypoglycaemia and perinatal death
- that treatment includes changes in diet and exercise and could involve medicines.

- Tailor blood glucose-lowering therapy to the blood glucose profile and personal preferences of the woman with gestational diabetes.
- Offer women advice about changes in diet and exercise at the time of diagnosis of gestational diabetes.
- Advise women with gestational diabetes to eat a healthy diet during pregnancy, and emphasise that foods with a low glycaemic index should replace those with a high glycaemic index.
- Refer all women with gestational diabetes to a dietitian.
- Advise women with gestational diabetes to take regular exercise (such as walking for 30 minutes after a meal) to improve blood glucose control.
- Offer a trial of changes in diet and exercise to women with gestational diabetes who have a fasting plasma glucose level below 7 mmol/litre at diagnosis.
- Offer metformin to women with gestational diabetes if blood glucose targets are not met using changes in diet and exercise within 1–2 weeks.
- Offer insulin instead of metformin to women with gestational diabetes if metformin is contraindicated or unacceptable to the woman.
- Offer addition of insulin to the treatments of changes in diet, exercise and metformin for women with gestational diabetes if blood glucose targets are not met.
- Offer immediate treatment with insulin, with or without metformin, as well as changes in diet and exercise, to women with gestational diabetes who have a fasting plasma glucose level of 7.0 mmol/litre or above at diagnosis.
- Consider immediate treatment with insulin, with or without metformin, as well as changes in diet and exercise, for women with gestational diabetes who have a fasting plasma glucose level of between 6.0 and 6.9 mmol/litre if there are complications such as macrosomia or hydramnios.
- Consider glibenclamide, for women with gestational diabetes:
  - in whom blood glucose targets are not achieved with metformin but who decline
    - § insulin therapy or
    - § who cannot tolerate metformin.

Antenatal care for women with diabetes

- Advise pregnant women with type 2 diabetes or gestational diabetes to test their fasting and 1-hour post-meal blood glucose levels daily during pregnancy if they are:
  - on diet and exercise therapy or
  - taking oral therapy (with or without diet and exercise therapy) or
  - single-dose intermediate-acting or long-acting insulin.
- Advise pregnant women with any form of diabetes to maintain their capillary plasma glucose below the following target levels
  - fasting: 5.3 mmol/litre **and**
  - 1 hour after meals: 7.8 mmol/litre or
  - 2 hours after meals: 6.4 mmol/litre.
- Advise pregnant women with diabetes who are on insulin or glibenclamide to maintain their capillary plasma glucose level above 4 mmol/litre.
- Measure HbA1c levels in all pregnant women with pre-existing diabetes at the booking appointment to determine the level of risk for the pregnancy.
- Consider measuring HbA1c levels in the second and third trimesters of pregnancy for women with pre-existing diabetes to assess the level of risk for the pregnancy.
- Measure HbA1c levels in all women with gestational diabetes at the time of diagnosis to identify those who may have pre-existing type 2 diabetes.
- Do not use HbA1c levels routinely to assess a woman's blood glucose control in the second and third trimesters of pregnancy.
- Be aware that the rapid-acting insulin analogues (aspart and lispro) have advantages over soluble human insulin during pregnancy and consider their use.
- Advise women with insulin-treated diabetes of the risks of hypoglycaemia and impaired awareness of hypoglycaemia in pregnancy, particularly in the first trimester.
- Advise pregnant women with insulin-treated diabetes to always have available a fast-acting form of glucose (for example, dextrose tablets or glucose-containing drinks).
- Offer women with insulin-treated diabetes continuous subcutaneous insulin infusion (CSII; also known as insulin pump therapy) during pregnancy if adequate blood glucose control is not obtained by multiple daily injections of insulin without significant disabling hypoglycaemia.
- Consider continuous glucose monitoring for pregnant women on insulin therapy:
  - who have problematic severe hypoglycaemia (with or without impaired awareness of hypoglycaemia) or

  - who have unstable blood glucose levels (to minimise variability) **or**
  - to gain information about variability in blood glucose levels.
- Test urgently for ketonaemia if a pregnant woman with any form of diabetes presents with hyperglycaemia or is unwell, to exclude diabetic ketoacidosis.
- At antenatal appointments, provide care specifically for women with diabetes, in addition to the care provided routinely for healthy pregnant women.
- During pregnancy, admit immediately women who are suspected of having diabetic ketoacidosis for level 2 critical care, where they can receive both medical and obstetric care.
- Offer pregnant women with pre-existing diabetes retinal assessment by digital imaging following their first antenatal clinic appointment (unless they have had a retinal assessment in the last 3 months), and again at 28 weeks. If any diabetic retinopathy is present at booking, perform an additional retinal assessment at 16–20 weeks.
- Ensure that women who have preproliferative diabetic retinopathy or any form of referable retinopathy diagnosed during pregnancy have ophthalmological follow-up for at least 6 months after the birth of the baby.
- If renal assessment has not been undertaken in the preceding 3 months in women with pre-existing diabetes, arrange it at the first contact in pregnancy. If the serum creatinine is abnormal (120 micromol/litre or more), the urinary albumin:creatinine ratio is greater than 30 mg/mmol or total protein excretion exceeds 0.5 g/day, referral to a nephrologist should be considered (eGFR should not be used during pregnancy). Thromboprophylaxis should be considered for women with nephrotic range proteinuria above 5 g/day (albumin:creatinine ratio greater than 220 mg/mmol).
- Offer women with diabetes an ultrasound scan for detecting fetal structural abnormalities, including examination of the fetal heart (4 chambers, outflow tracts and 3 vessels), at 20 weeks.
- Offer pregnant women with diabetes ultrasound monitoring of fetal growth and amniotic fluid volume every 4 weeks from 28 to 36 weeks.
- Diabetes should not be considered a contraindication to antenatal steroids for fetal lung maturation or to tocolysis.
- In women with insulin-treated diabetes who are receiving steroids for fetal lung maturation, give additional insulin according to an agreed protocol and monitor them closely.
- Do not use betamimetic medicines for tocolysis in women with diabetes.

Intrapartum care

- Discuss the timing and mode of birth with pregnant women with diabetes during antenatal appointments, especially during the third trimester.
- Advise pregnant women with type 1 or type 2 diabetes and no other complications to have an elective birth by induction of labour, or by elective caesarean section if indicated, between 37+0 weeks and 38+6 weeks of pregnancy.
- Consider elective birth before 37+0 weeks for women with type 1 or type 2 diabetes if there are metabolic or any other maternal or fetal complications.
- Advise women with gestational diabetes to give birth no later than 40+6 weeks, and offer elective birth (by induction of labour, or by caesarean section if indicated) to women who have not given birth by this time.
- Consider elective birth before 40+6 weeks for women with gestational diabetes if there are maternal or fetal complications.
- Diabetes should not in itself be considered a contraindication to attempting vaginal birth after a previous caesarean section.
- Explain to pregnant women with diabetes who have an ultrasound-diagnosed macrosomic fetus about the risks and benefits of vaginal birth, induction of labour and caesarean section
- Offer women with diabetes and comorbidities such as obesity or autonomic neuropathy an anaesthetic assessment in the third trimester of pregnancy.
- If general anaesthesia is used for the birth in women with diabetes, monitor blood glucose every 30 minutes from induction of general anaesthesia until after the baby is born and the woman is fully conscious.
- Monitor capillary plasma glucose every hour during labour and birth in women with diabetes and ensure that it is maintained between 4 and 7 mmol/litre.
- Intravenous dextrose and insulin infusion should be considered for women with type 1 diabetes from the onset of established labour.
- Use intravenous dextrose and insulin infusion during labour and birth for women with diabetes whose capillary plasma glucose is not maintained between 4 and 7 mmol/litr
- Babies of women with diabetes should stay with their mothers unless there is a clinical complication or there are abnormal clinical signs that warrant admission for intensive or special care.
- Carry out blood glucose testing routinely in babies of women with diabetes at 2–4 hours after birth. Carry out blood tests for polycythaemia, hyperbilirubinaemia, hypocalcaemia and hypomagnesaemia for babies with clinical signs.
- Perform an echocardiogram for babies of women with diabetes if they show clinical signs associated with congenital heart disease or cardiomyopathy, including heart murmur.

- Admit babies of women with diabetes to the neonatal unit if they have:
  - hypoglycaemia associated with abnormal clinical signs
  - respiratory distress
  - signs of cardiac decompensation from congenital heart disease or cardiomyopathy
  - signs of neonatal encephalopathy
  - signs of polycythaemia and are likely to need partial exchange transfusion
  - need for intravenous fluids
  - need for tube feeding (unless adequate support is available on the postnatal ward)
  - jaundice requiring intense phototherapy and frequent monitoring of bilirubinaemia
  - been born before 34 weeks (or between 34 and 36 weeks if dictated clinically by the initial assessment of the baby and feeding on the labour ward).
- Women with diabetes should feed their babies as soon as possible after birth (within 30 minutes) and then at frequent intervals (every 2–3 hours) until feeding maintains pre-feed capillary plasma glucose levels at a minimum of 2.0 mmol/litre.
- If capillary plasma glucose values are below 2.0 mmol/litre on 2 consecutive readings despite maximal support for feeding, if there are abnormal clinical signs or if the baby will not feed orally effectively, use additional measures such as tube feeding or intravenous dextrose.
- Test blood glucose levels in babies of women with diabetes who present with clinical signs of hypoglycaemia, and treat those who are hypoglycaemic with intravenous dextrose as soon as possible

Postnatal care

- Women with insulin-treated pre-existing diabetes should reduce their insulin immediately after birth and monitor their blood glucose levels carefully to establish the appropriate dose.
- Explain to women with insulin-treated pre-existing diabetes that they are at increased risk of hypoglycaemia in the postnatal period, especially when breastfeeding, and advise them to have a meal or snack available before or during feeds.
- Women who have been diagnosed with gestational diabetes should discontinue blood glucose-lowering therapy immediately after birth.
- Women with pre-existing type 2 diabetes who are breastfeeding can resume or continue to take metformin and glibenclamide immediately after birth, but should avoid other oral blood glucose-lowering agents while breastfeeding.
- Women with diabetes who are breastfeeding should continue to avoid any medicines for the treatment of diabetes complications that were discontinued for safety reasons in the preconception period.
- Refer women with pre-existing diabetes back to their routine diabetes care arrangements.

- Remind women with diabetes of the importance of contraception and the need for preconception care when planning future pregnancies.

- Remind women who were diagnosed with gestational diabetes of the symptoms of hyperglycaemia.
- Explain to women who were diagnosed with gestational diabetes about the risks of gestational diabetes in future pregnancies and offer them testing for diabetes when planning future pregnancies.
- For women who were diagnosed with gestational diabetes and whose blood glucose levels returned to normal after the birth:
  - Offer lifestyle advice (including weight control, diet and exercise).
  - Offer a fasting plasma glucose test 6–13 weeks after the birth to exclude diabetes.
  - If a fasting plasma glucose test has not been performed by 13 weeks, offer a fasting plasma glucose test, or an HbA1c test if a fasting plasma glucose test is not possible, after 13 weeks.
- Advise women with a fasting plasma glucose level below 6.0 mmol/litre & HbA1c level below 39 mmol/mol (5.7%) that:
  - they have a low probability of having diabetes at present
  - they should continue to follow the lifestyle advice (including weight control, diet and exercise) given after the birth
  - they will need an annual test to check that their blood glucose levels are normal
  - they have a moderate risk of developing type 2 diabetes, and offer them advice, guidance and interventions on preventing type 2 diabetes.
- Advise women with a fasting plasma glucose level between 6.0 and 6.9 mmol/litre & HbA1c level between 39 and 47 mmol/mol (5.7% and 6.4%) that
  - they are at high risk of developing type 2 diabetes, and offer them advice, guidance and interventions on preventing type 2 diabetes.
- Advise women with a fasting plasma glucose level of 7.0 mmol/litre or above & HbA1c level of 48 mmol/mol (6.5%) or above that
  - they are likely to have type 2 diabetes and offer them a diagnostic test to confirm diabetes.
- Offer an annual HbA1c test to women who were diagnosed with gestational diabetes who have a negative postnatal test for diabetes.
- Offer women who were diagnosed with gestational diabetes early self-monitoring of blood glucose or an OGTT in future pregnancies.

Green Top Guidelines

- The diagnosis of epilepsy and epileptiform seizures should be made by a medical practitioner with expertise in epilepsy, usually a neurologist.
- Women with a history of epilepsy who are not considered to have a high risk of unprovoked seizures can be managed as low-risk women in pregnancy.
- Women with epilepsy (WWE), their families and healthcare professionals should be aware of the different types of epilepsy and their presentation to assess the specific risks to the mother and baby.

Classification of Seizures

Common types of epilepsy/seizures	Clinical presentation	Effects on mother and baby
Tonic-clonic seizures (previously known as grand mal)	Dramatic events with stiffening, then bilateral jerking and a post-seizure state of confusion and sleepiness.	Sudden loss of consciousness with an uncontrolled fall without prior warning. Associated with a variable period of fetal hypoxia.[22] This seizure type is associated with the highest risk of SUDEP.
Absence seizures	Generalised seizures that consist of brief blank spells associated with unresponsiveness, which are followed by rapid recovery.	Effects mediated through brief loss of awareness although physiological effects are modest. Worsening absence seizures place the woman at high risk of tonic-clonic seizures.
Juvenile myoclonic epilepsy	Myoclonic jerks are the key feature of this form of epilepsy and often precede a tonic-clonic convulsion. These jerks present as sudden and unpredictable movements and represent a generalised seizure.	Occurs more frequently after sleep deprivation and in the period soon after waking or when tired. The sudden jerks may lead to falls or to dropping of objects, including the baby.
Focal seizures (previously defined as 'complex partial' if seizures impair consciousness and 'simple partial' if consciousness not impaired)	Symptoms are variable depending on the regions and networks of the brain affected. Within an individual, the attacks are recognisable and stereotypical. Seizures may impair consciousness. Primary focal seizures can undergo secondary generalisation. An aura is a primary focal seizure.	Impairment of consciousness increases risk of injury such as long bone fracture, dental or head injury, electrocution or burns compared with if consciousness is retained (an epileptic aura only). They can be associated with a variable period of hypoxia and risk of SUDEP.

- SUDEP is defined as 'sudden, unexpected, witnessed or unwitnessed, nontraumatic and nondrowning death in patients with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicologic or anatomic cause for death.

Aetiology

- In pregnant women presenting with seizures in the second half of pregnancy which cannot be clearly attributed to epilepsy, immediate treatment should follow existing protocols for eclampsia management until a definitive diagnosis is made by a full neurological assessment.
- Cardiac disorders
- Metabolic disorders
- Intracranial conditions
- Neuropsychiatric conditions including non-epileptic attack disorder

Prepregnancy counselling and management

- WWE who are planning their pregnancy should have a clinician competent in the management of epilepsy take responsibility for sharing decisions around choice and dose of AEDs, based on the risk to the fetus and control of seizures.
- WWE should be reassured that most mothers have normal healthy babies and the risk of congenital malformations is low if they are not exposed to AEDs in the periconception period.
- Women should be informed that the risk of congenital abnormalities in the fetus is dependent on the type, number and dose of AEDs.
- WWE and their partners need to be informed about the possible adverse impact on long-term neurodevelopment of the newborn following in utero exposure to sodium valproate.
- All WWE should be advised to take 5 mg/day of folic acid prior to conception and to continue the intake until at least the end of the first trimester to reduce the incidence of major congenital malformation.

- Prepregnancy folic acid 5 mg/day may be helpful in reducing the risk of AED-related cognitive deficits.
- The lowest effective dose of the most appropriate AED should be used.
- Exposure to sodium valproate and other AED polytherapy should be minimised by changing the medication prior to conception, as recommended by an epilepsy specialist after a careful evaluation of the potential risks and benefits.
- WWE should be informed that two-thirds will not have seizure deterioration in pregnancy.
- Pregnant women who have experienced seizures in the year prior to conception require close monitoring for their epilepsy.
- WWE should be provided with verbal and written information on prenatal screening and its implications, the risks of self-discontinuation of AEDs and the effects of seizures and AEDs on the fetus and on the pregnancy, breastfeeding and contraception.
- WWE should be informed that the introduction of a few safety precautions may significantly reduce the risk of accidents and minimise anxiety.
- Healthcare professionals should acknowledge the concerns of WWE and be aware of the effect of such concerns on their adherence to AEDs.

Antepartum management

- WWE taking AEDs who become unexpectedly pregnant should be able to discuss therapy with an epilepsy specialist on an urgent basis.
- It is never recommended to stop or change AEDs abruptly without an informed discussion.
- Early pregnancy can be an opportunity to screen for structural abnormalities. The fetal anomaly scan at 18+0–20+6 weeks of gestation can identify major cardiac defects in addition to neural tube defects.
- All WWE should be offered a detailed ultrasound.
- Routine monitoring of serum AED levels in pregnancy is not recommended although individual circumstances may be taken into account.
- Healthcare professionals should be alert to signs of depression, anxiety and any neuropsychiatric symptoms in mothers exposed to AEDs.

- Healthcare professionals need to be aware of the small but significant increase in obstetric risks to WWE and those exposed to AEDs, and to incorporate this in the counselling of women and the planning of management.
- In the antenatal period, WWE should be regularly assessed for the following: risk factors for seizures, such as sleep deprivation and stress; adherence to AEDs; and seizure type and frequency.
- If admission is required antenatally, WWE at reasonable risk of seizures should be accommodated in an environment that allows for continuous observation by a carer, partner or nursing staff.
- Serial growth scans are required for detection of small-for-gestational-age babies and to plan further management in WWE exposed to AEDs.
- There is no role for routine antepartum fetal surveillance with cardiotocography in WWE taking AEDs.
- All babies born to WWE taking enzyme-inducing AEDs should be offered 1 mg of intramuscular vitamin K to prevent haemorrhagic disease of the newborn.
- There is insufficient evidence to recommend routine maternal use of oral vitamin K to prevent haemorrhagic disease of the newborn in WWE taking enzyme-inducing AEDs.
- There is insufficient evidence to recommend giving vitamin K to WWE to prevent postpartum P haemorrhage.
- WWE should be reassured that most will have an uncomplicated labour and delivery. The diagnosis of epilepsy per se is not an indication for planned caesarean section or induction of labour.
- Inappropriate medical intervention, including AED administration and iatrogenic early delivery, should be avoided when there is a firm diagnosis of non-epileptic attack disorder.
- In WWE taking enzyme-inducing AEDs who are at risk of preterm delivery, doubling of the antenatal corticosteroid dose for prophylaxis against respiratory distress syndrome in the newborn is not recommended.

Intrapartum Care

- Pregnant WWE should be counselled that the risk of seizures in labour is low.
- Adequate analgesia and appropriate care in labour should be provided to minimise risk factors for seizures such as insomnia, stress and dehydration.
- Long-acting benzodiazepines such as clobazam can be considered if there is a very high risk of seizures in the peripartum period.
- AED intake should be continued during labour. If this cannot be tolerated orally, a parenteral alternative should be administered.
- Seizures in labour should be terminated as soon as possible to avoid maternal and fetal hypoxia and fetal acidosis. Benzodiazepines are the drugs of choice.
- Continuous fetal monitoring is recommended in women at high risk of a seizure in labour, and following an intrapartum seizure.
- Pain relief in labour should be prioritised in WWE, with options including transcutaneous electrical P nerve stimulation (TENS), nitrous oxide and oxygen (Entonox®), and regional analgesia.
- Pethidine should be used with caution in WWE for analgesia in labour. Diamorphine should be used in preference to pethidine.
- For WWE at risk of peripartum seizures delivery should be in a consultant-led unit with facilities for one-to-one midwifery care and maternal and neonatal resuscitation.

Postpartum Management

- WWE and their caregivers need to be aware that although the overall chance of seizures during and immediately after delivery is low, it is relatively higher than during pregnancy.
- WWE should be advised to continue their AEDs postnatally. Mothers should be well supported in the postnatal period to ensure that triggers of seizure deterioration such as sleep deprivation, stress and pain are minimised.
- If the AED dose was increased in pregnancy, it should be reviewed within 10 days of delivery to avoid P postpartum toxicity.
- Neonates born to WWE taking AEDs should be monitored for adverse effects associated with AED exposure in utero.

- WWE who are taking AEDs in pregnancy should be encouraged to breastfeed. Based on current evidence, mothers should be informed that the risk of adverse cognitive outcomes is not increased in children exposed to AEDs through breast milk.
- Postpartum safety advice and strategies should be part of the antenatal and postnatal discussions P with the mother alongside breastfeeding, seizure deterioration and AED intake.
- Postnatal mothers with epilepsy at reasonable risk of seizures should be accommodated in single P rooms only when there is provision for continuous observation by a carer, partner or nursing staff.
- WWE should be screened for depressive disorder in the puerperium. Mothers should be informed about the symptoms and provided with contact details for any assistance.

Contraception

- WWE should be offered effective contraception to avoid unplanned pregnancies. Copper intrauterine devices (IUDs), the levonorgestrel-releasing intrauterine system (LNG-IUS) and medroxyprogesterone acetate injections should be promoted as reliable methods of contraception that are not affected by enzyme-inducing AEDs.
- Women taking enzyme-inducing AEDs (carbamazepine, phenytoin, phenobarbital, primidone, oxcarbazepine, topiramate and eslicarbazepine) should be counselled about the risk of failure with some hormonal contraceptives.
- Women should be counselled that the efficacy of oral contraceptives (combined hormonal contraception, progestogen-only pills), transdermal patches, vaginal ring and progestogen-only implants may be affected if they are taking enzyme-inducing AEDs (e.g. carbamazepine, phenytoin, phenobarbital, primidone, oxcarbazepine and eslicarbazepine).
- All methods of contraception may be offered to women taking non-enzyme-inducing AEDs (e.g. sodium valproate, levetiracetam, gabapentin, vigabatrin, tiagabine and pregabalin).

- WWE taking enzyme-inducing AEDs should be informed that a copper IUD is the preferred choice for emergency contraception. Emergency contraception pills with levonorgestrel and ulipristal acetate are affected by enzyme-inducing AEDs.
- Women taking lamotrigine monotherapy and oestrogen-containing contraceptives should be informed of the potential increase in seizures due to a fall in the levels of lamotrigine.
- The risks of contraceptive failure and the short- and long-term adverse effects of each contraceptive method should be carefully explained to the woman. Effective contraception is extremely important with regard to stabilisation of epilepsy and planning of pregnancy to optimise outcomes.
- WWE should be informed of the effect of changing the dose of AED on seizures and its impact on driving privileges.

RCOG Green-top Guideline

Suitability for planned VBAC

- Planned VBAC is appropriate for and may be offered to the majority of women with a singleton pregnancy of cephalic presentation at 37+0 weeks or beyond who have had a single previous lower segment caesarean delivery, with or without a history of previous vaginal birth.

Contraindications to VBAC

- Women with previous uterine rupture or classical caesarean scar
- Women with previous inverted T or J incisions, low vertical uterine incisions or significant inadvertent uterine extension at the time of primary caesarean - caution should be exercised and decisions should be made on a case-by-case basis by a senior obstetrician with access to the details of previous surgery.
- Women who have other absolute contraindications to vaginal birth that apply irrespective of the presence or absence of a scar (e.g. major placenta praevia).
- Women who have had two or more prior lower segment caesarean deliveries may be offered VBAC after counseling about the risk of uterine rupture and maternal morbidity, and the individual likelihood of successful VBAC

Factors associated with increased risk of uterine rupture in women undergoing VBAC

- An individualised assessment of the suitability for VBAC should be made in women with factors that increase the risk of uterine rupture.

Antenatal counselling

- The antenatal counselling of women with a previous caesarean birth should be documented in the notes.
- A final decision for mode of birth should be agreed upon by the woman and member(s) of the maternity team before the expected/planned date of delivery.
- When a date for ERCS is being arranged, a plan for the event of labour starting before the scheduled date should be documented in the notes.
- The routine use of VBAC checklists during antenatal counselling should be considered, as they would ensure informed consent and shared decision making in women undergoing VBAC.
- A patient information leaflet should be provided with the consultation.

Risks and benefits of planned VBAC versus ERCS from 39+0 weeks of gestation

- Women should be made aware that successful VBAC has the fewest complications and therefore the chance of VBAC success or failure is an important consideration when choosing the mode of delivery.
- Women should be made aware that the greatest risk of adverse outcome occurs in a trial of VBAC resulting in emergency caesarean delivery.
- Women should be informed that planned VBAC is associated with an approximately 1 in 200 (0.5%) risk of uterine rupture.
- Women should be informed that the absolute risk of birth-related perinatal death associated with VBAC is extremely low and comparable to the risk for nulliparous women in labour.
- Women should be informed that ERCS is associated with a small increased risk of placenta praevia and/or accreta in future pregnancies and of pelvic adhesions complicating any future abdominopelvic surgery.
- The risk of perinatal death with ERCS is extremely low, but there is a small increase in neonatal respiratory morbidity when ERCS is performed before 39+0 weeks of gestation.
- The risk of respiratory morbidity can be reduced with a preoperative course of antenatal corticosteroids.

Likelihood of VBAC success

- Women should be informed that the success rate of planned VBAC is 72–75%.
- Women with one or more previous vaginal births should be informed that previous vaginal delivery, particularly previous VBAC, is the single best predictor of successful VBAC and is associated with a planned VBAC success rate of 85–90%.
- Previous vaginal delivery is also independently associated with a reduced risk of uterine rupture.

Intrapartum management of planned VBAC

- Planned VBAC should be conducted in a suitably staffed and equipped delivery suite with continuous intrapartum care and monitoring with resources available for immediate caesarean delivery and advanced neonatal resuscitation.
- Women with an unplanned labour and a history of previous caesarean delivery should have a discussion with an experienced obstetrician to determine feasibility of VBAC.
- Epidural analgesia is not contraindicated in a planned VBAC, although an increasing requirement for pain relief in labour should raise awareness of the possibility of an impending uterine rupture.
- Women should be advised to have continuous electronic fetal monitoring for the duration of planned VBAC, commencing at the onset of regular uterine contractions.
- Women should be informed of the two- to three-fold increased risk of uterine rupture and around 1.5-fold increased risk of caesarean delivery in induced and/or augmented labour compared with spontaneous VBAC labour.
- Induction of labour using mechanical methods (amniotomy or Foley catheter) is associated with a lower risk of scar rupture compared with induction using prostaglandins.

Clinical features associated with uterine scar rupture include:

- abnormal CTG
- severe abdominal pain, especially if persisting between contractions
- acute onset scar tenderness
- abnormal vaginal bleeding
- haematuria
- cessation of previously efficient uterine activity

- maternal tachycardia, hypotension, fainting or shock
- loss of station of the presenting part
- change in abdominal contour and inability to pick up fetal heart rate at the old transducer site.

Planning and conducting ERCS

- ERCS delivery should be conducted after 39+0 weeks of gestation. Antibiotics should be administered before making the skin incision in women undergoing ERCS.
- All women undergoing ERCS should receive thromboprophylaxis according to existing RCOG guidelines.
- Early recognition of placenta praevia, adopting a multidisciplinary approach and informed consent are important considerations in the management of women with placenta praevia and previous caesarean delivery.

Special circumstances

- There is uncertainty about the safety and efficacy of planned VBAC in pregnancies complicated by post-dates, twin gestation, fetal macrosomia, antepartum stillbirth or maternal age of 40 years or more. Hence, a cautious approach is advised if VBAC is being considered in such circumstances.
- Women who are preterm and considering the options for birth after a previous caesarean delivery should be informed that planned preterm VBAC has similar success rates to planned term VBAC but with a lower risk of uterine rupture.

RCOG Green top Guideline

Suitability for planned VBAC

- Small–for–gestational age (SGA) refers to an infant born with a birth weight less than the 10 centile.
- SGA birth is defined as an estimated fetal weight (EFW) or abdominal circumference (AC) less than the 10centile and severe SGA as an EFW or AC less than the 3 centile.
- Fetal growth restriction (FGR) is not synonymous with SGA. Some, but not all, growth restricted fetuses/infants are SGA while 50–70% of SGA fetuses are constitutionally small, with fetal growth appropriate for maternal size and ethnicity. The likelihood of FGR is higher in severe SGA infants. Growth restriction implies a pathological restriction of the genetic growth potential. As a result, growth restricted fetuses may manifest evidence of fetal compromise. Low birth weight (LBW) refers to an infant with a birth weight < 2500 g.
- Causes of Small fetuses are -
  - o normal (constitutionally) small,
  - o non–placenta mediated growth restriction, for example; structural or chromosomal anomaly
  - o inborn errors of metabolism
  - o fetal infection
  - o placenta mediated growth restriction.
  - o Maternal factors can affect placental transfer of nutrients, for example; low pre–pregnancy weight, under nutrition, substance abuse or severe anaemia.
  - o Medical conditions can affect placental implantation and vasculature and hence transfer, for example; pre-eclampsia, autoimmune disease, thrombophilias, renal disease, diabetes and essential hypertension.

Risk factors for a SGA fetus/neonate

- All women should be assessed at booking for risk factors for a SGA fetus/neonate to identify those who require increased surveillance.
- Women who have a major risk factor should be referred for serial ultrasound measurement of fetal size and assessment of wellbeing with umbilical artery Doppler from 26–28 weeks of pregnancy.
- Women who have three or more minor risk factors should be referred for uterine artery Doppler at 20–24 weeks of gestation

- Second trimester DS markers have limited predictive accuracy for delivery of a SGA neonate.
- A low level (< 0.415 MoM) of the first trimester marker PAPP–A should be considered a major risk factor for delivery of a SGA neonate.
- In high risk populations uterine artery Doppler at 20–24 weeks of pregnancy has a moderate predictive value for a severely SGA neonate.
- In women with an abnormal uterine artery Doppler at 20–24 weeks of pregnancy, subsequent normalisation of flow velocity indices is still associated with an increased risk of a SGA neonate. Repeating uterine artery Doppler is therefore of limited value.
- Women with an abnormal uterine artery Doppler at 20–24 weeks (defined as a pulsatility index [PI] > 95 centile) and/or notching should be referred for serial ultrasound measurement of fetal size and assessment of wellbeing with umbilical artery Doppler commencing at 26–28 weeks of pregnancy.
- Women with a normal uterine artery Doppler do not require serial measurement of fetal size and serial assessment of wellbeing with umbilical artery Doppler unless they develop specific pregnancy complications, for example antepartum haemorrhage or hypertension. However, they should be offered a scan for fetal size and umbilical artery Doppler during the third trimester.
- Serial ultrasound measurement of fetal size and assessment of wellbeing with umbilical artery Doppler should be offered in cases of fetal echogenic bowel.
- Abdominal palpation has limited accuracy for the prediction of a SGA neonate and thus should not be routinely performed in this context.
- Serial measurement of symphysis fundal height (SFH) is recommended at each antenatal appointment from 24 weeks of pregnancy as this improves prediction of a SGA neonate.
- SFH should be plotted on a customised chart rather than a population–based chart as this may improve prediction of a SGA neonate.
- Women with a single SFH which plots below the 10 centile or serial measurements which demonstrate slow or static growth by crossing centiles should be referred for ultrasound measurement of fetal size.
- Women in whom measurement of SFH is inaccurate (for example: BMI > 35, large fibroids, hydramnios) should be referred for serial assessment of fetal size using ultrasound.

Optimum method of diagnosing a SGA fetus and FGR

- Fetal abdominal circumference (AC) or estimated fetal weight (EFW) < 10 centile can be used to diagnose a SGA fetus.
- Use of a customised fetal weight reference may improve prediction of a SGA neonate and adverse perinatal outcome. In women having serial assessment of fetal size, use of a customised fetal weight reference may improve the prediction of normal perinatal outcome.

- Routine measurement of fetal AC or EFW in the third trimester does not reduce the incidence of a SGA neonate nor does it improve perinatal outcome. Routine fetal biometry is thus not justified.
- Change in AC or EFW may improve the prediction of wasting at birth (neonatal morphometric indicators) and adverse perinatal outcome suggestive of FGR.
- When using two measurements of AC or EFW to estimate growth velocity, they should be at least 3 weeks apart to minimise false–positive rates for diagnosing FGR. More frequent measurements of fetal size may be appropriate where birth weight prediction is relevant outside of the context of diagnosing SGA/FGR.
- Where the fetal AC or EFW is < 10 centile or there is evidence of reduced growth velocity, women should be offered serial assessment of fetal size and umbilical artery Doppler.

Investigations that are indicated in SGA fetuses

- Offer referral for a detailed fetal anatomical survey and uterine artery Doppler by a fetal medicine specialist if severe SGA is identified at the 18–20 week scan.
- Karyotyping should be offered in severely SGA fetuses with structural anomalies and in those detected before 23 weeks of gestation, especially if uterine artery Doppler is normal.
- Serological screening for congenital cytomegalovirus (CMV) and toxoplasmosis infection should be offered in severely SGA fetuses.
- Testing for syphilis and malaria should be considered in high risk populations.
- Uterine artery Doppler has limited accuracy to predict adverse outcome in SGA fetuses diagnosed during the third trimester.

Interventions to be considered in the prevention of SGA fetuses/neonates

- Antiplatelet agents may be effective in preventing SGA birth in women at high risk of pre-eclampsia although the effect size is small.
- In women at high risk of pre-eclampsia, antiplatelet agents should be commenced at, or before, 16 weeks of pregnancy.
- There is no consistent evidence that dietary modification, progesterone or calcium prevent birth of a SGA infant. These interventions should not be used for this indication.
- Interventions to promote smoking cessation may prevent delivery of a SGA infant. The health benefits of smoking cessation indicate that these interventions should be offered to all women who are pregnant and smoke.
- Antithrombotic therapy appears to be a promising therapy for preventing delivery of a SGA infant in high-risk women. However, there is insufficient evidence, especially concerning serious adverse effects, to recommend its use.

Interventions to be considered in the preterm SGA fetus

- Women with a SGA fetus between 24 and 35 weeks of gestation, where delivery is being considered, should receive a single course of antenatal corticosteroids.

Optimal method and frequency of fetal surveillance in SGA

- In a high–risk population, the use of umbilical artery Doppler has been shown to reduce perinatal morbidity and mortality. Umbilical artery Doppler should be the primary surveillance tool in the SGA fetus.
- When umbilical artery Doppler flow indices are normal it is reasonable to repeat surveillance every 14 days.
- More frequent Doppler surveillance may be appropriate in a severely SGA fetus.
- When umbilical artery Doppler flow indices are abnormal (pulsatility or resistance index > +2 SDs above mean for gestational age) and delivery is not indicated repeat surveillance twice weekly in fetuses with end–diastolic velocities present and daily in fetuses with absent/reversed end–diastolic frequencies.
- CTG should not be used as the only form of surveillance in SGA fetuses.
- Interpretation of the CTG should be based on short term fetal heart rate variation from computerized analysis.
- Ultrasound assessment of amniotic fluid volume should not be used as the only form of surveillance in SGA fetuses.
- Interpretation of amniotic fluid volume should be based on single deepest vertical pocket. Biophysical profile should not be used for fetal surveillance in preterm SGA fetuses.
- In the preterm SGA fetus, middle cerebral artery (MCA) Doppler has limited accuracy to predict academia and adverse outcome and should not be used to time delivery.
- In the term SGA fetus with normal umbilical artery Doppler, an abnormal middle cerebral artery Doppler (PI < 5 centile) has moderate predictive value for acidosis at birth and should be used to time delivery.
- Ductus venosus Doppler has moderate predictive value for academia and adverse outcome.
- Ductus venosus Doppler should be used for surveillance in the preterm SGA fetus with abnormal umbilical artery Doppler and used to time delivery.

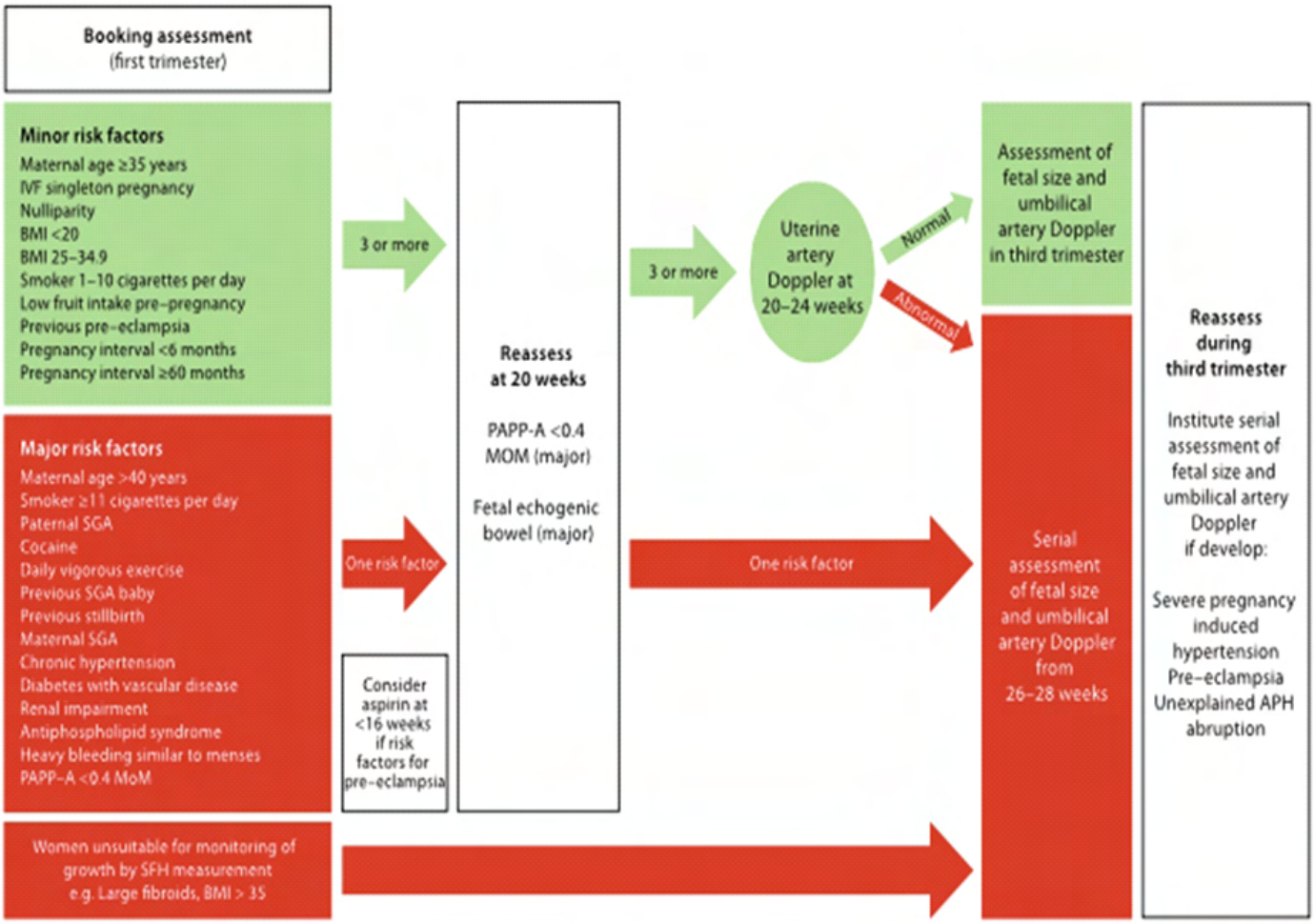
The optimal gestation to deliver the SGA fetus

- In the preterm SGA fetus with umbilical artery AREDV detected prior to 32 weeks of gestation, delivery is recommended when DV Doppler becomes abnormal or UV pulsations appear, provided the fetus is considered viable and after completion of steroids. Even when venous Doppler is normal, delivery is recommended by 32 weeks of gestation and should be considered between 30–32 weeks of gestation.
- If MCA Doppler is abnormal, delivery should be recommended no later than 37 weeks of gestation.
- In the SGA fetus detected after 32 weeks of gestation with an abnormal umbilical artery Doppler, delivery no later than 37 weeks of gestation is recommended.
- In the SGA fetus detected after 32 weeks of gestation with normal umbilical artery Doppler, a senior obstetrician should be involved in determining the timing and mode of birth of these pregnancies. Delivery should be offered at 37 weeks of gestation.

How the SGA fetus should be delivered

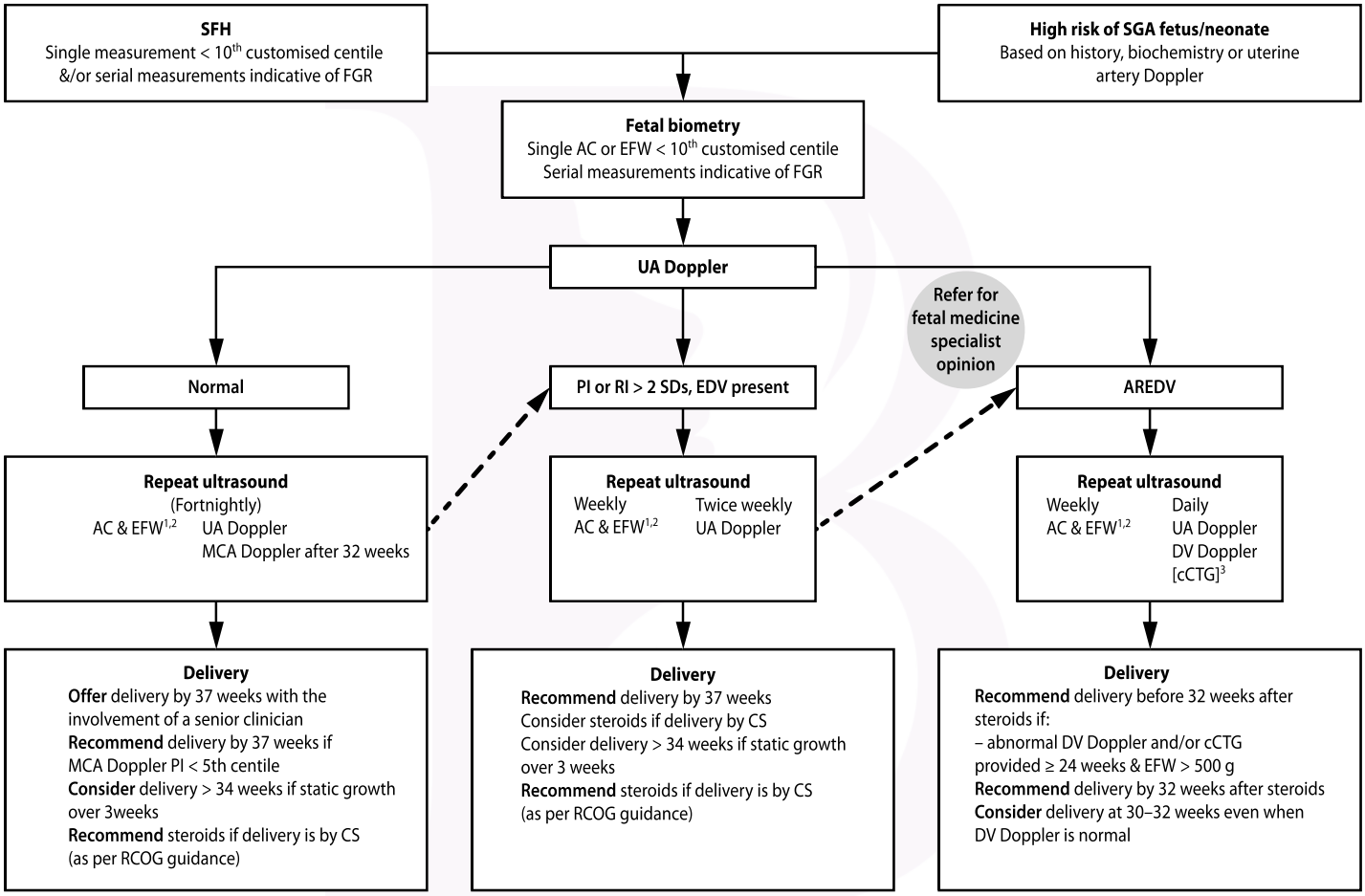
- In the SGA fetus with umbilical artery AREDV delivery by caesarean section is recommended.
- In the SGA fetus with normal umbilical artery Doppler or with abnormal umbilical artery PI but end–diastolic velocities present, induction of labor can be offered but rates of emergency caesarean section are increased and continuous fetal heart rate monitoring is recommended from the onset of uterine contractions.
- Early admission is recommended in women in spontaneous labor with a SGA fetus in order to instigate continuous fetal heart rate monitoring.

MANAGEMENT FOR SGA



Risk assessment must always be individualised (taking into account previous medical and obstetric history and current pregnancy history). Disease progression or institution of medical therapies may increase an individual's risk.

APPENDIX III: The Management of the Small–for–Gestational–Age (SGA) Fetus



[1] Weekly measurement of fetal size is valuable in predicting birthweight and determining size-for-gestational age
[2] If two AC/EFW measurements are used to estimate growth, they should be at least 3 weeks apart
[3] Use cCTG when DV Doppler is unavailable or results are inconsistent – recommend delivery if STV < 3 ms

Abbreviations: AC, abdominal circumference; EFW, estimated fetal weight; PI, pulsatility index; RI, resistance index; UA, umbilical artery; MCA, middle cerebral artery; DV ducts venosus; SD, standard deviation; AREDV., Absent/reversed end–diastolic velocities; cCTG, computerised cardiotography; STV, short term variation; SFH, symphysis–fundal height; FGR, fetal growth restriction; EDV, end–diastolic velocities.

NICE GUIDELINES

When giving information and support to women at increased risk of preterm labor, with suspected, diagnosed or established preterm labor, or having a planned preterm birth (and their family members or carers as appropriate):

- give this information and support as early as possible, taking into account the likelihood of preterm birth and the status of labor
- bear in mind that the woman (and her family members or carers) may be particularly anxious
- give both oral and written information
- describe the symptoms and signs of preterm labor
- explain to the woman about the care she may be offered.

For women who are having a planned preterm birth or are offered treatment for preterm labor, provide information and support that includes:

- information about the likelihood of the baby surviving and other outcomes and risks for the baby, giving values as natural frequencies.
- explaining about the neonatal care of preterm babies, including location of care explaining about the immediate problems that can arise when a baby is born preterm.
- explaining about the possible long-term consequences of prematurity for the baby ongoing opportunities to talk about and state their wishes about resuscitation of the baby
- an opportunity to speak to a neonatologist or pediatrician.

Offer a choice of prophylactic vaginal progesterone or prophylactic cervical cerclage to women who have both:

- a history of spontaneous preterm birth (up to 34+0 weeks of pregnancy) or mid- trimester loss (from 16+0 weeks of pregnancy onwards) and
- results from a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy that show a cervical length of 25 mm or less.

Consider prophylactic vaginal progesterone for women who have either:

- a history of spontaneous preterm birth (up to 34+0 weeks of pregnancy) or mid- trimester loss (from 16+0 weeks of pregnancy onwards) or
- results from a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy that show a cervical length of 25 mm or less.

When using vaginal progesterone, start treatment between 16+0 and 24+0 weeks of pregnancy and continue until at least 34 weeks.

Consider prophylactic cervical cerclage for women when results of a transvaginal ultrasound scan carried out between 16+0 and 24+0 weeks of pregnancy show a cervical length of 25 mm or less, and who have had either:

- preterm prelabor rupture of membranes (P-PROM) in a previous pregnancy or
- a history of cervical trauma.

If prophylactic cervical cerclage is used, ensure that a plan is in place for removal of the suture.

- `Do not use nitrazine to diagnose P-PROM.
- ` Do not perform diagnostic tests for P-PROM if labor becomes established in a woman reporting symptoms suggestive of P-PROM.
- Antenatal prophylactic antibiotics for women with P-PROM

- Offer women with P-PROM oral erythromycin 250 mg 4 times a day for a maximum of 10 days or until the woman is in established labor (whichever is sooner).
- For women with P-PROM who cannot tolerate erythromycin or in whom erythromycin is contraindicated, consider an oral penicillin for a maximum of 10 days or until the woman is in established labor (whichever is sooner).
- Do not offer women with P-PROM co-amoxiclav as prophylaxis for intrauterine infection.

Identifying infection in women with P-PROM

- Use a combination of clinical assessment and tests (C-reactive protein, white blood cell count and measurement of fetal heart rate using cardiotocography) to diagnose intrauterine infection in women with P-PROM.
- Do not use any one of the following in isolation to confirm or exclude intrauterine infection in women with P-PROM:
  - a single test of C-reactive protein
  - white blood cell count
  - measurement of fetal heart rate using cardiotocography.
- If the results of the clinical assessment or any of the tests are not consistent with each other, continue to observe the woman and consider repeating the tests.

'Rescue' cervical cerclage

- Do not offer 'rescue' cervical cerclage to women with:
  - signs of infection or
  - active vaginal bleeding or
  - uterine contractions.
- Consider 'rescue' cervical cerclage for women between 16+0 and 27+6 weeks of pregnancy with a dilated cervix and exposed, unruptured fetal membranes.
- take into account gestational age (being aware that the benefits are likely to be greater for earlier gestations) and the extent of cervical dilatation.
- discuss with a consultant obstetrician and consultant paediatrician.
- Explain to women for whom 'rescue' cervical cerclage is being considered (and their family members or carers as appropriate):
  - about the risks of the procedure
  - that it aims to delay the birth, and so increase the likelihood of the baby surviving and of reducing serious neonatal morbidity.
- If 'rescue' cervical cerclage is used, ensure that a plan is in place for removal of the suture.

Diagnosing preterm labor for women with intact membranes

- Explain to women reporting symptoms of preterm labour who have intact membranes (and their family members or carers as appropriate):
  - about the clinical assessment and diagnostic tests that are available
  - how the clinical assessment and diagnostic tests are carried out.
  - what the benefits, risks and possible consequences of the clinical assessment and diagnostic tests are, including the consequences of false positive and false negative test results taking into account gestational age.

- Offer a clinical assessment to women reporting symptoms of preterm labor who have intact membranes. This should include:
  - o clinical history taking
  - o the observations described for the initial assessment of a woman in labor
  - o guideline on intrapartum care
  - o a speculum examination (followed by a digital vaginal examination if the extent of cervical dilatation cannot be assessed).
- If the clinical assessment suggests that the woman is in suspected preterm labor and she is 29+6 weeks pregnant or less, advise treatment for preterm labor.

- If the clinical assessment suggests that the woman is in suspected preterm labor and she is 30+0 weeks pregnant or more, consider transvaginal ultrasound measurement of cervical length as a diagnostic test to determine likelihood of birth within 48 hours.
- Act on the results as follows:

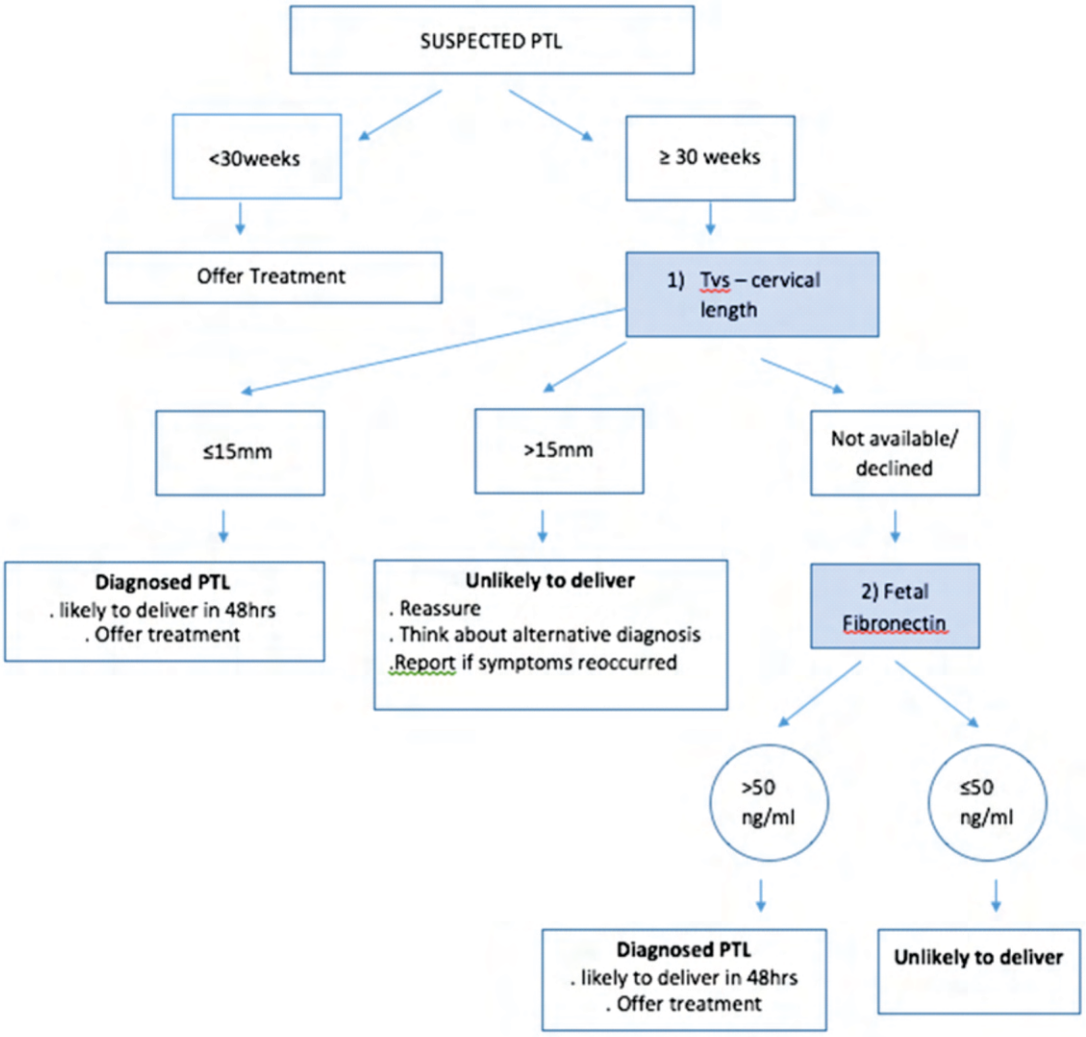
Ø if cervical length is more than 15 mm, explain to the woman that it is unlikely that she is in preterm labor and:
- o think about alternative diagnoses
- o discuss with her the benefits and risks of going home compared with continued monitoring and treatment in hospital
- o advise her that if she does decide to go home, she should return if symptoms suggestive of preterm labor persist or recur

Ø if cervical length is 15 mm or less, view the woman as being in diagnosed preterm labor and offer treatment
- o Consider fetal fibronectin testing as a diagnostic test to determine likelihood of birth within 48 hours for women who are 30+0 weeks pregnant or more if transvaginal ultrasound measurement of cervical length is indicated but is not available or not acceptable.

· Act on the results as follows:

Ø if fetal fibronectin testing is negative (concentration 50 ng/ml or less), explain to the woman that it is unlikely that she is in preterm labor and:
- o think about alternative diagnoses
- o discuss with her the benefits and risks of going home compared with continued monitoring and treatment in hospital

- o advise her that if she does decide to go home, she should return if symptoms suggestive of preterm labor persist or recur
- If fetal fibronectin testing is positive (concentration more than 50 ng/ml), view the woman as being in diagnosed preterm labour and offer treatment.
- If a woman in suspected preterm labr who is 30+0 weeks pregnant or more does not have transvaginal ultrasound measurement of cervical length or fetal fibronectin testing to exclude preterm labor, offer treatment consistent with her being in diagnosed preterm labor.
- Do not use transvaginal ultrasound measurement of cervical length and fetal fibronectin testing in combination to diagnose preterm labour.
- Ultrasound scans should be performed by healthcare professionals with training in, and experience of, transvaginal ultrasound measurement of cervical length.



Tocolysis

- Take the following factors into account when making a decision about whether to start tocolysis:
  - o whether the woman is in suspected or diagnosed preterm labor
  - o other clinical features (for example, bleeding or infection) that may
  - o suggest that stopping labor is contraindicated
  - o gestational age at presentation
  - o likely benefit of maternal corticosteroids
  - o availability of neonatal care (need for transfer to another unit)
  - o the preference of the woman.

- Consider nifedipin for tocolysis for women between 24+0 and 25+6 weeks of pregnancy who have intact membranes and are in suspected preterm labor.
- Offer nifedipine for tocolysis to women between 26+0 and 33+6 weeks of pregnancy who have intact membranes and are in suspected or diagnosed preterm labor.
- If nifedipine is contraindicated, offer oxytocin receptor antagonists for tocolysis.
- Do not offer betamimetics for tocolysis.

Maternal corticosteroids

- For women between 23+0 and 23+6 weeks of pregnancy who are in suspected or established preterm labor, are having a planned preterm birth or have P-PROM, discuss with the woman (and her family members or carers as appropriate) the use of maternal corticosteroids in the context of her individual circumstances.
- Offer maternal corticosteroids to women between 24+0 and 33+6 weeks of pregnancy who are in suspected, diagnosed or established preterm labor, are having a planned preterm birth or have P-PROM.
- Consider maternal corticosteroids for women between 34+0 and 35+6 weeks of pregnancy who are in suspected, diagnosed or established preterm labor, are having a planned preterm birth or have P-PROM.
- When offering or considering maternal corticosteroids, discuss with the woman (and her family members or carers as appropriate):
  - o how corticosteroids may help
  - o the potential risks associated with them.
- Do not routinely offer repeat courses of maternal corticosteroids, but take into account:
  - o the interval since the end of last course
  - o gestational age

- o the likelihood of birth within 48 hours.
- For women between 23+0 and 23+6 weeks of pregnancy who are in established preterm labor or having a planned preterm birth within 24 hours, discuss with the woman (and her family members or carers as appropriate) the use of intravenous magnesium sulfate for neuroprotection of the baby, in the context of her individual circumstances.
- Offer intravenous magnesium sulfate for neuroprotection of the baby to women between 24+0 and 29+6 weeks of pregnancy who are:
  - o in established preterm labor or
  - o having a planned preterm birth within 24 hours.
- Consider intravenous magnesium sulfate for neuroprotection of the baby for women between 30+0 and 33+6 weeks of pregnancy who are:
  - o in established preterm labor or
  - o having a planned preterm birth within 24 hours.
- Give a 4 g intravenous bolus of magnesium sulfate over 15 minutes, followed by an intravenous infusion of 1 g per hour until the birth or for 24 hours (whichever is sooner).
- For women on magnesium sulfate, monitor for clinical signs of magnesium toxicity at least every 4 hours by recording pulse, blood pressure, respiratory rate and deep tendon (for example, patellar) reflexes.
- If a woman has or develops oliguria or other signs of renal failure:
  - o monitor more frequently for magnesium toxicity
  - o think about reducing the dose of magnesium sulfate.

Fetal monitoring

- Monitoring options: cardiotocography and intermittent auscultation
- Discuss with women in suspected, diagnosed or established preterm labor (and their family members or carers as appropriate):
  - o the purpose of fetal monitoring and what it involves
  - o the clinical decisions it informs at different gestational ages
  - o if appropriate, the option not to monitor the fetal heart rate
- Involve a senior obstetrician in discussions about whether and how to monitor the fetal heart rate for women who are between 23+0 and 25+6 weeks pregnant.
- Explain the different fetal monitoring options to the woman (and her family members or carers as appropriate), being aware that:
  - o there is limited evidence about the usefulness of specific features to suggest hypoxia or acidosis in preterm babies
  - o the available evidence is broadly consistent with that for babies born at term
  - o a normal cardiotocography trace is reassuring and indicates that the baby is coping well with labor, but an abnormal trace does not necessarily indicate that fetal hypoxia or acidosis is present.

- Explain to the woman (and her family members or carers as appropriate) that there is an absence of evidence that using cardiotocography improves the outcomes of preterm labor for the woman or the baby compared with intermittent auscultation.
- Offer women in established preterm labor but with no other risk factors a choice of fetal heart rate monitoring using either:
  - cardiotocography using external ultrasound or
  - intermittent auscultation.

Fetal scalp electrode

- Do not use a fetal scalp electrode for fetal heart rate monitoring if the woman is less than 34+0 weeks pregnant unless all of the following apply:
  - it is not possible to monitor the fetal heart rate using either external cardiotocography or intermittent auscultation
  - it has been discussed with a senior obstetrician
  - the benefits are likely to outweigh the potential risks
  - the alternatives (immediate birth, intermittent ultrasound and no monitoring) have been discussed with the woman and are unacceptable to her.
- Discuss with the woman (and her family members or carers as appropriate) the possible use of a fetal scalp electrode between 34+0 and 36+6 weeks of pregnancy if it is not possible to monitor the fetal heart rate using either external cardiotocography or intermittent auscultation.

Fetal blood sampling

- Do not carry out fetal blood sampling if the woman is less than 34+0 weeks pregnant.
- Discuss with the woman the possible use of fetal blood sampling between 34+0 and 36+6 weeks of pregnancy if the benefits are likely to outweigh the potential risks.
- When offering fetal blood sampling, discuss this with the woman, and advise her that if a blood sample cannot be obtained a caesarean section is likely.

Mode of birth

- Discuss the general benefits and risks of caesarean section and vaginal birth with women in suspected, diagnosed or established preterm labor and women with P-PROM (and their family members or carers as appropriate)
- Explain to women in suspected, diagnosed or established preterm labour and women with P-PROM about the benefits and risks of caesarean section that are specific to gestational age. In particular, highlight the difficulties associated with performing a caesarean section for a preterm birth, especially the increased likelihood of a vertical uterine incision and the implications of this for future pregnancies.
- Explain to women in suspected, diagnosed or established preterm labor that there are no known benefits or harms for the baby from caesarean section, but the evidence is very limited.
- Consider caesarean section for women presenting in suspected, diagnosed or established preterm labor between 26+0 and 36+6 weeks of pregnancy with breech presentation.
- Timing of cord clamping for preterm babies (born vaginally or by caesarean section)

- If a preterm baby needs to be moved away from the mother for resuscitation, or there is significant maternal bleeding:
  - consider milking the cord and
  - clamp the cord as soon as possible.
- Wait at least 30 seconds, but no longer than 3 minutes, before clamping the cord of preterm babies if the mother and baby are stable.
- Position the baby at or below the level of the placenta before clamping the cord.

RCOG greentop guidelines

Optimal method for diagnosing late IUFD

- Auscultation and cardiotocography should not be used to investigate suspected IUFD.
- Real-time ultrasonography is essential for the accurate diagnosis of IUFD.
- Ideally, real-time ultrasonography should be available at all times.
- A second opinion should be obtained whenever practically possible.
- Mothers should be prepared for the possibility of passive fetal movement. If the mother reports passive fetal movement after the scan to diagnose IUFD, a repeat scan should be offered.

Best practice for discussing the diagnosis and subsequent care

- If the woman is unaccompanied, an immediate offer should be made to call her partner, relatives or friends.
- Discussions should aim to support maternal/parental choice.
- Parents should be offered written information to supplement discussions

Investigation of the cause of late IUFD

- Clinical assessment and laboratory tests should be recommended to assess maternal wellbeing (including coagulopathy) and to determine the cause of death, the chance of recurrence and possible means of avoiding further pregnancy complications.
- Parents should be advised that no specific cause is found in almost half of stillbirths.
- Parents should be advised that when a cause is found it can crucially influence care in a future pregnancy
- Women with an IUFD who are rhesus D-negative
    - Women who are rhesus D (RhD)-negative should be advised to have a Kleihauer test undertaken urgently to detect large feto–maternal haemorrhage (FMH) that might have occurred a few days earlier.
    - Anti-RhD gammaglobulin should be administered as soon as possible after presentation.
    - If there has been a large FMH, the dose of anti-RhD gammaglobulin should be adjusted upwards and the Kleihauer test should be repeated at 48 hours to ensure the fetal red cells have cleared.
    - If it is important to know the baby's blood group; if no blood sample can be obtained from the baby or cord, RhD typing should be undertaken using free fetal DNA (ffDNA) from maternal blood taken shortly after birth.

Table 1. Tests recommended for women with a late IUFD

Test	Reason(s) for test	Evidence level	Reference(s)	Additional comments
Maternal standard haematology and biochemistry including CRPs and bile salt	Pre-eclampsia and its complications Multi-organ failure in sepsis or haemorrhage Obstetric cholestasis	3	3, 19, 42	Platelet count to test for occult DIC (repeat twice weekly)
Maternal coagulation times and plasma fibrinogen	DIC	3	19	Not a test for cause of late IUFD Maternal sepsis, placental abruption and pre-eclampsia increase the probability of DIC Especially important if woman desires regional anaesthesia
Kleihauer	Lethal feto–maternal haemorrhage To decide level of requirement for anti- RhD gammaglobulin	2	25, 43	Feto–maternal haemorrhage is a cause of IUFD[43] Kleihauer should be recommended for all women, not simply those who are RhD-negative (ensure laboratory aware if a woman is RhD-positive) Tests should be undertaken before birth as red cells might clear quickly from maternal circulation In RhD-negative women, a second Kleihauer test also determines whether sufficient anti-RhD has been given

Table 1 *(continued)*. Tests recommended for women with a late IUFD

Test	Reason(s) for test	Evidence level	Reference(s)	Additional comments
Maternal bacteriology: blood cultures midstream urine vaginal swabs cervical swabs	Suspected maternal bacterial infection including *Listeria monocytogenes* and *Chlamydia* spp.	1++	32–34, 39 41, 44, 45	**Indicated in the presence of:** maternal fever flu-like symptoms abnormal liquor (purulent appearance/offensive odour) prolonged ruptured membranes before late IUFD Abnormal bacteriology is of doubtful significance in the absence of clinical or histological evidence of chorioamnionitis[46] (Evidence level 3) In one study, amniotic fluid culture was positive in only 1 of 44 women with IUFD despite evidence of chorioamnionitis in a further 9 women[47] (Evidence level 3) Also used to direct maternal antibiotic therapy
Maternal serology: viral screen syphilis tropical infections	Occult maternal–fetal infection	2+	30, 32–35, 48	Stored serum from booking tests can provide baseline serology Parvovirus B19, rubella (if nonimmune at booking), CMV, herpes simplex and *Toxoplasma gondii* (routinely) Hydrops not necessarily a feature of parvovirus-related late IUFD Treponemal serology – usually known already Others if presentation suggestive, e.g. travel to endemic areas
Maternal random blood glucose	Occult maternal diabetes mellitus	3	49, 50	Rarely a woman will have incidental type 1 diabetes mellitus, usually with severe ketosis Women with gestational diabetes mellitus return to normal glucose tolerance within a few hours after late IUFD has occurred
Maternal HbA_{1c}	Gestational diabetes mellitus	2+	3, 4, 51–53	Most women with gestational diabetes mellitus have a normal HbA_{1c} Need to test for gestational diabetes mellitus in future pregnancy Might also indicate occult type 1 and type 2 diabetes
Maternal thyroid function	Occult maternal thyroid disease	3	54, 55	TSH, FT4 and FT3
Maternal thrombophilia screen	Maternal thrombophilia	1++	56–58	**Indicated if** evidence of fetal growth restriction or placental disease The association between inherited thrombophilias and IUFD is weak, and management in future pregnancy is uncertain[56,58] Most tests are not affected by pregnancy – if abnormal, repeat at 6 weeks Antiphospholipid screen repeated if abnormal
Anti-red cell antibody serology	Immune haemolytic disease	3	59–62	**Indicated if** fetal hydrops evident clinically or on postmortem
Maternal anti-Ro and anti-La antibodies	Occult maternal autoimmune disease	3	63	**Indicated if** evidence of hydrops, endomyocardial fibro-elastosis or AV node calcification at postmortem
Maternal alloimmune antiplatelet antibodies	Alloimmune thrombocytopenia	3	64	**Indicated if** fetal intracranial haemorrhage found on postmortem

Table 1 *(continued)*. Tests recommended for women with a late IUFD

Test	Reason(s) for test	Evidence level	Reference(s)	Additional comments
Parental bloods for karyotype	Parental balanced translocation Parental mosaicism	3	65–67	**Indicated if:** fetal unbalanced translocation other fetal aneuploidy, e.g. 45X (Turner syndrome) fetal genetic testing fails and history suggestive of aneuploidy (fetal abnormality on postmorterm, previous unexplained IUFD, recurrent miscarriage)
Maternal urine for cocaine metabolites	Occult drug use	1++	68	With consent, if history and/or presentation are suggestive
Fetal and placental: microbiology fetal blood fetal swabs placental swabs	Fetal infections	2+ 3	33, 34, 69	More informative than maternal serology for detecting viral infections Cord or cardiac blood (if possible) in lithium heparin Written consent advisable for cardiac bloods Need to be obtained using clean technique
Fetal and placental tissues for karyotype (and possible single-gene testing): deep fetal skin fetal cartilage placenta	Aneuploidy Single gene disorders **See section 5.4 on sexing**	2+	70–74	**Absolutely contraindicated if** parents do not wish (written consent essential) Send several specimens – cell cultures might fail Culture bottles must be kept on labour ward in a refrigerator – stored separately from formalin preservation bottles Genetic material should be stored if a single-gene syndrome is suspected
Postmortem examination: external autopsy microscopy X-ray placenta and cord	**See section 5.6**		3, 4, 75, 76	**Absolutely contraindicated if** parents do not wish (written consent essential) External examination should include weight and length measurement IUGR is a significant association for late IUFD

Some tests should be taken before birth. Tests below the bold line are fetal. Shaded tests are selective.
AV = atrioventricular; CMV = cytomegalovirus; CRP = C-reactive protein; DIC = disseminated intravascular coagulation; FT3 = free triiodothyronine; FT4 = free thyroxin index; HbA1c = glycated haemoglobin; IUFD = intrauterine fetal death; IUGR = intrauterine growth restriction; RhD = rhesus D; TSH = thyroid-stimulating hormone

5.4 What precautions should be taken when sexing the baby?

Parents can be advised before birth about the potential difficulty in sexing the baby, when appropriate.

Two experienced healthcare practitioners (midwives, obstetricians, neonatologists or pathologists) should inspect the baby when examining the external genitalia of extremely preterm, severely macerated or grossly hydropic infants.

If there is any difficulty or doubt, rapid karyotyping should be offered using quantitative fluorescent polymerase chain reaction (QF-PCR) or fluorescence in situ hybridisation (FISH).

B

Females can be mistaken for males, and vice versa. Errors in fetal sexing can result in severe emotional harm for parents. Some practitioners who have incorrectly determined the sex on external inspection probably had no doubt at the time. Extreme prematurity, maceration and hydrops can all make the diagnosis difficult. If the sex cannot be determined clinically or if there is any difficulty or

Evidence level 3

- Postmortem examination –
  - Parents should be offered full postmortem examination to help explain the cause of an IUFD. Parents should be advised that postmortem examination provides more information than other (less invasive) tests and this can sometimes be crucial to the management of future pregnancy
  - Postmortem examination should include external examination with birth weight, histology of relevant tissues and skeletal X-rays.
  - Pathological examination of the cord, membranes and placenta should be recommended whether or not postmortem examination of the baby is requested.
  - The examination should be undertaken by a specialist perinatal pathologist.

Labour and birth

- Timing
  - Recommendations about labour and birth should take into account the mother's preferences as well as her medical condition and previous intrapartum history.
  - Women should be strongly advised to take immediate steps towards delivery if there is sepsis, preeclampsia, placental abruption or membrane rupture, but a more flexible approach can be discussed if these factors are not present. Well women with intact membranes and no laboratory evidence of DIC should be advised that they are unlikely to come to physical harm if they delay labour for a short period, but they may develop severe medical complications and suffer greater anxiety with prolonged intervals.
  - Women who delay labour for periods longer than 48 hours should be advised to have testing for DIC twice weekly.
  - Women contemplating prolonged expectant management should be advised that the value of postmortem may be reduced.
  - Women contemplating prolonged expectant management should be advised that the appearance of the baby may deteriorate.
  - Vaginal birth is the recommended mode of delivery for most women, but caesarean birth will need to be considered with some

- Induction of labour
  - A combination of mifepristone and a prostaglandin preparation should usually be recommended as the first-line intervention for induction of labour.
  - Misoprostol can be used in preference to prostaglandin E2 because of equivalent safety and efficacy with lower cost
  - Women should be advised that vaginal misoprostol is as effective as oral therapy but associated with fewer adverse effects.

- Mifepristone can be used alone to increase the chance of labour significantly within 72 hours (avoiding the use of prostaglandin).
- Mechanical methods for induction of labour in women with an IUFD should be used only in the context of a clinical trial.
- Women with a single lower segment scar should be advised that, in general, induction of labour with prostaglandin is safe but not without risk.
- Misoprostol can be safely used for induction of labour in women with a single previous LSCS and an IUFD but with lower doses than those marketed in the UK.
- Women with two previous LSCS should be advised that in general the absolute risk of induction of labour with prostaglandin is only a little higher than for women with a single previous LSCS.
- Women with more than two LSCS deliveries or atypical scars should be advised that the safety of induction of labour is unknown.

- Recommendations for intrapartum antimicrobial therapy
  - Women with sepsis should be treated with intravenous broad-spectrum antibiotic therapy (including antichlamydial agents).
  - Routine antibiotic prophylaxis should not be used.
  - Intrapartum antibiotic prophylaxis for women colonised with group B streptococcus is not indicated
- Recommendations for pain relief in labour
  - Diamorphine should be used in preference to pethidine.
  - Regional anaesthesia should be available for women with an IUFD.
  - Assessment for DIC and sepsis should be undertaken before administering regional anaesthesia.
- Recommendations for women labouring with a scarred uterus
  - Women undergoing VBAC should be closely monitored for features of scar rupture.
  - Oxytocin augmentation can be used for VBAC, but the decision should be made by a consultant obstetrician.

Puerperium

- Women should be cared for in an environment that provides adequate safety according to individual clinical circumstance.
- Women with no critical care needs should ideally be able to choose between facilities which provide adequate privacy.
- Thromboprophylaxis
  - Women should be routinely assessed for thromboprophylaxis, but IUFD is not a risk factor.
- o Heparin thromboprophylaxis should be discussed with a haematologist if the woman has DIC

- Suppression of lactation
  - Women should be advised that almost one-third of those that choose nonpharmacological measures are troubled by excessive discomfort.
  - Women should be advised that dopamine agonists successfully suppress lactation in a very high proportion of women and are well tolerated by a very large majority; cabergoline is superior to bromocriptine.
  - Dopamine agonists should not be given to women with hypertension or pre-eclampsia.
  - Estrogens should not be used to suppress lactation.

Psychological and social aspects of care

- Carers must be alert to the fact that mothers, partners and children are all at risk of prolonged severe psychological reactions including post-traumatic stress disorder but that their reactions might be very different.
- Counselling should be offered to all women and their partners.
- Other family members, especially existing children and grandparents, should also be considered for counselling.
- Debriefing services must not care for women with symptoms of psychiatric disease in isolation. Parents should be advised about support groups.

Follow-up

- Parents should be advised about the cause of late IUFD, chance of recurrence and any specific means of preventing further loss.
- Women should be offered general prepregnancy advice, including support for smoking cessation.
- Women should be advised to avoid weight gain if they are already overweight (body mass index over 25) and to consider weight loss.
- An offer should be made to discuss the potential benefit of delaying conception until severe psychological issues have been resolved.
- Carers should be aware that while mothers tend to experience greater anxiety when conception occurs soon after a fetal loss, partners are more likely to suffer anxiety if conception is delayed.
- Parents can be advised that the absolute chance of adverse events with a pregnancy interval less than 6 months remains low and is unlikely to be significantly increased compared with conceiving later.
- The meeting should be documented for the parents in a letter that includes an agreed outline plan for future pregnancy.

Pregnancy following unexplained stillbirth

- The history of stillbirth should be clearly marked in the case record and carers should ensure they read all the notes thoroughly before seeing the woman.
- Women with a previous unexplained IUFD should be recommended to have obstetric antenatal care. Women with a previous unexplained IUFD should be recommended to have screening for gestational diabetes.
- For women in whom a normally formed stillborn baby had shown evidence of being small for gestational age, serial assessment of growth by ultrasound biometry should be recommended in subsequent pregnancies

European society of cardiology, 2018

General recommendations

- Pre-pregnancy risk assessment and counselling is indicated in all women with known or suspected congenital or acquired cardiovascular and aortic disease.
- It is recommended to perform risk assessment in all women with cardiac diseases of childbearing age before and after conception, using the mWHO classification of maternal risk.
- It is recommended that high-risk patients are treated in specialized centres by a multidisciplinary pregnancy heart team.
- Foetal echocardiography by experienced specialists is recommended when there is an elevated risk of foetal abnormalities.
- Echocardiography is recommended in any pregnant patient with unexplained or new cardiovascular signs or symptoms.
- If cardiac surgery is to be performed after 24 weeks and before 37 weeks of gestation, then corticosteroids are recommended for the mother.
- Vaginal delivery is recommended as the first choice in most patients.
- Induction of labour should be considered at 40 weeks of gestation in all women with cardiac disease.
- Genetic counselling should be considered in women with congenital heart disease or congenital arrhythmia, cardiomyopathies, aortic disease, or genetic malformations associated with CVD.
- MRI (without gadolinium) should be considered if echocardiography is insufficient for a definite diagnosis.
- In patients with severe hypertension, vaginal delivery with epidural analgesia and elective instrumental delivery should be considered.
- Delivery before necessary surgery should be considered when gestational age is >_26 weeks.
- Caesarean delivery should be considered for obstetrical indications or for patients with dilatation of the ascending aorta >45 mm, severe aortic stenosis, pre-term labour while on oral anticoagulants, Eisenmenger's syndrome, or severe heart failure.
- A chest radiograph may be considered if other methods are not successful in clarifying the cause of dyspnoea.
- Cardiac catheterization may be considered with very strict indications.
- CT and electrophysiological studies may be considered in selected patients for vital indications.
- Coronary bypass surgery or valvular surgery may be considered during pregnancy when conservative and medical therapy has failed, and in situations that threaten the mother's life or that are not amenable to percutaneous treatment.
- Prophylactic antibiotic therapy to prevent endocarditis during delivery is not recommended.

Modified World Health Organization classification of maternal cardiovascular risk

	mWHO I	mWHO II	mWHO II–III	mWHO III	mWHO IV
Diagnosis (if otherwise well and uncomplicated)	Small or mild – pulmonary stenosis – patent ductus arteriosus – mitral valve prolapse Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) Atrial or ventricular ectopic beats, isolated	Unoperated atrial or ventricular septal defect Repaired tetralogy of Fallot Most arrhythmias (supraventricular arrhythmias) Turner syndrome without aortic dilatation	Mild left ventricular impairment (EF >45%) Hypertrophic cardiomyopathy Native or tissue valve disease not considered WHO I or IV (mild mitral stenosis, moderate aortic stenosis) Marfan or other HTAD syndrome without aortic dilatation Aorta <45 mm in bicuspid aortic valve pathology Repaired coarctation Atrioventricular septal defect	Moderate left ventricular impairment (EF 30–45%) Previous peripartum cardiomyopathy without any residual left ventricular impairment Mechanical valve Systemic right ventricle with good or mildly decreased ventricular function Fontan circulation. If otherwise the patient is well and the cardiac condition uncomplicated Unrepaired cyanotic heart disease Other complex heart disease Moderate mitral stenosis Severe asymptomatic aortic stenosis Moderate aortic dilatation (40–45 mm in Marfan syndrome or other HTAD; 45–50 mm in bicuspid aortic valve, Turner syndrome ASI 20–25 mm/m^2, tetralogy of Fallot <50 mm) Ventricular tachycardia	Pulmonary arterial hypertension Severe systemic ventricular dysfunction (EF <30% or NYHA class III–IV) Previous peripartum cardiomyopathy with any residual left ventricular impairment Severe mitral stenosis Severe symptomatic aortic stenosis Systemic right ventricle with moderate or severely decreased ventricular function Severe aortic dilatation (>45 mm in Marfan syndrome or other HTAD, >50 mm in bicuspid aortic valve, Turner syndrome ASI >25 mm/m^2, tetralogy of Fallot >50 mm) Vascular Ehlers–Danlos Severe (re)coarctation Fontan with any complication
Risk	No detectable increased risk of maternal mortality and no/mild increased risk in morbidity	Small increased risk of maternal mortality or moderate increase in morbidity	Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity	Signicantly increased risk of maternal mortality or severe morbidity	Extremely high risk of maternal mortality or severe morbidity
Maternal cardiac event rate	2.5–5%	5.7–10.5%	10–19%	19–27%	40–100%
Counselling	Yes	Yes	Yes	Yes: expert counselling required	Yes: pregnancy contraindicated: if pregnancy occurs, termination should be discussed
Care during pregnancy	Local hospital	Local hospital	Referral hospital	Expert centre for pregnancy and cardiac disease	Expert centre for pregnancy and cardiac disease
Minimal follow-up visits during pregnancy	Once or twice	Once per trimester	Bimonthly	Monthly or bimonthly	Monthly
Location of delivery	Local hospital	Local hospital	Referral hospital	Expert centre for pregnancy and cardiac disease	Expert centre for pregnancy and cardiac disease

ASI = aortic size index; EF = ejection fraction; HTAD = heritable thoracic aortic disease; mWHO = modied World Health Organization classication; NYHA = New York Heart Association; WHO = World Health Organization.

Predictors of maternal and neonatal events

Predictors of maternal cardiovascular events	Predictors of neonatal events
Prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia)[4,28,43,47,48]	NYHA class III/IV or cyanosis during baseline pre-natal visit
NYHA class III/IV[29,42,43,48,49]	Maternal left heart obstruction
Left heart obstruction (moderate to severe)[29,42]	Smoking during pregnancy
Reduced systemic ventricular systolic function (ejection fraction <40%)[29,43,49]	Low maternal oxygen saturation (<90%)
Reduced subpulmonary ventricular function[47,50] (TAPSE <16 mm)[49,51]	Multiple gestations Use of anticoagulants throughout pregnancy
Systemic atrioventricular valve regurgitation (moderate to severe)[42]	Cardiac medication before pregnancy 'At birth' cyanotic heart disease
Pulmonary atrioventricular valve regurgitation (moderate to severe)[42]	Mechanical valve prosthesis
Pulmonary arterial hypertension[43,48,49]	Maternal cardiac event during pregnancy
Cardiac medication before pregnancy[42,46]	Maternal decline in cardiac output during pregnancy
Cyanosis (O_2 saturation <90%)[29,49]	Abnormal uteroplacental Doppler ow
Natriuretic peptide levels (NT-proBNP >128 pg/mL at 20 weeks predictive of event later in pregnancy)[42,46]	
Smoking history[51]	
Mechanical valve prosthesis[42,47]	
Repaired or unrepaired cyanotic heart disease[42]	

Predictors identied in references [29,35,42,43,51]
NT-proBNP = N-terminal pro B-type natriuretic peptide; NYHA = New York Heart Association; TAPSE = tricuspid annular plane systolic excursion.