South Australian Perinatal Practice Guideline

Fetal Growth (Restricted)

Note:
This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate, and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Note: The words woman/women/mother/she/her have been used throughout this guideline as most pregnant and birthing people identify with their birth sex. However, for the purpose of this guideline, these terms include people who do not identify as women or mothers, including those with a non-binary identity. All clinicians should ask the pregnant person what their preferred term is and ensure this is communicated to the healthcare team.

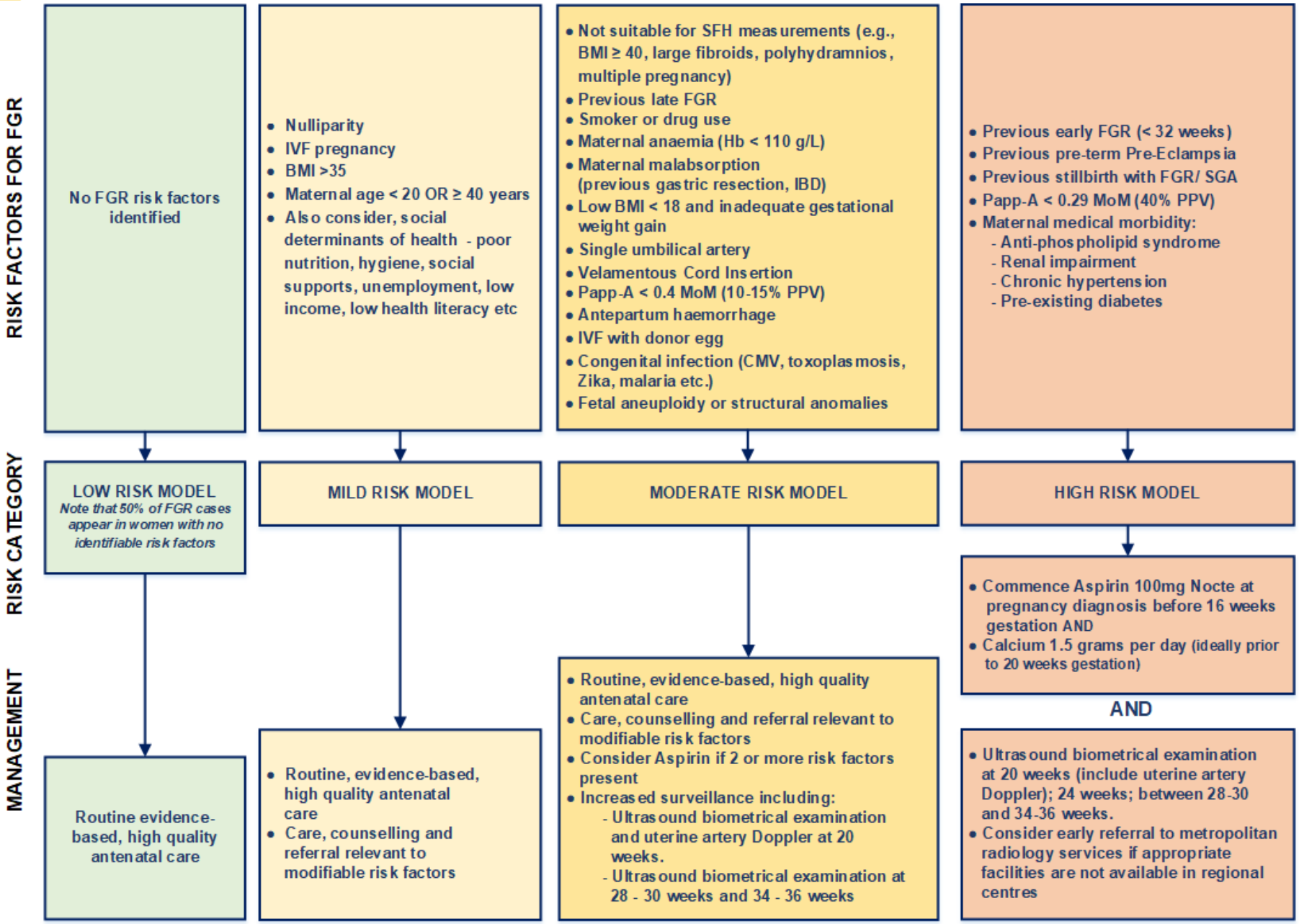
Explanation of the Aboriginal artwork:
The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics, the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectfully manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of Perinatal Practice Guideline (PPG)

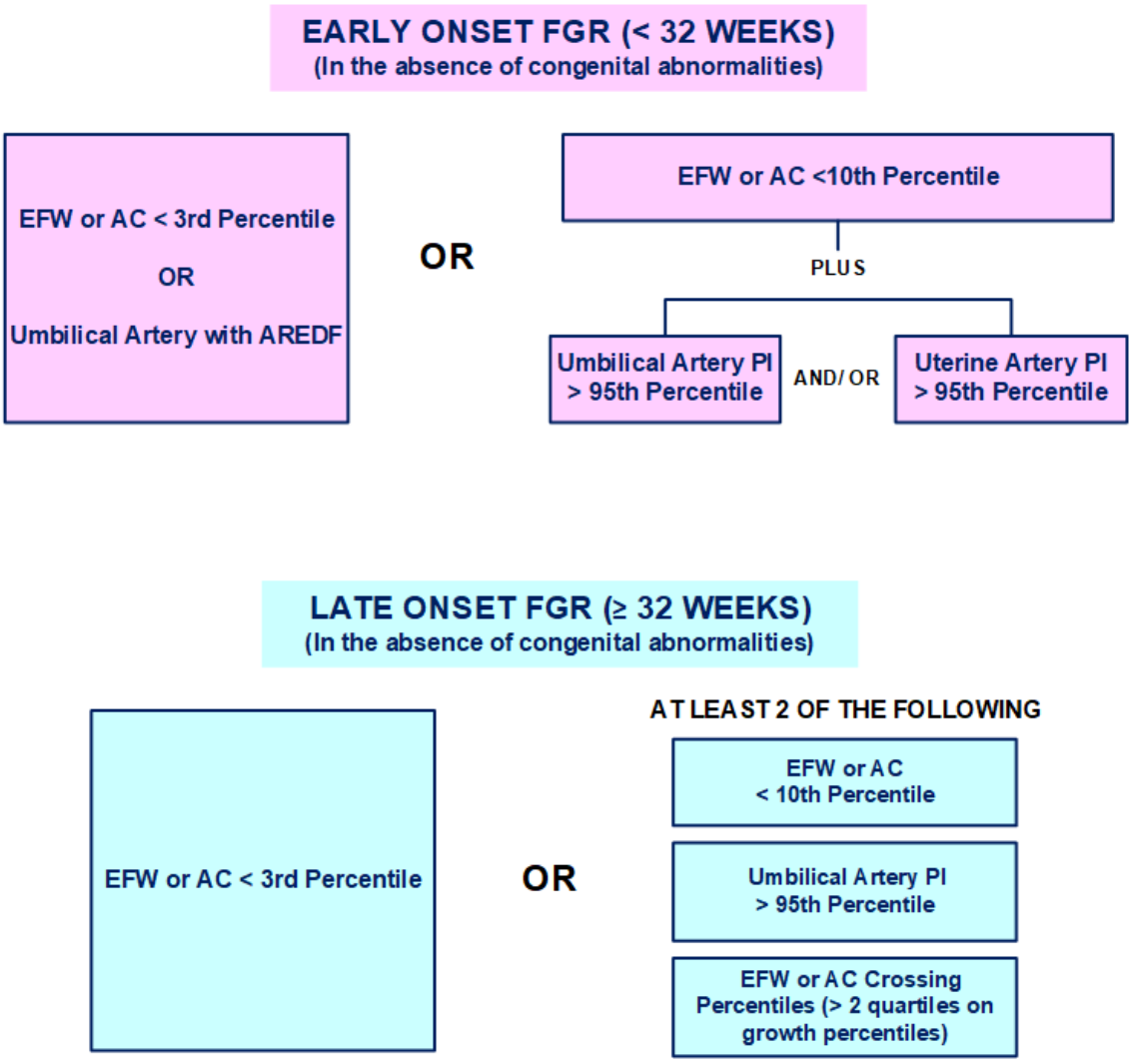
The *Fetal Growth (Restricted) PPG* will guide the screening, diagnosis, and management of fetal growth restriction. Fetal growth restriction is associated with an increased risk of stillbirth, neonatal death, short term and long term morbidity; therefore, the identification and management of these pregnancies is essential in preventing poor outcomes[1, 2].

Flowchart 1 | Risk Assessment and Screening for FGR



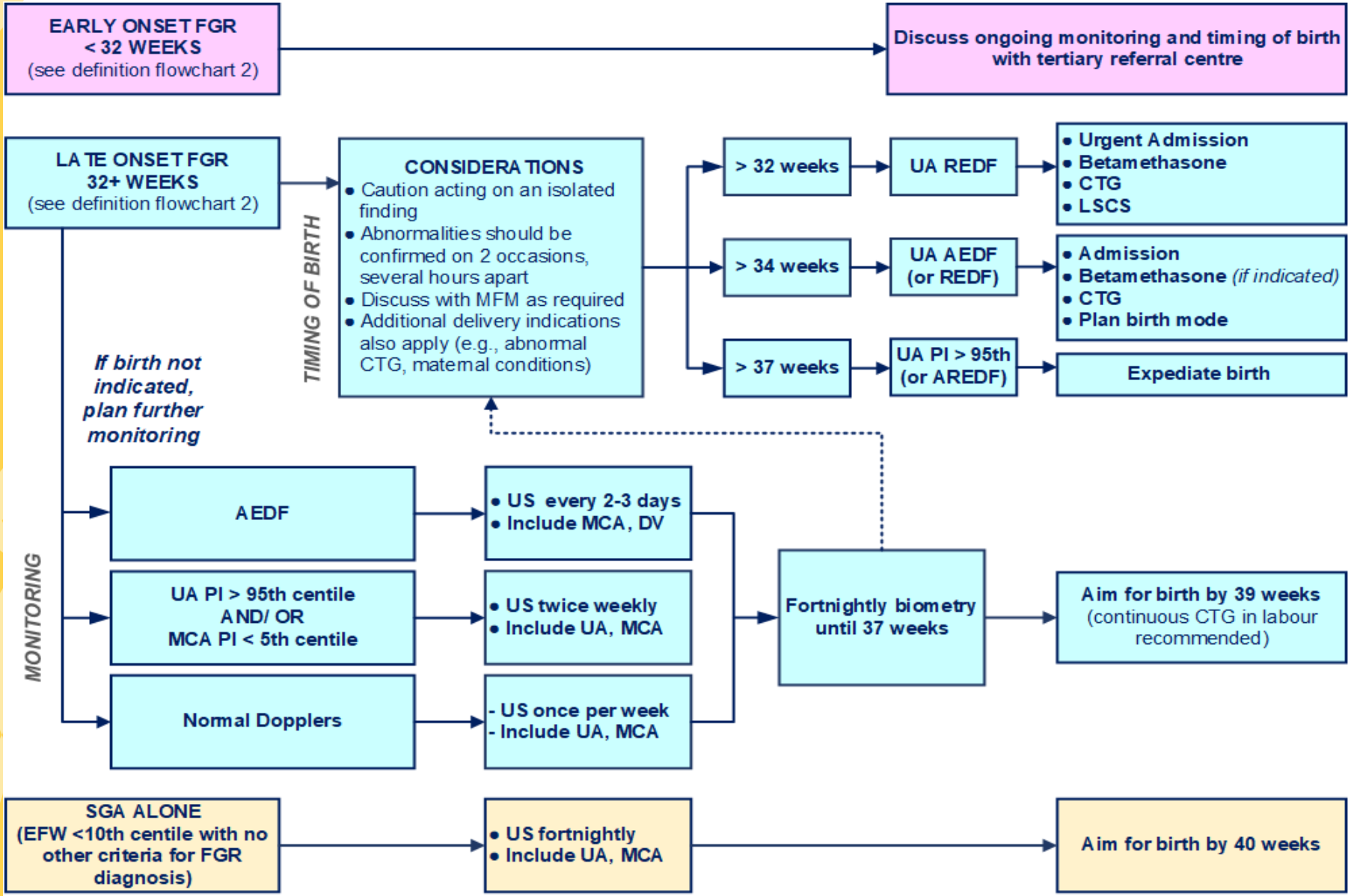
Flow Chart 2 | Diagnosis of FGR

Consensus-based Definitions for Fetal Growth Restriction to Aid Diagnosis (FGR)[3]



Note: Fetal growth restriction has previously been categorized as 'symmetrical' or 'asymmetrical' FGR. These have traditionally been associated with onset at early or later gestations, and thought to reflect separate disease processes, however it is now apparent that both can be associated with poor perinatal outcomes, and as such these descriptions are not part of the consensus definition of FGR. Doppler velocimetry findings and gestational age at onset are better predictors of outcome[4, 5]

Flowchart 3 | Monitoring and Management of FGR (with likely placental origin)



NOTE: ALWAYS CONSIDER FULL MATERNAL-FETAL CLINICAL PICTURE AND ADDITIONAL RISK FACTORS SUCH AS PRE-ECLAMPSIA, DECREASED FETAL MOVEMENTS, REDUCED AFI. ALL WOMEN WITH EARLY ONSET FGR SHOULD BE REFERRED FOR MFM SPECIALIST CONSULTATION.

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Summary of Practice Recommendations

Fetal Growth Restriction (FGR) is diagnosed by ultrasound measurements and Doppler abnormalities, in contrast to Small for Gestational Age (SGA), in which the estimated fetal weight or birth weight is below the 10th percentile for gestational age in the absence of pathology.

Most SGA pregnancies are constitutionally small and healthy, therefore differentiating between SGA and FGR is crucially important.

Identification of women at high and moderate risk of FGR is ideal to ensure targeted screening, diagnostic ultrasound and preventative interventions, without pathologizing or over-intervening in normal pregnancies.

Aspirin is not effective for prevention of FGR alone:

Use of aspirin in the prevention of pre-eclampsia, refer to **Flowchart 1 | Risk Assessment and Screening for FGR.**

Low Molecular Weight Heparin (LMWH) is also not effective for population level prevention of FGR. Use in women with risk factors for severe FGR may be discussed on an individual case basis.

LMWH should be used where indicated for the evidence-based treatment of concurrent medical conditions or complications.

Selective ultrasound based on risk factors is warranted for women at moderate and high risk of FGR. Whilst routine ultrasound at 28 - 36 weeks may slightly increase the detection rate of FGR, it has not so far been shown to improve outcomes and hence is not currently recommended.

Following a diagnosis of FGR, close monitoring and expert management is required to improve outcomes for FGR foetuses.

This may require referral to a tertiary centre or MFM unit for ongoing monitoring and Management, particularly for cases of early FGR (< 32 weeks).

Rural LHNs should have a documented process for referring women to metropolitan LHN high risk pregnancy or MFM units for advice and/or transfer of care.

If the referral is urgent, the referring doctor should call the Women's and Children's Hospital Switchboard (08 81617000) and request to speak to the Maternal Fetal Medicine Fellow on call.

Perinatal service providers need cultural sensitivity within a non-judgemental environment when planning care for the Aboriginal woman.

Health literacy and understanding may be limited for Aboriginal women whose primary language is not English. An interpreter should be offered where available, to support the understanding of management and treatment options in this scenario.

An AMIC or Aboriginal Healthcare Worker should be consulted with to ensure cultural safety and appropriateness is adhered and to ensure cultural beliefs and practices are understood by clinicians in the provision of care.

Abbreviations

>	Greater than
≥	Greater than or equal to
<	Less than
≤	Less than or equal to
AC	Abdominal Circumference
AGA	Appropriate for Gestational Age
AEDF	Absent End Diastolic Flow
AREDF	Absent or Reversed End-Diastolic Flow
BMI	Body Mass Index
CMV	Cytomegalovirus
CPR	Cerebro-Placental Ratio
CRL	Crown-Rump Length
EFW	Estimated Fetal Weight
FGR	Fetal Growth Restriction
FIGO	Federation of Gynecology[sic] and Obstetrics
FBE	Full blood examination
g	Gram(s)
g/L	Gram(s) per Litre
IBD	Inflammatory Bowel Disease
ICSI	Intra-Cytoplasmic Sperm Injection
IVF	Invitro fertilisation
Microg	Microgram(s)
mL	Millilitre(s)
mg	Milligram(s)
MoM	Multiples of Median
Papp-A	Pregnancy Associated Plasma Protein A
PI	Pulsatility Index
PPV	Positive Predictive Value
RCT	Randomised Controlled Trial
REDF	Reversed End-Diastolic Flow
SFH	Symphysio-Fundal Height
SGA	Small for Gestational Age
TORCH	**T**oxoplasmosis, **O**ther agents, **R**ubella, **C**ytomegalovirus, and **H**erpes simplex
UA	Umbilical Artery
UtA	Uterine Artery
US	Ultrasound

Definitions

Early onset FGR	FGR that is diagnosed before 32 weeks or has clinical signs that indicate early onset*
FGR	May be defined as a fetus not achieving its growth potential because of underlying disorders which may include placental pathology, maternal pathology or intrinsic fetal disorders, FGR is defined by FIGO[6] as being diagnosed by ultrasound measurements and Doppler abnormalities
Late onset FGR	FGR that is diagnosed after 32 weeks with evidence of recent deterioration in growth and Dopplers**
Severe FGR	Estimated fetal weight ≤ 3rd centile
SGA	An estimated fetal weight or birth weight below the 10th percentile for gestational age, most of whom are actually small healthy fetuses

***Early onset FGR** is more commonly associated with abnormal umbilical artery Doppler and early onset pre-eclampsia. Diagnosis is usually easier than late onset FGR and the main therapeutic dilemma for early onset FGR involves the risks of premature delivery. In early onset FGR (prior to 32 weeks), neonates have significantly lower survival rates than appropriately grown neonates. Gestational age and birth weight are the greatest determinants of outcome[7, 8].*

***Late onset FGR** refers to FGR diagnosed beyond 32 weeks gestation. The main difficulty with late onset FGR is accurate diagnosis- there is a high rate of false positive diagnoses which may lead to unnecessary intervention. The main risk of late FGR is sudden fetal decompensation and stillbirth, but both types of FGR have risks of adverse longer term outcomes for the child.*

Background

SGA is not a proxy for FGR; the definition of FGR aims to identify a subset of fetuses at higher risk of adverse outcomes.

Fetal growth restriction is associated with an increased risk of stillbirth, neonatal death, and short term morbidity; therefore the identification and management of these pregnancies is essential in preventing poor outcomes[1, 2].

Fetal growth restriction is also associated with higher incidence of neurodevelopmental delay, childhood and adult obesity and metabolic disorders[7, 9].

Sixty percent (60%) of SGA fetuses (< 10th centile) and 40% of severely SGA fetuses (< 3rd centile) are not suspected of FGR[2].

Antenatal detection of FGR is protective against stillbirth, however over 40% of stillbirths in SGA fetuses occurred despite the diagnosis of FGR[1].

FGR remains a leading cause of stillbirth, neonatal mortality, and short- and long-term morbidity.

Close monitoring and expert management of FGR is required to improve outcomes for FGR fetuses.

Causes of Fetal Growth Restriction (FGR)

Suboptimal placental transfer of maternal nutrition:

- Smoking
- Maternal anaemia
- Malabsorption

Placental causes:

- Infarction, fibrin deposition, chronic abruption, lack of spiral artery transformation
- Chronic placental inflammation / villitis
- Confined placental mosaicism
- Cord disorders – hyper-coiling, single umbilical artery, marginal/velamentous insertion

Fetal causes:

- Genetic (aneuploidy, deletions, mutations, epigenetic)
- Syndromal / structural disorders
- Congenital infection (CMV, Toxoplasmosis, Zika, Malaria)
- Teratogens (drugs / toxins)

Prevention of Fetal Growth Restriction (FGR)

Identification of risk factors that can be modified to prevent the development of FGR[9]:

- Smoking cessation
- Cessation or replacement of teratogenic or growth inhibiting drugs by safer medication pre conceptually or early in pregnancy
- Avoidance of environmental agents causing FGR
- Targeted use of aspirin:
  - Aspirin has not been shown to be independently effective in prevention of FGR in high quality trials[10] (although it is appropriate in targeted prevention of preeclampsia[11])
  - Since preeclampsia is strongly associated with early onset FGR, there is an obvious overlap in preventative strategies

- Aspirin (100mg nocte[12]) should be advocated for women at risk of preeclampsia by history or predisposition for preeclampsia because of medical risk factors (see below), as well as those at high risk of early FGR[9] (these risk factors will overlap significantly with risk factors for pre-eclampsia)

> Low Molecular Weight Heparin (LMWH) is not effective for population level prevention of FGR. Use in women with risk factors for severe FGR may be discussed on an individual case basis. LMWH is indicated as part of evidence-based treatment of concurrent medical conditions or complications [13]

Consider accessibility to medications for Aboriginal women who are from country and or remote communities. Seek advice from the woman and/or ALO to ensure medications can be accessed for appropriate treatment

All Aboriginal women requiring ongoing management with medications should be referred to register for the Closing the Gaps Medicines Access Program. Discuss with Pharmacy to ensure woman can access medicines at an affordable cost

Prediction of Fetal Growth Restriction (FGR) | Targeted Screening

> Current available evidence suggests that routine ultrasound in low-risk women is likely to increase detection of SGA (& FGR) babies but has not yet been shown to improve outcomes for the neonate and may result in a small increase in IOL[14-17].

> Prediction of FGR involves identification of women at high risk of FGR who may benefit from targeted screening, diagnostic ultrasound and preventative interventions, without pathologizing or over-intervening in normal pregnancies.

> Additional FGR screening by ultrasound should be undertaken only in women who:

- have identified risk factors (moderate or high risk) for FGR (see flowchart 1)
- are unsuitable for SFH monitoring alone (high BMI, uterine fibroids, polyhydramnios, multiple pregnancy)
- exhibit signs of fetal growth restriction
- demonstrate clinical concern over fetal size and growth.

> Importantly, half of the women diagnosed with fetal growth restriction have no identifiable risk factors,[2] highlighting the need for vigilance in SFH measurements and ongoing assessment of risk factors that develop over the pregnancy.

> Setting a threshold of risk is controversial, particularly as the outcomes being avoided such as stillbirth are relatively rare but are devastating.

> As most SGA fetuses are actually constitutionally small and healthy[17], differentiating FGR fetuses from SGA fetuses is crucially important.

High Risk Models

Risk factors that place women at high risk of fetal growth restriction include:

> history of previous early onset FGR affected pregnancies
> previous early-onset preeclampsia
> previous stillbirth with FGR/SGA
> pre-existing hypertension, diabetes or renal disease
> auto-immune disorders such as antiphospholipid syndrome, systemic lupus erythematosus and inflammatory bowel disease
> Papp-A value < 1st centile (< 0.29 MoM) has a 40% PPV of FGR.

The recommendations for women with any of these risk factors is:

> consider commencing Aspirin 100 mg nocte at 12-16 weeks gestation
> if there is a history or significant risk of developing pre-eclampsia, also consider use of calcium 1.5 grams per day commenced prior to 20 weeks gestation.

Ultrasound biometrical examination at:

> 20 weeks (+ uterine artery Doppler)
> 24 weeks
> 28-30 weeks
> 34-36 weeks

Note: Consider early referral to metropolitan radiology services if appropriate facilities are not available in regional centres (e.g., if advanced Doppler measurements not available at local facilities)

Moderate Risk Models

Risk factors that place women at moderate risk of fetal growth restriction include:

- previous late FGR
- smoking, Drug and Alcohol use
- maternal anaemia (Hb<110g/L)
- maternal malabsorption (previous gastric resection, IBD)
- low BMI <20 or inadequate gestational weight gain
- single umbilical artery
- velamentous cord insertion
- Papp-A <0.4MoM (10-15% PPV)
- antepartum Haemorrhage or Sub-chorionic haemorrhage
- IVF with donor egg
- congenital infection (CMV, toxoplasmosis, zika, malaria)
- fetal aneuploidy or structural abnormalities.

Note: A greater number of maternal risk factors is associated with increasing cumulative risk of fetal growth restriction[18]. Therefore, if a woman has multiple risk factors classified as "Moderate Risk", consideration should be given to the additional monitoring recommended for pregnancies at "High Risk" for FGR.

In depth literature review for each risk factor can be found under **Appendix 3 | Risk Factors Classified Under Moderate Risk Model**

Women with a moderate risk of FGR require:

- Routine, evidence - based, high quality antenatal care
- Care, counselling, and referral relevant to modifiable risk factors (i.e., smoking cessation support, DASSA referral, dietetics referral)
- Consider Aspirin 100 mg nocte commencing 12 – 16 weeks gestation if 2 or more risk factors apply
- Increased surveillance may be warranted, including:
- Ultrasound biometrical examination and uterine artery (UtA) Doppler at 20 weeks (consider referral for tertiary scan if facilities cannot perform UtA Doppler)
- Ultrasound biometrical examination at 28 - 30 weeks and 34 - 36 weeks.

Women who are unsuitable for SFH measurements require the same management recommended above. This includes women with:

- high BMI (e.g., ≥ 40, this will depend on the degree of impact on central adiposity and should be determined by the clinician)
- large fibroids
- polyhydramnios
- multiple pregnancy.

Mild Risk Models

Risk factors that place women at mild risk of fetal growth restriction include:

- nulliparity
- IVF pregnancy
- BMI > 35
- advanced maternal age ≥ 40 years
- maternal age < 20 years
- also consider social determinants of health, including poor nutrition, poor hygiene, lack of social supports, low income, homelessness, unemployment, poor health literacy.

Note: A greater number of maternal risk factors is associated with increasing cumulative risk of fetal growth restriction[18]. Therefore, if a woman has multiple risk factors classified as "Mild Risk", consideration should be given to additional ultrasound monitoring dependent on the severity of the risks.

Aboriginal Ethnicity

In South Australia, Aboriginal babies are 2-3 times more likely to be of low birth weight. The cumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services, and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Although Aboriginality is not an isolated risk factor for fetal growth restriction, it is recognised that concurrent socio-economic and health factors may contribute to a pregnancy affected by fetal growth restriction, and so these concurrent risk factors may be discussed with Aboriginal women and their support people to determine appropriate care and screening in pregnancy.

Low Risk Models

Women with pregnancies with none of the risk factors outlined above will, of course, require evidence based high quality antenatal care, but may have more options regarding frequency of visits [19] and the primary carer's need for consultation/referral [20].

Note: half of the women diagnosed with fetal growth restriction have no identifiable risk factors,[2] highlighting the need for vigilance in SFH measurements and ongoing assessment of risk factors that develop over the pregnancy.

Tools Used in Screening for Fetal Growth Restriction (FGR)

Symphysio Fundal Height (SFH) Measurement

- Reported sensitivity ranges from 17 - 86%.
- Using customised SFH charts (not yet widely available) does increase the detection rate of FGR[21].
- Using standardised SFH measurement methods and plotting the measurements on a growth chart increases the sensitivity as shown by the Intergrowth-21st project[22].
- SFH charts developed by the Intergrowth 21st project have been adopted by SA PPGs and incorporated in the SA Pregnancy Record (See **Appendix 1 – International Symphysis-Fundal Height Standards Chart**).
- For South Australian practice, referral for ultrasound is recommended if SFH measures are below the 10th centile (provided that the estimation of gestational age is accurate), or if repeat measures show a drop across centiles.

Procedure for Measuring of Symphysis Fundus Height[23]

The woman should lie in the **supine** position and should have an **empty bladder**.

- Technique for measuring uterine height:

1. Uterine height should be measured only using a **metric** tape of **non-elastic** material
2. Measurements are to be **blinded**, by turning the tape measure so that no numbers are visible during the measurement.
3. Hold the 0 cm marking of the tape with one hand, securing it over the upper border of the symphysis pubis bone.
4. With the palm of the other hand on the abdomen, pass the tape in a straight line from the symphysis pubis over the uterus to the fundus uteri until you feel a resistance in the abdominal wall. DO NOT HOLD THE TAPE BETWEEN THE FINGERS.
5. Use the cubital edge of the hand to sustain the tape in place at the point of the fundus uteri.
6. Carefully fold the paper at the level of the fundus. The tape should then be turned so that the numbers are visible, and the value can be determined.
7. Repeat the whole process a **second time**. If the second measure differs by more than one cm, repeat the measure a third time. Record the mean of the 2 closest measurements.
8. Chart the measurement on the SFH chart, See **Appendix 1 – International Symphysis-Fundal Height Standards Chart**

Fetal Growth Ultrasound Measurement Charts

- In the review paper by Ohuma et al [24], there is clearly a lack of consensus on how fetal charts should be constructed and whether an international chart that can be applied across populations is desirable. The Intergrowth - 21st project, described above, produced biometry charts which are an example of an international growth standard [25].
- However, at this time, there is no evidence to alter the use of fetal growth reference charts. For individual biometric measurements, there are reference charts based on Australian data (and currently endorsed by the Australian Society for Ultrasound in Medicine)[26].
- No suitable estimated fetal weight chart based on Australian sonographic measurements exists. The Hadlock charts[27] are an example of a well-produced fetal growth reference chart. Consistency of chosen weight formulas and growth charts within and between practices is recommended.

Monitoring and Management of FGR

- Following a diagnosis of FGR, close monitoring and expert management is required to improve outcomes for FGR fetuses.
- This may require referral to a tertiary centre or MFM unit. WCHN MFM referral form can be found in

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- **Appendix 4 | WCHN MFM** Referral Form or at Women's and Children's Hospital Maternal Fetal Medicine Service (MFMS)
- Rural LHNs should have a documented process for referring women to metropolitan LHN high risk pregnancy or MFM units for advice and/or transfer of care
- If the referral is urgent, the referring doctor should call the **Women's and Children's Hospital Switchboard (08 81617000)** and request to speak to the Maternal Fetal Medicine Fellow on call
- Identifying aetiology for FGR is important in monitoring and managing pregnancies affected by FGR[6]. Measures to identify aetiology include[6]:
- Taking a detailed history including maternal age, height and weight, nutritional status, socio-economic status, smoking, use of recreational drugs, chronic medical conditions, personal or family history suggestive of thrombophilia, genetic disorders or consanguinity, obstetric history including birth weights of previous children, and **careful consideration of pregnancy dating by examination of first trimester ultrasound** (if available)
- Dating based on last menstrual period is often unreliable
- pregnancies conceived with assisted reproductive technologies should be dated using the known conception date
- In all other pregnancies, first-trimester ultrasound is the most accurate method to date a pregnancy, with a precision of +/- 5 days in 95% of scans. Where multiple first trimester scans have occurred, the earliest scan with a Crown-Rump Length (CRL) of at least 10mm should be used.
- Consideration of risk for congenital infection, i.e., Frequent prolonged contact with children attending childcare (CMV), travel history to endemic regions (Zika virus or Malaria), history of febrile disease and/or rash in pregnancy or periconceptually or contact with domestic animals (toxoplasmosis). Additionally, consider risk for Syphilis and Varicella-Zoster virus.
- Screening for perinatal infections should be guided by the whole clinical picture and assessment of the likelihood of each individual infection, rather than a generic 'TORCH' panel[28] which is costly and of very limited benefit.
- When fetal infection is highly suspected based on serology or clinical findings, further consideration should be given to amniocentesis for testing of viral DNA[6]
- Doppler velocimetry is an integral part of the diagnosis and monitoring of FGR. Abnormal uterine, umbilical, or middle cerebral artery Doppler studies are suggestive of placental dysfunction as the underlying aetiology[6]. Dopplers may be normal in the early stages of FGR, therefore do not rule out placental dysfunction in this situation- serial monitoring is warranted to rule out placental dysfunction.

Management of FGR with Syndromal/ Chromosomal Origin

- In pregnancies with early FGR, with no signs suggestive of placental dysfunction, or with associated fetal structural anomalies, referral should be made for consideration of amniocentesis to detect underlying chromosome abnormalities.
- For women that have a diagnosis of fetal aneuploidy, ongoing care should be in consultation with a Maternal Fetal Medicine (MFM) clinician.
- Timing of birth will be determined by a number of factors, monitored by MFM, with a clearly documented plan made in consultation with the woman for clinicians at her birthing facility to follow. Birthing facility may also be determined by the anticipated needs of the baby relevant to neonatal unit capacity and ability.

Management of FGR with Placental Origin

- Suggestions regarding frequency of monitoring and timing of birth are outlined inFlowchart 3 | Monitoring and Management of FGR.

Timing of Birth

- The timing of birth varies according to severity and gestation. The risks of continuing the pregnancy must be balanced against the sequalae associated with pre-term birth. Iatrogenic early birth carries a high rate of neonatal complications, whereas delaying birth

is associated with higher risk of stillbirth[29]. In early FGR, evidence shows that each day gained in-utero increases survival by 1 - 2%[30].

> Consultation with clinicians experienced in the management of FGR is necessary to arrange appropriate surveillance and individualize management[4].

Labour and Birth Management

Labour (Including Induction of)

> For women who have a growth restricted fetus, cervical ripening using balloon catheterisation is preferable to avoid uterine hyperstimulation.
> Continuous fetal monitoring should occur where there is uterine activity, regardless of established labour as the growth restricted fetus may exhibit signs of hypoxia with any uterine activity.

Placental Examination

> The placenta should be sent for histopathological examination for all suspected fetal growth restriction (including those identified at birth i.e., Birth Weight < 3rd centile).

Neonatal Considerations and Management

Considerations

> Fetal growth restriction has multi-system effects in the newborn that reflect fetal hypoxia and malnutrition and the impact of preterm birth [5]
> Where there is marginal oxygenation of the fetus, the stress of labour increases the risks of intrapartum asphyxia and the likelihood of emergency caesarean section and need for resuscitation at birth.
> Hypothermia is more likely due to a relatively larger head to body ratio and reduced subcutaneous fat reserves.
> Hypoglycaemia is common in malnourished, preterm or sick growth restricted neonates, may occur due to increased glucose consumption for thermogenesis, reduced glycogen reserves and impaired gluconeogenesis
> Polycythaemia may be present reflecting in utero hypoxia and can be associated with jaundice and hyperviscosity.
> Constitutionally small neonates are not at increased risk of the above complications

Aboriginal women should be consulted on the care of the newborn baby in the first instance. Consult with their preferred Aboriginal health professional if requested

Early communication with the ALO or AMIC practitioner is recommended to ensure continuity of care and cultural support and advocacy is maintained is imperative in optimal outcomes for Aboriginal babies and their mothers

Management

> Where fetal growth restriction is known before birth, the birth should occur in a facility where there are facilities and staff to manage newborn resuscitation and stabilisation
> The immediate care of the newborn should pay careful attention to surveillance for complications of asphyxia, prematurity, respiratory distress, hypothermia and hypoglycaemia, following state PPG guidelines and local institutional protocols for transitional care.
> Paired cord gases are important to objectively document intrapartum asphyxia
> After stabilisation, the initial assessment of the newborn should include a careful examination to assess nutritional state and plotting of percentiles for weight, length and head circumference for gestational age. Examination should address whether the baby is constitutionally small or growth restricted, if clinical appearance is consistent with the gestation determined during pregnancy, the presence of syndromal features or congenital abnormalities, and features of a congenital infection.
> Breast feeding is encouraged with or without top-ups of expressed breast milk. Formula top-ups may be required to manage hypoglycaemia where medically indicated.

- Placental histopathology is important in the evaluation of the growth restricted neonate.
- Where the aetiology of the growth restriction is clear from the obstetric history, clinical examination and placental histopathology, further investigations for growth restriction are not required
- Subsequent growth patterns in infancy and childhood are dependent on the aetiology and severity of the growth restriction. Growth restriction with onset in the third trimester generally shows catch-up growth in the first 6 months, whereas more severe and earlier onset growth restricted neonates are more likely to remain smaller than their peers[31]
- Growth restricted neonates have a higher risk of long term neurological impairment at all birth gestations, and this is accentuated by preterm birth[32]
- All babies born at < 2000 grams at birth or < 34 weeks gestation are given ferrous sulfate and multivitamins (Pentavite) as per the SA Neonatal Medication Guidelines available at www.sahealth.sa.gov.au/neonatal

Consider accessibility to medications for Aboriginal women who are from country and or remote communities. Seek advice from the woman and/or ALO to ensure medications can be accessed for appropriate treatment.

All Aboriginal women and babies requiring ongoing management with medications should be referred to registering for the Closing the Gaps Medicines Access Program. Discuss with Pharmacy to ensure woman can access medicines at an affordable cost

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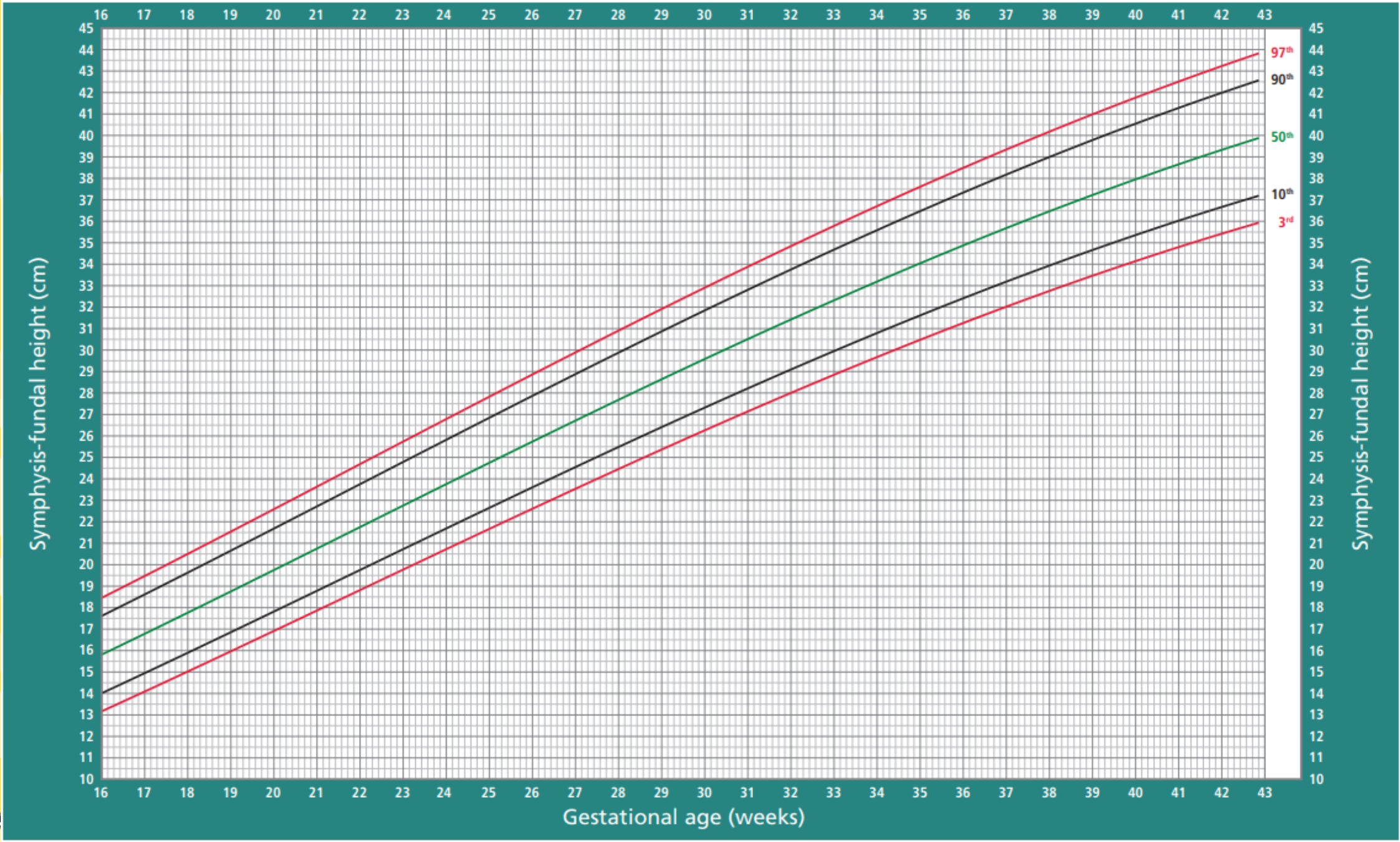
UNIVERSITY OF OXFORD

International Symphysis-Fundal Height Standards

INTERGROWTH-21st



Papageorghiou et al. *BMJ* 2016;355:i5662

Appendix 2 | Risk Factors Classified Under Mild Risk Model

<table>
<tr><td>Nulliparity</td><td>

Nulliparity is a risk factor for preeclampsia, and thus for FGR. Also, nulliparous women will not have the reassuring history of a previous pregnancy not affected by FGR. Thus, particular attention should be given to nulliparous pregnant women with respect to clinical monitoring for signs and symptoms of preeclampsia and symphysio fundal height measurement, as well as the fastidious adherence to the frequency of such monitoring
There is no consensus as to whether ultrasound screening for FGR or the use of aspirin is clinically or cost effective in women with nulliparous pregnancies without other risk factors[9]
To pathologise all nulliparous women without other risk factors “by promulgating practice directives that are marginally evidence based is both ineffective, and potentially harmful”[33]

</td></tr>
<tr><td>IVF Pregnancy (homologous ovum)</td><td>

A study of 246 singleton pregnancies indicated that there was no difference in centile birth weights of spontaneously conceived infants compared with IVF/ICSI conception[34]
A study of over 1100 singleton pregnancies with an FGR diagnosis or pre-eclampsia diagnosis (or both) were explored. Despite IVF pregnancies having older women, lower parity, and higher rates of hypertension and diabetes, they were significantly less likely to have an adverse neonatal outcome[35]
A study of nearly 70,000 pregnancies showed a much higher risk of ischaemic placental disease compared with spontaneously conceived pregnancies (4 times higher), even after adjustment for maternal age and parity[36]

</td></tr>
<tr><td>BMI > 35</td><td>

Increased maternal central adiposity presents a challenge for routine antenatal screening interventions. Accurate symphysio-fundal height measurements are difficult in this cohort, therefore additional screening through ultrasonography may be warranted to assess fetal growth. Women with increased BMI are at risk for both fetal growth restriction and fetal macrosomia[37], therefore careful monitoring of fetal size is needed and increased monitoring may be required based on clinical assessment. For women with a BMI over 40, increased monitoring is needed. Clinical discretion may be used for women with a BMI below 40

</td></tr>
<tr><td>Advanced Maternal Age ≥ 40 years</td><td>

A retrospective study of over 18million women indicates that maternal age of 40-50years is associated with an increase in fetal growth restriction, but not maternal age of 35-39years[38]
The increased risk is minor in comparison to other conditions

<table>
<tr><th>Age (years)</th><th>Risk (Odds Ratio) for FGR < 10th centile</th><th>Risk (Odds Ratio) for FGR < 5th centile</th></tr>
<tr><td>18-34</td><td>1.00</td><td>1.00</td></tr>
<tr><td>35-39</td><td>0.97</td><td>0.99</td></tr>
<tr><td>40-50</td><td>1.09</td><td>1.15</td></tr>
</table>
</td></tr>
</table>

Appendix 3 | Risk Factors Classified Under Moderate Risk Model

Unsuitable for SFH measurements:	• High BMI, polyhydramnios, multiple pregnancy and uterine fibroids are not necessarily risk factors for FGR, however they do make monitoring of fetal growth more difficult, therefore additional monitoring may be required. • For women who have a BMI over 40 or large uterine fibroids, fetal size monitoring is difficult through abdominal palpation and Symphysis Fundal Height alone. Ultrasound is necessary to monitor fetal size and detect abnormal growth trajectory.
Previous late FGR	• The risk of FGR, pre-term birth and stillbirth was moderately elevated for women who experienced these conditions in a previous pregnancy. • The risk is elevated further if two or more conditions occurred[39]
Smoking, Alcohol or drug use	• Tobacco use in pregnancy is associated with a 3-fold incidence of fetal growth restriction • Passive smoking is also a risk factor for fetal growth restriction, increasing the risk by 30%[40].This should be considered during antenatal care as a non-smoking mother living in a smoking environment will often be missed[40] • Alcohol consumption in pregnancy is associated with fetal growth restriction and a range of other sequalae including dysmorphia and poor neurodevelopmental outcomes[41] • Use of illicit substances such as cocaine, amphetamines and heroin increases risk of FGR[4] • A number of therapeutic medications have also been implicated in the aetiology of FGR including; antiepileptic medications, β-blockers, chemotherapy agents, and long-term fluorinated steroid use[4]
Maternal Anaemia (Hb <110g/L)	• Maternal anaemia (Hb < 110 g/L) and iron deficiency anaemia (Hb < 110 g/L and serum ferritin < 20) have a strong association with fetal growth restriction[42]. It is one of the leading causes of FGR in developing countries[43] • In a study of over 14,000 women in the UK, the risk of stillbirth and perinatal death in women with moderate to severe anaemia (haemoglobin < 100) at booking visit and 28 weeks was 3 and 5-fold, respectively[44]
Maternal malabsorption (previous gastric resection, IBD)	• Fetuses of women who had previous bariatric surgery are smaller, but this is not due to placental insufficiency and they are not necessarily at higher risk of FGR[45] • Women with inflammatory bowel disease are more likely to have inadequate weight gain in pregnancy. There is an association between inadequate maternal weight gain and inadequate nutrition (due to inflammatory bowel disease or gastrointestinal bypass surgery). These can cause lower birth weight due to decreased nutrition, however fetal growth restriction is not necessarily increased[46, 47]
Single umbilical artery	• A Single Umbilical Artery (SUA) is seen in 1 - 5% of pregnancies, with higher prevalence in multiple pregnancy and fetuses with abnormal karyotype. It is associated with congenital malformations including cardiac and genitourinary tract anomalies. Thus, detection of SUA warrants careful evaluation for additional abnormalities. • As an isolated finding, SUA occurs in 0.5 - 1% of pregnancies[48]. • For pregnancies with a SUA, there is an increased incidence of FGR therefore monitoring of fetal growth is recommended.

<table>
<tr><td>Low BMI <18 and inadequate gestational weight gain (GWG)</td><td>

Inadequate gestational weight gain is associated with SGA and adverse fetal and neonatal outcomes[46].
Inadequate GWG may be associated with inflammatory bowel disease and is strongly associated with Crohn’s disease and Ulcerative Colitis[46].
In this study, the American IOM recommendations for GWG were used

<table>
<tr><th>Pre-pregnancy BMI (kg/m2)</th><th>Recommended GWG (kg)</th></tr>
<tr><td><18.5</td><td>12.5 - 18</td></tr>
<tr><td>18.5 - 24.9</td><td>11.5 – 15</td></tr>
<tr><td>25 - 29.9</td><td>7 – 11.5</td></tr>
<tr><td>> 30</td><td>5 - 9</td></tr>
</table>
</td></tr>
<tr><td>Velamentous cord insertion</td><td>

Abnormal cord insertion, such as velamentous insertion is associated with lower mean birth weight[49].
Conception with assisted reproductive technologies (ART) has a high association with abnormal cord insertion[49].
There is a lower level of evidence for association of marginal cord insertion with lower birth weight.

</td></tr>
<tr><td>Papp-A</td><td>

Papp-A < 5th centile (< 0.4 MoM) has a 10 - 15% PPV based on 2019 - 2021 South Australian SAMSAS data. Papp-A is a positive regulator of insulin-like growth factors, influencing fetal growth and wellbeing[50]. International guidelines promote increased ultrasound surveillance for fetal growth restriction in women who have a Papp-A < 0.4 MoM (5th centile)[50, 51]

</td></tr>
<tr><td>Antepartum Haemorrhage and Subchorionic Haemorrhage</td><td>

Antepartum haemorrhage and subchorionic haemorrhage are associated with lower birth weight[52, 53], however evidence that it is linked specifically with fetal growth restriction is lacking.

</td></tr>
<tr><td>IVF with donor egg</td><td>

A number of confounding factors contribute to adverse fetal outcomes in pregnancies conceived using ART including multiple pregnancy, underlying subfertility, poor gamete quality and advanced maternal age[54].
The use of donor oocytes has allowed pregnancy to become more common at the extremes of reproductive age, where risks to mother and fetus are widely recognised.
It is difficult to examine the extent of which donor oocyte is singularly responsible for fetal growth restriction as several conditions are associated with both ART and oocyte donation including pregnancy induced hypertension, antepartum haemorrhage and pre-eclampsia. All of these conditions are associated with fetal growth restriction and an increase in iatrogenic preterm birth[54]. Additionally, fetal growth restriction is more common in women with subfertility, regardless of mode of conception, suggesting higher rates of abnormal placentation[55].

</td></tr>
<tr><td>Congenital infection (CMV, toxoplasmosis, rubella, Malaria, HSV etc.</td><td>

Most cases of FGR that are attributable to congenital infection arise from Cytomegalovirus (CMV), Rubella, Toxoplasmosis and Malaria[4]. Primary Herpes Simplex Virus (HSV) infection has also been implicated in causing FGR[4]. These infections are thought to result from insults to cellular proliferation, placental vascularisation, placental transport and immunologic milieu.
Gestation at which the infection occurs will impact the effect on fetal growth.

</td></tr>
</table>

Fetal Aneuploidy or structural anomalies	• Chromosomal abnormalities are responsible for 15 to 20% of cases of fetal growth restriction[56-58]. • FGR is frequently seen in fetuses with trisomy 18, and risk is elevated with other chromosomal abnormalities such as triploidy, sex chromosome abnormalities, other trisomies, deletions and duplications. • Confined placental mosaicism or uniparental disomy, though less frequently associated may also result in FGR[59, 60]. • The relationship between the two can be attributed to 3 mechanisms[61]: • FGR is a secondary disturbance to the presence of malformations • FGR can expose the fetus to malformations • FGR can co-exist with congenital malformations because of common aetiological factors

Referral Form – Maternal Fetal Medicine

Women's and Children's Health Network
72 King William Road, North Adelaide SA 5006
Tel: 08 8161 9263 Fax: 08 8161 9264

Government of South Australia
SA Health

Head of Unit: Dr Peter Muller Professor Jodie Dodd

Dr Rachel Earl Dr Mark Morton Dr Amanda Poprzeczny Dr Alice Robinson

Dr Victoria Snowball Dr Chris Wilkinson Dr Jane Woolcock

Dear (Dr's Name)_____

This referral has been discussed with (midwife/doctor) _____

PATIENT DETAIL

Name:_____

Address: _____

Date of Birth: _____ Phone:_____

Mobile: _____ Medicare Number:_____ Medicare Expiry: ____ ____

Support person:_____ Phone: _____

Interpreter required: ☐ No ☐ Yes Language: _____

ATSI Status: ☐ No ☐ Yes, Aboriginal ☐ Yes, Torres Strait Islander ☐ Yes, Aboriginal & Torres Strait Islander

REFERRING PRACTITIONER DETAILS

Referring Doctor: _____

Provider Number:_____ Phone:_____

Address: _____

Signature:_____ Date: _____

The below information **MUST** be provided with this referral request.

CLINICAL INFORMATION/REASON FOR REFERRAL (Page 1 of 2)

Gravidity/Parity:	EDC:

☐ Fetal Anomaly	☐ Current/Previous Pregnancy Complications
☐ Complex Multiple Pregnancy	☐ ADACS Follow up
☐ Severe Maternal Medical Conditions	☐ Pre/Post-Pregnancy Counselling
☐ Early Pregnancy Care Coordination	☐ Abnormal Maternal Serum Screening
☐ **Copy of ALL Ultrasounds attached**	☐ **Copy of Antenatal bloods attached**

Additional Clinical information or reason for referral inc. Previous Obs Hx and previous surgery Hx

Further information required – Please X reason for referral below

FETAL ANOMALY (MFM1)

☐ Second Opinion Ultrasound/Counselling
☐ Fetal congenital malformation requiring surveillance +/- intervention
☐ Inherited fetal endocrine anomalies requiring trans placental therapy
☐ Fetal congenital malformations requiring multi-specialty input and birth at WCH
☐ Fetal Palliative Care
☐ Fetal cardiac arrhythmias
☐ Fetal hydrops

CURRENT/PREVIOUS PREGANCY COMPLICATIONS (MFM2)

☐ Severe early IUGR requiring extended fetal Doppler / cardiac function / biophysical assessment Anti-Ro and/or Anti-La antibodies
☐ Rhesus and other blood group incompatibilities (titre ≥ 1:16 or previously affected fetus/neonate)
☐ Platelet incompatibilities (previously affected fetus/neonate)
☐ Primary infection or seroconversion with toxoplasmosis, cytomegalovirus, parvovirus, listeriosis
☐ Previous ≥ 2 Perinatal deaths (IUFD, NND)

PRE TERM BIRTH (MFM PTB)

☐ Previous spontaneous preterm birth ≤ 34 weeks
☐ Previous mid-trimester fetal loss OR previous cervical cerclage OR previous fully dilated Caesarean Section
☐ Previous Cervical surgery – 2 or more LLetz OR 1 Cone biopsy OR Radica trachelectomy
☐ Mullerian developmental anomaly OR Uterine Surgery such as Septum resection
☐ Ultrasound short cervix in current pregnancy - ≤ 15 mm at dating scan (11-14 weeks) or ≤25mm before 28 weeks

COMPLEX MULTIPLE PREGNANCY (MFM3)

☐ Monochorionic / Monoamniotic Twin Pregnancy
☐ Monochorionic / Diamniotic (MC/DA) Twin Pregnancy with Twin-Twin Transfusion Syndrome (TTTS) or discordant growth/nuchal translucency
☐ Triplet and Higher order multiple pregnancy
☐ Delayed interval deliveries

ADACS FOLLOW UP (MFM4)

☐ Stillbirth
☐ IUFD
☐ Fetal anomaly

SEVERE MATERNAL MEDICAL CONDITIONS (MFM5)

☐ Antiphospholipid syndrome
☐ Sickle Cell Anaemia or G6PD deficiency
☐ Cardiac disease (New York Heart Association Classification Grade III or IV)
☐ Maternal transplant
☐ Renal failure with dialysis
☐ Maternal current malignancy
☐ HIV

PRE/POST PREGNANCY COUNSELLING (MFM6)

☐ Pre-conception women with conditions listed in MFM5
☐ Pre-conception women with previous fetal anomaly and possible recurrence
☐ Postnatal Follow up

EARLY PREGNANCY CARE COORDINATION (MFM7)

☐ Women already known to MFM unit who require coordinated early / tertiary pregnancy care including focused morphology scanning

ABNORMAL MATERNAL SERUM SCREENING (MFM8)

☐ Counselling
☐ NIPT
☐ CVS
☐ Amnio

TELEHEALTH CONSULTATION (MFM9)

☐ *1-8 MUST be completed to identify consultation requirements*

Government of South Australia
SA Health

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