GUIDELINE FOR THE MANAGEMENT OF SUSPECTED SMALL FOR GESTATIONAL AGE SINGLETON PREGNANCIES AND INFANTS AFTER 34 WEEKS' GESTATION



This guideline has been developed to achieve a more consistent approach to management of small for gestational age (SGA) singleton pregnancies and infants in New Zealand. Copies of this guideline may be freely reproduced and distributed. District Health Boards may adapt and rename this document to suit local needs.

Authorship and consultation process

This guideline was written by Professors Lesley McCowan and Frank Bloomfield with input from Dr Emma Parry, Dr Katie Groom and sonographer Martin Necas in 2013. It was updated in October 2014 to obtain feedback from users and incorporate new evidence. Feedback was obtained from members of the NZ Maternal Fetal Medicine Network, Clinical Directors in Obstetrics and Gynaecology and Neonatology. The updated guideline was peer reviewed by Professor Peter Stone.

TABLE OF CONTENTS

			PAG					
1.	EX	ECUTIVE SUMMARY AND GRADES OF RECOMMENDATIONS	4					
2.	DE	FINITIONS	5					
3. BACKGROUND								
4.	RIS	RISK ASSESSMENT AND PREVENTION OF SGA						
	a.	Risk Assessment	5					
	b.	Primary prevention of SGA	5					
5.	EA	EARLY DETECTION OF SGA						
	a.	All Women	5					
	b.	Women at high risk of SGA	6					
6.	WHO SHOULD BE CONSIDERED FOR GROWTH SCANS?							
	a.	a. Previous SGA infant						
	b.	p. Underlying Medical Conditions						
	с.	Cigarette Smokers	7					
	d.	Obese Women	7					
	e.	Abnormal serum analytes	7					
	f.	Multiple pregnancies	7					
	g.	Late pregnancy risk factors-hypertension and antepartum haemorrhage	7					
7.	AN	ITENATAL MANAGEMENT OF SUSPECTED SGA	7					
	a.	Interpretation of growth scans	8					
		Fig 1a: EFW patterns on GROW charts that suggest suboptimal fetal growth	9					
		Fig 1b: EFW pattern on GROW chart that suggests normal fetal growth trajectory	9					
		Fig 2a: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound Chart	10					
		Fig 2b: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound Chart	11					
		Fig 2c: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound Chart	12					
	b.	SGA with abnormal UA Doppler	13					
	с.	SGA with normal UA Doppler	13					
	d.	Abnormal MCA Doppler or CPR indices	13					
	e.	Abnormal Uterine artery Doppler studies	13					
	f.	Severe SGA	13					
	g.	Normal MCA/CPR and uterine artery Doppler studies and EFW between 3 rd and 10 th centile	13					
8.	DELIVERY PLANNING							
	a.	Delivery at 38 weeks	14					
	b.	Management plan with MCA, uterine artery Doppler and severity of SGA (Fig 3)	14					
	c.	Method of induction of labour	15					
	d.	Labour and birth	15					
	e.	SGA with Absent (AEDV) or Reversed End-diastolic Velocity (REDV)	15					
9.	NEONATAL MANAGEMENT AFTER BIRTH							
	a.	Neonatal problems in SGA babies						
	b.	Postnatal growth standards	15					
	c.	Hypoglycaemia	16					
	d.	Monitoring at-risk babies for hypoglycaemia	16					
	e.	Management of hypoglycaemia	17					

	f. Management of hypothermia	17
	g. Monitoring and management of jaundice	18
	h. Investigation of underlying cause of SGA	18
	i. Preterm, SGA babies	18
10.	MATERNAL FOLLOW-UP/ADVICE FOR FUTURE PREGNANCIES	18
11.	SUGGESTED AUDIT TOPICS	18
	MANAGEMENT ALGORITHMS	
	Fig 3: Management of SGA ≥ 34 weeks gestation with detailed Doppler assessment	19
	Fig 4: Simplified algorithm for management of suspected SGA pregnancies based on umbilical	20
	artery Doppler indices	
APP	PENDICES	

I.	Quick reference tables for Umbilical Artery, MCA, Uterine artery Doppler and Cerebroplacental ratio Doppler reference range charts	21 22
I. I.	Main alterations in 2014 update of guideline Levels of evidence and grades of recommendations in executive summary	23 26
REI	FERENCES	27

1.	EXECUTIVE SUMMARY AND GRADES OF RECOMMENDATIONS	
	• SCA infants comprise approximately 40% of non-appmalous stillbirths born after 24 weeks	Level of
	 SGA infants comprise approximately 40% of non-anomalous stillbirths born after 34 weeks A minority of these SGA infants are currently detected before birth in New Zealand 	Evidence
	 Improved detection accompanied by careful management and timely delivery is associated 	B
	with reduced morbidity and mortality	В
	• Risk assessment for major risk factors for SGA should be undertaken at the booking visit	с
	• Utilisation of a GROW chart, associated with structured education, can increase antenatal	
	detection of SGA pregnancies and may be associated with reduced perinatal mortality	
	Routine growth scans in women at low risk of SGA do not improve perinatal outcomes	С
	• Women with major risk factors for SGA are recommended to have fetal growth assessed by	Α
	ultrasound	В
	• Women in whom it is not possible to reliably measure fundal height (e.g. BMI > 35, large	
	fibroids) should be referred for ultrasound assessment of growth	$\mathbf{\nabla}$
	• When an ultrasound is performed, it is recommended that the estimated fetal weight (EFW)	
	is plotted on a GROW chart and individual measurements on the population scan chart	С
	• Fetal abdominal circumference <=5 th centile or EFW <10 th centile can be used to diagnose	
	the suspected SGA fetus	Α
	• As >80% of SGA infants are born after 37 weeks' serial growth scans should continue until	
	delivery in high risk women	\checkmark
	All women in whom SGA is suspected on ultrasound scan should have umbilical artery	
	Doppler performed	Α
	If umbilical artery Doppler is abnormal, same day referral is recommended	_
	If there is absent or reversed end diastolic velocity, admission is recommended	
	• When umbilical artery Doppler is normal, specialist consultation is recommended within 1-2	
	weeks	$\mathbf{\nabla}$
	Management algorithms describe recommended fetal surveillance depending on Doppler	
	indices and severity of the suspected fetal growth restriction	С
	 Cardiotocography or biophysical profile should not be the <u>only</u> surveillance in the SGA pregnancy 	С
	 Delivery of the fetus suspected to be SGA at approximately 38 weeks is associated with 	В
	reduced perinatal morbidity compared with earlier or later delivery, is cost effective and is	_
	not associated with increased Caesarean section rates	
	• If women with suspected SGA infants are not induced twice weekly surveillance of fetal well	
	being is recommended	_
	Continuous fetal monitoring in labour is recommended for all pregnancies with suspected	В
	SGA fetuses	
	• Infants who are confirmed to be SGA or IUGR at birth are at increased risk of morbidity and,	В
	in particular, require monitoring for hypoglycaemia	
	Infants with a birthweight that is disproportionately low compared with other growth	В
	parameters (length and head circumference) are at increased risk of neonatal morbidity,	
	even if birthweight is >10 th percentile, and require assessment for IUGR and monitoring	
	• Treatment of neonatal hypoglycaemia with buccal dextrose gel reduces neonatal unit	А
	admission for hypoglycaemia and increases breastfeeding post- hospital discharge	

4

2. **DEFINITIONS**

Small for gestational age (SGA) is defined as an infant with birthweight less than the 10th birth weight centile or a fetus with an estimated fetal weight (EFW) on a customised growth chart less than the 10th customised centile for gestation. Definitions which use customised standards to define SGA have been shown to be better associated with perinatal morbidity and mortality than definitions of SGA derived from population-based standards [1-3]. Fetal growth restriction (a fetus that has failed to reach its growth potential) is another commonly used term which has considerable overlap with SGA but is more difficult to define in practice as not all growth restricted infants are SGA. SGA pregnancies identified before birth with evidence of abnormal blood flow patterns (abnormal umbilical artery , uterine artery, middle cerebral artery, or cerebro-placental ratio Doppler indices) or with an estimated fetal weight <3rd centile are considered to be growth restricted [4]. Note: a fetus with estimated fetal weight or abdominal circumference crossing centiles on serial scans or with a major discrepancy between head and abdominal circumference may also be growth restricted but may or may not meet the criteria for SGA.

3. BACKGROUND

SGA infants have increased rates of perinatal morbidity and mortality. New Zealand Perinatal and Maternal Mortality Review Committee (PMMRC) data show that approximately 40% of normallyformed stillborn infants born at \geq 24 weeks' have a birth weight < 10th customised centile [5]. In the Auckland Stillbirth Study 37% of late stillbirths (\geq 28 weeks) were SGA at birth. Twelve percent of SGA stillbirths were identified before birth compared with 32% of SGA infants in control (ongoing gestation matched) pregnancies [6]. Reductions in perinatal mortality and morbidity in these vulnerable SGA infants can occur with improved antenatal detection combined with careful management and timely delivery [7].

4. RISK ASSESSMENT AND PREVENTION OF SGA

a. Risk Assessment

All women require assessment at booking for risk factors for SGA infants. Those with major risk factors, defined in the RCOG guideline [8] as: a history of a previous SGA or stillborn infant; maternal age >40; maternal or paternal history of being SGA at birth; smoking >10 cigarettes daily; using cocaine, and maternal diseases associated with increased risk (e.g. chronic hypertension, renal disease, diabetes with vascular disease, anti-phospholipid syndrome) are recommended to have a plan for serial growth scans. Those who develop complications in the current pregnancy (heavy early pregnancy bleeding, fetal echogenic bowel, preeclampsia, severe pregnancy-induced hypertension, unexplained ante-partum haemorrhage or abruption and low gestational weight gain) are recommended to have a plan for serial growth scans in the third trimester [8].

b. Primary prevention of SGA

When women at high risk of SGA are seen by an obstetrician at \leq 16 weeks' gestation, prophylactic treatment with low dose aspirin (100 mg per day) may be considered as this reduces the risk of SGA, especially in women who also have risk factors for preeclampsia, such as those with underlying medical disorders [9-11].

5. EARLY DETECTION OF SGA

a. All women

Observational studies show that use of a gestation-related optimum weight (GROW) chart can significantly increase detection of SGA pregnancies [12-14]. The PMMRC has recommended that a GROW chart should be used to record symphysis-fundal height measurements to improve detection of SGA infants [5]. A recent UK publication has shown that implementation of the GROW program accompanied by a structured education program was associated with reduced stillbirth rates [15].

Use of the GROW program in the West-Midlands in the UK has been associated with reduced stillbirths in SGA infants [16]. The GROW program can be downloaded from

www.gestation.net/grow-nz.aspx and is also available on some DHB computer systems. The GROW chart calculates the woman's body mass index (BMI) and the birth weight centile of any previous infant(s). When using a GROW chart symphysis-fundal height (SFH) should be measured and plotted regularly (but not more frequently than fortnightly) from 26 to 28 weeks onwards using the standardised technique recommended in the GROW education program [17]. A growth scan is recommended if SFH is reducing centiles (e.g. >30%) or is < 10th % [17]. The ADHB GROW guideline has additional details on use of GROW for interested readers:

http://nationalwomenshealth.adhb.govt.nz/Portals/0/Documents/Policies/Customised%20Antenat al%20Growth%20Chart_.pdf.

NOTE:

A growth scan is not recommended in women where SFH is tracking along or above the 90th centile if gestational diabetes has been excluded and there is no clinical concern re polyhydramnios.

b. Women at high risk of SGA

It is recommended that women with major risk factors for SGA have serial growth scans [8] in addition to regular measurement of symphysis-fundal height plotted on a GROW chart.

It is recommended that individual ultrasound measurements of fetal head, abdomen and femur length are plotted on the population Australasian Society of Ultrasound in Medicine (ASUM) ultrasound charts and the estimated fetal weight plotted on the GROW chart. The information from both sources as well as the clinical information are used to make a full assessment. As >80% of SGA infants are born after 37 weeks' [18], it is recommended that serial growth scans are continued in women at high risk until delivery and <u>not</u> discontinued earlier in the third trimester if growth is normal at this time.

In women assessed to be at high risk of <u>severe</u> or <u>early</u> SGA (e.g. previous early SGA with delivery <34 weeks, anti-phospholipid syndrome, severe chronic hypertension, maternal renal disease or an autoimmune condition), uterine artery Doppler studies at 20-24 weeks may help to identify the subgroup at highest risk [19]. Those with very abnormal uterine artery Doppler studies have an approximately 60% risk of developing SGA or preeclampsia requiring delivery <34 weeks [20] and should have regular scans and maternal surveillance

6. WHO SHOULD BE CONSIDERED FOR GROWTH SCANS?

There is no <u>current</u> evidence that routine growth scans after 24 weeks' increase detection of SGA or improve perinatal outcomes in populations at low risk of SGA [21] but results from further ongoing trials are awaited.

a. Previous SGA infant

These women have a three-fold increase in risk of SGA [8]. The gestation at which growth scans are started can be individualised, depending on the gestation at delivery and the severity of SGA in the previously affected infant e.g. if a previous SGA infant was born at 32 weeks, 3-4 weekly scans may be planned from 24 weeks; if the previous SGA infant was born at term, 3-4 weekly scans from 30-32 weeks may be appropriate.

b. Underlying Medical Conditions

Serial growth scans (3-4 weekly) are recommended with more frequent growth scans (2-3 weekly) if sup-optimal growth is suspected. The gestation at which to initiate serial growth scans will be recommended by the specialist according to the estimated magnitude of risk.

c. Cigarette Smokers

Smoking >10 cigarettes daily is considered a major risk factor for SGA by the RCOG [8]. Women who become smoke-free by 15 weeks have no increase in risk of SGA compared with non-smokers [22]. As with non-smokers, local data show that 80% of SGA infants born to women who smoke are also born at term (Anderson N, personal communication) [23].

d. Obese Women

The BMI at which fundal height measurement is unreliable is difficult to prescribe as it depends on distribution of maternal fat and also height. A plan for growth scans is recommended with a BMI of >35 [8]. Antenatal detection of SGA is reduced in obese women [23] and risk of SGA is increased after adjustment for confounding factors such as chronic hypertension [24]. When it is not possible to assess fetal growth clinically, growth scans may be considered at 30-32 weeks' and at 36-38 weeks' to enable serial assessment of fetal growth [25]. If a single growth scan is performed, detection of size abnormalities is better at 36-38 weeks' [25] but will not enable assessment of late pregnancy growth velocity. More frequent and / or earlier initiation of growth scans may be indicated if additional risk factors for SGA, such as chronic hypertension, are present.

e. Abnormal Serum Analytes

First trimester aneuploidy screening includes measurement of PAPP-A . Low PAPP-A is associated with increased risks of SGA and preeclampsia and low PAPP-A is considered a major risk factor for SGA by the RCOG and an indication for serial growth scans [8]. First trimester aneuploidy screening currently reports PAPP-A results. Low dose aspirin (100 mg per day) is recommended in women with low PAPP-A (<0.2 MoM) starting at <16 weeks', especially in those who also have other risk factors.

f. Multiple Pregnancies

Monthly scans are recommended for di-chorionic di-amniotic twin pregnancies, and fortnightly scans for mono-chorionic di-amniotic twins – links to RANZCOG guidelines can be found at the following site: <u>http://www.ranzcog.edu.au/college-statements-guidelines.html#obstetrics</u> Under Multiple pregnancy select: Monochorionic Twin Pregnancy, Management of (C-Obs 42)

g. Late pregnancy risk factors: hypertension and antepartum haemorrhage

A recent New Zealand publication has identified late pregnancy risk factors for infants who are SGA by customised birthweight centiles including: preeclampsia aOR 2.94 (2.49-3.48), preeclampsia superimposed on chronic hypertension aOR 4.49 (2.94-6.88), abruption aOR 2.57 (1.74-3.78), APH of unknown origin aOR 1.71 (1.45-2.00) [24]. Women identified with these pregnancy complications should be considered for serial scans if the pregnancy is continuing after the condition is diagnosed [8].

7. ANTENATAL MANAGEMENT OF SUSPECTED SGA

In cases of very early onset SGA (<32 weeks'), the fetus is often symmetrically small and intrinsic fetal causes such as chromosomal abnormality, structural anomalies and fetal infection need to be considered. Women should be referred for specialist and/or MFM review and further investigation. Detailed management of early onset SGA is not considered further in this guideline.

When an infant is suspected to be SGA or growth restricted on ultrasound scan, umbilical artery (UA) Doppler studies should be performed at the same time as the growth scan to stratify risk and enable planning of on-going management [26]. Specialist referral is recommended when SGA is suspected on ultrasound and a follow up growth scan needs to be arranged (See Figures 3 and 4).

The optimum interval for serial scanning in suspected SGA is at least two weeks with fewer false positive diagnoses of SGA if the interval between scans is three weeks [27].

NOTE:

In all cases where SGA is suspected after scanning, antenatal surveillance should include advice about fetal movements. The ANZSA leaflet about fetal movements is a useful resource and can be found at the following site: http://www.stillbirthalliance.org.au/guideline4.htm In nulliparous women about 25% of SGA babies are born to women with hypertensive complications (preeclampsia, gestational hypertension, chronic hypertension) [18]. SGA can be the first presentation in hypertensive pregnancy and women should be informed about the symptoms of preeclampsia http://nzapec.com/resources and regular monitoring of BP and urinalysis performed at each clinical assessment in pregnancies with suspected SGA infants.

a. Interpretation of growth scans - definition of suspected SGA and FGR

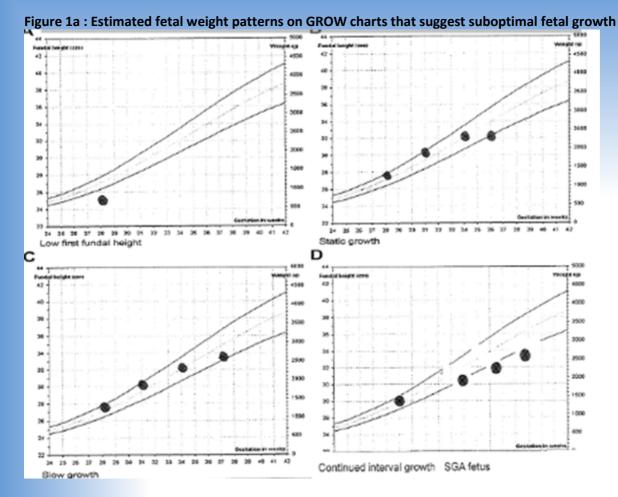
It is recommended that individual ultrasound measurements of the fetal head, abdomen and femur length are plotted on the Australasian Society of Ultrasound in Medicine (ASUM) population ultrasound charts and the estimated fetal weight plotted on the GROW chart. The information from **both** sources is used to make a full assessment. <u>http://www.asum.com.au/newsite/files/documents/policies/PS/D7_policy.pdf</u>

NOTE: The abdominal circumference (AC) is usually the first fetal measurement to become reduced in SGA. Suboptimal fetal growth is suspected when:

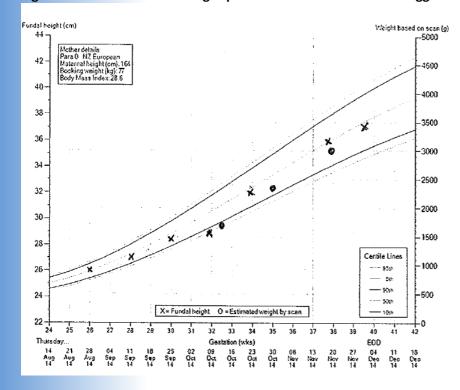
- The abdominal circumference on the population (ASUM) scan chart is <5th centile
- Discrepancy between head and abdominal circumferences (e.g. HC 75th centile and AC 20th centile which suggests wasting)
- AC is $>5^{th}$ centile but is crossing centiles by $> 30^{th}$ centile e.g. reduction from 50^{th} centile to 20^{th} centile
- A change in AC of <5 mm over 14 days [28]
- EFW on the GROW chart is <10th centile
- EFW on the GROW chart is crossing centiles with ≥one third reduction in EFW percentile (see examples in Figure 1) [29].

When interpreting growth scan results it is also important to consider the margin of error (which is usually about 10%) especially if measurements vary from one scan to the next e.g. if EFW or AC fluctuates around the 5th or 10th centile this is likely to be a fetus with a growth problem and a follow up scan is recommended. Interpretation of growth trend improves with a greater number of biometric data points. In general, it is more difficult to be certain of small changes in growth trend when only two sets of measurements are available, especially if these were not performed by the same practitioner.

Some babies who are initially suspected to be SGA will have subsequent accelerated growth velocity and can be reclassified as normally grown and low risk (see figure 3)

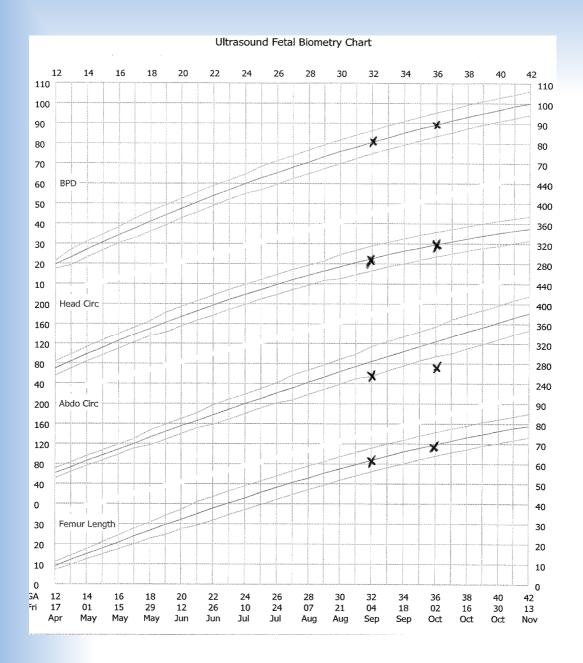






This woman does not need further growth scans after 38weeks and can be managed as low risk of SGA.

Figure 2a: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound chart



Asymmetric SGA with reduced interval growth of AC

Figure 2b: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound chart

Scan at 34 weeks suggests asymmetry between head and abdomen. The woman needs umbilical artery Doppler and follow up growth scan in 2-3 weeks.

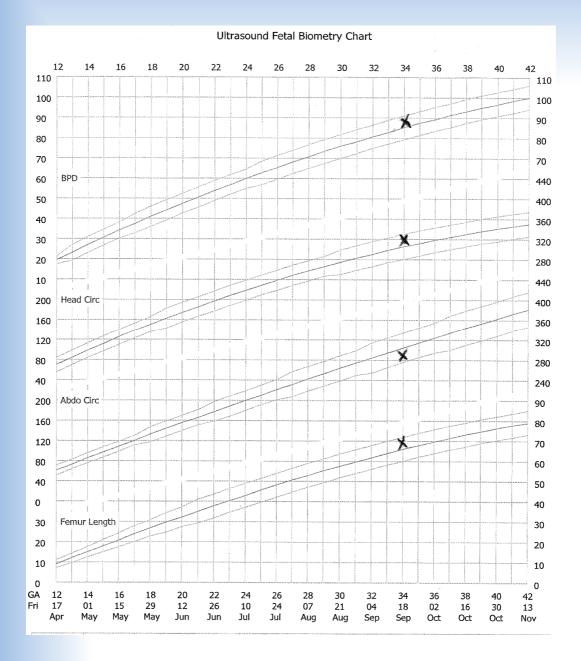
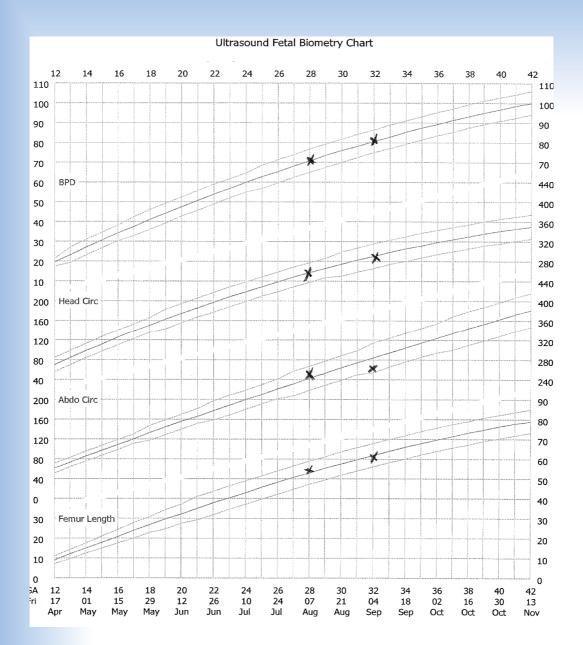


Figure 2c: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound chart



Minimal interval growth of abdominal circumference even though measurements still in normal range. The woman needs umbilical Doppler, specialist referral and ongoing scans.

b. SGA with abnormal UA Doppler

These pregnancies have elevated (>95th centile) pulsatility index in the umbilical artery but antegrade end-diastolic flow is still present [see appendix I for quick reference charts for Doppler ranges].They comprise a minority of SGA pregnancies identified after 34 weeks and association with maternal hypertension is common [30]. It is recommended that these pregnancies should have twice-weekly fetal and maternal surveillance as an outpatient (see Figure 3). If preeclampsia is confirmed admission may be recommended. Arrange surveillance through day assessment unit or local alternative.

A low threshold for delivery is recommended if there is any concern about maternal or fetal well-being or if there is suspected cessation of fetal growth.

c. SGA with normal UA Doppler

Approximately two thirds of SGA infants identified in the antenatal period will have normal UA Doppler studies (\leq 95th centile; see appendix I) and this is usual in SGA infants diagnosed after 34 weeks [31]. Normal UA Doppler findings exclude major feto-placental vascular pathology, but approximately three quarters of cases will have histological evidence of abnormal utero-placental perfusion and other pathological features [32]. The morbidity and mortality in these SGA infants with normal UA Doppler is increased compared with appropriate-for-gestational-age infants but to a lesser extent than in SGA infants with abnormal UA Doppler [30, 33, 34]. Subgroups of SGA infants with normal UA Doppler who are at higher risk of morbidity (acidosis at birth, LSCS for fetal distress) include those with:

- Abnormal middle cerebral artery (MCA) Doppler studies (<5th centile) [33, 34]
- Abnormal ratio of MCA / UA Doppler indices (cerebro placental ratio (CPR) <5th centile) [33, 34]
- Abnormal uterine artery Doppler studies (>95th centile) at time of diagnosis of SGA [34, 35]
- Extreme SGA with estimated fetal weight <3rd centile [36]

These babies can be considered to have fetal growth restriction [4]

It is recommended that delivery is undertaken in these higher risk pregnancies by 38 weeks', or earlier if additional maternal or fetal concerns arise [4, 8, 37].

A suggested management algorithm for clinical services with access to MCA and uterine artery Doppler assessments is outlined in Figure 3.

For units that do not have access to MCA and uterine artery Doppler studies or that decide not to undertake this more complex evaluation, a suggested management algorithm adapted from the Society of Maternal Fetal Medicine [38] is shown in Figure 4.

d. Abnormal MCA Doppler or CPR indices

Fetuses with abnormal MCA Doppler studies (<5th centile) or a low CPR (<5th centile) are at increased risk of acidosis at birth [30, 33] and may benefit from more frequent surveillance [39, 40] and, as suggested above, delivery by 38 weeks. Twice-weekly surveillance is recommended, including clinical review and CTG; at least weekly umbilical artery and MCA Doppler studies and amniotic fluid volume (single deepest vertical pool of amniotic fluid), and scans for growth every two to three weeks (see Figure 3). Document the management plan in the clinical record. It can be helpful for individual management to plot the sequential changes in Doppler indices (see Appendix I for Doppler reference charts).

e. Abnormal Uterine artery Doppler studies

SGA pregnancies with normal umbilical artery Doppler studies and abnormal mean uterine artery Doppler indices (>95th centile) (see Appendix I) or bilateral uterine artery notching at the time SGA is diagnosed are a subgroup with abnormal placental blood supply who are also at

increased risk of fetal compromise in labour [33, 34].

f. Severe SGA

Fetuses with EFW < 3rd centile with normal UA, MCA, CPR and uterine artery Doppler studies still have an increased risk of fetal compromise in labour and this may occur soon after the onset of contractions [36]. They therefore also comprise a high risk subgroup.

Note- when using GROW the clinician can identify babies with EFW below the 5th centile line who fit this more severe SGA category.

g. Normal MCA/CPR and uterine artery Doppler studies and EFW between 3rd and 10th centile Approximately 40% of suspected SGA pregnancies with normal umbilical artery Doppler indices will fall into this low risk sub-group [4]. It has been suggested that these small babies, who have low rates of hypoxia, may be considered constitutionally small and delivered at 40 weeks, unless there is other clinical concern [4]. Weekly clinical visits and growth scans and Doppler studies are recommended every two to three weeks when the above Doppler parameters are normal and the fetus is not suspected to have severe SGA (Figure 3). Delivery by term is recommended [4, 31].

8. DELIVERY PLANNING

a. Delivery at 38 weeks

This approach is recommended in centres where additional fetal assessment with MCA and uterine artery Doppler studies is not possible, to identify further the SGA infants at higher risk. This recommendation is in keeping with recent Society of Maternal Fetal Medicine guidelines which recommend induction at 38-39 weeks in SGA with normal umbilical artery Doppler studies (Figure 4) [38]. The consensus view from the recent Disproportionate Intrauterine Growth Intervention Study at Term (DIGITAT) is that the optimum time for delivery in SGA pregnancies is at around 38 weeks' - this was associated with the lowest risk of severe fetal growth restriction and perinatal morbidity [40, 41] and was cost effective [42]. This recommendation is in keeping with findings from population-based studies which demonstrate that stillbirth risk in SGA infants increases more steeply after 38 weeks of gestation [43]. Data from DIGITAT also showed that a policy of induction of labour in SGA pregnancies after 36-37 weeks' was not associated with a three-fold increase in severe IUGR and two-fold increase in risk of preeclampsia [40].

All women with SGA pregnancies need a plan for serial monitoring for maternal and fetal wellbeing.

In the DIGITAT study, surveillance with twice-weekly CTGs and daily fetal movement monitoring was undertaken in expectantly managed women. There is no good evidence to support this surveillance regimen other than the fact that in DIGITAT there were no perinatal deaths in over 600 SGA pregnancies. There were 4 stillbirths in 452 women eligible for DIGITAT who were not included in the trial, in whom fetal surveillance was not pre-specified (personal communication Prof S Scherjon, lead investigator DIGITAT study). Women with suspected SGA pregnancies and normal umbilical artery Doppler studies, who do not have additional Doppler parameters performed, should therefore be considered for twice-weekly surveillance as per DIGITAT [40].

b. Management plan with MCA, uterine artery Doppler and severity of SGA (Fig 3)

As outlined above, in District Health Boards where detailed assessment is possible with MCA and uterine artery Doppler, an alternative approach is recommended with induction of labour of the highest risk sub-groups by 38 weeks' (or earlier if concern).

The group of suspected SGA babies (approximately 40%) with normal MCA, CPR, uterine artery Doppler and with EFW not <3rd centile are likely to be constitutionally small and delivery at 40 weeks' is reasonable unless there is other clinical concern [4].

c. Method of induction of labour

The optimum mode of induction of labour for SGA pregnancies, in which it is not possible to perform artificial rupture of membranes, may be with a balloon catheter. This reduces the risk of hyper-stimulation associated with fetal heart changes [44] which the SGA fetus may tolerate less well than an appropriately-grown fetus.

d. Labour and birth

Management plans for labour/birth need to be individualised for each SGA pregnancy. SGA fetuses with abnormal Doppler indices or with severe SGA have increased rates of acidosis in labour (see section 7). Women in these subgroups who start spontaneous labour should be advised to be admitted early in labour to enable careful fetal monitoring. Those who are induced also require careful fetal monitoring from early labour.

i. SGA with abnormal umbilical artery Doppler

These fetuses are at high risk in labour; however, they may still tolerate vaginal birth. It is unusual for delivery to be required at less than 34 completed weeks' but if necessary and time allows, corticosteroids should be administered [45].

ii. SGA fetuses with normal umbilical artery Doppler and evidence of brain sparing
 When the MCA Doppler is abnormal the probability of requiring Caesarean section for
 suspected fetal distress after induction of labour is approximately 55% and elective Caesarean
 section may be considered in this context as an alternative to induction [33, 34].
 ii. SGA fetuses with abnormal uterine artery Doppler

These pregnancies with abnormal mean uterine artery pulsatility index or bilateral notches have abnormal placental blood supply and are recommended to have fetal monitoring from early in labour [34, 35].

iv. SGA with estimated fetal weight <3rd centile

As in categories i-iii above these SGA pregnancies also constitute a high risk subgroup in labour [36].

e. SGA with Absent (AEDV) or Reversed End-diastolic Velocity (REDV)

This markedly abnormal Doppler finding indicates major placental vascular pathology and occurs in 1-2% of all SGA pregnancies, usually in the second or early third trimester [30]. If this very abnormal Doppler finding is identified, same-day admission is recommended for assessment and management planning. Delivery by Caesarean section is recommended.

9. NEONATAL MANAGEMENT AFTER BIRTH

a. Neonatal problems in SGA babies

Babies born SGA (defined as birthweight <10th centile on whichever growth charts are used at the birth facility; see [46] for discussion of growth charts) are at increased risk for common neonatal morbidities, most notably hypoglycaemia, hypothermia and jaundice.

b. Postnatal growth Standards

The INTERGROWTH-21st population growth charts recently have been published and were developed from multi-ethnic women at low risk of impaired fetal growth using the same methodology as the WHO Child Growth Standards [47]. The WHO Child Growth Standards are recommended by the New Zealand Ministry of Health for monitoring early childhood growth and are reproduced in the Well Child / Tamariki Ora Healthbook. Plotting of birth anthropometry on the INTERGROWTH birth charts also facilitate ongoing monitoring with the NZ-WHO charts.

Note that a birthweight of <2.5 Kg (low birthweight) is substantially below the 10th centile at full

	Boys	Girls
37 weeks	2.38	2.33
38 weeks	2.57	2.50
39 weeks	2.73	2.65
40 weeks	2.88	2.78
41 weeks	3.01	2.89
42 weeks	3.12	2.98

term and represents a profoundly small infant; this criterion, therefore, is not a suitable lower limit for initiating monitoring of SGA babies. The figure on the left shows the 10th percentile for birth weight for boys and girls for each gestation between 37 and 42 weeks using INTERGROWTH birth charts [47]. Babies with birth weights below the 10th percentile are at increased risk for the complications outlined above.

If there is access to full growth standards (i.e. length and head circumference centile charts in addition to birthweight centiles) then disproportionate growth (length and head circumference on

significantly higher centiles than weight) may also be an indication for regarding the infant at risk secondary to IUGR, even if the birthweight is above the 10th centile, population or customised.

c. Hypoglycaemia:

In healthy, term babies, there is a transient rise in glucose concentrations around the time of birth secondary to glycogenolysis and gluconeogenesis. This, however, is followed by a rapid decline, reaching a nadir at 1-2 hours of age. Concentrations then rise to be similar to fetal concentrations (approximately two-thirds maternal concentrations) by about 3-4 hours of age. Adult concentrations usually are not reached until 3-4 days of age. SGA babies are at increased risk for hypoglycaemia secondary to decreased hepatic glycogen stores and, frequently, an inappropriately high level of insulin secretion for the prevailing glucose concentrations. This has the potential to make the hypoglycaemia more dangerous as glycogenolysis and production of alternative cerebral fuels are inhibited by insulin. Hypoglycaemia is common in SGA babies. A recent New Zealand study found that 52% of babies with a birthweight below the 10th population or customised percentile will have an episode of hypoglycaemia (blood glucose concentration <2.6 mmol/L [48]. Most of these (50%) occurred during the first 6 hours after birth but 37% of babies had their first low blood glucose concentration after three normal measurements. Low blood glucose concentrations are associated with brain injury [49, 50] and, therefore, babies at risk should have regular blood glucose monitoring until confirmation of transition. It is important to note that the majority of babies with hypoglycaemia will not exhibit any symptoms.

d. Monitoring at-risk babies for hypoglycaemia

- Only a device that uses the glucose oxidase method (e.g. blood gas analyser, EPOC, iSTAT, laboratory analyser) reliably detects hypoglycaemia. Point-of-care devices (e.g. BM Stix, Precision G monitors, Accu Chek) do not detect hypoglycaemia reliably.
- Blood glucose concentration should be measured at one to two hours of age and then prefeed thereafter
- Feeding should commence early; complementary feeds are not indicated unless the blood glucose concentration is <2.6 mmol/L.
- Blood glucose monitoring can be discontinued once three *consecutive* blood glucose concentrations are within the normal range (≥2.6 mmol/L)
- However, if the infant is not feeding well or there is a poor milk supply, ongoing monitoring, or recommencement of monitoring, is indicated and the infant may benefit from lactation consultant input if this is available.
- If the infant has any symptoms that may be due to hypoglycaemia (lethargy, irritability, jitteriness, hypothermia) on-going monitoring, or recommencement of monitoring, and paediatric review are indicated.

e. Management of hypoglycaemia

Many hospitals will have their own algorithm for the management of babies with hypoglycaemia detected on the postnatal ward and local guidelines should be followed until a national guideline is developed and adopted. Recent evidence from an NZ clinical trial demonstrates that treatment of hypoglycaemia with a buccal dextrose gel can reduce the need for admission to a neonatal unit for hypoglycaemia and also increase breast-feeding rates post-discharge [51]. The dose found to be effective was 0.5 mL/Kg, massaged into the buccal mucosa.

An example of an algorithm can be found at:

http://www.adhb.govt.nz/newborn/Guidelines/Nutrition/HypoglycaemiaManagement.htm

A flow chart for management of hypoglycaemia can be found at: http://www.adhb.govt.nz/newborn/Guidelines/Nutrition/Hypoglycaemia%20flow%20chartNov13.pdf

- Management of mildly or moderately low blood glucose concentrations (e.g 1.2 2.5 mmol/L) with buccal dextrose gel results in fewer admissions to NICU for hypoglycaemia, fewer complementary formula feeds and improved breast-feeding rates 2 weeks after discharge [51]. See flow chart above for an example of an algorithm for the management of hypoglycaemia with dextrose gel.
- If buccal dextrose gel is not available, mildly or moderately low blood glucose concentrations can be managed in the first instance with additional / complementary feeds followed by a repeat measurement after 30 minutes.
- Babies with moderately or profoundly low blood glucose concentrations (e.g. <1.2 mmol/L) should be referred urgently to the paediatric service for admission to NICU/SCBU. Consider administering a dose of buccal dextrose gel or an additional feed, using complementary feeds if necessary, pending admission.
- Babies with hypoglycaemia that does not respond to buccal dextrose gel, additional breast or complementary feeds, or that is recurrent, should be referred for paediatric assessment, even if the hypoglycaemia is only mild.
- Babies with symptomatic hypoglycaemia should be referred for paediatric assessment.

f. Management of hypothermia

Hypothermia is consequent upon an increased body surface area to weight ratio, augmenting heat loss.

- SGA babies should have their temperature monitored for at least 12 hours or until stable
- Ongoing hypothermia or temperature instability may be a sign of underlying metabolic illness or sepsis and further advice should be sought from a paediatrician.

g. Monitoring and management of jaundice

Jaundice in the newborn is a normal phenomenon, as bilirubin acts as a scavenger of free radicals which are high after birth. However, jaundice can also be a sign of underlying problems which may be serious and high levels of jaundice can cause kernicterus, a devastating neurological illness. The significance of jaundice in any given infant depends upon the maturity and age of the infant, on the clinical condition and whether there are any other conditions present.

- It is difficult to estimate serum bilirubin concentrations by skin colour alone: if there is concern, a blood test should always be taken.
- Any clinical jaundice in the first 24 hours after birth should be regarded as abnormal and should be referred to the paediatric service.
- Jaundice is more common in SGA and IUGR babies because they frequently have a degree of polycythaemia.

- Prolonged jaundice (definitions may vary, but generally beyond 10-14 days, serum bilirubin >150-200 µmol/L in term babies) should be evaluated to exclude a conjugated hyperbilirubinaemia or other underlying cause.
- Late onset jaundice (>7-10 days after birth) should also be evaluated as this is unlikely to be physiological.
- To assist in the evaluation of serum bilirubin concentrations, these should be plotted on a chart that gives guidance as to intervention (an example can be found at http://www.adhb.govt.nz/newborn/Guidelines/images/SBR%20Chart%20-%20term%20without%20haemolysis.jpg

The UK NICE treatment threshold graphs can be found here: http://www.nice.org.uk/guidance/cg98/chapter/appendix-d-the-treatment-thresholdgraphs

Note preterm babies, babies with ongoing haemolysis or those with co-existing conditions may have different thresholds for intervention (an example can also be found at http://www.adhb.govt.nz/newborn/Guidelines/images/SBR%20Chart%20-%20preterm%20and%20haemolysis.jpg.

h. Investigation of underlying cause of SGA

The pregnancy and maternal histories may provide an explanation for the cause of SGA or IUGR, such as pre-existing maternal disease, evidence of placental vascular disease, exposure to toxins such as cigarette smoking etc. However, consideration should be given as to whether further investigations are indicated. In the absence of an identifiable cause in the history, further investigations should be considered as this may impact on management of the SGA infant, the likely risk of recurrence in subsequent pregnancies and management of those pregnancies. Investigations may include the following:

- Placental histology (consent must be obtained).
- Karyotype (of the infant and, in cases of extreme IUGR with a very small placenta, of the placenta for confined placental mosaicism)
- Newborn blood samples to exclude congenital infection
- Additional investigations for rarer metabolic / endocrine / genetic causes if indicated

i. Preterm, SGA babies

Babies born preterm are at risk of similar morbidities as babies born SGA, regardless of whether they are themselves SGA. Babies born both preterm and SGA are, therefore, at increased risk and should be monitored closely, particularly for poor feeding, hypoglycaemia and hypothermia.

10. MATERNAL FOLLOW-UP/ADVICE FOR FUTURE PREGNANCIES

Women who have given birth to a SGA infant have an increased risk of recurrence in a future pregnancy [8]. Early booking in a future in a future pregnancy is recommended so that a specialist consultation can be performed and low dose aspirin prescribed if appropriate. Attention can be given to modifiable risk factors such as cigarette smoking and obesity. A care plan for a future pregnancy should be documented.

11. SUGGESTED TOPICS FOR AUDIT

- Rates of antenatal detection of SGA infants
- Proportion of women with suspected SGA who have umbilical artery doppler studies performed
- Proportion of women with major risk factors for SGA infants who have serial growth scans
- Proportion of women with suspected SGA pregnancies with abnormal Doppler indices
- Gestation at delivery in women with SGA pregnancies suspected in the antenatal period
- Proportion of non-anomalous singleton stillbirths ≥ 28 weeks' that are SGA at birth

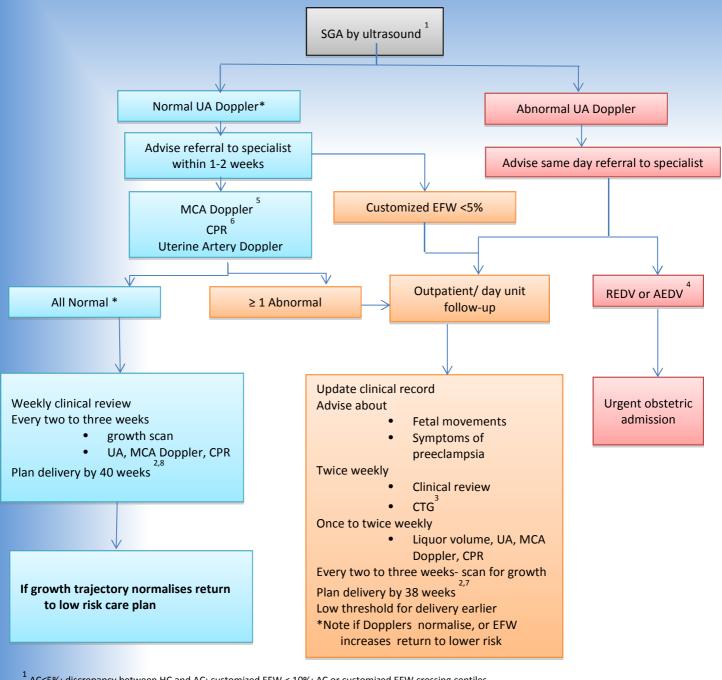


Figure 3: Management of SGA ≥ 34 weeks gestation with detailed Doppler assessment

¹ AC<5%; discrepancy between HC and AC; customized EFW < 10%; AC or customized EFW crossing centiles

² Recommend Foley catheter induction of labour ³ Recommend computerised cardiotocograph ⁵ Middle cerebral artery,

⁴ Reversed or absent end diastolic velocity

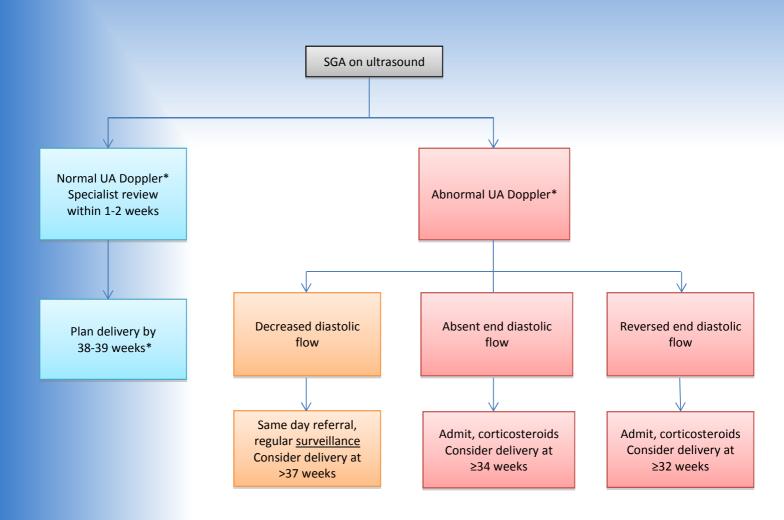
⁷ Continuous fetal heart rate monitoring from <u>onset</u> of contractions

⁸ Continuous fetal heart rate monitoring in established labour

* see appendix for reference ranges

⁶ Cerebro-placental ratio

Figure 4: Simplified algorithm for management of SGA based on umbilical artery Doppler indices



UA, umbilical artery, * see appendix for Doppler reference ranges

¹In conjunction with antepartum testing

Adapted from SMFM Guideline: SMFM Doppler assessment of fetus with IUGR. Am J Obstet Gynecol 2012.

*For recommendations re fetal surveillance if delivery not undertaken see sections 6 and 7 of guideline

APPENDIX I

1. Quick reference tables for Umbilical Artery, MCA, Uterine artery Doppler and Cerebroplacental ratio

	Umbilical Artery PI *		MCA PI ◆ <5 th percentile is abnormal		Cerebroplacental Ratio (CPR) ◆ CPR = MCA PI/UA PI <5 th percentile is abnormal			Mean Uterine Artery PI + Mean PI=(RT PI + LT PI)/2 >95 th percentile is abnormal		
Gestation	50 th	95 th	50 th	5th		50 th	5th	50 th	95th	
Weeks	percentile	percentile	percentile	percentile		percentile	percentile	percentile	percentile	
18		- •	·	·		•	·	1.20	1.79	
19	1.25*	1.63*						1.15	1.70	
20	1.22*	1.59*						1.10	1.61	
21	1.15	1.46						1.05	1.54	
22	1.13	1.43						1.00	1.47	
23	1.10	1.40						0.96	1.41	
24	1.08	1.38	1.86	1.38		1.74	1.16	0.93	1.35	
25	1.06	1.35	1.94	1.44		1.85	1.24	0.89	1.30	
26	1.04	1.33	2.01	1.50		1.95	1.32	0.86	1.25	
27	1.02	1.31	2.06	1.55		2.05	1.40	0.84	1.21	
28	1.00	1.28	2.11	1.58		2.14	1.47	0.81	1.17	
29	0.98	1.26	2.15	1.61		2.21	1.53	0.79	1.13	
30	0.96	1.24	2.16	1.62		2.28	1.58	0.77	1.10	
31	0.94	1.21	2.16	1.62		2.32	1.62	0.75	1.06	
32	0.92	1.19	2.14	1.61		2.35	1.64	0.73	1.04	
33	0.90	1.16	2.10	1.58		2.36	1.65	0.71	1.01	
34	0.88	1.14	2.04	1.53		2.35	1.63	0.70	0.99	
35	0.86	1.11	1.96	1.47		2.32	1.60	0.69	0.97	
36	0.84	1.09	1.86	1.39		2.27	1.55	0.68	0.95	
37	0.81	1.06	1.75	1.30		2.19	1.48	0.67	0.94	
38	0.79	1.03	1.63	1.20		2.09	1.40	0.66	0.92	
39	0.77	1.00	1.49	1.10		1.97	1.29	0.65	0.91	
40	0.75*	1.07*	1.29*	1.02*		1.80 [*]	1.24*	0.65	0.90	

References:

* Acharya G, et al. Reference ranges for serial measurements of blood velocity and pulsatility index at the intra-abdominal portion, and fetal and placental ends of umbilical artery. Ultrasound Obstet Gynecol 2005; 26:162-169.

* Ebbing, C., Rasmussen, S., & Kiserud, T. Middle cerebral artery blood flow velocities and pulsatility index and the cerebroplacental pulsatility ratio: longitudinal reference ranges and terms for serial measurements. Ultrasound Obstet Gynecol, 2007. 30(3): p. 287-96.

* Baschat AA, Gembruch U. The cerebroplacental Doppler ratio revisited. Ultrasound Obstet Gynecol 2003; 21:124-127.

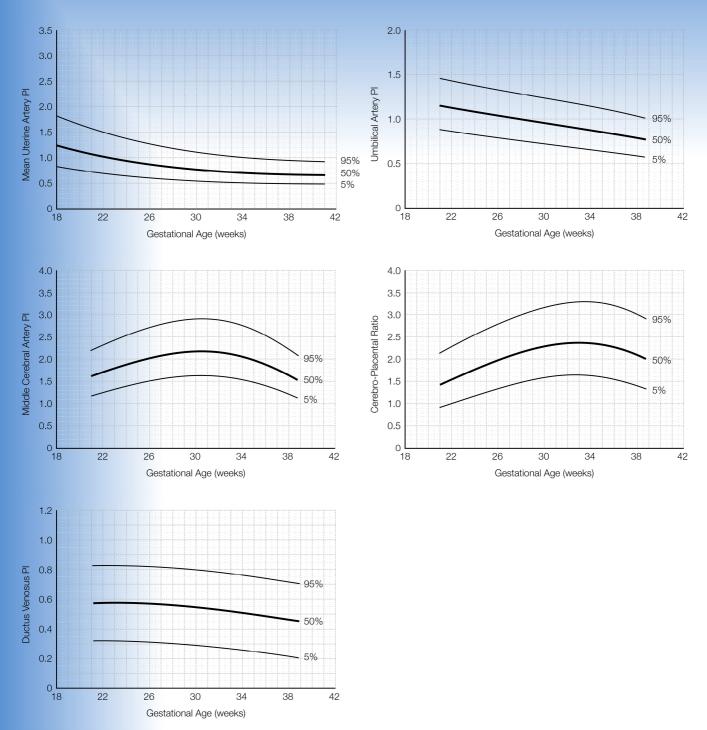
⁺ Gomez O, et al. Reference ranges for uterine mean pulsatility index at 11-41 weeks of gestation. Ultrasound Obstet Gynecol 2008; 32: 128-132.

Note to ultrasound practitioners:

Further information about the standards of performance and reference ranges of obstetric Doppler examinations is available in the NZMFMN Obstetric Doppler Guideline 2014 from the following web link.

http://www.healthpoint.co.nz/public/new-zealand-maternal-fetal-medicine-network/?solo=otherList&index=1

2. Doppler reference range charts



References:

Ebbing, C., Rasmussen, S., & Kiserud, T. Middle cerebral artery blood flow velocities and pulsatility index and the cerebroplacental pulsatility ratio: longitudinal reference ranges and terms for serial measurements. Ultrasound Obstet Gynecol, 2007. 30(3): p. 287-96.

Gomez O, et al. Reference ranges for uterine mean pulsatility index at 11-41 weeks of gestation. Ultrasound Obstet Gynecol 2008; 32: 128-132. Kessler, J., Rasmussen, S., Hnson, M., & Kiserud, T. Longitudinal reference ranges for ductus venosus flow velocities and waveform indices. Ultrasound Obstet Gynecol, 2006. 28: 890-898.

APPENDIX II

MAIN ALTERATIONS IN THE 2014 UPDATE OF THIS SGA GUIDELINE-

incorporated in response to feedback from reviewers or due to additional evidence.

1. Summary of key recommendations in guideline with grades of evidence –page 4.

2. Definitions: page 5:

Additional definition of fetal growth restriction has been added- "SGA pregnancies identified before birth with evidence of abnormal blood flow patterns (abnormal umbilical artery, uterine artery, middle cerebral artery, or cerebro-placental ratio Doppler indices) or with an estimated fetal weight <3rd centile are considered to be growth restricted [4]".

3. Background page 5:

Added reference to NZ research -"In the Auckland Stillbirth Study 37% of late stillbirths (\geq 28 weeks) were SGA at birth. Twelve percent of SGA stillbirths were identified before birth compared with 32% of SGA infants in control (ongoing gestation matched) pregnancies [6] ."

4. Risk Assessment- page 5:

Major risk factors for SGA as per RCOG guideline have been included in document rather than referring users to RCOG guideline to access this more detailed information.

5. Primary prevention of SGA page 5:

In response to feedback the recommended upper gestation for starting low dose aspirin in women considered at high risk has been reduced from 20 to \leq 16 weeks.

6. Early detection of SGA page 6:

New references have been added which report that implementation of formal training in standardised symphysis-fundal height measurement, plotting on a customised growth chart along with a guideline for management of SGA may have been associated with a reduction in perinatal mortality in regions of the UK [15-17].

7. Women at high risk of SGA page 6:

In women who remain at high risk of SGA it is recommended that growth scans are continued until delivery.

8. Who should be considered for growth scans page 7:

Cigarette Smoking

There has been some editing and abbreviating in the text. To align with the RCOG guideline the section on smoking now refers to women who smoke >10 cigarettes daily (rather than all smokers) as being at high risk of SGA. Also a comment that SGA babies born to women who smoke are generally born at term.

Obese women

There are new data that suggest that if a single growth scan is performed in obese women growth abnormalities are more likely to be detected if performed at 36-38 weeks compared with at 30-32 weeks [25].

Abnormal serum analytes

Elevated HcG has been removed as a major risk factor .

9. Interpretation of growth scans page 8:

An additional criterion for diagnosing SGA has been added, namely a change in AC of <5 mm over 14 days [28], and a new reference has been added which defines fetal growth restriction as > one third reduction in EFW centile on a GROW chart [29]. There is now an added comment that if babies initially suspected to be SGA have subsequent accelerated growth velocity with an EFW > 10th centile thay can

be reclassified as normally grown and at low risk. Figure 1b has been added to provide a graphic example of this scenario.

11. SGA with normal UA Doppler page 14

Reordered so SGA with abnormal umbilical artery Doppler section comes before SGA with normal umbilical artery Doppler.

A reference about placental pathology and Doppler indices is included [32]32].

A new simplified management algorithm, for DHBs that do not have access to MCA and uterine artery Doppler studies or decide not to undertake this more complex evaluation, has been incorporated based on SMFM guidelines [38] Figure 4.

Abnormal MCA Doppler or CPR indices

"It can be helpful for individual management to plot the sequential changes in Doppler indices (see Appendix I for Doppler reference ranges)".

Normal MCA/CPR and uterine artery Doppler studies and EFW between 3rd and 10th centile Reference added that 40% of suspected SGA pregnancies with normal umbilical artery Doppler indices will fall into this low risk sub-group [4].

11. DELIVERY PLANNING page 14-15

Delivery at 38 weeks

Added that expectant management in DIGITAT study was associated with a three-fold increase in severe IUGR and two-fold increase in risk of preeclampsia [40].

Added "there were 4 stillbirths in 452 eligible women who were not included in the DIGITAT trial, in whom fetal surveillance was not pre-specified (personal communication Prof Sicco Scherjon lead investigator DIGITAT study).

The labour and birth section was updated with subheadings as below:

a. Labour and birth

Management plans for labour/birth need to be individualised for each SGA pregnancy. SGA fetuses with abnormal Doppler indices or with severe SGA have increased rates of acidosis in labour (see section 7). These subgroups of women with SGA pregnancies, who start spontaneous labour, should be advised to be admitted early in labour to enable careful fetal monitoring. Those who are induced also require careful fetal monitoring from early labour.

i. SGA with abnormal umbilical artery Doppler

These fetuses are at high risk in labour; however, they may still tolerate vaginal birth. It is unusual for delivery to be required at less than 34 completed weeks' but if necessary and time allows, corticosteroids should be administered [45].

ii. SGA fetuses with normal umbilical artery Doppler and evidence of brain sparing

When the MCA Doppler is abnormal the probability of requiring Caesarean section for suspected fetal distress after induction is approximately 55% and elective Caesarean section may be considered in this context as an alternative to induction [33, 34].

ii. SGA fetuses with abnormal uterine artery Doppler

These pregnancies with abnormal mean uterine artery pulsatility index or bilateral notches have abnormal placental blood supply and are recommended to have fetal monitoring from early in labour [34, 35].

iv. SGA with estimated fetal weight <3rd centile

As in categories i-iii above these SGA pregnancies also constitute a high risk subgroup in labour [36].

12. NEONATAL MANAGEMENT AFTER BIRTH Page 15-18

Population Birthweight References

A reference to the recently published INTERGROWTH-21st population growth charts have been included and also a chart showing the 10th percentile for term babies from INTERGROWTH.

Management of hypoglycaemia

Information has been added about use of dextrose gel for treatment of hypoglycaemia "Recent evidence from an NZ clinical trial demonstrates that treatment of hypoglycaemia with a buccal dextrose gel can reduce the need for admission to a neonatal unit for hypoglycaemia and also increase breastfeeding rates post-discharge [51].

An example of an algorithm can be found at:

http://www.adhb.govt.nz/newborn/Guidelines/Nutrition/HypoglycaemiaManagement.htm A flow chart for management of hypoglycaemia can be found at: http://www.adhb.govt.nz/newborn/Guidelines/Nutrition/Hypoglycaemia%20flow%20chartNov13.pdf

The UK NICE treatment threshold graphs can be found here: <u>http://www.nice.org.uk/guidance/cg98/chapter/appendix-d-the-treatment-threshold-graphs</u>

"Management of mildly or moderately low blood glucose concentrations (e.g 1.2 - 2.5 mmol/L) with buccal dextrose gel results in fewer admissions to NICU for hypoglycaemia, fewer complementary formula feeds and improved breast-feeding rates 2 weeks after discharge [ref as above]. See flow chart above for an example of an algorithm for the management of hypoglycaemia with dextrose gel."

A number of new references have been added with the updated evidence especially reflecting new work presented at the Third International Fetal growth Conference in Oxford in 2014.

APPENDIX III

Levels of evidence and grades of recommendations in executive summary [8]

Classification of evidence levels

- 1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias
- 1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias
- Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias
- 2++ High-quality systematic reviews of case-control or cohort studies or highquality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
- 2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
- 2- Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
- 3 Non-analytical studies, e.g. case reports, case series
- 4 Expert opinion

Grades of recommendations At least one meta-analysis, systematic review or Α randomised controlled trial rated as 1++ and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results A body of evidence including studies rated as B 2++ directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+ A body of evidence including studies rated as C 2+ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++Evidence level 3 or 4; or D Extrapolated evidence from studies rated as 2+ **Good** practice point Recommended best practice based on the \checkmark clinical experience of the guideline development group

References

- 1. Anderson, N.H., et al., *Maternal and pathological pregnancy characteristics in customised birthweight centiles and identification of at-risk small-for-gestational-age infants: a retrospective cohort study.* BJOG: An International Journal of Obstetrics & Gynaecology, 2012. **119**(7): p. 848-56.
- Gardosi, J., B. Clausson, and A. Francis, *The value of customised centiles in assessing perinatal mortality risk associated with parity and maternal size*. BJOG: An International Journal of Obstetrics & Gynaecology, 2009. **116**(10): p. 1356-63.
- McCowan, L.M.E., J.E. Harding, and A.W. Stewart, *Customized birthweight centiles predict SGA pregnancies with perinatal morbidity*. BJOG: An International Journal of Obstetrics & Gynaecology, 2005. 112(8): p. 1026-33.
- 4. Figueras, F., et al., *An integrated model with classification criteria to differentiate late-onset fetal growth restriction vs. small-for-gestational age.* Ultrasound Obstetrics & Gynecology, Oct 31 2014 doi: 10.1002/uog.14714. [Epub ahead of print].
- 5. PMMRC, Sixth Annual Report of the Perinatal and Maternal Mortality Review Committee. Reporting mortality 2010. Wellington: Health Quality & Safety Commission 2012.
- 6. Stacey, T., et al., Antenatal care, identification of suboptimal fetal growth and risk of late stillbirth: findings from the Auckland Stillbirth Study. Australian & New Zealand Journal of Obstetrics & Gynaecology, 2012. **52**(3): p. 242-7.
- 7. Lindqvist, P.G. and J. Molin, *Does antenatal identification of small-for-gestational age fetuses significantly improve their outcome?* Ultrasound in Obstetrics & Gynecology, 2005. **25**(3): p. 258-64.
- 8. RCOG, The investigation and management of small-for-gestational-age fetus: Green-top guideline No 31. 2013.
- 9. Askie, L.M., et al., Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data. Lancet, 2007. **369**(9575): p. 1791-8.
- 10. Bujold, E., et al., *Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis.* Obstetrics & Gynecology, 2010. **116**(2 Pt 1): p. 402-14.
- **11.** Duley, L., et al., *Antiplatelet agents for preventing pre-eclampsia and its complications*. Cochrane Database of Systematic Reviews, 2007. **2**: p. CD004659.
- 12. Gardosi, J. and A. Francis, *Controlled trial of fundal height measurement plotted on customised antenatal growth charts*. British Journal of Obstetrics & Gynaecology, 1999. **106**(4): p. 309-17.
- 13. Roex, A., et al., Serial plotting on customised fundal height charts results in doubling of the antenatal detection of small for gestational age fetuses in nulliparous women. Australian & New Zealand Journal of Obstetrics & Gynaecology, 2012. **52**(1): p. 78-82.
- 14. Goodfellow, L., A. Sharp, and Z. Alfirevic Antenatal detection of small for gestational age before and after introduction of customised growth charts: experience of a large teaching hospital. Abstract 1.6, p40. . 2014.
- **15.** Gardosi, J., et al., Association between reduced stillbirth rates in England and regional uptake of accreditation training in customised fetal growth assessment. BMJ Open, 2013. **3**(12): p. e003942.
- 16. Gardosi, J., et al. *Reducing stillbirths in the West Midlands*. 2013; Available from: <u>http://medweb4.bham.ac.uk/websites/key_health_data/2011/pdf/KHD%202011-</u> <u>12%20Chapter%204%20Reducing%20Stillbirths.pdf</u>.
- 17. Clifford, S., et al., *The Growth Assessment Protocol: a national programme to improve patient safety in maternity care. Available from <u>http://www.perinatal.org.uk/GAP/Resources/GAP_article_MIDIRS_Dec_2013.pdf</u>. MIDIRS, 2013.
 23(4): p. 516-523.*
- 18. Groom, K.M., et al., *The association between customised small for gestational age infants and preeclampsia or gestational hypertension varies with gestation at delivery.* BJOG: An International Journal of Obstetrics & Gynaecology, 2007. **114**(4): p. 478-84.

- 19. Cnossen, J.S., et al., *Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis.* CMAJ Canadian Medical Association Journal, 2008. **178**(6): p. 701-11.
- 20. Coleman, M.A., L.M. McCowan, and R.A. North, *Mid-trimester uterine artery Doppler screening as a predictor of adverse pregnancy outcome in high-risk women.* Ultrasound in Obstetrics & Gynecology, 2000. **15**(1): p. 7-12.
- 21. Bricker, L., J.P. Neilson, and T. Dowswell, *Routine ultrasound in late pregnancy (after 24 weeks' gestation).* Cochrane Database of Systematic Reviews, 2008(4): p. CD001451.
- 22. McCowan, L.M.E., et al., Spontaneous preterm birth and small for gestational age infants in women who stop smoking early in pregnancy: prospective cohort study.[Erratum appears in BMJ. 2009;338. doi: 10.1136/bmj.b1558]. BMJ, 2009. **338**: p. b1081.
- Williams, M., M. Southam, and J. Gardosi, Antenatal detection of fetal growth restriction and stillbirth risk in mothers with high and low body mass index. Arch Dis Child Fetal Neonatal Ed, 2010.
 95: p. Fa92.
- 24. Anderson, N.H., et al., *Independent risk factors for infants who are small for gestational age by customised birthweight centiles in a multi-ethnic New Zealand population.* Australian & New Zealand Journal of Obstetrics & Gynaecology, 2013. **53**(2): p. 136-42.
- 25. Harper, L., et al., *The utility of ultrasound surveillance of fluid and growth in obese women.* Am J Obstet Gynecol, 2014: p. pii: S0002-9378(14)00388-3.
- 26. Alfirevic, Z., T. Stampalija, and G.M. Gyte, *Fetal and umbilical Doppler ultrasound in normal pregnancy*. Cochrane Database of Systematic Reviews, 2010(8): p. CD001450.
- 27. Mongelli, M., S. Ek, and R. Tambyrajia, *Screening for fetal growth restriction: a mathematical model of the effect of time interval and ultrasound error.* Obstetrics & Gynecology, 1998. **92**(6): p. 908-12.
- 28. Owen, P., et al., *Standards for ultrasound fetal growth velocity*. British Journal of Obstetrics & Gynaecology, 1996. **103**(1): p. 60-9.
- 29. Fung, A.M., et al., *Effects of maternal obstructive sleep apnoea on fetal growth: a prospective cohort study.* PLoS ONE [Electronic Resource], 2013. **8**(7): p. e68057.
- 30. Trudinger, B.J., et al., *Fetal umbilical artery velocity waveforms and subsequent neonatal outcome.* British Journal of Obstetrics & Gynaecology, 1991. **98**(4): p. 378-84.
- **31.** Savchev, S., F. Figueras, and E. Gratacos, *Survey on the current trends in managing intrauterine growth restriction.* Fetal Diagnosis & Therapy, 2014. **36**(2): p. 129-35.
- **32.** Parra-Saavedra, M., et al., *Placental findings in late-onset SGA births without Doppler signs of placental insufficiency*. Placenta, 2013. **34**(12): p. 1136-41.
- **33.** Cruz-Martinez, R., et al., *Fetal brain Doppler to predict cesarean delivery for nonreassuring fetal status in term small-for-gestational-age fetuses.* Obstetrics & Gynecology, 2011. **117**(3): p. 618-26.
- 34. Severi, F.M., et al., Uterine and fetal cerebral Doppler predict the outcome of third-trimester smallfor-gestational age fetuses with normal umbilical artery Doppler. Ultrasound in Obstetrics & Gynecology, 2002. **19**(3): p. 225-8.
- **35.** Ghosh, G.S. and S. Gudmundsson, *Uterine and umbilical artery Doppler are comparable in predicting perinatal outcome of growth-restricted fetuses.* BJOG: An International Journal of Obstetrics & Gynaecology, 2009. **116**(3): p. 424-30.
- **36.** Savchev, S., et al., *Estimated weight centile as a predictor of perinatal outcome in small-forgestational-age pregnancies with normal fetal and maternal Doppler indices.* Ultrasound in Obstetrics & Gynecology, 2012. **39**(3): p. 299-303.
- **37.** Savchev, S., et al., *Evaluation of an optimal gestational age cut-off for the definition of early- and late-onset fetal growth restriction.* Fetal Diagnosis & Therapy, 2014. **36**(2): p. 99-105.
- Society for Maternal-Fetal Medicine Publications, C., et al., Doppler assessment of the fetus with intrauterine growth restriction.[Erratum appears in Am J Obstet Gynecol. 2012 Jun;206(6):508].
 American Journal of Obstetrics & Gynecology, 2012. 206(4): p. 300-8.
- **39.** Baschat, A.A., *Fetal growth restriction from observation to intervention.* Journal of Perinatal Medicine, 2010. **38**(3): p. 239-46.

- 40. Boers, K.E., et al., *Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT).* BMJ, 2010. **341**: p. c7087.
- 41. Boers, K.E., et al., *Neonatal morbidity after induction vs expectant monitoring in intrauterine growth restriction at term: a subanalysis of the DIGITAT RCT*. American Journal of Obstetrics & Gynecology, 2012. **206**(4): p. 344.e1-7.
- 42. Vijgen, S.M.C., et al., *Economic analysis comparing induction of labour and expectant management for intrauterine growth restriction at term (DIGITAT trial)*. European Journal of Obstetrics, Gynecology, & Reproductive Biology, 2013. **170**(2): p. 358-63.
- 43. Vashevnik, S., S. Walker, and M. Permezel, *Stillbirths and neonatal deaths in appropriate, small and large birthweight for gestational age fetuses.* Australian & New Zealand Journal of Obstetrics & Gynaecology, 2007. **47**(4): p. 302-6.
- 44. Jozwiak, M., et al., *Mechanical methods for induction of labour*. Cochrane Database of Systematic Reviews, 2012. **3**: p. CD001233.
- 45. Roberts, D. and S. Dalziel, *Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth.* Cochrane Database of Systematic Reviews, 2006(3): p. CD004454.
- 46. Tudehope, D., et al., *Growth monitoring of low birthweight infants: what references to use?* Journal of Paediatrics & Child Health, 2012. **48**(9): p. 759-67.
- 47. Villar, J., et al., *The likeness of fetal growth and newborn size across non-isolated populations in the INTERGROWTH-21(st) Project: the Fetal Growth Longitudinal Study and Newborn Cross-Sectional Study.* The Lancet Diabetes & Endocrinology, 2014. **2**(10): p. 781-92.
- 48. Harris, D.L., P.J. Weston, and J.E. Harding, *Incidence of neonatal hypoglycemia in babies identified as at risk.* Journal of Pediatrics, 2012. **161**(5): p. 787-91.
- 49. Boardman, J.P., C.J. Wusthoff, and F.M. Cowan, *Hypoglycaemia and neonatal brain injury*. Archives of Disease in Childhood Education & Practice, 2013. **98**(1): p. 2-6.
- 50. Burns, C.M., et al., *Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia*. Pediatrics, 2008. **122**(1): p. 65-74.
- 51. Harris, D.L., et al., *Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial.* Lancet, 2013. **382**(9910): p. 2077-83.