# Introduction of the Growth Assessment Protocol at Counties Manukau Health, New Zealand: Effect on detection of small for gestational age pregnancy, and maternal and neonatal outcomes

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## Abstract

Timely identification of the small for gestational age (SGA) fetus is pivotal in high-quality antenatal care. Non-detection of poor fetal growth multiplies the risk of morbidity, stillbirth, and neonatal death amongst these vulnerable pregnancies. It is crucial that the tools used for detection of SGA are effective and appropriate for the target population to modify risk by optimal management.

The United Kingdom (UK) based Perinatal Institute's Growth Assessment Protocol (GAP) is being introduced in New Zealand district health boards (DHBs), and while it has been associated with improved detection of fetal growth restriction in the UK and Australia, the programme has not been evaluated in a New Zealand, a unique setting in that antenatal care is usually provided by a single maternity provider.

GAP education incorporates SGA risk selection, with specialist review and a schedule of growth scans for high risk pregnancies, serial fundal height measurement, use of customized growth standards, and an evidence-based guideline for management if SGA is detected. Counties Manukau Health (CMH) is New Zealand's largest DHB and was the first New Zealand DHB to implement GAP. CMH serves a multi-ethnic population with high obesity and high rates of socio-economic deprivation and has the highest perinatal mortality in New Zealand.

The primary objective of this thesis is to determine whether introduction of GAP at CMH has increased antenatal detection of SGA. The secondary objectives are to determine if GAP is associated with increased induction of labour, caesarean birth, and reduced composite adverse neonatal outcome (Apgar score <7 at 5 minutes, admission to the neonatal unit for >48 hours, and ventilation).

A retrospective before and after study was undertaken, using routinely collected data from two 12-month epochs: pre-GAP 2012, before widespread use of any element of GAP; and post-GAP 2017, one year after introduction of GAP education. The study population comprised women with singleton non-anomalous pregnancies, booked by 20 weeks with a DHB midwife, and who gave birth after 24 weeks of gestation. At CMH, a team of DHB midwives provide continuity of antenatal and postnatal care, which is the model of care provided for pregnancies in the study. This differs from the model of care provided by community (self-employed) midwives who provide full continuity of care.

Maternal and neonatal outcomes were compared in the pre- and post-GAP cohorts for pre-specified outcomes by logistic regression, with adjustment for potential confounding by factors associated with SGA, including New Zealand

deprivation index, ethnicity, maternal age, body mass index (BMI) and cigarette smoking. Pre- and post-GAP cohorts were compared by non-SGA and SGA subgroups, and by SGA identification status. The difference in exposure effect between these respective subgroups was assessed by an interaction test.

Antenatal detection of SGA increased significantly after introduction of GAP from 22.9% to 57.9% (aOR=4.81, 95% CI 2.82, 8.18; p<0.0001) with very similar SGA rates across epochs (13.8% vs 12.9%; p=0.68). The increase in SGA detection was greater in Maaori and Pacific Island women (pre-GAP 18.9% vs post-GAP 63.8%) compared with other ethnicities (pre-GAP 28.6% vs post-GAP 52.1%; interaction p=0.049) but was similar among BMI groups. Induction of labour and caesarean birth increased between epochs, but this increase was similar in SGA and non-SGA pregnancies. Among those with SGA, increased antenatal identification of SGA post-GAP appeared to be associated with lower composite adverse neonatal outcome (identified SGA: pre-GAP 32.4% vs post-GAP 17.5%, aOR=0.44, 95% CI 0.17, 1.15; non-identified SGA: pre-GAP 12.3% vs post-GAP 19.3%, aOR=1.81, 95% CI 0.73, 4.48; interaction p=0.03). Identification also appeared to reduce prolonged (>48 hours) neonatal unit admission (identified SGA: pre-GAP 29.4% vs post-GAP 16.3%, aOR=0.42, 95% CI 0.15, 1.15; non-identified SGA pre-GAP 9.6% vs post-GAP 15.8%, aOR=1.86, 95% CI 0.63, 5.52; interaction p=0.04).

It is acknowledged that the study was undertaken by the New Zealand GAP lead educator, who recognised and managed the potential conflict of interest.

In conclusion, introduction of the GAP programme in a multi-ethnic population with high obesity appeared to be associated with a 5-fold increase in likelihood of SGA detection, without increasing obstetric intervention for SGA. GAP also appeared to be associated with reduced composite adverse neonatal outcome and prolonged neonatal unit admission amongst identified SGA, which will likely result in cost savings. The detection of SGA post-GAP in the CMH community was similar to the best performing GAP units in the UK and similar to rates of detection using routine late pregnancy ultrasound scan. GAP is effective in a New Zealand setting with a continuity of midwifery care model.

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## Attestation of Authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except the literature review on the link between neonatal encephalopathy and small for gestational age pregnancy, which I co-authored), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

Joyce Cowan

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*Every day I see or hear*
*something that more or less*
*kills me with delight,*
*that leaves me like a needle*
*in the haystack of light.*

*It is what I was born for-*
*to look, to listen*
*to lose myself inside this soft world-*
*to instruct myself over and over*
*in joy, and acclamation.*

*Nor am I talking about the exceptional,*
*the fearful, the dreadful, the very extravagant-*
*but of the ordinary, the common, the very drab,*
*the daily presentations.*

*Oh, good scholar, I say to myself,*
*how can you help but grow wise*
*with such teachings as these-*
*the untrimmable light of the world,*
*the ocean's shine*
*the prayers that are made out of grass?*

'Mindful' by Mary Oliver (2005) from *Why I Wake Early*.

# Chapter 1: Introduction

Being born small for gestational age (SGA) has a frequent association with stillbirth, with a population attributable risk of 30% (Audette & Kingdom, 2018). There is increased risk of perinatal morbidity such as asphyxia, hypoglycaemia, and hypothermia (Sharma, Farahbakhsh, Shastri, & Sharma, 2016); as well as the possible lifetime effects of increased neurodevelopmental delay, obesity, and metabolic disease (McCowan, Figueras, & Anderson, 2018). In New Zealand, the Perinatal and Maternal Mortality Review Committee (PMMRC) reports annually on deaths of mothers and babies. Reporting on data collected in 2016, the committee found that the death rate is approximately three times higher for SGA babies compared to appropriately grown or large for gestational age babies (PMMRC, 2018). International literature tells us that many of these SGA stillborn babies are not recognised to be SGA before their birth, removing the opportunity for careful surveillance and timely birth. The death of each baby is tragic for grieving parents and families and devastating for the professionals involved with their care. A key aim of antenatal care is to monitor fetal growth in order to identify those pregnancies with SGA babies. This study concerns introduction of the Growth Assessment Protocol (GAP), a programme designed to increase detection of SGA in pregnancy and reduce stillbirth.

Currently a number of district health boards (DHBs) in New Zealand are implementing GAP, a training programme developed in the United Kingdom (UK) by the Perinatal Institute (http://www.perinatal.org.uk). The programme has been associated with increased detection of SGA pregnancies (Gardosi, Francis, Turner, & Williams, 2018; Jayawardena & Sheehan, 2018; Roex, Nikpoor, van Eerd, & Hodyl, 2012). In turn, improved detection has been linked with a reduction in stillbirth in the UK (Clifford, Giddings, Southam, Williams, & Gardosi, 2013) and, more recently, in New Zealand (PMMRC, 2017).

## *1.1 Elements of GAP*

The comprehensive programme involves education of clinicians regarding risk assessment for SGA at booking, evidence-based protocols for management of pregnancies at low or increased risk of SGA, standardised fundal height measurement, and use of customized gestation related optimal weight (GROW) charts. Ongoing three monthly reports and regular audits of missed cases of SGA are key elements of the programme (Gardosi, 2014; Williams, Turner, Butler, & Gardosi, 2018).

Accurate standards to monitor fetal growth are essential to enhance early recognition of the fetus at risk of unfavourable immediate and long term outcomes, and use of customized fetal growth standards, based on maternal characteristics of ethnicity, height, weight at first antenatal visit, and parity, are central to the GAP programme. Prior to the development of customized fetal growth standards (Gardosi, Chang, Kalyan, Sahota, & Symonds, 1992), population standards were used to assess fetal growth and birth weight. Observational studies have demonstrated that population standards do not perform as well as customized standards in identification of small babies at risk of perinatal morbidity and mortality (Clausson, Gardosi, Francis, & Cnattingius, 2001; Gardosi, Clausson, & Francis, 2009); and this is particularly important in the New Zealand setting, where population standards may not perform well in the modern diverse multi-ethnic context.

### *1.2 FGR and SGA terminology*

In writing this thesis I have used the first person to refer to myself as the researcher, and first-person plural when referring to the research findings to acknowledge the collaborative work involved when accessing and analysing data, as well as the support of my supervisors. Throughout this document, I will refer to the terms SGA and FGR[1]. These terms are often used interchangeably in the literature, and their use may overlap in practice. However, to improve outcomes it is important to distinguish between the constitutionally small fetus and one that is not growing well. There is no internationally agreed definition of FGR and SGA, but FGR refers to a fetus who has not reached his/her biological growth potential and SGA refers to a fetus or neonate with a weight $<10^{th}$ centile for gestational age. In New Zealand SGA is defined using customized standards (McCowan & Bloomfield, 2014; McCowan et al., 2018). Nevertheless, many authors continue to use the terms SGA and FGR interchangeably, in part because it is often not possible to distinguish between a growth restricted fetus and a healthy constitutionally small baby until the birth, unless ultrasound examination has revealed severe growth restriction and/or abnormalities of Doppler velocimetry (Figueras, Savchev, Triunfo, Crovetto, & Gratacos, 2015). Consequently, SGA is often used as an umbrella term. Where the distinction is clear from sources quoted, I will use the appropriate terminology; otherwise, SGA will be used to cover both possibilities.

[1] A complete list of abbreviations used in this thesis is included in Appendix A.

### *1.3 Objectives*

The primary objective of this study is to assess the effect that introduction of GAP has on the detection of SGA babies at a large New Zealand DHB–Counties Manukau Health (CMH). A secondary objective is to assess the impact of GAP on maternal and neonatal outcomes, with a particular focus on SGA pregnancies. GAP was introduced at CMH at the beginning of 2016 but, prior to this study, there has been no formal evaluation of the effect of the use of the programme in a New Zealand setting.

### *1.4 The New Zealand context, Counties Manukau DHB*

My study is the first to assess the impact of GAP in the context of a New Zealand DHB. CMH provides primary, secondary, and tertiary level maternity care. The population served by the DHB is ethnically diverse and, according to the 2013 census, 36% of the population lived in areas classified as the most socio-economically deprived (NZ Deprivation Indices 9 and 10) (Atkinson, Salmond, & Crampton, 2014; CMH, 2017). Data from a later census in 2018 were not available at time of writing (http://www.stats.govt.nz). An improvement in perinatal morbidity and mortality is urgently required at CMH as it has the highest rate of perinatal death in New Zealand (PMMRC, 2017). Introduction of GAP to CMH , if effective in increasing detection of SGA, has the potential to contribute to reducing perinatal death, while recognising that service provision is only one aspect of addressing the problem, as social determinants of health, such as finance, culture, housing, ethnicity and education are the key drivers of inequity (Winnard, Lee, & Macloed, 2015).

### *1.5 Significance of the study*

This research will provide evidence about the effect of the use of GAP in New Zealand maternity practice. It is important that research is carried out in the New Zealand context. While observational studies from other countries have shown that introduction of the GAP programme is associated with an increased rate of detection of SGA and a reduction of stillbirth, the New Zealand model of maternity care is unique, as most women have their own lead maternity care provider in a continuity of care model. While the study was conducted on data from pregnancies managed by DHB midwives, the model of care included continuity of antenatal and postnatal care, usually from the same midwife. This differs from care provided by self-employed midwives who also provide intra-partum care. However, the study relates to antenatal care, with a similar model regardless of employed or self-employed status of the midwife. Findings from other

countries are not necessarily transferrable, and local validation is essential to inform practice at DHB levels and guide decisions regarding ongoing policy and funding by the Ministry of Health (MoH).

### *1.6 The wider New Zealand context*

GROW charts have been used in New Zealand maternity practice since approximately 2007 when the computerised application for generation of GROW charts became freely available from the Perinatal Institute website. At that time, education for clinicians was not required and simple instructions were included on the Perinatal Institute website (www.gestation.net). Over the following years, more formal education was provided as part of the New Zealand Action on Preeclampsia (NZAPEC) annual study days, occasional presentations by leaders in Maternal Fetal Medicine, and as a small component of the New Zealand recertification education required by the Midwifery Council, which was provided by the New Zealand College of Midwives (NZCOM), between 2011 and 2014. The New Zealand Maternal Fetal Medicine Network (NZMFMN) (www.healthpoint.co.nz/public/new-zealand-maternal-fetal-medicine-network) provided information about risk factors for SGA and use of GROW in the context of guidelines for management of SGA pregnancies (McCowan & Bloomfield, 2014), but uptake of formal education varied.

Accredited GROW workshops were introduced in 2014 and the full GAP programme was available in New Zealand from 2016. However, while the MoH supported the introduction of GAP nationally, there was no financial support available from the MoH for DHBs to implement the programme, which involved a service agreement between the Perinatal Institute and the DHB with a small annual cost to cover education, software, and ongoing support. Some DHBs self-funded the programme but many delayed introduction in the hope that there would eventually be a national funding solution.

### *1.7 Funding from the Accident Compensation Corporation for national introduction of GAP*

In 2017 the Accident Compensation Corporation (ACC) Neonatal Encephalopathy Taskforce (Accident Compensation Commission, n.d.) committed to fund the national introduction and evaluation of GAP for a three year period following consideration of the evidence linking SGA and neonatal encephalopathy (NE). During the ACC's evaluation of the business case for GAP, I co-authored a literature review presenting the

evidence linking NE and SGA, and the increased risk of NE when SGA is not detected antenatally (Appendix B). This literature review was considered by ACC, alongside the business plan, as evidence to support ACC funding of the national introduction of GAP.

### *1.8 GAP as component of NE reduction strategy*

GAP is now established as one of the four programmes adopted in 2017 to reduce NE (Appendix C). In May 2018, as the national lead educator for GAP, I was appointed to the ACC GAP working group which will oversee and evaluate the roll out of GAP across New Zealand.

### *1.9 Research approach*

On enrolment in the Doctor of Health Science programme, I was unclear about my research approach. My methodology for previous postgraduate study had been qualitative. As my focus clarified, it became apparent that my research approach would need to be quantitative. I had identified a need for research in New Zealand to inform maternity care providers about the appropriateness and possible value of GAP, and it was clear that the effect of introduction of GAP at a DHB would need to be measured statistically. I met with a bio-statistician at Auckland University of Technology (AUT) and discussed possible approaches before presenting my research proposal. My primary hypothesis was based on the expectation that the GAP programme would increase detection of pregnancies with SGA babies; my secondary hypotheses were based on the expectation that amongst SGA pregnancies, introduction of the GAP programme would be associated with improved neonatal outcomes, an increase in induction of labour to ensure timely birthing for at risk babies, and no increase in caesarean section. While a randomised controlled trial (RCT) is optimal for this form of evaluation, it would not be possible to conduct an RCT at CMH. There was an existing commitment to the introduction of GAP from 2016 and some midwives and doctors had been using GROW for several years; therefore, a pre- and post-intervention study seemed the best fit for the project.

### *1.10 Time period of pre- and post-GAP study*

The time period selected for the pre-GAP audit was January 1$^{st}$ to December 31$^{st}$ 2012; a period which predated any knowledge of the GAP programme or accredited education for GROW, and it was prior to the publication of the SGA guideline (McCowan & Bloomfield, 2014). The post-GAP audit was conducted for the period April 1$^{st}$ 2017 to

March 31st 2018, a year following the first round of GAP workshops and introduction of the programme.

### *1.11 The study population and analysis sets*

The study population was comprised of all births for women at CMH during the time periods selected, and following exclusions outlined in Chapter 4. As it is not possible to access large numbers of maternity records held in the community by self-employed midwives, births for women whose care was provided by self-employed midwives were excluded from the study population. The final datasets for the pre- and post-GAP audits were obtained following additional exclusion of records for women who booked after 20 weeks, had no documented booking weight or height, gave birth before 24 weeks of pregnancy, had a multiple pregnancy, or a baby with a congenital anomaly.

### *1.12 Antenatal detection of SGA*

Antenatal SGA detection was assessed on evidence in the maternity record of an ultrasound scan reporting suspected growth restriction. Rates of detection were assessed depending on whether the birth occurred before or after protocol introduction. All other maternal and neonatal outcomes were assessed on the antenatal detection status outcome. Maternal characteristics were assessed as potential confounders.

### *1.13 Confounding variables*

Analysis of demographic variables and pregnancy characteristics revealed significant differences between the pre- and post-GAP epochs for maternal age, body mass index (BMI), ethnicity, New Zealand Deprivation Indices and smoking status. A regression model was constructed to adjust for these variables.

### *1.14 What brought me to this study*

In 1993, while working as a midwife, one of my clients experienced severe preeclampsia and suffered life threatening complications. Upon her recovery, we collaboratively established New Zealand Action on Preeclampsia (NZAPEC) (http://www.nzapec.com/) to raise awareness of preeclampsia, support sufferers and promote research into this condition. In my role as director of NZAPEC I have organised annual study days for midwives and doctors for almost 25 years. The focus of these days has included SGA as it is closely related to preeclampsia. I was employed as a midwifery lecturer at AUT from 2000 until recently, and, because I had gained a

special interest in SGA pregnancy through my involvement with NZAPEC, I developed a postgraduate paper for midwives which focussed on fetal growth and wellbeing.

In 2013, to expand my knowledge of fetal growth, I attended the second international Fetal Growth conference in Baltimore, United States of America, where I was introduced to Professor Jason Gardosi, the founder of the Perinatal Institute. At that time, Professor Gardosi was interested in offering training to a New Zealand midwife educator, to in turn provide accredited education for the use of GROW charts in New Zealand. Until that time, midwives and doctors could use GROW charts without accredited education; however, the Perinatal Institute had begun to require users of GROW to be educated and accredited for safe and optimal use of the tool. This led to my visiting the Perinatal Institute in the UK, in early 2014, accompanied by a New Zealand midwifery colleague, where we worked with the Perinatal Institute midwifery educators to learn how to conduct GROW workshops, which we subsequently offered nation-wide on return to New Zealand.

At the same time, I had enrolled in the Doctor of Health Science programme at AUT and had been considering a focus for my study in fetal growth and wellbeing. The following year when I was refining my research question, CMH expressed interest in the introduction of the GAP programme. I realised this would be an opportunity to conduct research on the effectiveness of the programme in a New Zealand setting.

### *1.15 Assumptions and pre-understandings*

While I was aware of the research showing the effect of GAP in the UK, I realised that for acceptance of the programme in New Zealand it would be essential to evaluate it in the local context. Additionally, I was aware that the model of maternity care in New Zealand is unique and that research findings from overseas may not be transferable. As the remaining New Zealand educator for the Perinatal Institute, following the resignation of my colleague, I was aware that my contract with the Perinatal Institute as a GAP educator could be viewed as a conflict of interest. However, as a researcher I have been aware that my approach must be objective and independent of my education role to honestly report my findings, whether or not they show that the GAP programme is effective at CMH. I have been supported by my supervisors and the processes we have in place to ensure rigour about the data collection and analysis. I have received no funding for my research.

### *1.16 Overview of thesis*

This study starts with an introduction outlining the GAP programme, and the significance of the study in the context of CMH. Chapter 2 comprises the literature review, presented in two sections. The first section defines FGR and SGA in more detail, provides an overview of historical and current methods of assessing fetal growth, evidence for GAP, as well as a summary of the importance of detecting SGA and the potential problems associated with failure to reach growth potential from pregnancy throughout the lifespan. The second section addresses the controversial topic of which growth standards should be used in pregnancy.

Chapter 3 reports the New Zealand story surrounding the introduction of GAP with the political complexity of introducing change within the health system. Methodology and methods for the study are presented in Chapter 4, including the pre-GAP audit, introduction of GAP and the post GAP audit. Maternal and neonatal findings are presented in Chapter 5. Chapter 6 is the discussion chapter in which a summary and discussion, including strengths and weaknesses, with suggestions for further research, education and practice are presented.

### *1.17 Review and summary*

This chapter has introduced my study, the setting in which it is conducted and myself as researcher. I have discussed why it is important to conduct this research. The methodology and methods are briefly explained, with a description of the pre-and post-intervention audits in the context of introduction of the GAP programme to CMH.

At the beginning of my doctoral studies, the leader of the Doctor of Health Science programme, Professor Liz Smythe, gave me a card featuring a photograph of a smiling child. She wrote these words of encouragement:

**‘Let the smile of this child inspire you.**
**There will be children who live because of**
**your investment in this work.**
**You will never know their names,**
**but feel their smiles in your heart.’**

It is my hope that my study will play a part in improving perinatal outcomes for the babies at CMH, and beyond. In the following chapters I address the importance of

detecting SGA during pregnancy and describe the introduction of GAP at CMH, and the wider context of effecting change within the New Zealand health system.

# Chapter 2: Literature Review

## *Part one: Historical and current methods of detection and overview of SGA*

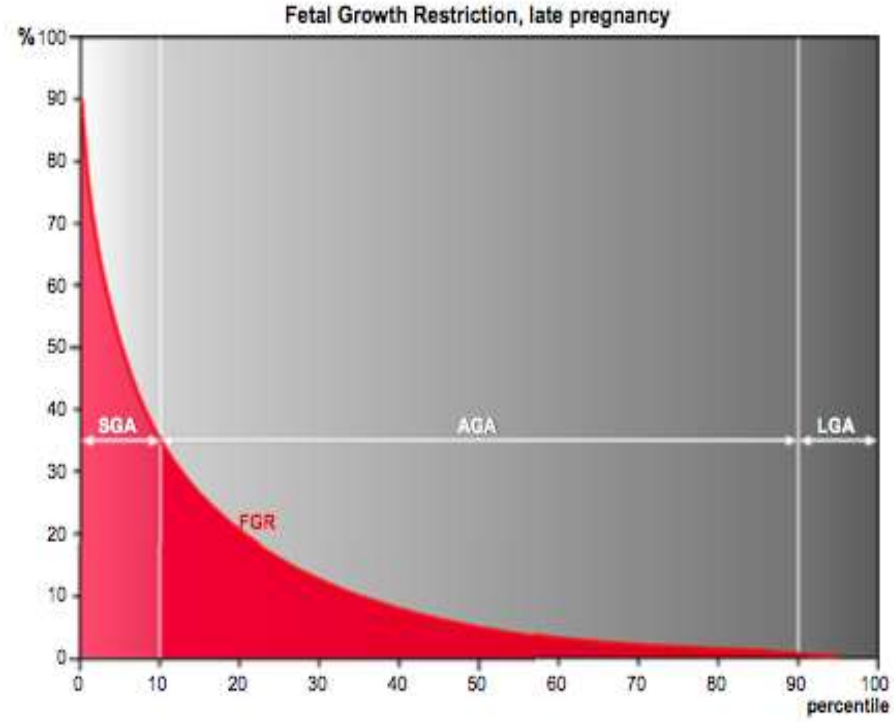
### *2.1 Definitions of SGA and FGR*

As mentioned in Chapter 1, SGA and FGR are often used synonymously in the literature. SGA commonly refers to a fetus with an estimated fetal weight <10$^{th}$ centile or a neonate with a birth weight <10$^{th}$ centile, either by population (Villar et al., 2014; World Health Organization, 2006) or customized standards (Anderson, Sadler, Stewart, & McCowan, 2012; Gardosi, 2014). In New Zealand SGA at birth is defined as a baby with birthweight <10$^{th}$ customized centile (McCowan & Bloomfield, 2014). Not all SGA babies are growth restricted, and the term FGR refers to a fetus or infant that has failed to reach its growth potential (McCowan et al., 2018). FGR and SGA may overlap and can be challenging to differentiate in pregnancy as a fetus can be growth restricted while having an estimated weight >10$^{th}$ centile; as may a neonate with a birth weight >10$^{th}$ centile (Figure 1). A comparison of international standards for the detection and management of FGR highlighted the differences in definition of FGR, with most using the 10$^{th}$ centile as a cut off for FGR diagnosis (i.e., using same definition for FGR and SGA) but some requiring evidence of abnormal Doppler studies or an estimated weight <3$^{rd}$ centile for diagnosis of pathological growth restriction (McCowan et al., 2018). Furthermore, early onset FGR (which by definition is diagnosed at or before 32 weeks) differs from late onset FGR in relation to aetiology, clinical manifestation, placental dysfunction, and patterns of deterioration (Dall'Asta, Brunelli, Prefumo, Frusca, & Lees, 2017; Lees et al., 2013). The focus of the GAP programme is identification of the SGA fetus defined as birthweight <10$^{th}$ customized centile.

### *2.2. Literature search*

#### *2.2.1 Overview*

The literature review is presented in two sections. While my research question primarily concerns the effect of introduction of GAP at a New Zealand maternity facility, I have chosen to situate my research within a wider review of literature. The reason for the breadth of this literature review is twofold. Firstly, it is not possible to present the research about GAP without the context of the problems associated with SGA, and consequent need for timely detection with optimal management. Secondly, while there are numerous publications concerning customized fetal growth standards, there is currently a paucity of literature which specifically addresses GAP.




**SGA**
Small for gestational age

**AGA**
Appropriate for gestational age

**LGA**
Large for gestational age

*Figure 1. Schematic depiction of overlap and difference between FGR and SGA*

x-axis represents growth percentile, y-axis represents percentage of the population, red area represents fetuses with growth restriction. Shows that a fetus/baby may have a weight <10$^{th}$ centile and be appropriately grown or above the 10$^{th}$ centile but also be growth restricted.

Reproduced with permission (Ganzevoort, Thilaganathan, Baschat, & Gordijn, 2019, p. 76)

Part one explores historical and current methods of screening for, and detection of, SGA. Methods range from simple use of maternal abdominal landmarks, through to advanced Doppler velocimetry. The evidence in relation to GAP is introduced. Part two overviews SGA, including risk factors, pathophysiology, and prophylaxis. Potential problems associated with failure to reach optimal growth, from pregnancy throughout the lifespan, are addressed. The controversial topic of which standards should be applied to assess optimal fetal growth concludes this chapter.

### *2.2.2 Search strategy*

The review of literature has continued throughout the duration of my study—from writing my research proposal to the writing of results. I have sourced literature published throughout my study through regular database searching, conference attendance, and active communication with experts in the field. Literature reviewed is primarily from the last 10 years, except for seminal works published previously. Most papers report international studies, and key New Zealand research is included.

Multiple databases were searched including CINAHL, Medline, Google Scholar, Cochrane, and Web of Science. Further literature was sourced from the reference lists of papers retrieved. For key literature, such as publications regarding GAP, key points were tabulated. To access literature on GAP, the following search terms were used: (1) Growth Assessment Protocol; (2) GAP. Secondary sources were searched (Cochrane database) but no relevant systematic review articles were found specifically for GAP. Primary sources were searched with no limitations for date or language but restricted to English. Eight relevant papers were identified using this process. The process for accessing literature on fetal growth standards is described in part two. The last search was completed on June 11$^{th,}$ 2019.

### *2.3 Methods of antenatal detection of SGA*

#### *2.3.1 Historical methods of assessing fetal growth*

The art of assessing fetal growth is a cornerstone of antenatal care and predates academic literature. The following section reviews practices which have developed over the last 250 years, with varying levels of evidence and effectiveness.

*a) Abdominal palpation, callipers, and tape measures*

Abdominal palpation is an ancient art which has been used to assess fetal growth, position, and lie; while more formal methods of fetal growth measurement are relatively recent. In 1752, William Smellie, cited in Engstrom and Sittler (1993), described the growth of the uterus by comparing it to a goose egg at 3 months, mid-way between the symphysis pubis and navel at 5 months, mid-way between the navel and scrobiculum cordi (xiphisternum) at 8 months, and at the scrobiculum cordi at 9 months. Subsequently, writers such as Sutugin (1875), cited in Engstrom and Sittler (1993) began to report large differences in abdominal measurements between women, and recommended that the pregnant uterus be measured with a pelvimetry calliper.

Early calliper techniques were invasive and involved one branch of the calliper being placed in the woman's vagina against the fetal head and the other branch placed at the uterine fundus against the upper pole of the fetus. While various calliper techniques were employed, and measurements were found to be have better inter-user reliability than those obtained by use of a tape measure, the latter were found to correlate better with gestation. Thankfully the use of callipers has been discontinued.

*b) Early measurement techniques*

Over a century ago, a detailed method of measurement of the pregnant woman's abdomen was described by McDonald (1906), although this was intended primarily as a

technique to assess gestation from the size of the uterus rather than to assess the growth of the baby. Gestation was assessed by measuring the abdomen from the fundus of the uterus to the symphysis pubis, and this measurement was divided by 3.5 to give the duration of pregnancy in lunar months. However, this technique was reported as applicable only after the sixth month of gestation. McDonald recommended measurement from the fundus to the symphysis, following the contour of the abdominal wall, as in current practice. However, in contrast to usual modern practice, he recommended that for multiparous women with soft uteri and lax abdominal muscles, an assistant should support the uterus to maintain the fetal axis in a longitudinal lie to enable reliable measurement. McDonald observed that 35cm was the usual height of the uterus at full term, and that it depended mainly on the fetal occipito-coccygeal measurement, claiming that this varied 'but little' in babies of various weights. Further, McDonald added that the average fetal weight at term was 3300gm and that for every centimetre measurement in fundal height above 35cm, 200gm should be added to the estimated fetal weight. However, in 1906, concern about fetal size related more to whether the baby would safely traverse the maternal pelvis rather than whether optimal fetal growth had been reached (McDonald, 1906). Since McDonald's time, many techniques have been proposed to monitor fetal growth

### *c) Maternal landmarks*

While use of maternal landmarks to assess gestation is not evidence based, the practice of using abdominal landmarks, such as the symphysis pubis, umbilicus, and the xiphisternum; has existed for some time in midwifery and obstetric care (Beazley & Underhill, 1970). Practices, such as using the level of the umbilicus to represent 20 weeks' gestation, remain current in obstetric texts (Magowen, Owen, & Thomson, 2018). Measurements have also been recorded as finger breadths above or below a landmark, or as a proportion of the distance between them, such as mid-way between the symphysis pubis and the umbilicus (Engstrom, 1988). However, even in 1906, it was recognised that use of landmarks was questionable. A study involving measurements of several thousand pregnant women showed that the height of the umbilicus varied from 12-20cm above the symphysis (McDonald, 1906). A study reported by Beazley and Underhill (1970), demonstrated a biological variation in the length of women's abdomens of 17.5cm, which refutes the utility of landmarks completely, even if fetal growth was standard in all women, although this idea has now been largely negated through the development of customized standards for fetal growth (Gardosi et al., 1992). While use of a tape measure to record growth had been practiced

for several decades (Wallin, Gyllensward, & Westin, 1981), it was not until the 1980s that a chart for plotting symphyseal-fundal height (SFH[2]) measurements was developed (Quaranta, Currell, & Redman, 1981). An overview of current methods to assess fetal growth is described next.

### *2.3.2 Current methods of assessing fetal growth*

#### *a) Palpation vs tape measure*

Simple use of a tape measure to record the distance between the top of the fundus of the uterus and the symphysis pubis is common in practice and has been compared to use of palpation alone. A systematic review of literature (Robert, Ho, Valliapan, & Sivasangari, 2015), which compared abdominal palpation with measurement of SFH for detection of poor fetal growth, identified only one high quality paper (Lindhard et al., 1990). This RCT compared prediction of SGA, interventions, additional diagnostic procedures, and neonatal outcome between pregnancies of 804 women, who had SFH measurements plotted on a gravidogram, a reference chart developed by Westin (1977); and 835 women who were not measured. It was found that SFH measurement was not helpful in the detection of SGA; in fact, abdominal palpation alone was superior in sensitivity and specificity, although frequency of measurements was reported as few as 3 in 79% of pregnancies, which may have been insufficient to promptly detect slowing of fetal growth. There were no significant differences between the two groups in the number of diagnostic procedures (ultrasound scans and cardiotocography), interventions (induction of labour and caesarean birth), and neonatal outcome (Apgar score, umbilical artery pH< 7.15, admission to neonatal special care unit, and neonatal death) (Lindhard et al., 1990).

#### *b) McDonald's rule*

While numerous references cite the use of McDonald's rule, I was not able to identify a primary source apart from the previously mentioned historic work by McDonald (1906). Current reference to McDonald's rule in practice is based on the expectation that each week of gestation equates to an incremental one centimetre measurement with a 2-3cm variability under or over this standard (Magowen et al., 2018; Mathai, 1988; Morse, Williams, & Gardosi, 2009; Wallin et al., 1981). Two international guidelines (American College of Obstetricians and Gynecologists, 2013; Lausman & Kingdom, 2013) continue to recommend this technique despite the lack of robust evidence, and the

[2] While the abbreviation **SFH** is commonly used to denote symphyseal fundal height, GAP education recommends measuring **from** the uterine fundus **to** the symphysis pubis. In the context of GAP, the term **fundal height** will be used in this thesis.

fact that it does not allow for the wide variation in measurements due to maternal body mass index, ethnicity and parity, particularly in the modern-day obesity epidemic.

*c) Population fundal height charts*

If a tape measure is used to track fetal growth, it is important that fetal growth standards are reliable and relevant. None of the current methods described above provide a reference against which to assess whether the fetus is growing appropriately. Growth references were originally derived from population standards first described by Quaranta et al. (1981). These growth standards were developed from SFH measurements recorded for a group of women in Oxford, UK, with babies whose birth weights were between the 25$^{th}$ and 90$^{th}$ centiles. When clinicians used these standards, 73.1% of infants with birth weight of <10$^{th}$ were accurately predicted by SFH measurement. However, numbers were small (n=103) and with today's diverse multi-ethnic population mix it is unlikely that this standard would perform as well. I was not able to find any further publication reporting ongoing use of this measurement reference. In New Zealand, there are no SFH charts recommended for use, apart from customized fetal growth charts developed and licenced by the Perinatal Institute (http://www.perinatal.org.uk), the charitable trust responsible for the development of GAP.

*d) Standardised fundal height measurement and plotting on GROW chart*

Morse et al. (2009) reviewed the literature on fetal growth screening by fundal height measurement and found the evidence was restricted by a wide range of methods and endpoints as described above. She recommended that a standardised pathway was needed and proposed a screening and detection programme for SGA. It included serial standardised fundal height measurement, plotting on a customized growth chart (in the context of an evidence-based care pathway), clear indications for referral for ultrasound growth scanning, and follow up with Doppler velocimetry if required. The combination of techniques is now the basis of GAP, as introduced earlier in this chapter. The evidence for use of customized standards will be explored later in this section. The techniques to assess fetal growth described above are 'screening' tools rather than 'diagnostic' measures, as SGA and FGR are 'diagnosed' by ultrasound estimation of growth, biometric measurements, and Doppler velocimetry.

*e) Ultrasound*

*(i) Ultrasound estimated fetal weight and biometric measurements used to define SGA*

When SGA is suspected from assessment of the fundal height (according to guidelines provided in GAP education), a growth scan is recommended and an estimated fetal weight (EFW) is calculated by use of a formula utilising biometric measurements of head circumference (HC), biparietal dimeter (BPD), femur length (FL), and abdominal circumference (AC). Commonly, the equation utilised is the one attributed to Hadlock, Harrist, Sharman, Deter, and Park (1985). The EFW calculated by Hadlock et al.'s formula is based on population growth standards, and measurements for the original model were taken from an unselected population of women within a week of giving birth. The sample included preterm, term, and post-term pregnancies and included SGA or LGA babies. It is important, therefore, to plot the EFW on a customized growth chart to more accurately identify the fetal weight centile based on the individual mother's characteristics and gestation.

*(ii) New Zealand definition of SGA/FGR by ultrasound findings*

In New Zealand, SGA is defined by an EFW <10$^{th}$ centile on a customized antenatal growth chart or an abdominal circumference ≤ 5$^{th}$ centile on the population biometry chart. FGR is defined, amongst non-SGA fetuses, when there is a major discrepancy between the head and abdominal circumference (e.g., HC 75$^{th}$ centile and AC 20$^{th}$ centile), an abdominal circumference >5$^{th}$ centile but crossing centiles by >30%, or an EFW on the customized chart reducing centiles by >30% (McCowan & Bloomfield, 2014). In addition to the above, criteria recommended by Figueras et al. (2015), are also used in New Zealand to differentiate between FGR in SGA fetuses and constitutional SGA. FGR is diagnosed amongst SGA fetuses if EFW is <3$^{rd}$ percentile, and/or there is an abnormal cerebro-placental ratio (CPR), and/or umbilical (UA) or uterine artery (Ut. A) Doppler indices. SGA (constitutional) is present if EFW is 3-10$^{th}$ percentile and all Doppler indices are normal. This definition informs the New Zealand Maternal Fetal Medicine Network (NZMFMN) SGA guideline (McCowan & Bloomfield, 2014).

*f) Doppler studies*

The Doppler effect, first described by Christian Doppler in 1842, is the apparent change in frequency of light or sound as the source approaches or moves away from the observer. This effect has been utilised in clinical practice to assess the flow of blood within an artery or vein as high frequency sound waves are bounced off circulating red blood cells and represented by an image which depicts the velocity of blood flow. Over 40 years ago, Fitzgerald and Drumm (1977) pioneered use of Doppler in pregnancy as

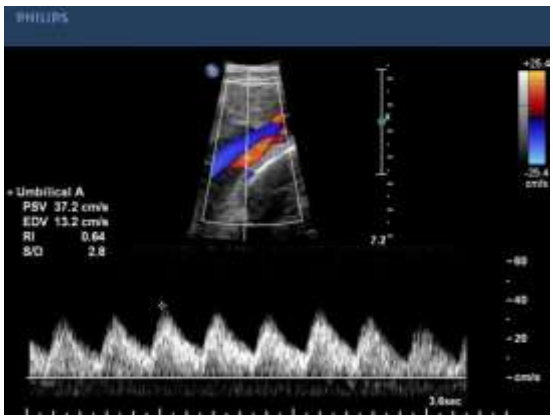
they combined two ultrasound techniques to develop a method of viewing blood flow in the fetal umbilical arteries and vein.

The purpose of fetal surveillance once SGA has been diagnosed antenatally is to avoid fetal acidaemia, which results from a period of chronic or acute hypoxia. Tyrrell, Obaid, and Lilford (1989) demonstrated the association between abnormal umbilical artery Doppler waveforms, fetal hypoxia, and acidosis; and the technique is now used widely in high risk pregnancies to assess the degree of placental dysfunction caused by abnormal blood flow. A Cochrane systematic review of 18 studies comparing use of Doppler to non-use of Doppler in high risk pregnancy, found that use of Doppler was associated with a reduction in perinatal deaths [relative risk (RR)=0.71, 95% confidence interval (CI) 0.52, 0.98], fewer inductions of labour (RR=0.89, 95% CI 0.8, 0.99), and fewer caesarean births (RR=0.90, 95% CI 0.84, 0.97). There was no difference in the rate of operative vaginal births (RR=0.95, 95% CI 0.84, 1.14) or Apgar scores <7 at 5 minutes (RR=0.92, 95% CI 0.69-1.24). However, the quality of included studies was often unclear (Alfirevic, Stampalija, & Gyte, 2010).

Currently there are several types of Doppler studies utilised in the assessment of FGR. Following a growth scan, if the EFW, AC or growth velocity indicates SGA, a series of Doppler studies can be performed, starting with umbilical artery Doppler velocimetry (Figure 2).

*(i) Umbilical Artery (UA) Doppler*

As healthy pregnancy progresses, the resistance to blood flow within the UA reduces due to progressive placental vascular dilatation. Figure 2 shows a normal umbilical artery waveform with healthy diastolic blood flow velocities. Where there is increased placental resistance to blood flow, the diastolic velocity is reduced resulting in an increased pulsatillity index or resistance index, leading to reduced placental blood flow. In extreme cases, absent and eventually reversed flow velocity may occur indicating severe placental disease (Trudinger et al., 1991) (Figure 3). While deterioration to this degree is rare, and indicates need for urgent review in hospital, any finding of abnormal UA Doppler must be followed up with further investigation, and stepwise ongoing management (McCowan & Bloomfield, 2014) (see Appendix D). Further Doppler studies are described below:




UA Doppler image shows normal peak systolic and end diastolic velocity, with normal pulsatillity index.

Reproduced with permission from Dr. Sarah Constantine.

*Figure 2. Normal UA Doppler image*

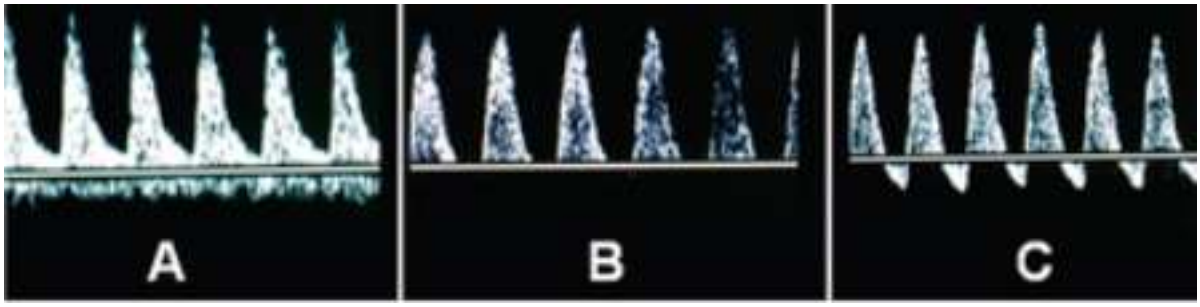



*Figure 3. Abnormal UA Doppler image*

Abnormal UA Doppler image shows (A) decreased end-diastolic velocity, (B) absent end-diastolic velocity, and (C) reversed end-diastolic velocity

(Adapted from Fig. 22-4; (Abuhamad, 2016) (https://radiologykey.com/the-role-of-doppler-ultrasound-in-obstetrics ).

### *(ii) Which SGA babies with normal UA Doppler are at increased risk of morbidity?*

A finding of normal UA Doppler, in the context of SGA, does not exclude pathology. SGA infants with normal UA Doppler but abnormal middle cerebral artery (MCA) or cerebro-placental ratio (CPR) (Cruz-Martinez, Figueras, Hernandez-Andrade, Oros, & Gratacos, 2011; Severi et al., 2002), and/or uterine artery (Ut. A) Doppler (Ghosh & Gudmundsson; Severi et al., 2002) at time of diagnosis of SGA, and those with EFW <3$^{rd}$ centile (Savchev et al., 2012) can be considered to have FGR (Figueras et al., 2015) and are at higher risk of adverse outcome, including emergency caesarean birth for fetal distress and acidosis at birth.

### *(iii) Middle Cerebral Artery (MCA) Doppler*

As placental function deteriorates, the resulting chronic hypoxia leads to the adaptive response known as ‘brain sparing’ in which blood flow is redistributed to favour vital organs as the resistance within the MCA reduces to enhance blood flow to the brain, resulting in an increase in end diastolic velocity (Figure 4). While this may seem to be a

useful adaptation, the response does not ensure normal neurodevelopment as it is associated with worsening hypoxaemia and acidosis (Cruz-Martinez et al., 2011; S. Miller, Huppi, & Mallard, 2016).

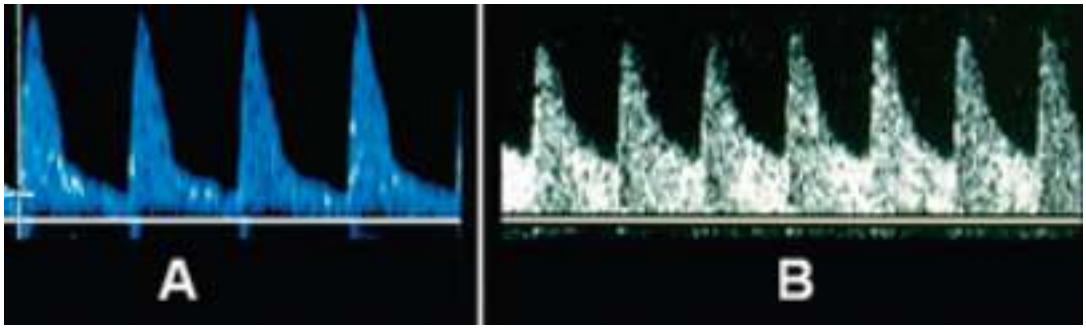



*Figure 4. Normal and abnormal MCA waveform images(A) Normal MCA Doppler waveforms (B) Abnormal MCA Doppler waveforms with increased end-diastolic velocity indicating possible hypoxia*

(Adapted from Fig. 22-5; (Abuhamad, 2016) (https://radiologykey.com/the-role-of-doppler-ultrasound-in-obstetrics ).

*(iv) Cerebro-placental ratio (CPR)*

The CPR is the ratio of the pulsatillity index of the MCA/the pulsatillity index of the UA and reflects placental status and fetal response. This ratio may be abnormal even if the MCA and UA are normal, so may reflect an increase in placental resistance and mild reduction in MCA resistance. Abnormal CPR has been associated with poor outcomes such as intrapartum hypoxia, increased rates of emergency caesarean birth, admission to the neonatal unit, and poor neurological outcome (Cruz-Martinez et al., 2011; Flood et al., 2014).

*(v) Uterine Artery (Ut. A) Doppler*

Blood flow in the uterine arteries can also be assessed by Ut. A Doppler. As healthy pregnancy advances, resistance in these arteries gradually reduces as the trophoblast invades and replaces the muscular media of the maternal spiral arteries. High resistance may persist in pregnancy with preeclampsia or FGR. Abnormal Ut. A. Doppler reflects disturbed utero-placental blood flow; therefore, less blood flow to the fetus. It is a surrogate measure for placental disease, and predicts increased risk of intrapartum fetal compromise (Ghosh & Gudmundsson, 2009; Severi et al., 2002).

### *2.3.3 Holistic approach*

Knowledge that the fetus is growing to potential is important to the pregnant woman and her family/whanau, as well as to her midwife and obstetrician. While the preceding sections address ‘tools’ to assess fetal growth, none of these can be used in isolation. It is acknowledged that the woman has knowledge of her baby’s wellbeing, and a skilled

clinician gains important information from the maternal history, inspection, and hands-on assessment of the woman's abdomen, before starting to use a tape measure, growth chart, or requesting an ultrasound growth scan or Doppler velocimetry. These tools provide information, in the context of holistic clinical assessment, to guide clinical decisions and optimal timing for birth of the baby.

## *2.4 What is the GAP?*

### *2.4.1 Background*

GAP (http://www.perinatal.org.uk/GAP/GAP.aspx) is a comprehensive programme for the detection and management of SGA. The programme was developed in the UK, following recognition that SGA was the most common cause of stillbirth and the realisation from confidential inquiry, that better recognition in pregnancy could reduce the burden of stillbirth for babies who were not reaching their growth potential (Gardosi, Giddings, Buller, Southam, & Williams, 2014). GAP has been available in the UK since 2009 when a regional version was introduced in the West Midlands, and in New Zealand since 2016 when it was introduced at Counties Manukau and Tairawhiti DHBs.

### *2.4.2 History*

The GAP programme originated with the discovery that population fetal growth standards, which did not adjust for maternal physiological variables, did not accurately predict fetal growth potential. In a review of 4129 pregnancies in Nottingham, UK, Gardosi et al. (1992) found that, in addition to fetal sex and gestation, maternal weight at booking, height, parity, and ethnicity were significant determinants of birthweight. A computer programme was developed that adjusted for each of these factors enabling calculation of optimal birthweight centile limits. Application of these centiles showed that 28% of babies designated SGA by conventional (population) standards were in fact appropriately grown, and 24% of those designated SGA by 'customized' standards would have been missed by population standards (Gardosi et al., 1992).

### *2.4.3 Origin of GROW charts*

The use of GROW charts is a key element of GAP. The concept for GROW was based on the above findings and, subsequently, coefficients from 30,000 pregnancies were used to develop software for the generation of 'customized' growth standards for individual women during pregnancy, including the concept 'term optimal weight' (TOW). This is the weight the baby is expected to reach at 40 weeks 0 days in the absence of pathology such as maternal diabetes, hypertension, and cigarette smoking.

Therefore, the standards represent optimal growth (Gardosi et al., 1992; Gardosi, Mongelli, Wilcox, & Chang, 1995). The original coefficients have now been superseded by those obtained from large international databases and incorporated into country specific versions of GROW. See below for example of a New Zealand GROW chart (Figure 5).

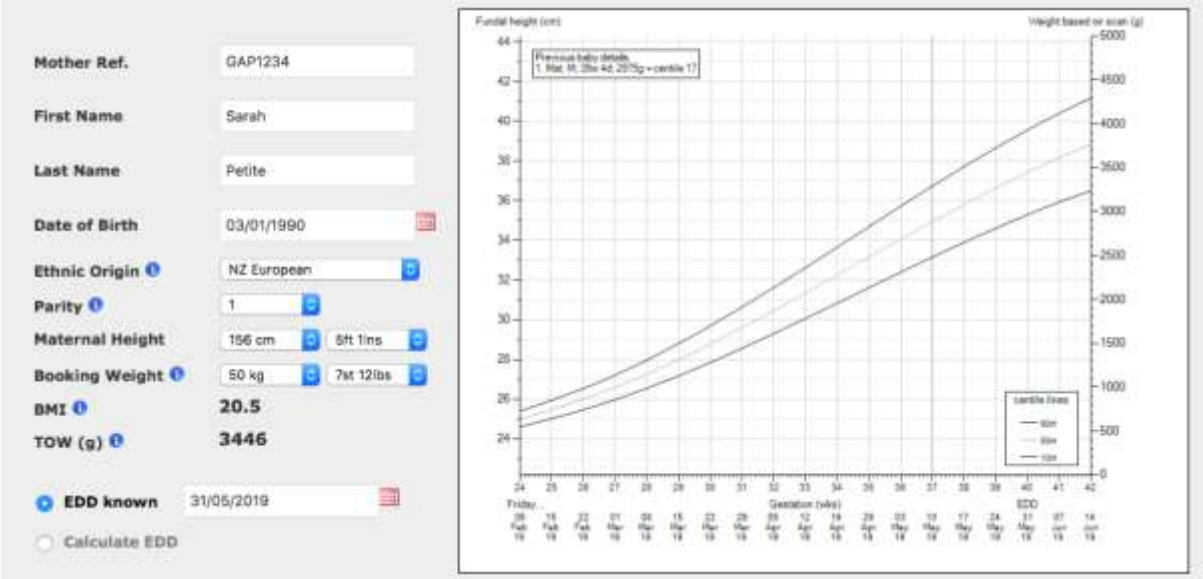



*Figure 5. Example of a GROW chart*

In the above chart, the 10th, 50th, and 90th centile lines are displayed. These are calculated from a mathematical formula for intra-uterine weight gain (Gardosi et al., 1992). The *y* axes represent fundal height in centimetres (left) and EFW in grams, from ultrasound measurement (right). The *x* axis represents gestation in weeks and days. The TOW is calculated as 3446gm in Figure 5, and the previous baby's birth weight has been calculated as the 17th customized centile. The fundal height can be plotted on the chart and represents uterine growth, as distinct from EFW, but the growth trajectory is expected to follow the curve of a centile line between the 10th and 90th delineation, and an ultrasound scan can be requested if the uterine growth trajectory is not tracking according to guidelines provided with the GAP education programme.

### *2.5 The use of GROW and GAP*

Use of GROW charts has been recommended in the Royal College of Obstetricians and Gynecologists' (RCOG) guidelines (RCOG, 2013), and GAP was recommended by the National Health Service (NHS) as part of a UK care bundle for stillbirth prevention launched in 2015 (O'Connor, 2014; Widdows, Roberts, Camancho, & Heazell, 2018).

GROW has also been used in maternity practice in New Zealand since 2007, and currently GAP is recommended by the New Zealand PMMRC (2018).

### *2.5.1 Introduction of GAP*

Introduction of GAP at a DHB involves a contractual arrangement between the Perinatal Institute and the DHB. The Perinatal Institute provides the initial education, with ongoing support and resources for cascade education and local introduction. In turn, the DHB nominates a GAP lead, multidisciplinary team, and champion to provide cascade education and encourage full introduction of the programme.

### *2.5.2 Face to face and E-learning*

An initial face to face multidisciplinary workshop is presented by a GAP educator to launch introduction of GAP, with a follow up e-learning tool for annual updating of clinicians. The New Zealand educational material has recently been extensively reviewed, by an advisor for the New Zealand College of Midwives and me, to ensure the material is appropriate for New Zealand clinicians, and aligns with local guidelines and philosophy. The education focusses on recognition of risk factors for SGA, provision of the appropriate care pathway, standardised fundal height measurement, plotting on a GROW chart, and the use of evidence-based protocols for detection and management of pregnancies with suspected and detected SGA.

### *2.5.3 The GROW-App*

The GROW-App, a web based electronic application used for generation of customized antenatal growth charts and birth weight centiles, enables routine monitoring and reporting of detection rates for SGA. Another electronic tool is provided for estimation of a baseline SGA detection rate, and systematic electronic auditing of missed cases of SGA. Calculation of a baseline detection rate is important to assess effectiveness of the programme. The baseline detection average was 18.7% for GAP hospitals in the UK (Williams, Turner, Butler, et al., 2018), which is consistent with earlier published research (Kean & Liu, 2009; Roex et al., 2012).

### *2.5.4 Auditing of GAP*

While a baseline audit is necessary to establish whether introduction of GAP improves detection of SGA, ongoing auditing is also a crucial element of GAP. Findings from auditing enable recognition of education needs and system issues in fetal growth surveillance for ongoing quality improvement, as well as recognition of resource constraints which may be addressed locally and nationally (Williams, Turner, Butler, et al., 2018).

### *2.5.5 Appropriate care depending on risk of SGA*

The emphasis of GAP is on longitudinal assessment throughout pregnancy, preferably by the same maternity care provider. Women who are considered low risk for SGA are assessed by serial fundal height measurements, with clear guidance concerning referral for a growth scan should the sequential fundal height measurements indicate suboptimal uterine growth. Women who are considered high risk for SGA are generally referred for obstetric review and assessed by serial growth scans with upscaling of surveillance with Doppler ultrasound according to evidence-based guidelines.

## *2.6. What is the evidence for GAP?*

### *2.6.1 United Kingdom*

Accredited education in customized fetal growth assessment has been associated with increased antenatal detection of SGA with a reduction in stillbirth in areas of high uptake, and the lowest recorded stillbirth rates in each of these regions (Gardosi, Giddings, Clifford, Wood, & Francis, 2013); and in over 90 NHS trusts between 2015 and 2018 (Williams, Turner, Hugh, Francis, & Gardosi, 2018). Following recognition of the link between accredited education, improved detection of SGA, and reduced rates of stillbirth, the Perinatal Institute developed the enhanced education programme which became GAP, available in the UK from 2013 (Clifford et al., 2013). Two years later, as previously mentioned, the programme was adopted as one of four components of the UK NHS ‘Saving Babies Lives Care Bundle’ (O'Connor, 2014). The care bundle also included programmes to reduce cigarette smoking in pregnancy, improve awareness and management of reduced fetal movements, and promote effective fetal monitoring in labour. A review of the care bundle (Widdows et al., 2018) concluded that while the stillbirth rate reduced by 20% in participating units, it was not possible to unambiguously attribute this to any particular aspect of the care bundle. However, it was agreed that the association was highly likely, and acknowledged that detection of SGA increased (from 33.8% to 53.7%) due to better surveillance through the use of GROW charts and serial growth scans (Widdows et al., 2018).

### *2.6.2 New Zealand*

While there have been no studies published to date reporting on the detection of SGA following the formal GAP programme in New Zealand, unpublished audits from National Women’s Hospital in Auckland showed that detection of SGA for pregnancies managed by community midwives, who routinely used customized antenatal growth charts, was higher than for a group of self-employed midwives in the same area (who

generally did not use customized antenatal growth charts) (L. McCowan, personal communication, May 7th 2019).

### *2.6.3 Australia*

Two studies have been published following Australian work on the introduction of aspects of the GAP programme. Roex et al. (2012) reported on antenatal detection of SGA after introduction of structured education and use of GROW charts, compared to an historical control group for whom GROW and formal clinician education about detection of SGA was not available. Antenatal detection of SGA in the control group was 24.8% and increased to 50.6% in the post intervention group [odds ratio (OR)=3.10, 95% CI 1.73, 5.57; $p < 0.001$]. However, the study was restricted to nulliparous women, and excluded Pakistani, Indian, and indigenous Australian women.

In a more recent study (Jayawardena & Sheehan, 2018), GAP was implemented in a large Melbourne hospital with a diverse cultural mix of clients, and included multiparous as well as nulliparous women, as for my study. The GAP programme was implemented into the care of women under the same team, with one group who gave birth to their babies prior to, and another following, introduction of GAP. Antenatal identification of SGA increased from 21% to 41% following the introduction of GAP (OR=2.6, 95% CI 1.3, 4.9; $p < 0.05$). While the above evidence is encouraging, it is observational and not generally viewed as being as robust as data from a RCT.

### *2.6.4 Lack of RCT evidence*

The gold standard RCT is challenging to implement for a programme such as GAP, as benefits have been reported from observational evidence. The programme has been recommended by professional bodies, such as RCOG in the UK, and in New Zealand the PMMRC (2018) and the New Zealand Maternal Fetal Medicine Network (NZMFMN) (McCowan & Bloomfield, 2014). It would also be difficult to conduct an RCT on GAP in New Zealand as the use of GROW is now widespread amongst maternity care providers. However, at the time of writing, a cluster RCT to evaluate the introduction of GAP is in progress in London, UK, and will provide important evidence regarding GAP, including maternal and neonatal clinical outcomes and economic analysis. Qualitative data will be also gathered to assess education and explore barriers to introduction. Data were to be collected on all babies born in participating units from 1st June to 31st July 2018. There is a need for more international research on the full introduction of GAP, as currently most evidence is UK based. However, the London RCT will have the potential to guide policy makers for future maternity care beyond the UK (Vieira et al., 2019). See Table 1 for summary of published literature on the GAP.

### *2.7 Aetiology and risk factors for SGA*

Fetal growth is contributed to by genetic potential but modified by fetal, maternal, and placental factors (Dall'Asta et al., 2017; J. Miller, Turan, & Baschat, 2008).

#### *2.7.1 Fetal factors*

Fetal factors are associated with 5-20% of all cases of SGA and are more likely when the condition arises early in pregnancy. Conditions include chromosome abnormalities, especially trisomy 13, 18, and 21; inborn errors of metabolism and genetic syndromes (Guibaud et al., 2017); and infection such as toxoplasmosis, varicella zoster, rubella, and cytomegalovirus (Leeper & Lutzkanin, 2018), as well as multiple gestation (Sherer, 2001).

#### *2.7.2 Maternal risk factors*

*a) Major maternal risk factors*

Recognition of those pregnancies with a higher chance of SGA at pregnancy booking is important to plan the most appropriate care pathway and, where appropriate, facilitate care and interventions to reduce the risk of adverse outcome. For this literature review, the focus will be on maternal conditions recognised as being major risk factors for SGA, as these are important in the context of the GAP programme, and minor risk factors will be briefly mentioned. An algorithm has been developed for New Zealand, adapted from the NHS England Stillbirth Care Bundle (O'Connor, 2014) and based on the NZMFMN SGA Guideline (McCowan & Bloomfield, 2014). See Figure 6, which includes a list of major risk factors for SGA that may be recognised at booking or during ongoing pregnancy. Pathways for screening, detection and management of SGA are represented in the algorithm, which is provided to all clinicians who engage with GAP. Major risk factors (OR or RR >2) are listed in Table 2.

*Table 1. Included studies: The Growth Assessment Protocol (GAP)*

| Author (Journal, Year) | Country | Purpose | Methods | Context | Findings | Limitations |
|---|---|---|---|---|---|---|
| Clifford, Giddings, Southam, Williams & Gardosi (Midirs, 2013) | UK | Report on the origin of the Perinatal Institute's GAP programme | N/A | Maternity units in West Midlands | Detection of SGA relative to uptake of education and associated with reduction in stillbirth rate. Recognition led to development of comprehensive GAP programme. | N/A |
| Gardosi, Giddings, Clifford, Wood & Francis (BMJ Open, 2013) | UK | To assess the effect of accredited education in fetal growth surveillance and evidence-based protocols on stillbirth rates in England and Wales | Case review: Analysis of mortality data from Office of National Statistics (ONS) | 3 NHS regions in England, which had implemented education for detection of SGA | Significant drop in stillbirth rates in England between 2007 and 2012. Lowest recorded stillbirth rates on record in regions with education. In contrast, there was no significant change in stillbirth rates in the remaining English regions and Wales, where uptake of education had been low. | Confounders may have been responsible for changes; however, none were identified by causality model |
| Jayawardena & Sheehan (ANZJOG, 2018) | Australia | To assess the effectiveness of GAP in a multicultural population in Royal Women's Hospital, Melbourne | Pre- and post-GAP intervention study. The GAP programme was introduced for 882 women, and outcomes were compared to outcomes for 942 women who gave birth after routine care before the introduction of the GAP | GAP implemented at Royal Women's Melbourne | Detection of SGA increased from 21% to 41% with the GAP program (OR 2.6, 95% CI 1.3, 4.9, $p < 0.05$). Following the GAP vaginal birth increased. No increase in induction or caesarean birth Reduced admission to neonatal unit | Model of care with all pregnancies managed by employed staff. Results may not be generalizable to settings with self-employed midwives such as New Zealand |

| Author (Journal, Year) | Country | Purpose | Methods | Context | Findings | Limitations |
|---|---|---|---|---|---|---|
| Turner, Butler, Giddings, Wood, and Gardosi (2016) http://www.perinatal.org.uk/gap/SaBiNE.aspx | UK | Report on SaBiNE project | The GAP team and champions work closely to implement the GAP, provide cascade education, baseline audit of SGA detection, rolling reporting of SGA detection, and missed case analysis for quality improvement | Intensive GAP education over 4 months across 3 North of England regions with designated champions-midwives | Significant increase in AN detection of SGA stillbirth rates dropped to lowest ever levels, resulting in 84 less stillbirths, but no change in rest of UK<br>Cost effective- estimated 14-fold return on investment | Intensive support of designated clinical midwives cannot be sustained economically. Potential for strength of programme to reduce without close support from the GAP champion |
| Turner, Williams, Wood & Gardosi (BJOG, 2016) | UK | Assess impact of the GAP education on identification of SGA pregnancies by symphyseal fundal height measurement | Collection of anonymised data from pre- and post-GAP. Electronic baseline audit tool for pre-GAP and data from GROW App post GAP | 31 NHS trusts, 19,432 pregnancies pre-GAP and 68,742 post- GAP | 70% increased referral for ultrasound scan in pregnancy. False positive referral increased from 8-11% | |
| Widdows, Roberts, Camancho & Heazell (Maternal and Fetal Health Research Centre, University of Manchester, 2018) | UK | To determine impact of care bundle on UK maternity services and perinatal outcomes.<br>(1) Evaluate effectiveness of care bundle in reducing stillbirth; (2) Assess degree to which each element has been implemented; (3) Understand processes and contexts of introduction success; (4) Estimate cost of introduction | Review of outcomes for 20 trusts (100,000 births) that implemented the care bundle for 2 years in 2015<br><br>The GAP was one of four strategies implemented. | Need for review of first saving babies lives care bundle. Varying introduction and effectiveness across NHS trusts | 20% reduction in stillbirth rates during study period. No (direct) evidence that of SBLCB interventions increase SGA detection but better monitoring of fetal growth with the GAP can lead to improved antenatal identification antenatal of SGA | Some units did not implement the GAP effectively. Depended on enthusiasm/ commitment of staff<br>Success reflects engagement as well as the elements of the individual elements of the care bundle |

| Author (Journal, Year) | Country | Purpose | Methods | Context | Findings | Limitations |
|---|---|---|---|---|---|---|
| Williams, Turner, Hugh, Francis & Gardosi (2018) (Presented at International Fetal Growth conference, Milan 2018) | UK | Assess whether the reduction in stillbirth rates in UK reflected fewer deaths of SGA babies | Analysis of prospectively collected audit data at time of birth. | Anonymised information from 96 NHS trusts between 2015 and 2018<br>748,415 pregnancies | 748,415 births were recorded on GROW software during 2015-2018 including 3,142 stillbirths (4.2/1000). Of these 1,074 (34.2%) were SGA at birth. The proportion of SGA cases decreased significantly from 38.3% in 2015/16 to 33.3% in, 2018/19 | SGA includes constitutionally small babies and detection of SGA defined as <10$^{th}$ centile does not distinguish between healthy small babies and those with growth restriction. Further analysis based on distinction between SGA and FGR warranted |
| Vieira et al (Trials, 2019) | UK | First RCT to evaluate clinical effectiveness, cost effectiveness, and introduction of the GAP<br><br>Published study protocol | Cluster RCT. Introduction of GAP/controls with standard AN care. Perinatal Institute present the programme and support hospitals for cascade education and auditing | Clusters (either NHS trusts or hospitals) in UK. | Not published yet<br><br>Recruitments are completed and data will be collected for all babies born 1$^{st}$ June to 31$^{st}$ November 2018 | Data has not yet been fully analysed<br>Some trusts were not using the GAP and some had not fully implemented it |

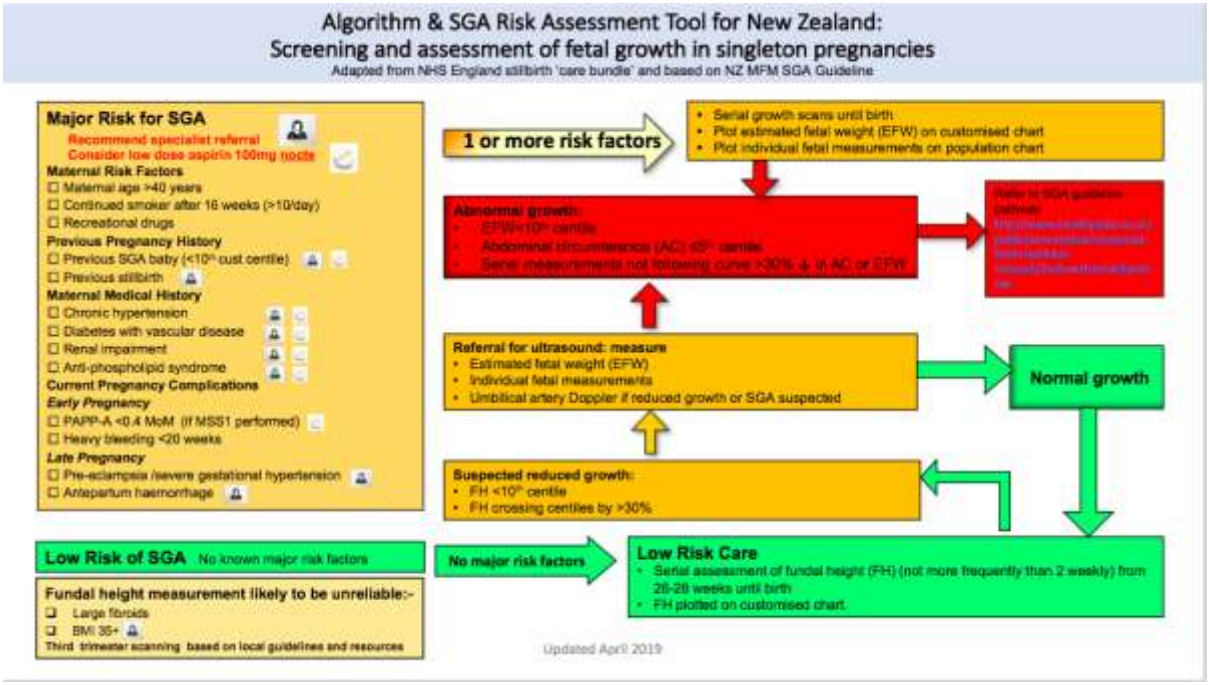



*Figure 6. Algorithm and SGA Risk Assessment tool New Zealand*

The image icons represent indication for specialist review and recommendation for SGA prophylaxis with low dose aspirin .

*Table 2. Major risk factors for SGA according to NZ SGA algorithm*

| **Definition of Risk** | **References** | **Estimate measure*** | **Point estimate and 95% CI** |
|---|---|---|---|
| Maternal Age >40 years | Odibo, Nelson, Stamilio, Sehdev, and Macones (2006) | OR | 3.2 (1.9-5.4) |
| Smoker ≥11 cigarettes/day | Cnattingius (2004); McCowan and Horgan (2009) | OR | 2.21 (2.03-2.4) |
| Recreational drug use | Gouin, Murphy, and Shah (2011) | OR | 3.23 (2.43-4.3) |
| Previous SGA (<10$^{th\%}$ customized) | Kleijer, Dekker, and Heard (2005) | OR | 3.9 (2.14-7.12) |
| Previous stillbirth | Ananth (2007) | OR | 6.4 (0.78-52.56) |
| Chronic hypertension | Allen, Joseph, Murphy, Magee, and Ohlsson (2004) | ARR | 2.5 (2.1-2.9) |
| Diabetes with vascular disease | Howarth, Gazis, and James (2007) | OR | 6 (1.5-2.3) |
| Renal impairment | Fink , Schwartz, Benedetti, and Stehmann (1998) | AOR | 5.3 (2.8-10) |
| Anti-phospholipid syndrome | Yasuda, Takakuwa, Tokunaga, and Tanaka (1995) | RR | 6.22 (2.43-16.0) |
| PAPP-A <0.4 MoM | Dugoff et al. (2004) | AOR | 2.47 (2.16-2.81) |
| Heavy bleeding early pregnancy | Weiss et al. (2004) | AOR | 2.6 (1.2-5.6) |
| Pre-eclampsia | Ananth (2007) | AOR | 2.6 (1.22-4.18) |
| Severe gestational hypertension | Allen et al. (2004) | RR | 2.5 (2.3-2.8) |
| Unexplained APH | McCowan and Horgan (2009) | OR | 5.6 (2.5-12.2) |

* **OR** Odds ratio, **AOR** adjusted odds ratio, **RR** Relative risk, **ARR** Absolute risk reduction, **MoM** Multiples of the median

### *b) Minor maternal risk factors*

While the above table lists the major risk factors according to the New Zealand SGA algorithm, the list does not include the numerous minor/moderate risk factors. The presence of minor/moderate risk factors is not an indication for serial growth scanning or prophylaxis according to current New Zealand guidelines (McCowan & Bloomfield, 2014); but guides practice in other countries, such as in the UK, where a combination of three or more minor risk factors is included in the rationale for ultrasound investigation from 20-24 weeks (RCOG, 2013). Minor risk factors include: maternal age ≥35 yrs. (Odibo et al., 2006), IVF singleton pregnancy (Jackson, Gibson, Wu, & Croughan, 2004), nulliparity (Shah, 2010), BMI <20 or >25, but only when SGA is defined by customized standards (Gardosi & Francis, 2009), previous pre-eclampsia (Ananth, 2007), low fruit intake pre-pregnancy (McCowan, Roberts, et al., 2009), and pregnancy interval <6 and >60 months (Conde-Agudelo, 2006).

### *c) Placental factors*

"It is not small size that puts a fetus at risk but placental dysfunction" (Bobrow & Soothill, 1999, p.1460). The placenta has been termed 'a diary of intra-uterine life' that determines fetal growth potential (Redline, 2008). Most cases of SGA, which are not a result of fetal genetic anomalies, congenital malformations or infection, are associated with inadequate utero-placental circulation from the end of the first trimester (Burton & Jauniaux, 2018). There are three overlapping gestational periods with important milestones necessary for successful maternal fetal exchange and optimal fetal growth. The first trimester involves maternal adaptations to pregnancy, the second includes progression of placental function to meet fetal growth needs, and the third prepares the fetus for extra-uterine life (Baschat, 2004). Depending on the gestation and extent of placental pathology, differing complications may arise. For instance, failed placental adherence results in miscarriage, but if adaptive mechanisms allow continuing pregnancy, growth restriction may affect fetal organs. Further, if compensatory measures are unsuccessful, the pregnancy may end in stillbirth. However, in many cases placental/fetal adaptation may provide sufficient nutrients for survival of the fetus while subclinical SGA goes unnoticed until apparent at the time of usual exponential growth in the third trimester, or until decreased adipose tissue and abnormal body proportions are noticed at birth (Baschat, 2004).

#### *(i) Impaired spiral artery remodelling*

Placental-related SGA is primarily a result of deficient remodelling of the uterine spiral arteries, which takes place during the end of the first trimester and early second

trimester. Following fertilisation, the cytotrophoblast forms anchoring sites in the uterus, establishing placental adherence with anchoring villi. Concurrently, vascular connections are formed between the maternal circulation and the intervillous space.

Adequate dilatation of the spiral arteries to provide for increased utero-placental circulation with rapidly developing placental villi, is crucial for optimal placental development and fetal growth. The spiral arteries are the terminal branches of the uterine arteries that supply the placenta and during the non-pregnant state they provide blood to the endometrium. The physiological changes before 20 weeks in a normal pregnancy result in widening of the vessel lumen and elimination of the muscular and elastic components of the arteries extending to the inner third of the myometrium. This process enables a high capacity, low resistance placental compartment capable of receiving 600ml of maternal blood flow per minute by term (Baschat, 2004). Figure 7 (A) shows a healthy maternal spiral artery at the beginning of pregnancy and Figure 8 (B), depicts a normal maternal spiral artery by 20 weeks when the remodelling is complete. The depth of invasion is important and in a sub-set of women the invasion does not extend beyond the decidua resulting in circulation with high resistance (Roberts, 2014). Figure 9 (C) represents the shallow remodelling that can be seen in some cases of FGR and pre-eclampsia. The consequent malperfusion results in reperfusion injury, oxidative stress and an imbalance of angiogenic/antiangiogenic factors (Groom & David, 2018).The cellular stress within the placenta limits cell proliferation and selectively suppresses protein synthesis (Burton & Jauniaux, 2018).

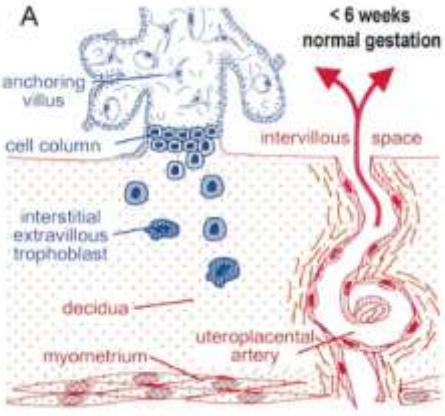



*Figure 7. Schematic representation of interstitial and endovascular trophoblastic invasion of spiral artery before 6 weeks of pregnancy*

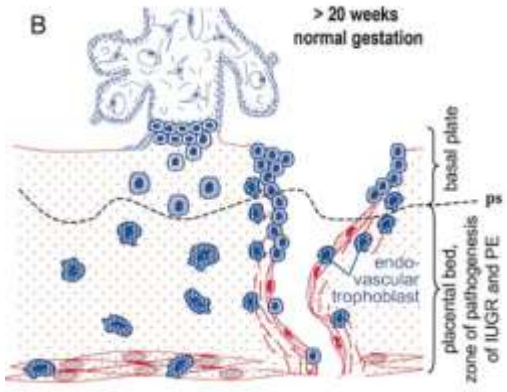



*Figure 8. Schematic representation of uterine artery remodelling by 20 weeks of normal pregnancy*

ps = zone of placental separation, where basal plate separates from placental bed at the birth. Blue represents fetal, red represents maternal tissues. Spiral artery remodelling by trophoblast invasion shown.

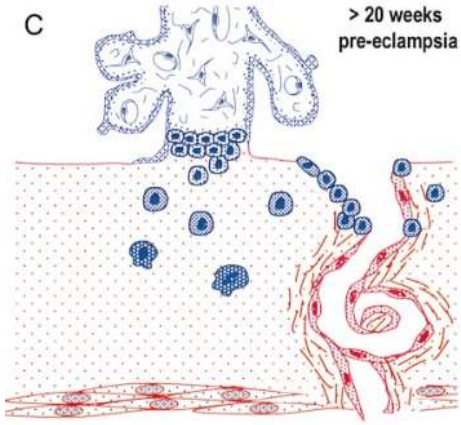



*Figure 9. Schematic representation of failure of endovascular trophoblast invasion*

Trophoblast invasion is shallow, leaving arteries narrow and inelastic, as in some cases of FGR and pre-eclampsia (PE), with subsequent malperfusion

Reproduced with permission from Kaufmann, Black, and Huppertz (2003, p. 2).

### *(ii) SGA and maternal hypertension*

There has been an assumption that the common co-existence of SGA and hypertensive disease in pregnancy may reflect the same placental pathology but different clinical manifestations, suggesting that SGA may include two distinct subgroups. A study which compared pregnancy outcome and placental pathology in pregnancies with SGA with and without preeclampsia, found there were significantly different pregnancy outcomes and placental pathology between the two groups (Groom, North, Poppe, Sadler, & McCowan, 2007). While the majority of neonates with SGA are born to normotensive women (approximately 75%), the risk of SGA is increased when the woman has preeclampsia compared to the risk for normotensive controls (Groom et al.,

2007; McCowan, Roberts, et al., 2009; Xiao, Sorenson, Williams, & Luthy, 2003). Although risk depends on onset and severity of preeclampsia, and parity, Odegard, Vatten, Nilsen, Salvesen, and Austgulen (2000) found that the risk of SGA was four times greater (RR=4.2, 95% CI 2.2, 8.0) for babies born after pre-eclampsia compared to normotensive controls.

Severe early onset SGA often occurs in the context of severe early onset preeclampsia featuring impaired maternal utero-placental circulation because of defective spiral artery remodelling and its effects. However, there are less characteristic histological changes with late onset SGA which represents a more heterogeneous group with less characteristic placental pathology (Groom et al., 2007).

## *2.8 Prevention of SGA*

### *2.8.1 Low dose aspirin*

*a) Action*

Low dose aspirin (LDA) suppresses production of prostaglandins including thromboxane, a powerful vasoconstrictor with prothrombotic and antiplatelet effects (Patrignani, Filabozzi, & Patrono, 1982). Long term use of LDA irreversibly blocks formation of thromboxane A2 in platelets inhibiting platelet aggregation; thereby enhancing placental circulation (Taubert et al., 2004). Additionally, LDA has cytoprotective and anti-oxidant properties, induces the release of the vasodilator nitric oxide from the vascular endothelium (Taubert et al., 2004), and increases the activity of heme-oxygenase-1 to break down heme, with consequent reduction in oxidative stress, cell injury, and inflammation (Grosser et al., 2003).

*b) Evidence*

It has been recognised for some years that LDA provides a modest reduction in risk for SGA, especially in high risk women (Bujold, Roberge, & Nicolaides, 2014). Early studies have been supported by more recent evidence. In a meta-analysis, Roberge et al. (2017) found LDA was associated with 10% reduction in risk of SGA (RR=0.90, 95% CI 0.81, 1.00), while an individual patient data meta-analysis, including over 22,000 women, showed that the relative risk for SGA was 0.76 (95% CI 0.61, 0.94) (Meher, Duley, Hunter, & Askie, 2017).

*c) Dosage and timing*

In New Zealand, the recommended dose of LDA for SGA prophylaxis is 100mg daily (McCowan & Bloomfield, 2014). Although lower doses have been tested, 100-150mg commenced prior to 16 weeks of pregnancy provides a modest benefit in women

identified as at risk of SGA from history taking at booking (Groom & David, 2018). There is evidence to support evening rather than morning administration of LDA as reduction of risk was reported to be insignificant when LDA was taken on awakening, and most effective when taken at bedtime (Ayala, Ucieda, & Hermida, 2013).

### *2.8.2 Unfractionated heparin and low molecular weight heparin*

*a) Action*

Unfractionated heparin (UF), is a naturally occurring polysaccharide that acts as an anti-coagulant and fractionated or low molecular weight heparin (LMWH) is a product of the fractionation of UF. While it has a similar mechanism, UF has more predictable anticoagulant activity. Both UF and LMWH have been used in pregnancy for thromboprophylaxis and treatment of venous thromboembolism, and are considered safe (Groom & David, 2018). While the anticoagulant action of heparins suggests a potential role in prevention of placental pathology such as thrombosis and infarction, there are other effects including anti-inflammatory (Mousavi, Moradi, Khorshidahmad, & Motamedi, 2015), and pro-angiogenic; improving endothelial function and promoting the release of placental growth factor (McLaughlin et al., 2017). These actions add strength to the hypothesis that heparins may be useful in the prophylaxis of placenta-mediated SGA. However, the evidence for clinical use is not strong.

*b) Evidence*

Early RCTs suggested that heparin might reduce the risk of SGA but results were heterogeneous. A systematic review of RCTs between 2000 and 2013 (Rodger et al., 2016), concluded that LMWH did not reduce the risk of placenta mediated pregnancy complication in at risk women. More recently, a multi-centre RCT, the Enoxaparin for the Prevention of Preeclampsia and IUGR (EPPI) trial assessed the effectiveness of LMWH to prevent recurrent preeclampsia and SGA in a sample of women at high risk of both conditions (Groom et al., 2017). All women received high risk care including LDA and calcium (if appropriate to reduce risk of preeclampsia). This study did not find that addition of LMWH to standard high-risk care reduced the risk of SGA or preeclampsia and the researchers concluded that use of heparin as prophylaxis for placenta mediated conditions, such as preeclampsia and SGA, should be restricted to the research setting.

### *2.8.3 Smoking cessation*

While LDA currently remains the only evidence based pharmaceutical prophylaxis with modest benefits for reduction of risk of placenta mediated SGA, it is of key importance to address modifiable lifestyle risk factors such as smoking. Smoking cessation is

recommended in all evidence based guidelines for the prevention of SGA (McCowan et al., 2018). Maternal cigarette smoking is a leading cause of SGA, with growth restriction thought to be due to intrauterine exposure to carbon monoxide and nicotine as well as numerous toxins which affect the fetus at a cellular level (Regan et al., 2015). McCowan, Dekker, et al. (2009) found there was no difference in the rates of SGA between women who were non-smokers and those who stopped before 15 weeks' gestation, suggesting that the adverse effects of smoking were prevented by cessation in early pregnancy. This evidence offers a positive message for midwifery practice. Incentive based smoking cessation programmes are the most effective in assisting pregnant women to quit (Tappin, 2015). An incentive-based smoke free programme, in which grocery vouchers are provided to women as a reward for achieving smoke free status, has been in place at CMH since 2013. The programme has been very successful compared to a previous non-incentive-based programme. During the first three years of the programme, twice as many women accessed the service and three times as many women (70%) succeeded in being smoke free one month after their quit dates (CMH, 2018).

### *2.9 Why does detection of SGA matter?*

Morbidity and mortality rates are higher for the infant with early onset SGA (born at <32 weeks) compared to late onset (Lees et al., 2013; Nardozza et al., 2017). Yet, at any gestation the risks associated with suboptimal fetal growth are considerable, as described next.

#### *2.9.1 Mortality – Association between stillbirth and SGA*

Stillbirth is a tragedy for parents and families as well as being extremely distressing for clinicians. The World Health Organization (n.d.) defines stillbirth as a third trimester fetal death (≥1000gm or ≥28 weeks). In New Zealand, a stillbirth is a death of a fetus ≥20 weeks' gestation or weighing ≥400gm if the gestation is unknown (PMMRC, 2016). In 2016, in New Zealand, there were 325 stillbirths which equated to 5.5 per 1000 births. It is important to interpret stillbirth rates with the knowledge that international differences in definition exist. For instance, the UK definition is death of a fetus ≥24 weeks; thus, applying this definition, the New Zealand stillbirth rate for 2016 would be 3.3 per 1000.

Similarly, in a large population based UK study, Gardosi and colleagues (2013) found that the overall stillbirth rate was 4.2 per 1000 births but only 2.4 per 1000 in pregnancies without growth restriction (FGR was defined as birthweight <10$^{th}$

customized centile). In the group of antenatally detected FGR pregnancies the stillbirth rate was 9.7 per 1000 births but if not detected the rate was 19.8 per 1000 births (See Figure 10).

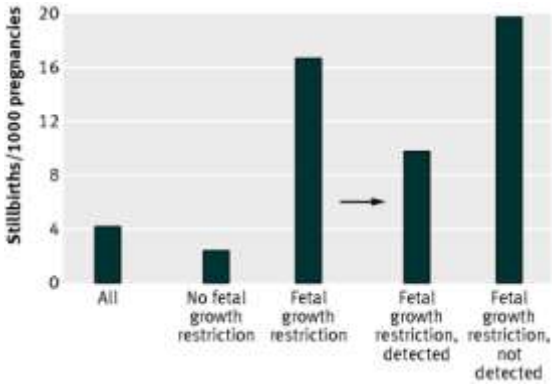



*Figure 10. Stillbirth rate with and without antenatal detection*

Reproduced with permission from Gardosi, Madurasinghe, et al. (2013, p. 14).

### *2.9.2 Morbidity – Immediate and long term risks*

Immediate risks for the growth restricted newborn include perinatal asphyxia, hypothermia, hypoglycaemia, polycythaemia, jaundice, thrombocytopenia, respiratory distress syndrome, sepsis, necrotising enterocolitis, intraventricular haemorrhage, neonatal seizures, and hypoxic ischaemic encephalopathy (Chauhan et al., 2014; Sharma et al., 2016). While the aim of timely detection and optimal management of SGA is to avoid the complications associated with SGA, the effects may extend to childhood and beyond. NE is arguably the most devastating outcome of SGA, apart from stillbirth.

*(a) Neonatal encephalopathy*

NE is a syndrome characterised by neurological dysfunction (Nelson et al., 2012), and associated with adverse outcomes including neonatal death, cerebral palsy, epilepsy, and other cognitive and behavioural problems (Kurinczuk, White-Koning, & Badawi, 2010). The syndrome presents in the first hours of life in term and late preterm infants. For many of these infants, there have been no recognised asphyxial intrapartum or acute birth events. In a major case control study (Badawi et al., 1998), FGR was associated with a significantly increased risk of neonatal encephalopathy compared with a control group of term infants without NE. For infants with a birth weight <3$^{rd}$ centile, the risk of NE was 38.23 per 1000 births. Nelson at al. (2014) reviewed the maternal and infant records of 4165 singleton neonates with a gestational age of ≥36 weeks that met the criteria for inclusion in the Vermont Oxford Network Neonatal Encephalopathy Registry (VON) (Horbar, Soll, & Edwards, 2010). Data from the VON can be used to

examine patterns of perinatal care and identify need for improvement in care, and includes information on clinical antecedents of NE. Nelson et al. (2012) confirmed the findings of previous studies that several non-asphyxial factors such as infection, inflammation, birth defects, and intrauterine growth restriction are associated with NE. In 46% of cases there was an abnormal maternal or fetal condition prior to labour, including maternal hypertension (16%) and FGR (16%). Of all fetal conditions, growth restriction was the most common. The importance of antenatal recognition of SGA was emphasised by Locatelli et al. (2010), who investigated antenatal and intrapartum antecedents for NE, in a case controlled study of 27 infants with NE. Eleven percent of the babies were SGA, versus four percent of controls, suggesting that future strategies to reduce NE should focus on identification of antepartum risk factors as in cases such as SGA, there may be a lower threshold for hypoxic or ischaemic events during late pregnancy and labour. Similarly, in an earlier study by West et al. (2005), 17% of term babies with NE were SGA, with no confirmed evidence of antenatal diagnosis in most cases.

In a recent New Zealand multidisciplinary review of contributory factors and avoidability of NE, it was found that in 9 per 83 (10.8%) cases there were factors relating to failure of best practice in appropriate antenatal assessment of fetal growth and recognition of SGA pregnancies (Sadler, Farquhar, Masson, & Battin, 2016). The New Zealand and international literature raises the likelihood that better detection of SGA and timely delivery through introduction of GAP may reduce the burden of NE.

*(b) Neurodevelopmental delay*

Placental dysfunction resulting in FGR is an important risk factor for neurodevelopmental delay, even in the absence of NE. Preterm growth restriction is associated with abnormal motor skills and neurological delay, while cognitive impairment is more common in FGR that occurs at later gestations (Baschat, 2011). This suggests that pathophysiology may differ depending on gestation and the time sensitive vulnerability of the developing fetal brain (Baschat, 2011). Comparison of outcomes between preterm and term SGA infants found that term SGA infants had more problems with scholastic and vocational attainments (Shah & Kingdom, 2011), while preterm infants with severe SGA were more likely to suffer adverse motor and neuro-behavioural outcomes in childhood and adolescence.

*(c) SGA and childhood growth*

A challenge with interpretation of data concerning children born SGA is the lack of consistency on the definition of SGA. Historically, many have used population standards; yet, globally definition remains inconsistent. Despite inconsistency in definitions, it is established that a failure to reach optimal birth weight can affect the child's growth potential well beyond the perinatal period. Children born SGA are at risk of short stature and, according to Argente, Mehls, and Barrios (2010), 10% continue to be below the 3$^{rd}$ centile for height in adulthood. In this study, SGA was defined as a birthweight and/or length at least two standard deviations below the mean for gestational age. Similarly, US data from a study of 1100 children born SGA (birth weight <10$^{th}$ centile) showed that the risk of stunted growth (defined as height for age z score of -2) at five years was 6.8% (Xie et al., 2015). Those infants whose mothers were of short stature, including the co-occurrence of cigarette smoking during pregnancy, were at particular high risk. The link between sub-optimal fetal growth and poor growth in childhood might be multifactorial, as hypothesised by Xie et al. (2015) suggesting that stunted growth of children born SGA to short mothers could also be due to the limited genetic potential or possibly due to shared disadvantaged socio-economic factors.

*(d) SGA and renal function*

Children born with a very low birth weight are predisposed to kidney disease as they may have less nephrons compared to children with birth weights appropriate for their gestational age. In a study of kidney function in five year olds (Basioti, Giapros, Kostoula, Cholevas, & Andronikou, 2009), it was found that children born SGA had increased blood pressure, and alteration in uric acid and calcium excretion. These findings were related to the degree of growth restriction. As most nephrons form during the third trimester, impairment of fetal growth during this time may affect nephrogenesis and reduce the overall number of nephrons. This could increase the risk of future chronic renal disease (Luyckx et al., 2017), and be one of the pathways leading to an increased risk of adult cardiovascular disease as low nephron numbers are associated with hypertension (Luyckx et al., 2017).

*(e) Effects of SGA throughout a lifetime*

Barker and colleagues conducted the first research showing that adults born at low birthweights were at higher risk of cardiovascular disease (Barker & Osmond, 1986). Low birth weight has been linked with altered glucose tolerance (Newsome et al., 2003), and birth weight and abdominal circumference at birth have been inversely

related to systolic blood pressure in children, adolescents, and adults (Huxley, Shiell, & Law, 2000). There are several possible mechanisms leading to poor fetal growth and, while pathogenesis varies between early and late onset SGA, there is evidence that fetal adaptation to a reduced supply of nutrients permanently alters metabolism and physiology. Maternal undernutrition is one mechanism that has been extensively studied (Barker, 2003; Roseboom et al., 2001). It appears that the long-term effects depend on the timing during gestation at which the undernutrition occurred. There are critical periods for growth and development of fetal tissues and organs and the effect of undernutrition is gestation specific. For example, in the follow up study of babies born during the Dutch famine in World War Two, it was found that people exposed to famine at mid-gestation as fetuses were more likely to develop obstructive airway disease. As the bronchial tree grows most rapidly in mid pregnancy this may support the hypothesis that inadequate fetal nutrition permanently affects the fetal tissues during critical periods of growth and development (Roseboom et al., 2001).

Another hypothesis suggests that poor fetal growth may affect the endocrine system and alter the way that glucose and insulin metabolism are programmed during fetal development, leading to permanent alterations in physiology. A systematic review of 48 publications found that people who were born small had an adverse profile of glucose and insulin metabolism as adults, evidenced by higher insulin resistance but not insulin deficiency (Newsome et al., 2003). While it may not be possible to prevent many of the long-term effects of SGA, the GAP programme is designed to identify at risk pregnancies, provide a tool for improved antenatal detection, and to offer an evidence-based management plan to optimise outcome. In the next section, the question of whether detection improves neonatal and maternal outcome is addressed.

### *2.10 Does detection of SGA improve outcomes?*

While my study is focussed on improved antenatal recognition of SGA, there would be little incentive to adopt a programme such as GAP without evidence of improved outcome following detection of SGA.

#### *2.10.1 Neonatal outcome following detection of SGA*

A cohort study conducted by Gardosi, Madurasinghe, et al. (2013) showed that in a population of 92,218 singleton births including 389 stillbirths from 24 weeks, the risk of stillbirth amongst SGA babies was five times greater when undetected compared to when detected antenatally. While this study provides evidence that increased detection

of SGA is associated with a reduction in stillbirth risk, it is also necessary to establish if improved detection results in reduced perinatal morbidity.

A Swedish study by Lindqvist and Molin (2005) reviewed outcomes for 26,968 SGA babies. Composite neonatal outcome included serious fetal complications: hypoxic neonatal encephalopathy, intracranial haemorrhage, Apgar score <4 at 5 minutes, neonatal convulsions, umbilical artery pH <7, cerebral palsy, cognitive delay, stillbirth, and neonatal death. When compared to SGA babies who were identified antenatally, those SGA babies who were not identified antenatally had a 4-fold increased risk of adverse outcome. Additionally, the severity of adverse outcome was associated with the degree of growth restriction when non-detected, but not when detected. This study suggests that a structured antenatal programme for fetuses identified as SGA results in a lower risk of adverse outcome compared with outcome for cases of SGA not identified. In New Zealand, the NZMFMN SGA guideline recommends a schedule for follow up of SGA pregnancies once a diagnosis of SGA has been made by ultrasound (McCowan & Bloomfield, 2014). It is expected that antenatal detection will improve outcomes, but research in the New Zealand context is needed to confirm this.

### *2.10.2 Maternal Outcomes*

*a) Effect of detection of SGA on induction of labour and operative birth*

While it is important to ensure that management of pregnancy with a presumed diagnosis of SGA maximises safety for mother and baby, there is currently no internationally agreed consensus for timing of birth. Induction of labour is indicated when continuation of the pregnancy would increase maternal or fetal risk. Wood, Cooper, and Ross (2014) conducted a systematic review and meta-analysis to establish whether induction of labour for women with intact membranes increased the caesarean delivery rate. Out of 37 trials reviewed, only two related to FGR (Boers et al., 2010; van den Hove, Willekes, Roumen, & Scherjon, 2006). However, there was no associated increase in operative delivery; in fact, induction reduced the rate of caesarean section, compared to expectant management (OR=0.83, 95% CI, 0.76, 0.92). Conversely, Visentin et al. (2014) found that there was higher risk of caesarean section with SGA than for appropriately grown babies whether or not SGA was recognised antenatally. Timing of induction may affect maternal outcome, as found by Ofir et al. (2013), who reported a doubling of caesarean section rate when women with SGA pregnancies were induced between 37 and 38 weeks. In contrast, Bond et al. (2015) reviewed three trials which met the criteria for a Cochrane review of randomised or quasi-randomised controlled trials comparing expectant management versus planned early delivery for

women with a suspected compromised fetus from 37 weeks' gestation or more. Fetal compromise included SGA, decreased fetal movements or abnormal cardio-tocograph (CTG) or ultrasound findings. Two of the three trials involved induction for SGA (Boers et al., 2010; van den Hove et al., 2006), and one for oligohydramnios (Ek, Andersson, Johansson, & Kublicas, 2005). While confirmed pathological findings indicated need for urgent delivery, early delivery in term pregnancies with suspected fetal compromise did not reduce perinatal morbidity or increase the risk of caesarean birth. However, as the review was informed by only three trials, the authors cautioned against generalisation of findings for all term pregnancies with suspected fetal compromise. A more individualised approach seems warranted.

More recently a study in the UK (Veglia, Cavallaro, Papageorghiou, Black, & Impey, 2018) has contrasted outcomes following management of SGA according to the RCOG (2013) guideline which recommends induction of labour for all SGA pregnancies at 37 weeks, with a stratified induction of labour protocol. The stratified protocol recommends delivery at 37 weeks for those pregnancies where the estimated fetal weight is <3$^{rd}$ centile, there is an abnormal CPR (<5$^{th}$ centile) on Doppler velocimetry, an abnormal Ut. A Doppler at the 20-week scan, a reduced pregnancy-associated plasma protein A (PAPP-A) level or maternal hypertension. For pregnancies with a lower risk SGA fetus (i.e., EFW 3-10$^{th}$ centile, and a normal PAPPA-A finding, normal Dopplers and no maternal hypertension), the recommendation is for birthing by 40-41 weeks. With this risk stratification, there was a reduction in maternal and neonatal morbidity in both the high and low risk groups (see Figure 11). This approach fits well with the NZMFMN SGA guideline (McCowan & Bloomfield, 2014), recommended by GAP.

*b) Emotional wellbeing*

Pregnancy and the postpartum period can be stressful for women regardless of pregnancy complications, and there are multiple factors involved with maternal mental health during the transition to motherhood. Fairbrother (2017) reported on the prevalence and incidence of maternal anxiety disorders in pregnancy and postpartum across levels of pregnancy complications, including stillbirth. As expected, the degree of anxiety correlated with the degree of pregnancy risk, and the author concluded that screening for anxiety should be implemented in pregnancy, particularly when the pregnancy is complicated. With more specific regard to maternal mental health, in the context of this thesis, a report on maternal health related quality of life for women who had been induced for SGA or managed expectantly during the DIGITAT

(Disproportionate Intrauterine Growth Intervention Trial At Term) study (Boers et al., 2010) showed that there was no difference in long term mental and physical health between the two groups at 6 weeks and 6 months postpartum. Notably, overall mental health in the two groups was worse than in the general population, perhaps due to anxiety over their complicated pregnancies and vulnerable babies (Bijlenga et al., 2011).

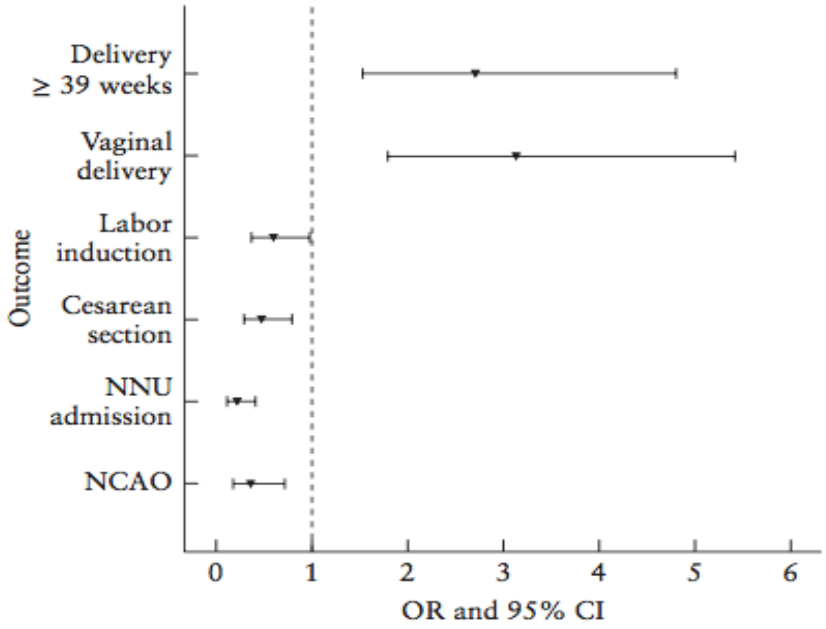



**Figure 1** Plot of odds ratios (OR) with 95% CI for risk of main maternal and neonatal outcomes for pregnancies complicated by small-for-gestational-age (SGA) fetus managed expectantly following risk stratification, with SGA group managed by delivery at 37 weeks as reference (dashed line). NCAO, neonatal composite adverse outcome; NNU, neonatal unit.

*Figure 11. Outcomes for SGA pregnancies managed expectantly according to risk stratification vs delivery at 37 weeks*

Reproduced with permission from Veglia et al. (2018, p. 69).

### *2.11 Conclusion*

In conclusion, the aim of GAP is to improve detection of SGA, in the context of evidence which shows that timely detection of SGA improves neonatal outcomes. Introduction of GAP in the UK has been associated with stillbirth reduction and has the potential to improve perinatal outcome in New Zealand. While pregnancy complications are inevitably associated with maternal stress, holistic evidence based professional care has the capacity to reduce perinatal mortality, neonatal morbidity as well as maternal psychological stress.

The preceding section has introduced the GAP programme, and the problems associated with being born too small. While there is growing international support for the programme, there is lack of consensus about whether use of customised standards is superior to use of other growth references. In the context of introduction of GAP to a New Zealand DHB, and subsequently more widely through national introduction, it is important to be informed about other approaches and ensure the tools adopted are the best for the local context. The following section provides a discussion on customized compared with other growth standards.

## *Part two: Which fetal and birthweight growth standards should be used?*

### *2.12 Introduction*

In the context of international debate about customized versus population standards, part two of this chapter explores the issue of which standards should be used to assess fetal and newborn weight.

#### *2.12.1 Literature search*

The following search criteria were used: (1) SGA or small for gestational age or FGR or fetal growth restriction AND (2) customized growth charts or GROW AND (3) Intergrowth. Secondary sources (Cochrane database): No relevant systematic review articles were found. Primary Sources: Cinahl, Medline via EBSCO interface and Web of Science were searched with no limitations for date or language but restricted to English. Reference lists of selected papers provided further sources.

### *2.13 Fetal growth standards*

While I have discussed the importance of appropriate monitoring of fetal growth and accurate identification of SGA as a key aspect of safe perinatal care, there is lack of international consensus on which fetal growth and birth weight standards should be used. While this thesis focuses on use of customized standards, the following section presents a review of other standards in use globally. It is important to review and critique all options to ensure the standards adopted serve the population well.

Fetal growth charts may be derived from ultrasound fetal measurements or from birth weight data, and there may be considerable differences depending on whether the standards represent a population or individual growth potential. Hui (2008) stated that the "ideal fetal growth chart should be created from a representative sample of the local population" (p. 12). However, standards derived from populations include data from premature births and prematurity is frequently associated with pathology; therefore, the

complication which leads to spontaneous or iatrogenic preterm birth may affect fetal growth. It is recognised that premature babies are disproportionally affected by FGR; consequently, standards derived from birthweights of premature babies are likely to involve negatively skewed linear growth curves (Hui, 2008). As previously mentioned, the commonly used population fetal growth charts developed by Hadlock et al. (1985) were derived from an unselected population including women who gave birth prematurely. Conversely, customized antenatal growth charts are derived from fetal growth standards in ongoing pregnancies. An optimal, individually adjusted weight at term, is combined with a proportionality growth curve, derived from an intrauterine growth formula. Thus, customized fetal growth is defined by the GROW curve (Gardosi, 2005), introduced in section 2.4.3; whereas population fetal growth standards represent the population from which data was derived but may not apply to the population for which they are used, and do not adjust for individual maternal variables which may affect fetal growth.

### *2.14 The variables that affect fetal growth*

Gardosi et al. (1992) demonstrated, using regression analysis, that in addition to gestational age and fetal sex, four maternal characteristics were significant independent determinants of birthweight in a cohort of 4179 women in Nottingham. These were: weight at first antenatal visit, height, ethnic group, and parity (all $p < 0.0001$). Subsequently, the inclusion of ethnic group has been challenged (Braun & Wentz, 2017; Lockie, McCarthy, Hui, Churilov, & Walker, 2017; Papageorghiou et al., 2018; Villar et al., 2014); hence, the following discussion will explore the question of ethnicity as a determinant of fetal growth.

#### *2.14.1 Ethnic origin - does it matter?*

The accuracy of self-reported ethnicity has been examined in a recent Australian study (Lockie et al., 2017), and it has been argued that infant smallness in some ethnic groups may be due to pathology related to nutrition, environment, and socio-demographic factors. Additionally, in non-isolated populations, factors such as invasion and migration add to the complexity of race and ethnicity (Papageorghiou et al., 2018). Furthermore, Braun and Wentz (2017) proposed that continued use of ethnicity as a variable in customized growth models is not socially or scientifically defensible as customized growth standards may mask underlying socio-economic circumstances that affect fetal growth.

### *2.14.2 Ethnic specific standards and perinatal outcome*

Kierans et al. (2008) tested the case for ethnic-specific standards of fetal growth with data from all births covering a 20-year period in British Columbia. They compared four ethnic groups, Chinese, South Asian, North American Indian, and 'other' for perinatal mortality, mean birth weight, and SGA based on both a single population standard and ethnic specific standards. Findings revealed a concordance of perinatal mortality with SGA rates when ethnic specific standards were used but not when a population standard was used. Further convincing evidence to support inclusion of ethnicity as a variable in a customized standard was presented with the results of a study involving 100,463 pregnancies in the US (Hanley & Janssen, 2013). Using multivariable logistic regression, the study compared the ability of ethnicity specific and population-based growth standards to predict Apgar <7 at 5 minutes, extended hospital stay, hypoglycaemia, and infection. Newborns considered SGA by ethnic specific growth standards had double the risk of adverse outcomes compared to those considered SGA by population standards, suggesting that ethnic specific standards perform better than population standards at identifying which babies are most at risk. While the concept of ethnicity is debatable in modern society, the preceding evidence suggests that inclusion of ethnicity in a customisation model for fetal growth remains valid, although socio-economic factors may overlap with ethnicity and merit consideration.

### *2.14.3 Socio-economic factors*

While it has been suggested that differences in fetal weight may be more affected by socio-economic factors than ethnicity, the social determinants of FGR are not well understood. In an American study with 2463 women enrolled in 52 community clinics across 5 Michigan communities, multiple indicators of socioeconomic status from childhood to adulthood (socioeconomic mobility) were measured (Slaughter-Acey, Holzman, Calloway, & Tian, 2016). Upward mobility from low to middle/upper class was associated with a reduced risk of delivering a growth restricted baby (OR=0.34, 95% CI 0.17, 1.69). Conversely, the risk of delivering a growth restricted baby for downwardly mobile women was increased (OR=2.23, 95 % CI 1.10, 4.51). Nevertheless, white women who experienced downward mobility retained an advantage in fetal growth compared to their black counterparts.

Likewise, a Swedish study (Dejin-Karlsson & Ostergren, 2004) suggested that the almost doubled risk of SGA in mothers of foreign origin was most probably linked to a disadvantaged social situation. Whether this effect is due to social or ethnic determinants is not clear, but it is established that a disadvantaged social situation

influences uptake of smoking in young people (Mathur, Erickson, Stigler, Forster, & Finnegan, 2013) and that smoking affects fetal growth (McCowan, Dekker, et al., 2009; Naeye, 1978; Sabra, Gratacos, & Gomez Roig, 2017). The model used by Gardosi (1995) for calculating customized growth potential addresses this question and calculates the differences in growth and weight which still exist after excluding pathological factors such as smoking.

### *2.15 Customized fetal growth standards in the New Zealand context*

In the New Zealand diverse multi-ethnic population, customized standards perform well at identifying SGA babies at risk of adverse outcome (Anderson, Sadler, Stewart, & McCowan, 2012). The following GROW charts show the difference in term optimal weight and growth curves for an Indian baby (3303g.) (Figure 12) compared to a Tongan baby (3536g.) (Figure 13. GROW chart for a Tongan woman (fictitious name) where both mothers have the same BMI and parity.

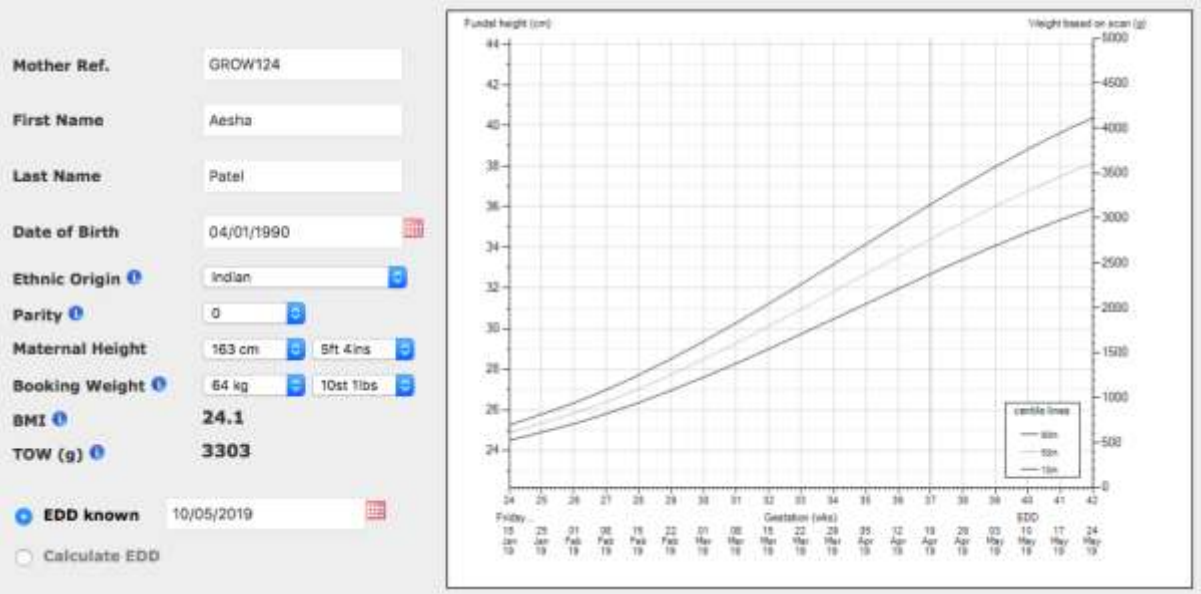



*Figure 12. GROW chart for an Indian woman (fictitious name)*

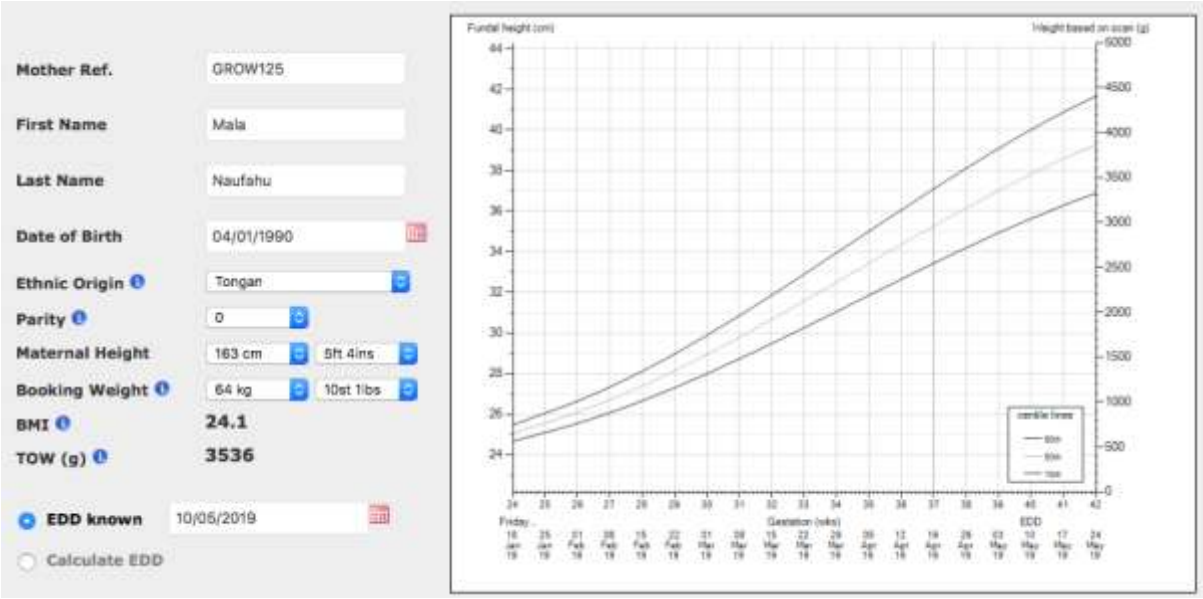



*Figure 13. GROW chart for a Tongan woman (fictitious name)*

### *2.16 International fetal growth standards*

While I have presented an argument in favour of customized standards, it is useful to consider other research which has led to the development of alternative models. There are four major longitudinal cohort studies that have developed growth charts; the Eunice Kennedy Shriver National Institute of Child Health and Human Development Fetal Growth Study (NICHD) (Buck Louis et al., 2015), which was designed to assess whether there were differences in ethnic specific fetal growth standards in the US, the WHO Multicentre Growth Reference (MCGRS) study (World Health Organization, 2006), the WHO fetal study (Kiserud et al., 2017; Merialdi et al., 2014), and the Intergrowth 21$^{st}$ study (Villar et al., 2014).

#### *2.16.1 NICHD*

For the NICHD study, data were derived from women in 12 states in the US, including 2334 healthy women with low risk singleton pregnancies. Exclusions were preterm birth, stillbirth, and fetal structural and karyotype anomalies. NICHD intended to develop a pooled standard for fetal growth if no racial/ethnic differences were found but the study identified significant differences in birthweight between ethnicities resulting in their publication of standards based on ethnicity/race.

#### *2.16.2 WHO MCGRS*

The WHO MCGRS study aimed to develop a universally applicable international growth reference to describe the growth of healthy children from birth to 5 years, based on the impression that babies and children raised in environments with no constraints on

growth, and who were breast fed according to WHO criteria would grow to an optimal size (World Health Organization, 2006). Data were derived from six international sites and included 8440 children. While WHO MCGRS is not a fetal growth reference it is included here for context, as the WHO fetal study, described next, was designed to add a reference to WHO MCGRS to complete a seamless fetal/childhood growth reference.

### *2.16.3 WHO fetal*

The WHO fetal study (Kiserud et al., 2017; Merialdi et al., 2014) included data from 1387 healthy women with low risk pregnancies from 10 countries in Africa, Asia, Europe, and South America. Repeated ultrasound biometric measurements were performed, showing that fetal growth varied significantly between countries, particularly in late pregnancy. There were also significant differences in EFW between the NICHD individual ethnicities, WHO fetal, and Intergrowth 21st pooled (**Error! Reference source not found.**) as well as between some countries (Table 4). The researchers concluded that the pooled data could be used cautiously internationally, especially where no local data exist, but may need customisation or adjustments for specific populations.

*Table 3. EFW at 50th centile at 39 weeks for NICHD, WHO fetal, and Intergrowth 21st*

| Standard | EFW (grams) |
|---|---|
| **NICHD** | |
| White | 3502 |
| Hispanic | 3330 |
| Asian | 3263 |
| Black | 3256 |
| **WHO Fetal (pooled)** | 3403 |
| **Intergrowth 21st (pooled)** | 3186 |

### *2.16.4 Intergrowth 21st*

The Intergrowth 21st study (Villar et al., 2014) was based on the premise that educated well women would give birth to babies with an optimal birth weight unaffected by ethnicity. In a seemingly contradictory finding, with data from births across eight countries, birth weights at term varied from Indian with a term birthweight of 2.9kg to the UK with a term birthweight of 3.5kg. In response to challenges regarding the findings, Intergrowth 21st researchers (Villar et al., 2015) stated that they did not intend

to compare birth weight or newborn length between countries; rather develop a tool to compare values against international standards that were constructed with all populations combined.

While the principles of Intergrowth 21st may have been interpreted as leading to the debatable finding that all babies, regardless of ethnicity, grow to the same optimal birthweight if maternal conditions are ideal, the matter is not so simple. More precisely, Intergrowth 21st researchers have demonstrated that measures of skeletal growth are similar across diverse geographical settings when mothers' health needs are met in the absence of environmental constraints on growth. Skeletal growth was chosen as the outcome measure to avoid fat-based indicators such as the abdominal circumference when comparing populations to formulate growth standards. For example, mean term birth length varied only a small amount from 48.6-49.8cm between ethnic groups. Markers of skeletal or linear growth are recommended by Intergrowth 21st because they are mostly resistant to skewing in response to excessive maternal nutrition and unlike fat-related indicators they are more precisely measurable. Regardless of this, the important consideration must be the detection of the at-risk fetus and baby, and the relative performance of each growth standard.

### *2.16.5 Comparison of NICHD, WHO Fetal and Intergrowth 21st fetal growth standards*

A comparison of the above studies was conducted with a focus on the aims, analytical approaches, and sampling frames (Grantz, Hediger, Liu, & Buck Louis, 2018). A key point of difference was the question of whether a single growth reference can be used to assess fetal growth, irrespective of ethnicity or country of origin. Analytical approaches between the three studies varied. Fetal weight and biometry were estimated by NICHD and WHO Fetal, using the Hadlock formula which uses FL, AC, and HC (Hadlock et al., 1985); while Intergrowth 21st estimated fetal weight and biometry by creating a new formula based on HC and AC, but not FL. This discrepancy may render the comparison of EFW between the standards less meaningful.

Additionally, comparison of the 50th centile for EFW at 39 weeks using the three studies suggests that there may be considerable differences according to ethnicity/race, and that pooled data may not be accurate for detection of abnormal fetal growth (Table 3).

Despite the subsequent pooling of data to derive an international standard for fetal growth, the WHO fetal study found country specific differences which compared

to the NICHD findings for ethnicity/race. For example, the 5th centile varied as below (Table 4).

*Table 4. Country specific differences in EFW at 5th centile in WHO fetal study*

| Country | EFW (grams) |
|---|---|
| Norway | 3200 |
| Egypt | 2700 |
| Pooled data from all countries | 2800 |

While these differences were reported, the WHO fetal study proceeded to pool data as the primary aim of the study was to be consistent with principles used in the WHO MCGRS study which had pooled data for growth from 0-5 years. Similarly, Intergrowth 21st examined the differences in crown rump length, head circumference and newborn length among countries; while they found differences between countries, these were not considered important and data was similarly pooled. Despite this, in their analysis, Grantz et al. (2018) concluded that the reported magnitude of variation between and within sites reported in Intergrowth 21st could be highly significant. The variation between and within populations does open the question of whether a customized model of fetal growth might perform better at identifying inappropriate fetal growth and, in so doing, improve perinatal morbidity and mortality.

### *2.16.6 Risk of perinatal death according to GROW or Intergrowth 21st*

Using a UK National Health database of 148,276 pregnancies, fetal weight curves based on Intergrowth 21st ultrasound scan parameters were compared with GROW customized standards to determine which birth weight standards best identified at risk SGA babies (Francis & Gardosi, 2015). 19,990 (13.5%) of the babies were SGA by customized standards, whereas only 9,100 were SGA (6.1%) by Intergrowth standards. Of these, 432 (4.7%) babies classified as SGA by Intergrowth 21st were not SGA by customized standards, highlighting significant differences. Compared to babies who were not SGA by either standard, the group who were SGA by customized standards only, had a significantly increased risk of perinatal death (OR=2.0, 95% CI 1.6, 2.5). In contrast, babies who were SGA only by Intergrowth standards had no increased risk of perinatal death (RR=1.1, 95% CI 0.1, 3.4). This suggests that a birth weight standard based on Intergrowth 21st may fail to recognise many SGA babies who are at risk of perinatal death.

Many studies have found that being SGA by customized standards is associated with increased risk of pathological outcomes compared to SGA defined by population

standards, including Intergrowth 21st (Anderson, Sadler, McKinlay, & McCowan, 2016; Clausson et al., 2001; Figueras et al., 2007; McCowan, Harding, & Stewart, 2005).

### *2.16.7 Comparison of Customized and Intergrowth 21st fetal growth standards*

In the first published multinational comparison of customized standards and Intergrowth 21st (Francis, Hugh, & Gardosi, 2018), both standards were applied to a cohort of 1.25 million term pregnancies from 10 countries. There were wide differences between the two standards in the proportions identified as both SGA and LGA.

Using Intergrowth 21st standards, the range of SGA for the cohort was 3.1-16.8% (average 4.4%) while the range for LGA was 5.1-27.5% (average 20.6%). This could represent physiological variation between populations. For instance, the high SGA rate reported for India (16.8%) in a cohort of middle-class Indian women seems high compared to the rate of 11.3% calculated for this cohort by customized standards. In contrast, application of customized standards showed that the range of SGA was 10.1-12.7% (average 10.5%) and the range for LGA was 7.3-9.9% (average 9.5%) (Francis et al., 2018).

Over-estimation of SGA may lead to parental concern and unnecessary investigations or interventions for the pregnant woman and neonate. Conversely, at risk pregnancies and neonates may not be recognised as small and may be missed by Intergrowth 21st standards. In the comparison of customized versus Intergrowth 21st standards (Francis et al., 2018), of the 10.5% of cases defined as SGA customized, 4.3% were also SGA by Intergrowth 21st with a relative risk for stillbirth of 3.5 (95% CI 3.1, 4.1). According to Francis et al. (2018), 60% of the customized SGA babies were not SGA by Intergrowth 21st; therefore, would be missed by Intergrowth 21st, but had a relative risk of 1.9 (95% CI 1.6, 2.2) for stillbirth. In contrast, a prospective observational study of 1055 women in Washington, US, compared customized and Intergrowth 21st standards for detection of neonatal SGA and adverse neonatal outcome. While the customized standard performed better at detection of neonatal SGA, neither of the standards performed well in prediction of immediate neonatal adverse outcome (Odibo, Nwabuobi, Odibo, & Tuuli, 2018).

## *2.17 Birth weight standards*

### *2.17.1 Intergrowth 21st birth weight standards in the New Zealand setting*

In their New Zealand based study, Anderson and co researchers compared adverse neonatal outcomes among SGA infants between the Intergrowth -21st and customized birthweight standards in a sample of 53,484 births at ≥33 weeks from the general

population of women birthing in Auckland between 2006 and 2013. Composite adverse neonatal outcome was defined as neonatal death, neonatal intensive care admission >48 hours, or ventilation >4 hours, or 5-minute Apgar score <7.

The Intergrowth 21st standard failed to detect a significant number of at-risk SGA infants, in particular amongst ethnic groups with larger maternal size, while identifying a disproportionate number of SGA in ethnicities with women of smaller size. Using the Intergrowth 21st standards, the incidence of SGA was 4.5%, while using customized standards it was 11.6%. Compared to those not identified as SGA by either standard, those identified by both Intergrowth 21st and customized standards had the highest risk of adverse outcome (RR 4). Customized standards identified more than three times as many SGA babies amongst Maaori[3], European, and Pacific ethnicities; and twice as many amongst Asian ethnicities compared to Intergrowth 21st. Intergrowth 21st birth weight standards need further evaluation before being implemented in a New Zealand multi-ethnic setting.

### *2.17.2 Customized and population birth weight standards*

There are several key players in the debate concerning which birth weight standards should be used. Customized fetal growth standards have been described in the context of GAP earlier, and I have compared customized and Intergrowth 21st fetal and birth weight standards. While customized birth weight standards are gradually being implemented internationally (Gardosi et al., 2018), it is important to recognise that there are alternative standards in use. The use of population birthweight centiles was reported almost 60 years ago (Lubchenco, Hansman, Dressler, & Boyd, 1963) following a study at Colorado General hospital in the US. Data were limited, however, in that it only included Caucasian infants and contained an undeterminable bias because of the inclusion of premature infants to provide a continuum of birth weights between 24 and 42 weeks. While it has been common practice to use population birth weight centiles with neonates being classified as SGA if the birth weight is less than the 10th centile, the use of population standards may under or overestimate the risk of SGA. For example, in ethnic groups with smaller than average maternal size, infants may be naturally (constitutionally) smaller but not growth restricted and the opposite applies to ethnicities with larger than average maternal size. While current population standards may represent a range of variables within a given population, customized birth weight

[3] This is the spelling for the Tangata Whenua (people of the land), who belong to the Tainui Rohe (territory) in which CMH is situated.

standards, adjusted for maternal physiological variables have been found to perform better at identification of SGA at risk of morbidity and mortality in the New Zealand context (Anderson, Sadler, Stewart, Fyfe, & McCowan, 2012).

### *2.17.3 Birth weight centiles in New Zealand*

Currently, in New Zealand, where customized antenatal growth charts are well established in pregnancy care and a customized birth weight centile is generated at birth as part of the GAP programme, there is ongoing discussion as to the most appropriate birth weight centiles to guide neonatal practice. The WHO (2006) population standards and Intergrowth 21$^{st}$ (Villar et al., 2014) birth weight standards are in use internationally, including in some New Zealand hospitals. However, with the introduction of GAP, use of customized birth weight centiles is increasing. The first global customized birthweight centile calculator has recently been released by the gestation network, and is adjusted for more than 100 ethnicities or countries of origin, as well as maternal parity, height, early pregnancy weight, and baby's sex (https://www.gestation.net/cc/about.htm).

## *2.18 Unwanted effects of misclassification*

### *2.18.1 Over and under-diagnosis of SGA*

Antenatal over-diagnosis of SGA could lead to unnecessary investigations and intervention as well as considerable parental anxiety when in fact babies may be growing appropriately for their individual potential. Conversely, with the low SGA rate using the Intergrowth 21$^{st}$ it is possible that many SGA babies will be unrecognised after birth because they are assessed as being above the 10$^{th}$ centile and any increased risk of morbidity in the neonatal period remains unknown. This potential misclassification raises the issue of safety and the possibility of incorrect allocation of resources with financial implication for health providers.

## *2.19 Conclusion*

The concept of a seamless growth standard and one international standard to monitor growth from conception to 5 years ("womb to classroom") (Villar et al., 2015, p. 494) is very attractive. However, at the point of writing, there is no evidence to support Intergrowth 21$^{st}$ as a tool which is superior in the identification of SGA and prediction of perinatal risk. The tool does not perform well in the New Zealand multi-ethnic population for fetal or newborn birth weight standards. Further research is needed to

evaluate the utility of Intergrowth 21st as a prediction model for SGA and perinatal risk internationally.

Arguments about the pitfalls of self-reported ethnicity are valid and the issue of what defines ethnicity remains debatable. In the meantime, the global version of GROW provides a universally applicable, yet customized standard, for fetal growth (Francis et al., 2018). Many studies indicate that customized standards perform better at identification of SGA at risk of morbidity and mortality but there needs to be a structured and evidence-based programme such as GAP to monitor pregnancy once SGA is detected. Introduction of GAP at a DHB, in conjunction with the NZMFMN SGA guideline, potentially provides a framework for a seamless programme from identification of risk for SGA at booking through to planning for optimally timed and safe birthing. Evaluation of this introduction at CMHh is the driving force for this study.

# Chapter 3. Introducing Change in Maternity Practice: The GAP and the New Zealand Context

## *3.1 Introduction*

In 2009, obstetrician Alphonse Roex, triggered by concern about the number of undetected cases of SGA babies, introduced the use of the Perinatal Institute's GROW charts into a large teaching hospital in Adelaide, Australia (Roex et al., 2012). Roex reported a doubling of detection of SGA following introduction of GROW charts. However, success was not without challenges and he received some resistance; "Change, even for the better, is hard to achieve, as is clinicians' compliance" (Roex et al., 2012, p. 81).

As described in Chapter 1, use of GROW charts is a key element in the GAP programme. This chapter focuses on the politics of change in a national maternity system, in respect to introduction of the GAP programme nation-wide in New Zealand.

## *3.2 Background: Implementing GAP in the UK*

The GAP programme, as introduced in Chapter 2, section 2.4, originated in the West Midlands, UK, in 2009, and gradually extended to other regions (Clifford et al., 2013). Prior to availability of GAP, there had been education for the use of GROW charts. However, it was evident that the comprehensive expanded programme was associated with better detection of SGA and perhaps a reduction in stillbirth (Gardosi, Giddings, et al., 2013). To date, GAP has been implemented in 80% of NHS trusts in the UK (Perinatal Institute, 2018).

## *3.3 Introduction of GROW and GAP in New Zealand*

### *3.3.1 Early use of GROW*

From 2007, the use of GROW charts and customized birthweight centiles slowly began in New Zealand. During this period, individual practitioners and DHBs intending to use GROW requested a licence from the Perinatal Institute and were supplied with the software free of charge. Practitioners using GROW charts were not required to undergo formal education during this time, but there were simple instructions about interpretation of fundal height and examples of GROW charts with normal and suboptimal growth patterns available on the Perinatal Institute website. There was no nationally accepted guideline for management of SGA pregnancies in New Zealand

until some years later when the NZMFMN developed their guideline (McCowan & Bloomfield, 2014).

### *3.3.2 Education for use of GROW*

Professor Lesley McCowan, a recognised international expert in fetal growth, delivered lectures on the use of GROW to detect SGA at various professional meetings in New Zealand from 2007. Following this, in 2010, Professor Jason Gardosi, the director of the Perinatal Institute, whose original work in the 1990s led to development of customized growth standards and the formulation of GROW charts (Gardosi et al., 1992), visited New Zealand and was invited to present several regional lectures on the topic of fetal growth restriction and the use of GROW, co-sponsored by the NZCOM and the Midwifery and Maternity Providers Organisation (MMPO) (https://mmpo.org.nz). Then, for a three-year period (1st April 2011 to 31st March 2014), a very brief overview of use of GROW was included in the technical skills component of the New Zealand Midwifery Council's compulsory recertification programme.

While, for several years, individual practitioners could use GROW charts without formal education, detection and follow up of suspected SGA was inconsistent across the country. After the realisation in the UK that formal education in the context of the comprehensive GAP programme was associated with better detection of SGA and perhaps an associated reduction in stillbirth (Clifford et al., 2013), the Perinatal Institute required users of GROW in the UK to undertake education and accreditation. Nonetheless, in New Zealand it was not mandatory until some years later, when access to the software was associated with a requirement for clinicians to attend a workshop or complete e-learning to become accredited users.

In February 2014, Professor Gardosi invited two New Zealand midwives (one of whom is me) to Birmingham to work for 2 weeks with the Perinatal Institute team, to be able to offer accredited education for the use of GROW charts in New Zealand. Following this, the two New Zealand trainers offered free workshops on the use of GROW in every New Zealand DHB. The workshops were enthusiastically attended in 14 out of the 20 DHBs. The remaining DHBs had initially accepted the offer of workshops but subsequently cancelled due to uncertainty about support from professional colleges.

Between 2014, when accredited GROW education became available in New Zealand, and 2016, when the first DHBs introduced GAP (GROW now combined with education about risk selection and management of SGA), the Perinatal Institute advised all New Zealand GROW chart users that accredited education was required to have

continued access to the GROW software. However, this mandate was not strictly adhered to. Consequently, many midwives and doctors continued to use GROW charts without formal education. To address this issue, a series of online workshops were made available for practitioners who were unable to attend a face to face workshop, and the option of e-learning was also available during this time.

### *3.3.3 Implementation process*

While the lack of a formal process of implementation based on a recognised theory may be viewed as a limitation, the programme is well established in the UK, and aspects of the programme such as education and guidelines were adapted to suit the New Zealand maternity system. In comparison with a recognised structure for design and evaluation of complex interventions to improve health as proposed by Campbell et al. (2000), the key phases are in fact aligned. For example, the introduction of GAP in New Zealand is based on a theoretical framework, including studies which have demonstrated effectiveness in the UK, and components of the intervention have been, and continue to be evaluated as part of the auditing which is an element of GAP.

## *3.4 Change is challenging*

There had been no apparent tension around use of GROW in New Zealand while it was entirely up to the practitioner to adopt the tool or not, with or without education. However, the requirement to undertake education to use GROW led to professional tension. Change in practice can be fraught with challenges and the move to require clinicians to engage in accredited education met with some fierce resistance.

### *3.4.1 Professional tensions*

Following the introduction of accredited GROW workshops in New Zealand, and the ensuing professional tension, a series of maternity sector meetings were held as professional body leaders and the MoH maternity advisors argued in support of, or against, use of GROW. Evidence was debated, philosophical differences were raised, and concerns expressed.

While use of the GROW tool had started to be positively assimilated into New Zealand maternity practice and supported by midwifery and obstetric professional bodies over the years, the introduction of a requirement for users to undergo accredited education triggered serious concerns. These concerns included the perception that an education programme was being imposed on New Zealand clinicians by an overseas organization, a lack of structured central administration by the MoH, cost to DHBs of supporting staff to attend education, lack of RCT evidence for use of customized growth

charts, medicalization of midwifery practice, and unintended consequences such as false positive diagnoses of SGA leading to unnecessary intervention. Further concerns related to increasing workload, technical system challenges, overuse of stretched ultrasound resources, inequity of access to scanning services, undermining of professional expertise, extra educational and practice requirements for already over-worked professionals, and vulnerability of those who chose not to engage.

### *3.5 Considering the issues*

While some of the concerns are valid, many can be addressed; and all are interesting when viewed in the context of an initiative to offer free education for clinicians who had already chosen to use GROW charts in practice, although without formal education. The offer of education was to support a practice already established by many midwives and doctors, not to roll out a new initiative. Although a comprehensive GAP programme would be implemented a few years later, this was not anticipated at the time. There is still no RCT evidence to support use of customized growth charts but evidence from observational studies is increasing (Jayawardena & Sheehan, 2018; Roex et al., 2012). Importantly, Anderson et al. (2016) have demonstrated the advantage of customized compared with Intergrowth 21$^{st}$ birthweight standards to identify pregnancies at high risk of stillbirth and neonatal morbidity in the New Zealand population.

Fears that use of GROW would lead to medicalization of pregnancy care can be understood in the context of a strong New Zealand midwifery profession, characterized by partnership with women and a holistic continuity of care model which enhances and protects the normal process of childbirth. Alternatively, it could be argued that improved skills for recognition of at-risk SGA pregnancies would enhance rather than threaten the midwifery model of care. New Zealand midwives are scientifically informed and can work within the biomedical model of care without losing the unique woman-focused model of care that has always been at the heart of midwifery. Concern, such as the risk of false positive diagnoses as a possible unintended consequence, is reasonable, but it could be argued that missed SGA can lead to more devastating consequences. Another concern is increased demand for ultrasound services, but skilled use of GROW will reduce unnecessary scanning as well as target resources appropriately. There are inequities in access to and funding available for ultrasound in New Zealand; for example, in one DHB all growth scans may be provided free of charge and available within hours of request, whereas in another area most scans are provided in the community, require a co-payment from the woman, and may not be

available for several days, or in some cases, weeks. It might be argued that it is the under-resourced ultrasound services that should be addressed rather than serving as a barrier to introduction of best practice. Professional tension is inevitable when a tool which is perceived as a threat to a model of care is proposed, and when inequity of access to services is highlighted, but it is enlightening to view this through a philosophical lens as follows.

### *3.6 Professional tension examined*

The conflicting viewpoints of players within the maternity system may be understood through an exploration of their history. It ensures that past experiences affect the present and deposit within everyone, schemes of perception, thought and action, and an attitude of correctness of practice and its constancy over time. Midwives have been described as "guardians of normal birth" (Thompson, 2004, p. 215). The 'midwifery model' of care, seen as a model which protects physiological birth and promotes woman centred care, may at times appear to conflict with the 'obstetric model' of care, even when this is evidence based. It is apparent that clinicians may view evidence differently through the clarity of their individual lenses.

Paradoxically, the use of GROW reduces medical intervention in small women whose babies may be considered to be failing to reach their growth potential according to population standards. In the context of the debate about research evidence for GROW and GAP, it may be that the validity of research can be questioned by a profession because it is led by professionals from another discourse. The discourse around customized growth charts was introduced chiefly by an obstetrician (Gardosi et al., 1992), fuelled by a desire to prevent the tragedy of stillbirth associated with fetal growth restriction. Without doubt, this desire is shared by all parents and providers of maternity care. However, the introduction of GAP in New Zealand was challenged robustly by some midwifery leaders.

#### *3.6.1 Balance of power in maternity care*

As stated above, debate about the value or possible unintended consequences of GROW/GAP has led to strong professional tension and conflict.

In the GROW/GAP debate, midwifery leaders challenged the robustness of research underpinning the use of GROW. Science was formerly the domain of 'medical men', and the philosophical division in the field of maternity care was clearer. The balance of power appears to have changed, with more equal players, as well-informed and academically skilled midwives are able to access, question, and critique scientific

evidence. The tensions are now not primarily philosophical; although viewpoints and critique of research may be influenced by the philosophical lens of the viewer.

### *3.6.2 Newcomer increases tension*

The Perinatal Institute may be viewed as a newcomer in the field of maternity care that increases the tension between those currently in the field and itself. The current players in the field of maternity care are many and include, pregnant women and their families/whānau[4], the MoH, the National Maternity Monitoring Group (NMMG) (https://www.health.govt.nz/our-work/life-stages/maternity-services/national-maternity-monitoring-group), as well as the professional colleges.

GROW had been used for several years in New Zealand maternity care. However, if not for two politically naïve New Zealand midwives visiting the UK to train as GROW educators, the concerns and issue of whether the tool should be promoted nationally may never have been raised at MoH level in 2014. Their endeavours to offer GROW education on return to New Zealand unwittingly set in motion a lengthy debate which is outlined in the following section.

## *3.7 The path to consensus*

On 12th May 2014, a meeting of New Zealand maternity sector leaders, representing the NZCOM, DHB midwifery leaders, and The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), was held to discuss 'Systems for identifying and addressing the needs of growth restricted babies'. Introduction of accredited GROW education was debated, and it was accepted that, while it is not a perfect tool, GROW currently enables the best detection of small babies. It was recognised that growth restriction is associated with stillbirth and a range of other poor life course outcomes as evidenced from the PMMRC (2013) report which identified that approximately 40% of normally formed stillborn babies born after 24 weeks were growth restricted.

However, several issues of concern were raised at the meeting, including the timing of the introduction of accredited education in New Zealand, logistical problems regarding IT issues, clinical cover for DHB staff to attend workshops, possible cost of the license for GROW, access to ultrasound, and other urgent priorities within the health system such as mental health of mothers. It was agreed that more time would be needed to develop an integrated programme allowing for standardisation, education, quality

[4] Maaori term for family, used widely in New Zealand.

improvement and wider education about the correct application of GROW and management of babies suspected to be growth restricted. The suggestion was made that the nation-wide rollout of the GROW/SGA education programme should be deferred. An agreed action from this meeting was that the maternity advisors to the MoH, Dr Pat Tuohy and Ms Bronwen Pelvin, would draft a letter to the MoH regarding the adoption of a growth restriction detection and management programme by the Maternity Quality and Safety Programme (MQSP)[5], and to seek centralised funding for the project, and GROW licencing costs.

Later, in 2014, at the 21st November meeting of the NMMG, the issue of a nationwide rollout of GROW education was debated further. The NMMG was established by the Director General of Health in 2012 to provide oversight of New Zealand's maternity system, acts as strategic advisor to the MoH on areas for improvement in the maternity sector and provides a national overview of the quality of New Zealand's maternity services. While this meeting did not lead to a resolution, a positive outcome was achieved on 19th June 2015, when it was decided by all stakeholders involved at the final meeting of maternity leaders and MoH advisors that use of GROW should be implemented in each DHB. As such, a letter was sent from the MoH to all DHB clinical directors with the following message:

> ***GROW system of detecting Intrauterine Growth Restriction/Small for Gestational Age***
>
> *Through discussions with the stakeholders, the Ministry has developed the view that the GROW system that produces a customized growth chart is the agreed tool for use in New Zealand and is already in use in several DHBs. As the DHB clinical directors have decided a customized growth chart is necessary for an obstetric referral for suspected IUGR/SGA, the tool needs to be available to referring clinicians. It is each DHB's responsibility to ensure the GROW tool is available and to pay any licence fees required. They also need to ensure that all the clinicians who are using the tool have the necessary education to use it correctly as this is an essential component of the GROW system's efficacy-that clinicians are taking the measurements in the same way.* (Full letter, Appendix E)

While key maternity stakeholders eventually reached official consensus, and most New Zealand midwives and obstetricians have now incorporated GROW into their practice, individual opinions still reflect tensions with varying levels of engagement and commitment to the GAP programme.

[5] MSQP is part of the New Zealand Maternity Quality Initiative, involved with reporting and monitoring maternity services to the MoH (MoH, 2011).

### *3.8 Funding of GAP in New Zealand*

Following the communication from the MoH, the clinical directors responded collectively, stating that the funding for introduction of the GROW system should be provided by the MoH rather than the individual DHBs. However, there was no MoH funding available. By this time, the full GAP programme was available, and the Perinatal Institute offered this to New Zealand DHBs, rather than the use of GROW as a stand-alone package of software. Although several DHBs engaged with the GAP programme, on the understanding that costs would be reimbursed once a nationally funded program was established, the likelihood of a national GAP programme being established seemed increasingly unlikely.

Towards the end of 2016, the possibility of funding through the New Zealand ACC ( https://www.acc.co.nz/ ) was raised, as part of the strategy to reduce NE, under the umbrella of the NE taskforce. The lifetime cost of supporting one child with NE has been estimated at NZ$33-55 million (ACC, n.d.). In 2016, in New Zealand, there were 56 cases of NE in babies born from 37 weeks, an incidence of 1 per 1000 term births (PMMRC, 2018). While this incidence is low, the impact is high and affects the individual and family through and beyond their lifetime.

In New Zealand babies who are born SGA by customized birthweight centiles are twice as likely to be diagnosed with NE as babies whose weights are appropriate for gestational age (PMMRC, 2018). In 2013, the MoH, the Health Quality and Safety Commission (HQSC), and ACC agreed to work together on a joint treatment injury project. It was agreed that NE should be one of the first treatment injuries to be targeted. Therefore, introduction of GAP as a strategy which may increase detection of babies at risk of hypoxia, and lead to increased surveillance and optimal management, was to be considered by a multidisciplinary group of experts comprising the NE taskforce (ACC, n.d.).

The NE taskforce was set up in November 2015 to bring together experts from the health care workforce including clinicians, professional bodies, patient advocacy groups related to NE, and government agencies. The objectives of the NE taskforce are to design and establish an evidence-based improvement programme to reduce the number and severity of avoidable NE cases in New Zealand by:

a) Investigating, researching, identifying and describing the scope of the problem
b) Identifying, prioritising and testing potential solutions based on national and international best practice interventions; and

c) Co-ordinating and delivering effective evidence-based initiatives aimed at mitigating NE and establishing the monitoring and evaluation necessary to track the impact of these initiatives.

### *3.9 Business case for GAP*

A business case in support of ACC funding of the national GAP project, supported by a literature review which I co-authored with another research midwife and my supervisor (LM) (Appendix B), on the association between SGA and NE, was presented to the ACC NE taskforce on 24th October 2017. The outcome was that ACC agreed to fund the national introduction of GAP in New Zealand over a 3-year period. After several months of negotiations between the provider of GAP—the Perinatal Institute, and ACC, a contract was signed by both parties in July 2018. This was an agreement to fund GAP in New Zealand until July 2021, with a commitment to securing ongoing funding through the MoH, providing the introduction of the programme improved neonatal outcomes.

### *3.10 ACC GAP working group*

A multi-disciplinary working group was established to support the national introduction of GAP, with members representing the NZCOM, the Midwifery Council, and the RANZCOG, a senior neonatologist, a radiologist, a family representative, and myself as the New Zealand GAP lead educator. All members share the goal of improved outcomes for mothers and babies and, while each is shaped by their own perspective, they are collectively committed to the success of the programme, within and outside of the working group.

### *3.11 Evaluation of GAP in New Zealand*

While research in the UK has shown that introduction of GAP has been associated with a reduction in stillbirth (Clifford et al., 2013), this study is the first to evaluate the programme in New Zealand. The GAP programme includes software to provide quarterly reporting of suspicion and detection of SGA antenatally. Each DHB that engages with the GAP programme is required to conduct a baseline audit of detection of SGA prior to the introduction of GAP. Following introduction of GAP, clinicians in the hospital can access reports through GAP software to track the rates of suspected SGA (through fundal height measurement) and detected SGA (through ultrasound scan). A tool is provided to audit missed cases for ongoing quality assurance by identification of

themes regarding issues contributing to missed cases. All data are kept securely on a New Zealand server and in compliance with national privacy legislation.

### *3.11.1 Early evidence*

Between 2008 and 2016 in New Zealand, perinatal related mortality rates for SGA babies were approximately three times higher than for appropriate and large for gestational age babies. However during the same time, there has been a significant reduction in perinatal related mortality amongst singleton non-anomalous SGA babies (from 26 weeks), from 10.38 to 7.28 per 1000 ($p<0.05$ for trend) (PMMRC, 2018).There was no simultaneous reduction in perinatal mortality for appropriate and large for gestational age babies. Increased education about SGA in pregnancy, introduction of GROW charts, and use of the NZMFMN SGA guideline (McCowan & Bloomfield, 2014) have been acknowledged amongst factors likely contributing to this reduction in mortality amongst SGA babies (PMMRC, 2017).

### 3.11.2 National data

The data which will be available through the national introduction of GAP will be a valuable tool to evaluate the effectiveness of GAP programme by individual DHBs and at a national level. It is important to study the impact of national quality improvement programmes to ensure they are having the desired effect; therefore, ongoing collection of high-quality data is important. Each DHB will be supported to collect data on baseline detection of SGA prior to introduction of GAP and this will enable evaluation in practice as quarterly reports on detection of SGA following introduction are collated.

## *3.12 Significance of this study*

This study provides evidence about the effect of introduction of GAP at a large New Zealand DHB, which serves a population with a heavy burden of perinatal morbidity and mortality (PMMRC, 2018), and information which may inform ongoing wider introduction of the programme. While findings from one DHB may not be generalisable to another setting, this research is a beginning piece of evidence about GAP in New Zealand. Ongoing data collection can inform government policy makers, DHB managers, and clinicians to address how challenges might be overcome, and potential benefits of introduction can be developed further.

## *3.13 Conclusion*

Debate about the appropriateness of a programme which impacts on all clinicians and users of a maternity system is necessary and healthy. Midwives and obstetricians have

the shared goal of a healthy mother and baby at the end of every pregnancy. While tensions inevitably exist in the face of proposed change, a multi-disciplinary approach enables each player to be heard and respected, and for change to progress appropriately for the benefit of women and their babies.

While national data indicate that increased education about SGA, use of GROW and introduction of GAP are likely factors associated with a reduction in perinatal death amongst SGA babies, this study is the first to formally report the effect of GAP in a New Zealand DHB. At the time of writing this thesis, 13 out of 20 DHBs have implemented GAP, and dates are planned for 2 more DHBs before the end of 2019. It is hoped the remaining 5 DHBs will implement in 2020. While funding is currently secured through the ACC NE taskforce until July 2021, success of the programme will determine the case for longevity with ongoing support at national level.

# Chapter 4: Methods

## *4.1 Introduction*

This study included collecting data from all eligible births during defined audit periods prior to, and following, the introduction of GAP at CMH. The rationale was to evaluate the introduction of GAP at CMH and test the primary hypothesis that GAP would improve antenatal detection of pregnancies with SGA babies. This chapter will present ethical considerations, study objectives, hypotheses and outcomes, location of the study and the women served, the pre-GAP audit, introduction of GAP, the post-GAP audit, relevant definitions, and the research methods for comparison of pre-GAP and post-GAP outcomes.

## *4.2 Ethical considerations*

### *4.2.1 Ethical and facility research approval*

Approval for the study was initially sought through application to the Health and Disability Commission Ethics Committee, but this was deemed out of scope and the committee advised that ethical approval should be sought through Auckland University of Technology Ethics Committee (AUTEC). Approval was subsequently obtained from AUTEC—approval number 16/68 (Appendix F). Facility approval for research at CMH was then obtained through the CMH research office, approval number 7 (Appendix G).

### *4.2.2 Consent and confidentiality*

The study involved analysis of data from electronic and hard copy health records. There was to be no communication with participants or their care providers. To maintain confidentiality, all data were de-identified as soon as practicable during the research process. Excel spreadsheets containing data were password protected, and hard copies of notes were kept in a secure office in the medical records department at all times during retrieval and checking of data.

## *4.3 Objectives, hypotheses and study outcomes*

### *4.3.1 Objectives*

*(a) Primary objective*

To assess the effect of introduction of GAP on detection of SGA at CMH.

*(b) Secondary objectives*

1. To assess the impact of GAP on maternal outcomes in SGA pregnancies.
2. To assess the impact of GAP on neonatal outcomes in SGA pregnancies.

### *4.3.2 Hypotheses*

*(a) Primary hypothesis*

Introduction of GAP will improve antenatal detection of pregnancies with SGA babies.

*(b) Secondary hypotheses*

1. Amongst SGA pregnancies, introduction of GAP will be associated with:
    a) An increase in induction of labour
    b) No increase in caesarean section
    c) Reduced neonatal composite morbidity

### *4.3.3 Outcomes*

*(a) Primary outcome*

Antenatal detection of SGA babies; defined as those with birthweight less than the 10$^{th}$ customized birthweight centile (Anderson, Sadler, Stewart, & McCowan, 2012).

*(b) Secondary outcomes*

*(i) Maternal*

1. Proportion of women with induction of labour
2. Proportion of women with caesarean birth
3. Gestation at birth: proportion of preterm and post-term births

*(ii) Neonatal composite morbidity*

1. Neonatal unit admission for >48 hours
2. Apgar score <7 at 5 minutes
3. Respiratory positive pressure support (mechanical and non-invasive).

## *4.4 Location of the study*

### *4.4.1 Geographical location of Counties Manukau*

CMH is based in the region of Manukau in the upper North Island of New Zealand, and covers Manukau City, Franklin, and Papakura Districts. Small areas at the southern extent of the DHB area are part of Waikato and Hauraki District. The section shaded in red, in Figure 14, depicts the region covered by CMH.


*Figure 14. CMH catchment area*

Image: https://www.google.com/maps/d/viewer?mid=1B1MIBJx6zE3oK26SPB9lZHexW5U&ll=-37.21727439361485%2C174.92975450000006&z=10

### *4.4.2 CMH maternity facilities and the women served*

*(a) CMH maternity facilities*

CMH is the largest provider of maternity services in New Zealand (PMMRC, 2018), with 8079 women giving birth in 2012. For the period of the post-GAP study period, 1st April 2017 to 31st March 2018, 7409 women gave birth. CMH has one secondary/tertiary birthing unit and three primary birthing units. In 2012, 15% of women gave birth at one of the 3 primary birthing units, compared to 11% in 2017.

*(b)Women served by CMH*

*(i) Ethnicity*

CMH has one of the fastest growing DHB populations in New Zealand; and is ethnically diverse. The ethnicities of Counties Manukau women who gave birth in 2012 were reported as Maaori 22.4%, Pacific Island 35.6%, Chinese 8.4%, Indian 3.9%, other Asian 4.3%, and New Zealand European/other 25.4% (CMH, 2013b). Ethnicity is prioritised, which means that the ethnicity of a woman who identifies as more than one ethnicity is assigned with Maaori prioritised first, followed by Pacific, Asian, and then European. Prioritisation eliminates multiple ethnicities from hospital data but also under-represents individual diversity (CMH, 2018; Ministry of Health, 2004).

*(ii) Socio-economic deprivation*

More than 50% of the CMH population reside in areas of the highest deprivation as determined by the New Zealand Deprivation Index (NZDep) deciles 9 and 10. NZDep is an index of socio-economic deprivation (Atkinson, Salmond, & Crampton, 2014),

informed by census data on income, qualifications, family structure, housing, access to transport and communication. Scores 1-10 are assigned to areas; where 1 represents areas with the least deprived scores and 10 those with the most. The score relates to areas of residence; therefore, cannot be assigned to individual people. However, deprivation is an observable and demonstrable disadvantage relative to the community in which a person lives, although it is acknowledged to be an incomplete measure of the complexity of socio-economic status (Salmond & Crampton, 2012).

*(iii) Body Mass Index (BMI)*

CMH also serves a population with very high rates of obesity. Data for the population of women who gave birth at CMH during 2012/2017 showed that for women with a known BMI at booking, 1.2% were categorised as underweight, 31% normal weight, 26% overweight and 42% obese (BMI $\geq$30kg/m$^2$). The booking BMI was not known for all women (CMH, 2013a, 2018). There are marked inequities in rates of obesity amongst women in CMH, with rates in Maaori (50.6%) and Pacific (68.8%) much higher than in European women (27.8%) (CMH, 2018)

### *4.4.3 CMH maternity care providers*

Three models of maternity care have been available at CMH during the study periods. Each woman chooses a lead maternity carer (LMC) to provide maternity care from booking to completion of postnatal care at six weeks postpartum. In 2012, LMC options included self-employed (community) midwife or obstetrician; hospital led care, with all care provided by CMH midwives and obstetricians; and shared care, with most of the care provided by a general practitioner but intrapartum care and postnatal care provided by a hospital employed midwife. In 2012, 56% of women were booked by self-employed LMCs, 32% booked under the hospital care, and 11% received shared antenatal care (CMH, 2013a). In 2017, 71% of women booked with self-employed midwives, while 29% booked under hospital care, and there was no shared care. There are demographic differences between caseloads of self-employed and DHB employed midwives. European women, and those residing in areas of lower deprivation, more frequently booked with a self-employed LMC than a hospital LMC in both epochs (CMH, 2013a, 2018). If a woman is unable to enrol with a self-employed midwife LMC, because she books late for maternity care or has complex needs due to medical or maternity history, the woman generally accesses care from a CMH midwife or midwife specialist who provides antenatal and postnatal care at a community clinic or the woman's home.

### *4.5 The pre-GAP audit*

#### *4.5.1 Time period and study population for the pre-GAP audit*

*(a) Time period*

The rationale for choosing the time periods has been described in Chapter 1, section 1.10, so is only briefly revisited in this chapter. The pre-GAP epoch, January 1st to December 31st, 2012, was selected to be prior to introduction of formal education for users of GROW charts and predated every aspect of GAP apart from informal ad hoc use of GROW charts.

*(b) Study population*

The study population for the pre-GAP audit comprised all mothers who gave birth in the period at any of the CMH maternity facilities. The 5694 births booked under the care of self-employed midwives required exclusion from the audit as records for these pregnancies are retained by the midwives and were not accessible for review to determine the audit outcome of whether SGA had been detected or not. The remaining 2385 pregnancies for women whose care had been provided by hospital employed staff comprised the eligible study population prior to further exclusions.

#### *4.5.2 Retrieval of data for the pre-GAP audit*

Data for the pre-GAP audit were obtained through three electronic CMH databases: (1) Healthware ™, which is used for recording and storing clinical data; (2) the patient information management system (PiMS ™), primarily used for tracking, coding, and resource allocation; and (3) Concerto, a clinical workstation which allows access to clinical records including ultrasound scan reports. A senior clinical analyst for CMH Health Intelligence and Informatics Department obtained the required demographic and clinical data for all births from 1st January, to 31st December 2012 from Healthware ™ and PiMS™. Data included a randomly assigned number to replace the woman's specific national health index (NHI) number, maternal age, ethnicity[6], deprivation index, parity, date of last menstrual period (LMP), estimated date of delivery (EDD) by LMP, EDD by ultrasound scan, gestation and weight at booking, height, smoking, pre-existing hypertension, pre-eclampsia, stillbirth, induction of labour, date of delivery, gestation at birth, type of birth, sex of baby, birth weight, Apgar score at 5 minutes, any neonatal ventilation, admission to the neonatal unit for >48 hours, and neonatal death. All information was recorded on an Excel spreadsheet (Version 15.32) and a passcode

[6] Ethnicity was described according to New Zealand MoH level 1 ethnic codes (MoH, n.d.-a), rolled up from the level 2 MoH codes listed in Healthware™ for the pre-GAP epoch and in the Maternity Clinical Information System (MCIS) for the post-GAP epoch.

was required for access. The passcode was known only to the researcher and analyst. After calculation, using the bulk birth weight centile tool, as described in section 4.5.5, the customized birthweight centile was added to the dataset, and detection of SGA was included in the spreadsheet once determined according to the process described in section 4.5.7.

### *4.5.3 Data checking*

Data obtained from Healthware™ were checked for missing fields and major outliers in numerical variables (e.g., maternal age, booking gestation, and gestation at baby's birth). For all missing fields and information which appeared to have been entered in Healthware™ inaccurately, such as unlikely booking or delivery gestation, the clinical charts were hand searched and all fields were subsequently updated with accurate information. Where maternal booking weight but not height was available, data from previous pregnancies was obtained to complete the height data.

### *4.5.4 Exclusion criteria*

From the eligible population of 2395 pregnancies, further exclusions (with rationale in parentheses) were made as follows:

- Women booked >20 weeks 0 days (n=1008) (unreliable estimated date of delivery for accurate calculation of birthweight centile).
- Women booked <20 weeks and 0 days but no BMI (n=50) (unable to calculate customized centile as height and booking weight required).
- Women who gave birth <24 weeks and 0 days (n=15) (too early for fundal height measurement and plotting; therefore, effect of GAP not able to be assessed).
- Babies with congenital anomalies (n=143).
- Multiple pregnancies (n=128 babies) (unsuitable for fundal height measurement on GROW chart).

These exclusions resulted in a remaining eligible sample of 1105 pregnancies. See

Figure 15 for process of exclusion and identification of SGA pregnancies.

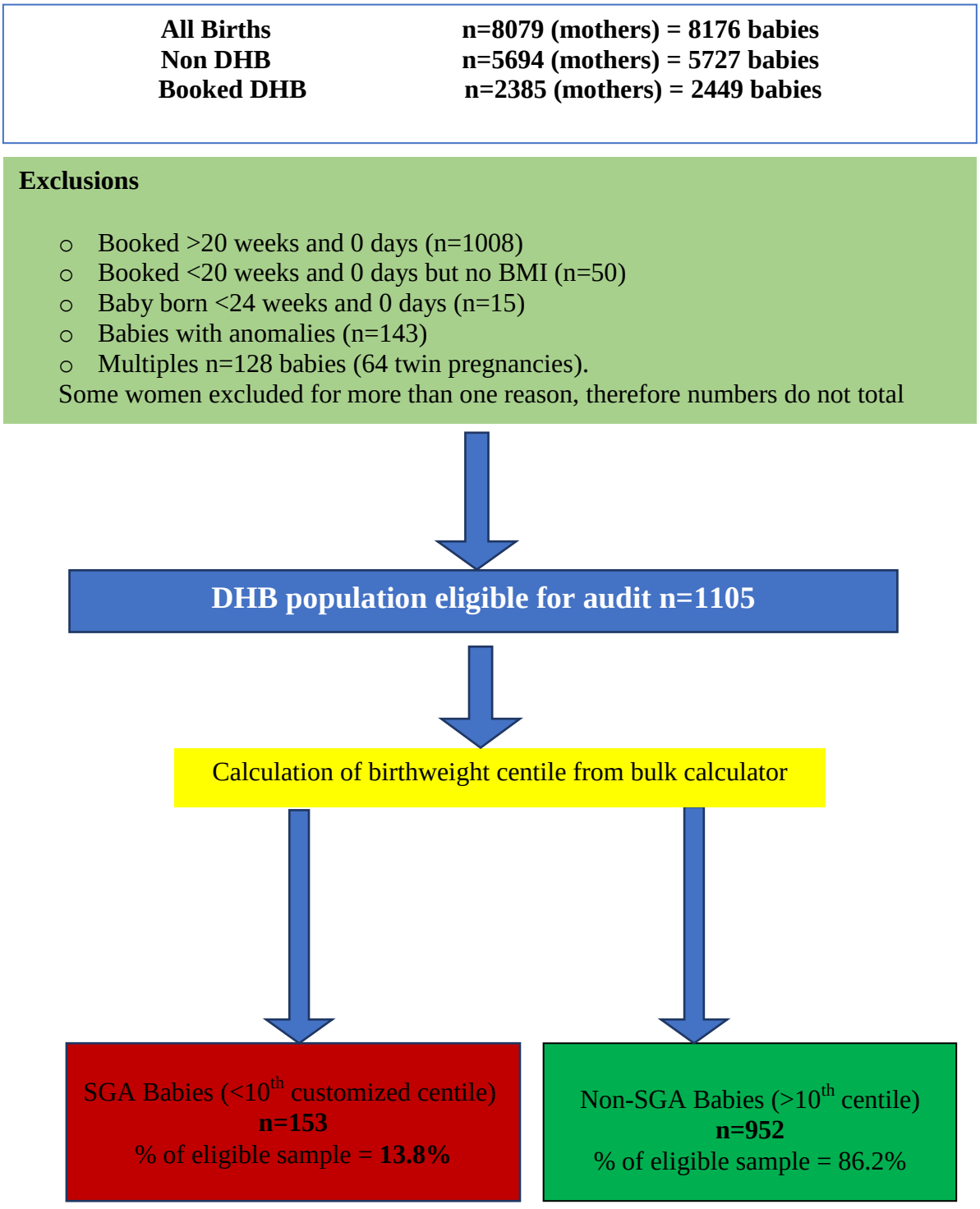



*Figure 15. Pre-GAP audit. Identifying the eligible population and SGA subgroup*

### *4.5.5 Determining the SGA sample*

Once all fields were accurately completed, a separate spread sheet was created with study number, maternal ethnicity, parity, height, weight at booking, gestation at baby's

birth, and baby's sex and birthweight. These data were applied to the Gestation Network's New Zealand bulk birthweight centile calculator version 6.7.8 (Anderson, Sadler, Stewart, & McCowan, 2012; Gardosi & Francis, 2016) (www.gestation.net) to identify the SGA babies (<10$^{th}$ customized centile). The calculator is an Excel spreadsheet into which a data base including maternal height, weight at booking, parity, ethnic group, gestational age at birth in days, sex, and weight of baby is applied. The tool calculates the customized birthweight centile for each baby. One hundred and fifty-three (13.8%) babies were found to be SGA and 952 (86.2 %) were non-SGA.

### *4.5.6 Pilot audit of clinical notes*

A pilot audit of 20 sets of notes was conducted to ascertain whether the required data points to describe the study population and pregnancy outcomes, as well as whether SGA was detected or not, were consistently recorded, before conducting the manual search of all notes for the 153 SGA babies. This audit revealed that maternal demographic and clinical variables, and maternal and neonatal outcomes, were consistently available. However, information regarding detection of SGA was inconsistently documented.

### *4.5.7 Process of establishing whether SGA was detected*

The notes of all women whose babies were identified as SGA using the bulk calculator were hand checked to ascertain whether SGA was detected by ultrasound scan. Ultrasound results were rarely documented in the notes, and growth scan reports were missing from the clinical record in 96/153 (63%) SGA cases.

To address the missing scan data, the missing scan reports were accessed electronically through the Concerto database, and information from scan reports were recorded on a separate Excel spreadsheet. Definition of detection/diagnosis of SGA in the pre-GAP audit was the same as in the post-GAP audit.

**Antenatal detection/diagnosis of SGA** was defined as an ultrasound estimated fetal weight (EFW) below the 10$^{th}$ customized centile or sequential measurements of EFW or AC with slow or no growth, and/or one or more abnormal Dopplers.

In 24 cases, where detection of SGA was uncertain after review of the scan reports, discussion occurred with a supervisor (Professor Lesley McCowan) who is a maternal fetal medicine specialist and international expert on SGA, and a decision was made based on all available information. Out of these 24 cases, 7 (29%) were classified as detected and 17 (71%) were classified as not detected using the prespecified parameters.

The preceding section has discussed the process of selecting the study population and establishing whether SGA was detected by ultrasound scan. The following section will describe the introduction of GAP at CMH.

### *4.6 Introduction of GAP at CMH*

The introduction of GAP at CMH commenced with a service level agreement between the Perinatal Institute and the DHB, signed on 16th February 2016. The agreement involves a commitment from the DHB to work with the Perinatal Institute to implement the programme, based on the following elements:

#### *4.6.1 Education and accreditation of all clinicians involved in maternity care*

The aim of GAP education is that all maternity care providers should receive instruction on:

- Awareness of major risk factors for SGA
- Relationship between SGA/FGR and perinatal mortality
- Standardised fundal height measurement
- Principles and use of customized antenatal growth charts
- Clinical implications of suboptimal growth, appropriate referral and care pathway

Due to the large numbers of staff at CMH, a series of workshops was presented over several months. Clinicians were provided with an algorithm and SGA risk assessment tool, summarising the major risk factors for SGA, allocation of appropriate care plan depending on risk of SGA, and a guide to management once SGA is suspected (Appendix H). Education is scenario based and interactive, with a focus on standardised fundal height measurement, accurate use and interpretation of GROW charts, and evidence-based management of SGA pregnancies, according to the New Zealand SGA guideline (McCowan & Bloomfield, 2014). A written test is completed by attendees to assess learning at completion of the workshop. Additionally, an e-learning programme is available for consolidation, and it is recommended that clinicians undertake this annually. Standardised fundal height measurement is a key element of the education and improves inter-and intra-user reliability. After demonstration by the instructor in the appropriate methodology to measure the fundal height, each participant demonstrates their technique which is assessed for accuracy compared with the standard. Key to consistency is the use of the correct landmarks as illustrated below, with identification of the highest point of the uterus (Figure 16). Next, with the tape measure starting at

zero centimetres, the measurement is taken from this point to the centre of the upper border of the symphysis pubis as illustrated below Figure 17).

The measurement is plotted in centimetres on the customized GROW chart, and if the uterine growth velocity is unsatisfactory an ultrasound scan is recommended for assessment of fetal weight and biometry.

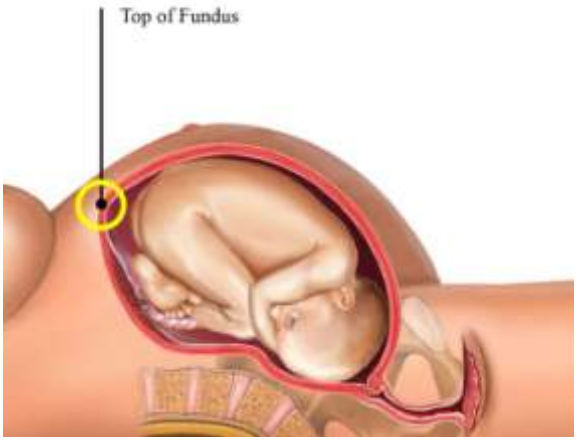



*Figure 16. Longitudinal view. Indicating top of fundus*

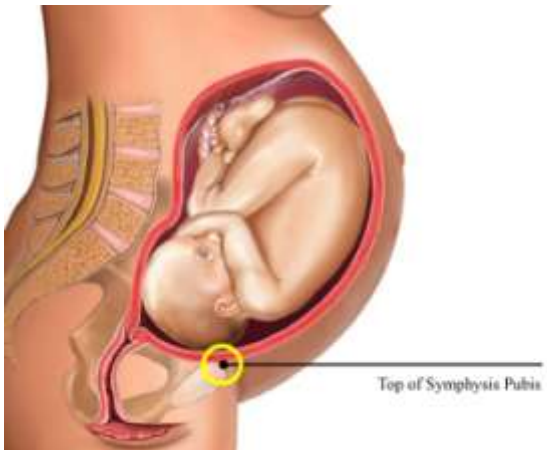



*Figure 17. Sagittal view. Indicating upper border of symphysis pubis*

Image adapted from: www.parents.com/pregnancy/week-by-week/your-third-trimester-of-pregnancy-week-by-week

See example below for satisfactory growth (Figure 18), and slowed fundal height growth velocity (Figure 19), indicating recommendation for a growth scan.

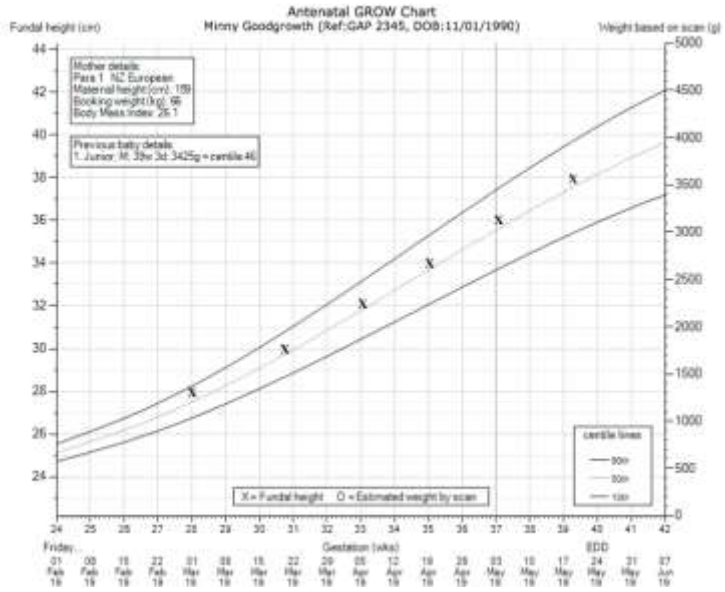



*Figure 18. GROW chart showing satisfactory growth of fundal height*

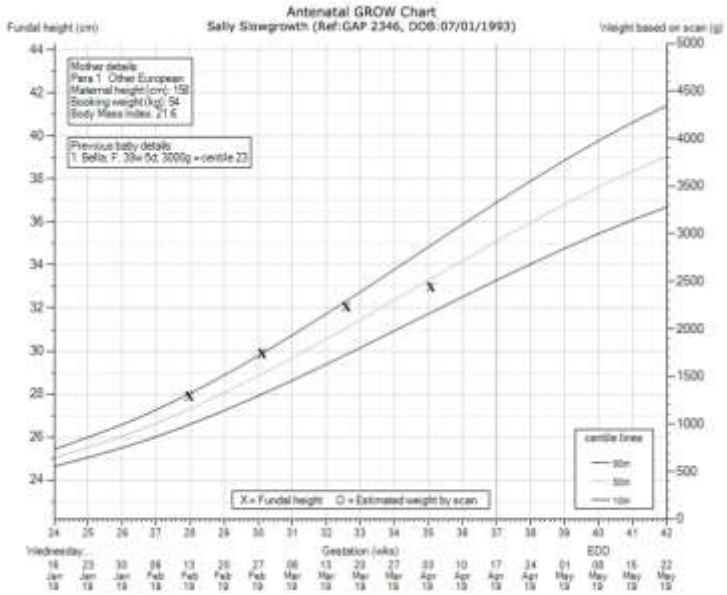



*Figure 19. GROW chart showing reduced fundal height growth velocity*

Following a finding of sub-optimal uterine growth from the fundal height measurement, it is recommended that the midwife/doctor requests an ultrasound scan to assess fetal growth and liquor volume. If there is evidence of SGA or suboptimal interval growth from fetal ultrasound measurements, the woman is referred for specialist review for a plan for ongoing care. Planning for optimal timing of the birth is determined by the NZMFMN SGA guideline, in the context of an individual schedule of holistic maternal and fetal assessment (McCowan & Bloomfield, 2014).

### *4.6.2 Adoption of evidence-based protocols and guidelines*

The NZMFMN SGA guideline is an integral component of the New Zealand GAP education programme (McCowan & Bloomfield, 2014). Utilisation of the guideline had begun at CMH prior to GAP introduction following publication in late 2013, and revision in 2014. The guideline includes information about SGA risk factors and appropriate ongoing pregnancy care based on regular holistic assessment. Following assessment of risk of SGA at booking, women are offered serial fundal height measurement every 2-3 weeks from 26-28 weeks, if identified as low risk of SGA. Measurements are electronically plotted on the GROW chart within the maternity clinical information system (MCIS). Alternatively, where the woman has a major risk factor for SGA at booking (defined as a risk factor with an odds ratio or relative risk $\geq$2) an individual schedule of serial growth scans is planned. Where fundal height measurements are likely to be unreliable, for example BMI $\geq$35kg/m$^2$, large fibroids or polyhydramnios, serial assessment of fetal growth by ultrasound is recommended. EFW is plotted on the electronic GROW chart. The guideline also provides a decision tool for evidence-based care after SGA or FGR has been detected in pregnancy.

### *4.6.3 Integration of GROW software in the CMH electronic MCIS*

The Perinatal Institute provided the software for use of GROW charts, and worked with Clevermed (https://www.clevermed.com), the software company which developed the MCIS, to ensure the software was implemented effectively in the CMH clinical information system.

### *4.6.4 Rolling audit, reporting of outcomes, and benchmarking.*

Software within the GROW application enables a quarterly report to be generated for the DHB on two criteria: 1) referral rates for growth scans for suspected SGA based on fundal height measurement, and 2) detection rates of SGA based on ultrasound findings. An electronic tool is provided for auditing of missed cases of SGA to promote learning opportunities and improve detection of SGA within the DHB. Following the introduction of GAP, a multidisciplinary team of GAP leaders continue to promote the programme in the DHB, with a link person supported by the Perinatal Institute. Currently, the UK GAP user average detection rate is reported as a benchmark, but it is envisaged that the New Zealand GAP user average will eventually replace this.

### *4.7 The post-GAP audit.*

#### *4.7.1 Time period and study population for post-GAP epoch*

*(a) Time period*

The post-GAP audit was conducted on data from births of babies born from 1st April 2017 to 31st March 2018, allowing time for the impact of GAP to be reflected in clinical outcomes.

*(b) Study population*

The study population for the post-GAP audit comprised all mothers who gave birth in the period at any of the CMH maternity facilities. With exclusions, as for the pre-GAP audit, the remaining 2021 pregnancies to women whose care had been provided by hospital employed staff comprised the eligible study population prior to further exclusions (Figure 21).

#### *4.7.2 Retrieval of data for the post-GAP audit*

The process of data collection differed from the process with the pre-GAP audit as by 2017 all maternity records were electronic, with the introduction of the MCIS in 2015. All post-GAP data were retrieved from the MCIS, PiMS™, and Concerto systems. The senior clinical analyst for CMH Health Intelligence and Informatics Department, who had accessed the pre-GAP data, retrieved all demographic and clinical post-GAP data for the total study population, as for the pre-GAP cohort. Missing or unlikely information was checked in the individual electronic records. All data were recorded on an Excel spreadsheet (Version 15.32) with a passcode known only to the researcher and analyst.

#### *4.7.3 Exclusion process*

From the initial sample of total births for the post-GAP period (n=7409), after exclusion of all records of pregnancies with self-employed LMC care (n=5388), there were 2021 pregnancies (2073 babies) remaining. Further exclusions were made as follows:

- Women booked >20 weeks 0 days (n=794)
- Women booked ≤20 weeks and 0 days but no booking BMI (n=0)
- Women who gave birth <24 weeks and 0 days (n=10)
- Babies with congenital anomalies (n=84)
- Multiple pregnancies (n=103 babies, 50 twin and 1 triplet pregnancy)

These exclusions resulted in a final eligible sample of 1082 pregnancies.

### *4.7.4 Retrieval of missing birthweight centiles and determining the SGA sample*

In the post-GAP data set, following exclusions, there were 109/1082 (10%) of records without a recorded birthweight centile in the MCIS. Within the MCIS, SGA status is automatically calculated through a function of the GROW-App, using the same coefficients to calculate the customized birthweight centile applied in the pre-GAP audit. The birthweight centile is calculated after response to questions completed at the time of entering birth details. The person entering data after the birth (usually the midwife) is asked to answer yes or no to 'whether SGA or FGR was detected antenatally by ultrasound scan' (the pop-up prompt on MCIS for this data-point is '**Antenatal detection/diagnosis of SGA** indicates an ultrasound estimated fetal weight (EFW) below the 10$^{th}$ centile, or sequential measurements with slow or no growth, and/or one or more abnormal Dopplers') (See Figure 20 below).

For pregnancies with no birthweight centile in MCIS, the electronic clinical records and scan reports were searched, enabling calculation of missing birthweight centiles. Sixteen out of one hundred and nine (14.7%) of these birthweight centiles were <10$^{th}$, and there was documented evidence from ultrasound scans retrieved from concerto that 10/16 (62.5%) of these SGA cases had been detected as such antenatally. Following completion of birthweight centile data, the number of SGA babies could be calculated for the post-GAP epoch. One hundred and forty (12.9%) babies were found to be SGA and 942 (87.1 %) were non-SGA. (See Figure 21).

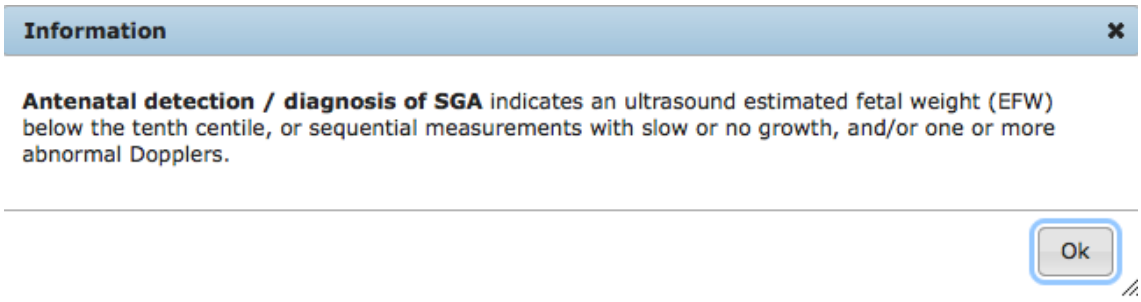



*Figure 20. Criteria for antenatal detection/diagnosis of SGA in MCIS*

| | |
|---|---|
| **All Births** | **n=7409 (mothers) = 7493 babies** |
| **Non DHB** | **n=5388 (mothers) = 5420 babies** |
| **Booked DHB** | **n=2021 (mothers) = 2073 babies** |

**Exclusions from Booked DHB n= 2073**

- Booked >20 weeks and 0 days (n=794)
- Booked <20 weeks and 0 days but no BMI (n=0)
- Baby born <24 weeks and 0 days (n=10)
- Babies with anomalies (n=84)
- Multiples n=103 babies (50 twin pregnancies, one triplet pregnancy).

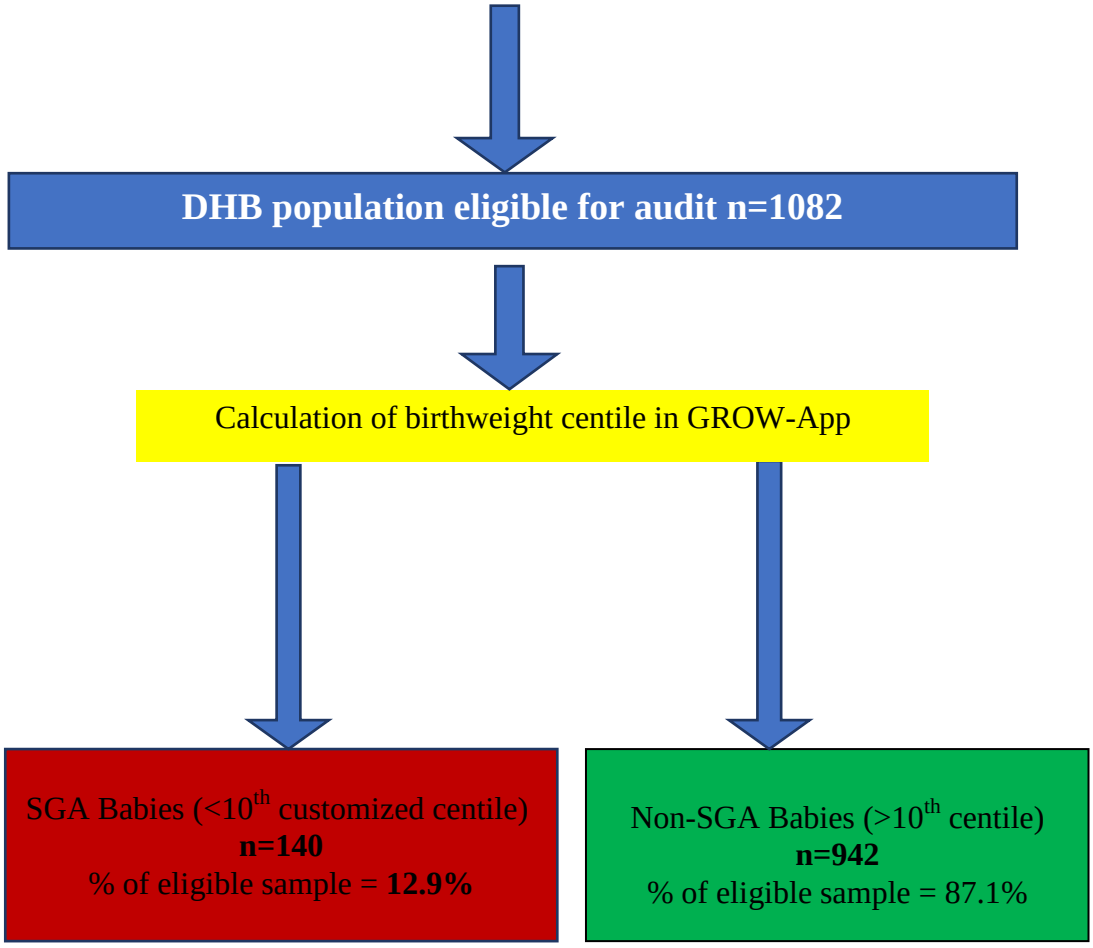



*Figure 21. Post-GAP audit. Identifying the eligible population and SGA subgroup*

### *4.7.5 Process of establishing whether SGA was detected*

An electronic report of detection status was available through the electronic clinical record. Because the report quality depends on accuracy of inputting of data by midwives in the birthing unit, an independent audit of detected SGA/FGR was conducted for all SGA pregnancies in the post-GAP sample of SGA pregnancies.

*(a) Audit Process*

Two year six medical students conducted the audit as part of their Counties Manukau Obstetrics and Gynecology Quality Improvement Project. Both were working on placement in the CMH maternity unit, had received education from the GAP lead educator on definition of SGA and parameters used to indicate antenatal detection, and education from the MCIS specialist midwife in the use of MCIS. The electronic antenatal and neonatal MCIS records were demonstrated live to the students and they were instructed in search strategies to locate the relevant information from the records to conduct the audit. Subsequently, they conducted the audit to assess the accuracy of MCIS data for the question regarding detection of SGA, in the post-GAP cohort.

The students checked each record for accuracy to the question: 'Was SGA or FGR detected antenatally by ultrasound scan?' They were given an Excel spreadsheet to record these data with NHI numbers of all eligible women in the post-GAP cohort who had given birth to an SGA baby. As for the pre-GAP audit, antenatal detection of SGA was defined as '**Antenatal detection/diagnosis of SGA** indicates an ultrasound EFW below the 10$^{th}$ centile, or sequential measurements with slow or no growth, and/or one or more abnormal Dopplers'. This instruction is included in the software via an information button which can be used to display the criteria before answering the question (as in Figure 20). The students sought further clarification during the audit, where they were unsure about detection status, to ensure decisions consistently reflected the agreed parameters. After detection status was confirmed, according to agreed parameters, MCIS data were updated accordingly.

*(b) Audit findings*

The audit revealed that there was an accuracy rate of 85.7% (120/140) for responses to the question regarding detection of SGA. Of the 20 inaccurate responses, 7 (35%) records inaccurately reported that SGA was detected, and 13 (65%) records inaccurately reported non-detection of SGA. Prior to the audit, the MCIS record indicated that there were 75/140 (53.6%) detected SGA; following the audit, this was corrected to 81/140 (57.9%) after individual records were checked and detection status for each record was either verified or updated.

### *4.8 Comparison of the pre-GAP and post-GAP findings*

An Excel (Version 15.32) spreadsheet was created for the post-GAP data to enable comparison of pre- and post-GAP data. Data points included in the post-GAP dataset were identical to those in the pre-GAP dataset.

#### *4.8.1 Definitions*

- **Anomalies.** Babies with congenital malformations, deformations, and chromosome abnormalities (Q 00-99) according to International Classification of Diseases and Related Health Problems (MoH, n.d.-b).
- **Deprivation Index.** An estimate of the relative socio-economic deprivation of a residential area (Salmond & Crampton, 2012).
- **Estimated date of delivery.** For pre-GAP data (2012), EDD was recorded in Healthware™, transferred from the midwife's booking form, and established from first ultrasound scan or calculated from the LMP if no early scan was performed. For the post-GAP data (2017-18) EDD was recorded in MCIS by the midwife at booking, using the same criteria.
- **Induction of labour.** An intervention to stimulate the onset of labour by pharmacological or other means (CMH, 2018).
- **Lead maternity carer.** The LMC provides a woman with continuity of care throughout pregnancy, labour and birth, and the postnatal period. Includes a midwife, obstetrician, or a general practitioner with a diploma in obstetrics[7] and can be either a maternity provider in his or her own right, or an employee or contractor of a maternity provider, and has been chosen by the woman to provide her lead maternity care (CMH, 2018).
- **Neonatal composite morbidity.** One or more of the following: a) neonatal unit admission for >48 hours; b) Apgar score <7 at 5 minutes; c) infant required ventilation.
- **Neonatal death.** The death of any baby showing signs of life at 20 weeks' gestation or beyond or weighing at least 400gm if gestation is unknown.
- **Pre-eclampsia.** Includes ICD 10 codes 0141 (severe pre-eclampsia) and 0149 (pre-eclampsia unspecified) (ICD10Data, 2019).
- **Pre-existing (chronic) hypertension.** Hypertension prior to onset of pregnancy.
- **Preterm birth.** Birth <259 days of gestation.
- **Post-term birth.** Birth >280 days of gestation.
- **Smoking.** History of maternal smoking within the last month by self-report at admission for birth.
- **Stillbirth.** A fetal death at ≥20 weeks or weighing at least 400gm if gestation is unknown (PMMRC, 2017).
- **Any ventilation.** Includes ICD codes (MoH, n.d.-b). 569 (continuous ventilatory support) and 570 (non-invasive ventilatory support). Both codes include 3 subcategories for time periods covering ≤ 24 hours through to ≥ 96 hours.

#### *4.8.2 Statistical analysis*

Analyses were conducted using SAS 9.4 (SAS Institute INC., Cary, NC, USA).

Demographic, maternal and neonatal outcomes were compared in the pre- and post-

[7] General practitioners may have provided shared maternity care in 2012 without a diploma in obstetrics.

GAP cohorts using chi-square and t-tests, for categorical and continuous data, respectively. The pre- and post-GAP cohorts were compared for the pre-specified outcomes, with exposure effect expressed as odds ratio and 95% confidence interval (CI). Analyses were adjusted for potential confounding by factors known to be strongly associated with SGA, including NZDep., ethnicity, maternal age, BMI, and cigarette smoking. For some outcomes with few events, adjustment was not possible due to non-convergence of models.

Two types of analysis were undertaken for each outcome. First, the pre- and post-GAP cohorts were compared by non-SGA and SGA subgroups, defined according to birthweight. The difference in exposure effect between subgroups was assessed by a test of interaction at an alpha level of 0.05. A significant exposure effect in either subgroup (95% CI excluding 1.0) in combination with a non-significant interaction ($p<0.05$) was interpreted as an epoch effect unrelated to the exposure of interest (i.e., the GAP programme).

Second, the SGA subgroup was further divided into babies who were and were not identified antenatally as SGA. The difference in exposure effect pre- and post-GAP among SGA babies who were and were not identified antenatally was also assessed by a test of interaction at an alpha level of 0.05. A significant exposure effect in the identified group, in combination with a significant interaction between identified and non-identified groups, was interpreted as an exposure effect directly related to the GAP programme.

### *4.9 Conclusion*

This chapter has introduced the study hypotheses, provided detailed methods for the pre- and post-GAP audits, a summary of the introduction of GAP at CMH, and a description of the process of data analysis. Maternal and neonatal findings following introduction of GAP will be presented in the next chapter.

# Chapter 5. Maternal Characteristics and Pregnancy and Neonatal Outcomes

## *5.1 Introduction*

This chapter compares the demographic characteristics and pregnancy outcomes of the pre-and post-GAP cohorts, including the primary outcome, detection of SGA, and secondary maternal and neonatal outcomes.

## *5.2 Maternal characteristics*

### *5.2.1 Age*

Maternal age differed significantly between the pre- and post-GAP epochs (p<0.0001) Table 5). While most women in both cohorts were aged between 20 and 39 years, there were fewer younger and older mothers in the post-GAP compared with pre-GAP cohorts (<20 years 8.6% pre-GAP vs 4.4% post-GAP; p < 0.0001) (>40 years 6.7% pre-GAP vs 3.7% post-GAP; p=0.002) (Figure 22).

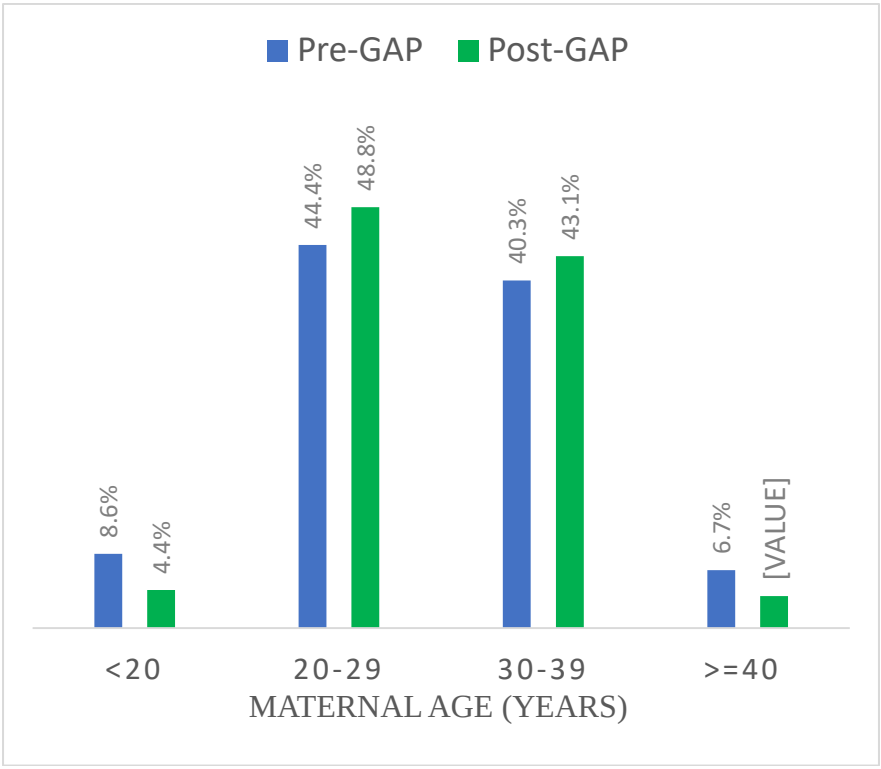



*Figure 22. Maternal age distribution in pre- and post-GAP cohorts*

### *5.2.2 Ethnicity*

Ethnicity differed significantly between the two epochs (p=0.0007). This was due to a reduction in the proportion of Pacific women (41% pre-GAP vs 33.3% post-GAP) and an increase in the proportion of Asian women (25.9% pre-GAP vs 33.3% post-GAP) (see Table 5, and Figure 23).

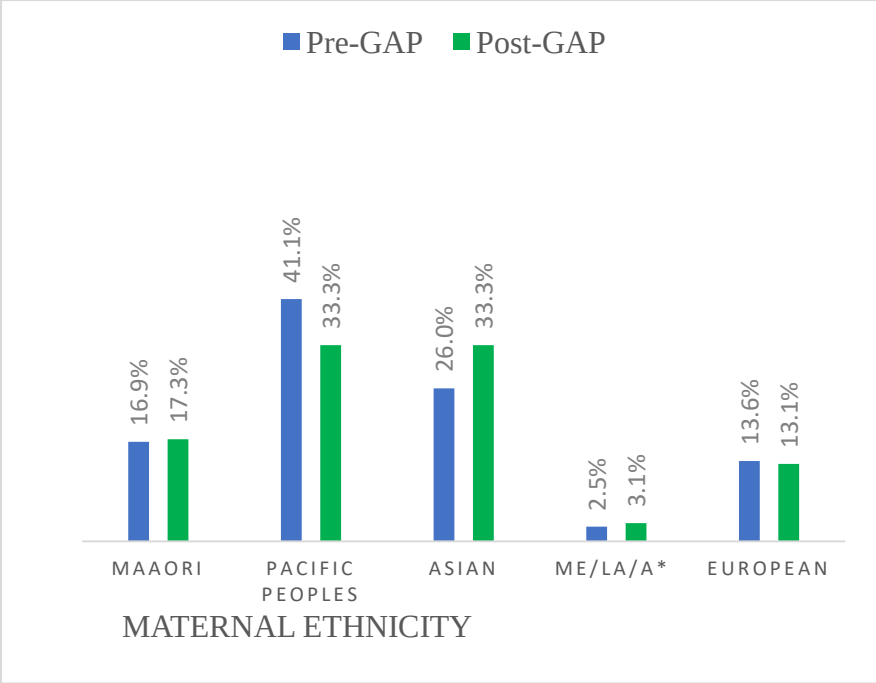



*Figure 23. Maternal ethnicity in pre- and post-GAP cohorts*

*Middle Eastern/Latin American/African

### *5.2.3 New Zealand deprivation centile*

The data for the pre- and post-GAP cohorts included in this study shows that the distribution of NZDep. centile indices is similar to the overall CMH community, with the minority residing in the more affluent areas designated as centiles 1-2, and the majority in the most deprived areas designated as centiles 9-10. There was no significant difference in deprivation between epochs (p=0.06) (see Figure 24).

### *5.2.4 Booking BMI*

There was a significant difference in maternal BMI between the two epochs (p=0.0025) with a small reduction in rates of obesity (Figure 25).

### *5.2.5 Smoking*

There was a significant reduction in rates of women self-reporting smoking within a month of the baby's birth (17.7% pre-GAP vs 11.9% post-GAP; p=0.0002).

### *5.2.6 Chronic hypertension*

The prevalence of chronic hypertension was similar in both epochs (4.7% pre-GAP vs 5.7% post-GAP; p=0.28).

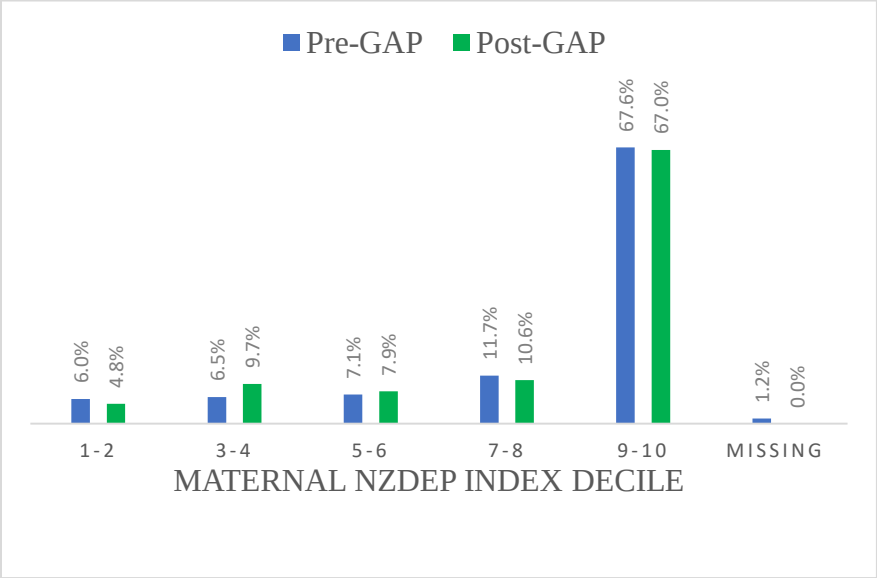



*Figure 24. Maternal deprivation index decile in pre-and post-GAP cohorts*

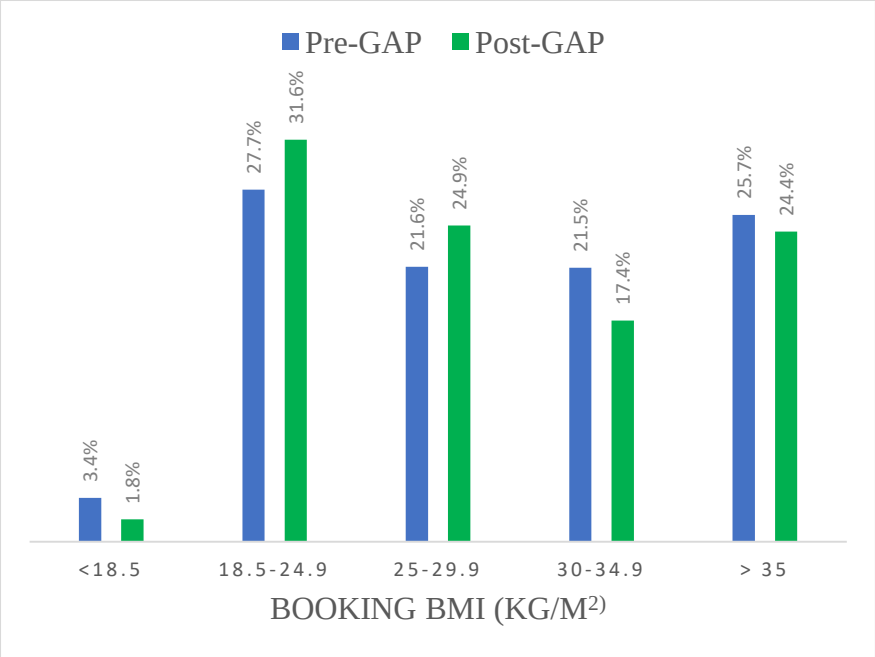



*Figure 25. Maternal BMI in pre- and post-GAP cohorts*

### *5.3 Pregnancy outcomes*

#### *5.3.1 Pre-eclampsia*

Rates of pre-eclampsia were similar in both epochs (5.8% pre-GAP vs 7.1% post-GAP; p=0.21).

#### *5.3.2 Gestation at birth*

The mean (SD) gestation at birth reduced slightly from 273.4 (12.3) days pre-GAP to 271.9 (12.4) days post-GAP (p=0.005).

#### *5.3.3 Mean birthweight*

There was a small but significant reduction in mean birthweight between epochs. Pre-GAP the mean (SD) birthweight was 3420g (596), and post-GAP 3353g (605) (p=0.009).

#### *5.3.4 Stillbirth*

There were six stillbirths in the pre-GAP cohort and seven in the post GAP cohort, giving rates of 5.4/1000 and 6.5/1000 pregnancies respectively. In the pre-GAP cohort, four of the six stillborn babies were SGA, but only one was detected antenatally. Four out of six were preterm, born at 24.4, 24.9, 28.9, and 33 weeks; and of these preterm babies, three out of four were severely SGA, with birthweight centiles 2.1, 0.4, and 0.4% respectively. The birthweight centile for the baby who was stillborn at 28.9 weeks was 11.3%. Of the remaining two stillbirths, both were born at term, with one SGA (birthweight centile 0.2%) and one large for gestational age (centile 100%).

In the post-GAP cohort, three of the seven stillborn babies were SGA, of whom one was detected antenatally. Three of the seven post-GAP still births, were born preterm at 26.7, 27.0, and 29.6 weeks' gestation; and all three were severely SGA (all had birthweight centiles of 0.0%). Of the remaining four stillbirths, two were born at term, with birthweight centiles 13.4% and 26.7%, while the other two were born at 28.7 and 30.9 weeks with birthweight centiles 85.0%, and 79.8%.

#### *5.3.5 Neonatal death*

In the pre-GAP cohort, there was one early neonatal death of a baby born at a very preterm gestation (birthweight centile 22.9%). In the post-GAP cohort, there were two neonatal deaths one of which occurred in a baby born at 40 weeks and who was SGA (birthweight centile 1.9%) and was not detected antenatally. This baby died at three days due to hypoxic ischaemic encephalopathy, pulmonary haemorrhage, and pneumothorax. The other neonatal death occurred at 25 days of age for a late preterm baby who was not SGA (35 weeks' gestation, birthweight centile 35.6%).

*Table 5. Maternal characteristics, and pregnancy and neonatal outcomes in pre- and post- GAP cohorts.*

| | **Pre-GAP n=1105** | **Post-GAP n=1082** | ***P*** |
|---|---|---|---|
| **Maternal Characteristics** | | | |
| **Age group (years)** | | | |
| <20 | 95 (8.6) | 48 (4.4) | <0.0001 |
| 20-29 | 491 (44.4) | 528 (48.8) | |
| 30-39 | 445 (40.3) | 466 (43.1) | |
| ≥40 | 74 (6.7) | 40 (3.7) | |
| **Ethnicity** | | | |
| Maaori | 186 (16.8) | 187 (17.3) | 0.0007 |
| Pacific Peoples | 453 (41.0) | 360 (33.3) | |
| Asian | 286 (25.9) | 360 (33.3) | |
| ME/LA/A | 27 (2.4) | 33 (3.1) | |
| European | 150 (13.6) | 142 (13.1) | |
| Residual categories | 3 (0.3) | 0 (0.0) | |
| **NZ Dep.** | | | |
| 1-2 | 66 (6.0) | 52 (4.8) | 0.06 |
| 3-4 | 72 (6.5) | 105 (9.7) | |
| 5-6 | 78 (7.1) | 85 (7.9) | |
| 7-8 | 129 (11.7) | 115 (10.6) | |
| 9-10 | 747 (67.6) | 725 (67.0) | |
| Missing | 13 (1.2) | 0 (0.0) | |
| **Booking BMI ($kg/m^2$)** | | | |
| <18.5 | 38 (3.4) | 19 (1.8) | 0.0025 |
| 18.5-24.9 | 306 (27.7) | 342 (31.6) | |
| 25-29.9 | 239 (21.6) | 269 (24.9) | |
| 30-34.9 | 238 (21.5) | 188 (17.4) | |
| ≥35 | 284 (25.7) | 264 (24.4) | |
| **Smoker** | 194 (17.6) | 29 (11.9) | 0.0002 |
| **Chronic Hypertension** | 52 (4.7) | 62 (5.7) | 0.28 |
| **Pregnancy and Neonatal Outcomes** | | | |
| **Pre-eclampsia** | 64 (5.8) | 77 (7.1) | 0.21 |
| **Gestation at birth* (days)** | 273.4 (12.3) | 271.9 (12.4) | 0.005 |
| **Birthweight* (g)** | 3420 (596) | 3353 (605) | 0.009 |
| **Stillbirth** | 6 (5.4/1000) | 7 (6.5/1000) | 0.75 |
| **Neonatal death** | 1 (0.9/1000) | 2 (1.9/1000) | 0.55 |

Data are mean (standard deviation), number (%) or rate/1000 births as appropriate
*Live births

### *5.4 Identification of SGA*

In the pre-GAP cohort, of 153 babies born SGA, 35 were detected antenatally as being SGA (22.9%). In the post GAP cohort, of 140 babies born SGA, 81 were detected antenatally as being SGA (57.9%). In adjusted analyses, the likelihood of SGA being detected antenatally increased almost five-fold in the post-GAP cohort (Table 6).

### *5.5 Influence of maternal characteristics on identification of SGA*

To assess the influence of maternal characteristics on identification of SGA, subgroup analysis was performed. To reduce the risk of type 2 error, several maternal characteristics were collapsed to binary categories: maternal ethnicity was categorised as Maaori or Pacific and compared with all other ethnicities; and NZDep. deciles 1-8 were compared to deciles 9 and 10 (high deprivation). For BMI, underweight and normal weight were combined into one group.

#### *5.5.1 Identification of SGA by maternal ethnicity*

Detection of SGA in both Maaori and Pacific women and non-Maaori and non-Pacific women increased between epochs (Maaori and Pacific 18.9% pre-GAP vs 63.8% post-GAP; non-Maaori and non-Pacific 28.6% pre-GAP to 52.1% post-GAP). Subgroup analysis suggested that the increase in detection of SGA between epochs was greater for Maaori and Pacific women (interaction p=0.049) (see Table 7).

#### *5.5.2 Identification of SGA by NZDep.*

Detection of SGA increased in both women with low and high deprivation (residing in areas 1-8 17.4% pre-GAP vs 57.1% post-GAP; women residing in areas 9-10, 25.2% pre-GAP vs 58.2% post-GAP), with no evidence that this differed by subgroup (interaction p=0.46).

#### *5.5.3 Identification of SGA by booking BMI*

As shown in Table 5 there was a significant difference in distribution of BMI between the two epochs. While detection of SGA increased for all BMI groups across epochs with no significant interaction (p=0.75), it was encouraging to see that SGA detection for women classified as morbidly obese, also increased substantially from 20.5% pre-GAP to 66.7% post-GAP.

### *5.5.4 Identification of SGA by smoking status*

While the numbers of women who reported smoking within the last month of pregnancy had reduced in the post-GAP epoch, there was a similar increase in the number of SGA babies detected amongst smoking and non-smoking women (interaction p=0.66), suggesting the effect of GAP did not differ by smoking status.

### *5.5.5 Identification of SGA by pre-eclampsia status*

While there were higher SGA detection rates in both epochs for women who developed pre-eclampsia compared to those who did not, there was a similar increase in the proportion of SGA babies detected amongst women with pre-eclampsia (40% pre-GAP to 72.7% post-GAP) and for those without pre-eclampsia (19.5% pre-GAP to 55.1% post-GAP; interaction p=0.74), suggesting that the effect of the GAP did not differ by pre-eclampsia status.

*Table 6. Identification of SGA pre-GAP and post-GAP*

| | Pre-GAP | Post-GAP | Unadjusted OR (95%CI) | *P* | Adjusted OR* (95%CI) | *P* |
|---|---|---|---|---|---|---|
| **Total Cohort** | n=1105 | n=1082 | | | | |
| **Total SGA** | 153 (13.8) | 140 (12.9) | 0.93 (0.72, 1.18) | 0.53 | 0.95 (0.74, 1.22) | 0.68 |
| **Total SGA** | n=153 | n=140 | | | | |
| **Identified SGA** | 35 (22.9) | 81 (57.9) | 4.63 (2.79, 7.67) | <0.0001 | 4.81 (2.82, 8.18) | <0.0001 |

***** Adjusted for NZDep., ethnicity, maternal age, maternal BMI, smoking

*Table 7. Identification of SGA pre-GAP and post-GAP by maternal demographic and clinical characteristics*

| | **SGA Pre-Gap Cohort n=153/1105 (13.8%)** | **SGA Post-GAP Cohort n=140/1082 (12.9%)** | |
|---|---|---|---|
| **Maternal Characteristics** | **SGA Detected N (%)** | **SGA Detected N (%)** | ***P interaction**** |
| **Maaori or Pacific Ethnicity** | | | |
| Yes | 17/90 (18.9) | 44/69 (63.8) | 0.049 |
| No | 18/63 (28.6) | 37/71 (52.1) | |
| **NZ Dep.** | | | |
| 1-8 | 8/46 (17.4) | 24/42 (57.1) | 0.46 |
| 9-10 (most deprived) | 27/107 (25.2) | 57/98 (58.2) | |
| **Booking BMI (kg/m$^2$)** | | | |
| <25 | 8/38 (21.1) | 24/46 (52.2) | 0.75 |
| 25-29.9 | 11/39 (28.2) | 20/34 (58.8) | |
| 30-34.9 | 8/37 (21.6) | 15/27 (55.6) | |
| ≥35 | 8/39 (20.5) | 22/33 (66.7) | |
| **Smoker** | | | |
| Yes | 7/36 (19.4) | 14/24 (58.3) | 0.66 |
| No | 28/117 (23.9) | 67/116 (57.8) | |
| **Pre-eclampsia** | | | |
| Yes | 10/25 (40.0) | 16/22 (72.7) | 0.74 |
| No | 25/128 (19.5) | 65/118 (55.1) | |

* Fisher's exact or chi-square test as appropriate.

### *5.6 Secondary maternal outcomes*

Maternal outcomes were induction of labour, caesarean birth, pre-term and post-term birth, and mean gestation at birth.

#### *5.6.1 Induction of labour*

The induction of labour (IOL) rate rose between the pre-GAP and post GAP epochs in both non-SGA (27.7% pre-GAP vs 32.3% post-GAP; aOR=1.23, 95% CI 1.01, 1.51) and SGA pregnancies (31.4% pre-GAP vs 45.7% post-GAP; aOR=1.70, 95% CI 1.03, 2.79). There was no evidence that this increase in rate of IOL differed in SGA and non-SGA pregnancies (interaction p=0.19) (Table 8).

In the SGA subgroup, the IOL rate increased between epochs in both pregnancies where SGA was identified (42.9% pre-GAP to 54.3% post-GAP; aOR= 1.51, 95% CI 0.65, 3.55) and pregnancies where SGA was not identified (28% pre-GAP to 33.9% post-GAP; aOR=1.15,95% CI 0.55, 2.39). Again, there was no evidence that this increase differed by SGA identification status (interaction p=0.60) (Table 8).

#### *5.6.2 Caesarean birth*

The caesarean birth rate also rose between the pre-GAP and post-GAP epochs, in both non-SGA (30.4% pre-GAP to 34.8% post-GAP; aOR=1.2, 95% CI 0.97,1.46) and SGA pregnancies (38.6% pre-GAP to 47.9% post-GAP; aOR=1.68, 95% CI 1.02, 2.77). There was no evidence that this increase in caesarean birth differed by SGA versus non-SGA subgroup (interaction p=0.58) (Table 8).

In the SGA subgroup, the caesarean birth rate increased between epochs in both pregnancies where SGA was identified (51.4% pre-GAP to 55.6% post-GAP; aOR =1.29, 95% CI 0.55, 3.05) and pregnancies where SGA was not identified (34.8% pre-GAP to 37.3% post-GAP; aOR=1.26, 95% CI 0.61, 2.61). Again, there was no evidence that this increase differed by SGA identification status (interaction p=0.86) (Table 8).

#### *5.6.3 Preterm birth*

The pre-term birth rate increased between the pre-GAP and post-GAP epochs, in both non-SGA (6.1% pre-GAP to 8.1% post-GAP; aOR=1.37, 95% CI 0.96,1.96) and SGA pregnancies (15.0% pre-GAP to 20.0% post-GAP; aOR=1.50, 95% CI 0.79, 2.84). There was no evidence that this increase in preterm birth differed by SGA versus non-SGA subgroup (interaction p=0.88).

In the SGA subgroup, the preterm birth rate decreased between epochs in pregnancies where SGA was identified (34.3% pre-GAP to 23.5% post-GAP); [adjusted odds ratio (aOR)=0.76, 95% CI 0.29, 1.95] but increased in pregnancies where SGA

was not identified (9.3% pre-GAP to 15.3% post-GAP; aOR=1.30, 95% CI 0.46, 3.65). However, the increase in preterm between epochs did not differ significantly by SGA identification status (interaction p=0.16) (Table 9).

### *5.6.4 Post-term birth*

The post-term birth rate decreased between the pre-GAP and post-GAP epochs, in both non- SGA (26.6% pre-GAP to 22.7% post-GAP; aOR=0.83, 95% CI 0.67,1.02) and SGA pregnancies (28.1% pre-GAP to 19.3% post-GAP; aOR=0.65, 95% CI 0.37, 1.16). There was no evidence that this decrease in post-term birth differed by SGA versus non-SGA subgroup (interaction p=0.32) (Table 9).

In the SGA subgroup, the post-term birth rate decreased between epochs in pregnancies where SGA was identified (8.6% pre-GAP to 7.4% post-GAP; aOR=0.82, 95% CI 0.17, 4.03), but increased in pregnancies where SGA was not identified (33.9% pre-GAP to 35.6% post-GAP; aOR=1.21, 95% CI 0.59, 2.48). There was no evidence that post-term birth differed by SGA identification status (interaction p=0.64) (Table 9).

*Table 8. Secondary maternal outcomes (IOL and C/S) pre- and post-GAP*

| | Pre-GAP | | Post-GAP | | Unadjusted OR (95%CI) | *P interaction* | Adjusted* OR (95%CI) | *P interaction* |
|---|---|---|---|---|---|---|---|---|
| | N | n (%) | N | n (%) | | | | |
| **Induction of labour** | | | | | | | | |
| Total | 1105 | 312 (28.2) | 1082 | 368 (34.0) | 1.31 (1.09, 1.57) | | 1.29 (1.07, 1.55) | |
| Non-SGA | 952 | 264 (27.7) | 942 | 304 (32.3) | 1.24 (1.02, 1.52) | | 1.23 (1.01, 1.51) | |
| SGA | 153 | 48 (31.4) | 140 | 64 (45.7) | 1.84 (1.14, 2.97) | 0.13 | 1.70 (1.03, 2.79) | 0.19 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 35 | 15 (42.9) | 81 | 43 (54.3) | 1.59 (0.71, 3.53) | | 1.51 (0.65, 3.55) | |
| Non-identified | 118 | 33 (28.0) | 59 | 20 (33.9) | 1.32 (0.67, 2.59) | 0.73 | 1.15 (0.55, 2.39) | 0.60 |
| **Caesarean Birth** | | | | | | | | |
| Total | 1105 | 348 (31.5) | 1082 | 395 (36.5) | 1.25 (1.05, 1.49) | | 1.23 (1.02, 1.48) | |
| Non-SGA | 952 | 289 (30.4) | 942 | 328 (34.8) | 1.23 (1.01, 1.49) | | 1.20 (0.97, 1.46) | |
| SGA | 153 | 59 (38.6) | 140 | 67 (47.9) | 1.46 (0.92, 2.33) | 0.49 | 1.68 (1.02, 2.77) | 0.58 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 35 | 18 (51.4) | 81 | 45 (55.6) | 1.18 (0.53, 2.61) | | 1.29 (0.55, 3.05) | |
| Non-identified | 118 | 41 (34.8) | 59 | 22 (37.3) | 1.12 (0.58, 2.14) | 0.92 | 1.26 (0.61, 2.61) | 0.86 |

* Adjusted for NZ Deprivation Index, ethnicity, maternal age, maternal BMI, smoking.

*Table 9. Secondary maternal outcomes (preterm and post-term birth) pre- and post-GAP*

| | Pre-GAP | | Post-GAP | | Unadjusted OR (95%CI) | *P interaction* | Adjusted* OR (95%CI) | *P interaction* |
|---|---|---|---|---|---|---|---|---|
| | N | n (%) | N | n (%) | | | | |
| **Preterm birth (<259 days)** | | | | | | | | |
| Total | 1105 | 81 (7.3) | 1082 | 104 (9.6) | 1.34 (0.99, 1.82) | | 1.36 (1.00, 1.86) | |
| Non-SGA | 952 | 58 (6.1) | 942 | 76 (8.1) | 1.35 (0.95, 1.93) | | 1.37 (0.96, 1.96) | |
| SGA | 153 | 23 (15.0) | 140 | 28 (20.0) | 1.41 (0.77, 2.59) | 0.90 | 1.50 (0.79, 2.84) | 0.88 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 35 | 12 (34.3) | 81 | 19 (23.5) | 0.59 (0.25, 1.40) | | 0.76 (0.29, 1.95) | |
| Non-identified | 118 | 11 (9.3) | 59 | 9 (15.3) | 1.75 (0.68, 4.50) | 0.09 | 1.30 (0.46, 3.65) | 0.16 |
| **Post term birth (>280 days)** | | | | | | | | |
| Total | 1105 | 296 (26.8) | 1082 | 241 (22.3) | 0.78 (0.64, 0.95) | | 0.80 (0.66, 0.98) | |
| Non-SGA | 952 | 253 (26.6) | 942 | 214 (22.7) | 0.81 (0.66, 1.00) | | 0.83 (0.67, 1.02) | |
| SGA | 153 | 43 (28.1) | 140 | 27 (19.3) | 0.61 (0.35, 1.06) | 0.34 | 0.65 (0.37, 1.16) | 0.32 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 35 | 3 (8.6) | 81 | 6 (7.4) | 0.85 (0.20, 3.63) | | 0.82 (0.17, 4.03) | |
| Non-identified | 118 | 40 (33.9) | 59 | 21 (35.6) | 1.08 (0.56, 2.08) | 0.77 | 1.21 (0.59, 2.48) | 0.64 |

* Adjusted for NZ Deprivation Index, ethnicity, maternal age, maternal BMI, smoking.

### *5.7 Neonatal outcomes among live births*

#### *5.7.1 Composite adverse neonatal outcome*

Composite adverse neonatal outcome (morbidity) was defined as one or more of the following: neonatal unit admission for >48 hours; Apgar score <7 at 5 minutes; and respiratory positive pressure support (mechanical and non-invasive).

There was a significant increase in composite adverse neonatal outcome between epochs in non-SGA babies (5.3% pre-GAP vs 9.8% post-GAP; aOR=1.98, 95% CI 1.38, 2.84) but not amongst SGA babies (16.9% pre-GAP vs 18.2% post-GAP; aOR= 1.05, 95% CI 0.55, 1.10), although the evidence for a difference in epoch effect between SGA versus non-SGA subgroups was not strong (interaction p=0.09).

In the SGA subgroup, there was evidence that increased identification of SGA post-GAP may be associated with lower composite adverse neonatal outcome (SGA identified: 32.4% pre-GAP vs 17.5% post-GAP; aOR=0.44, 95% CI 0.17, 1.15); SGA non-identified: 12.3% pre-GAP to 19.3% post-GAP; aOR=1.81, 95% CI 0.73, 4.48); (interaction p=0.03).

#### *5.7.2 Neonatal unit admission >48 hours*

There has been an overall increase in prolonged NNU admission between the two epochs. However, increased admission to the NNU for more than 48 hours was not more pronounced in the SGA subgroup compared with non-SGA.

There was no significant difference in prolonged NNU admission between epochs in non-SGA babies (3.3% pre-GAP vs 4.7% post-GAP; aOR=1.54, 95% CI 0.96, 2.47) or amongst SGA babies (14.1% pre-GAP to 16.1% post-GAP, aOR=1.08, 95% CI 0.54, 2.17) (Table 10).

There was no evidence that prolonged NNU admission differed by SGA versus non-SGA subgroup (interaction p=0.52) In the SGA subgroup, there was evidence that increased identification of SGA post-GAP may be associated with lower incidence of prolonged NNU admission (SGA identified: 29.4% pre-GAP to 16.3% post-GAP; aOR=0.42, 95% CI 0.15, 1.15); but in SGA non-identified: an increase from 9.6% pre-GAP to 15.8% post-GAP; aOR=1.86, 95% CI 0.63, 5.52; interaction p=0.04) (Table 10).

On review of birthweight centiles, for the pre-GAP SGA babies identified antenatally, those who received NNU care >48 hours had customized birthweight

centiles from 0.0 to 4.5%. Of those post-GAP SGA babies identified antenatally, who received NNU care >48 hours, customized birthweight centiles ranged from 0.0 to 6.9%. This suggests that admission and length of stay was associated with the neonates' degree of SGA in both epochs.

### *5.7.3 Apgar <7 at 5 minutes*

There was no significant difference in Apgar scores <7 at 5 minutes between epochs in non-SGA babies (1.4% pre-GAP and 1.7% post-GAP; aOR=1.24, 95% CI 0.59, 2.60 or amongst SGA babies 3.4% pre-GAP and 2.9% post-GAP; aOR=1.07, 95% CI 0.26, 4.49). There was no evidence that Apgar score <7 at 5 minutes varied by SGA versus non-SGA subgroup (p=0.65) (Table 11).

In the SGA subgroup, there was no evidence that Apgar score <7 at 5 minutes differed by identification status (SGA identified 2.9% pre-GAP and 1.3 % post-GAP; unadjusted OR 0.42, 95% CI 0.03, 6.88) and in SGA non-identified (3.5% pre-GAP and 5.3% post-GAP; unadjusted OR 1.53, 95% CI 0.33, 7.07; interaction p=0.43) (Table 11). Because of small numbers of babies with low Apgar scores in SGA subgroups, it was not possible to undertake multi-variable analysis for this outcome.

### *5.7.4 Any ventilation*

Any ventilation comprised two ICD code categories, 569 (continuous ventilatory support) and 570 (non-invasive ventilatory support). There was an increase in numbers of babies requiring any ventilation between the pre- and post-GAP epochs.

There was an increase in ventilation between epochs in non-SGA babies (2.6% pre-GAP to 8.3% post-GAP; aOR=3.36, 95% CI 2.12, 5.31) and amongst SGA babies (5.4% pre-GAP to 8.0% post-GAP; aOR=1.70, 95% CI 0.63, 4.59), although there was no evidence that ventilation differed by SGA versus non-SGA subgroup (interaction p=0.13) (Table 11).

In the SGA subgroup, while it was not possible to undertake multi-variable analysis due to small numbers, there was no evidence that ventilation differed by identification status. Ventilation rates for identified SGA were 5.9% pre-GAP and 6.3% post-GAP; (unadjusted OR 1.07, 95% CI 0.20, 5.79) and in non-identified SGA 5.2% pre-GAP to 10.5 % post-GAP; (unadjusted OR 2.1, 95% CI 0.66, 6.95; interaction p=0.51) (Table 11).

*Table 10. Neonatal outcomes ( composite adverse outcome and NNU admission > 48hr) pre- and post-GAP ( among livebirths)*

| | Pre-GAP | | Post-GAP | | Unadjusted OR (95%CI) | *P interaction* | Adjusted* OR (95%CI) | *P interaction* |
|---|---|---|---|---|---|---|---|---|
| | N | n (%) | N | n (%) | | | | |
| **Composite adverse neonatal outcome**** | | | | | | | | |
| Total | 1098 | 75 (6.8) | 1075 | 117 (10.9) | 1.67 (1.23, 2.26) | | 1.66 (1.22, 2.26) | |
| Non-SGA | 950 | 50 (5.3) | 938 | 92 (9.8) | 1.96 (1.37, 2.80) | | 1.98 (1.38, 2.84) | |
| SGA | 148 | 25 (16.9) | 137 | 25 (18.2) | 1.10 (0.60, 2.02) | 0.11 | 1.05 (0.55, 1.10) | 0.09 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 34 | 11 (32.4) | 80 | 14 (17.5) | 0.44 (0.18, 1.11) | | 0.44 (0.17, 1.15) | |
| Non-identified | 114 | 14 (12.3) | 57 | 11 (19.3) | 1.71 (0.72, 4.05) | 0.04 | 1.81 (0.73, 4.48) | 0.03 |
| **Neonatal Admission >48h** | | | | | | | | |
| Total | 1099 | 52 (4.7) | 1075 | 66 (6.1) | 1.32 (0.91, 1.91) | | 1.33 (0.91, 1.94) | |
| Non-SGA | 950 | 31 (3.3) | 938 | 44 (4.7) | 1.46 (0.91, 2.33) | | 1.54 (0.96, 2.47) | |
| SGA | 149 | 21 (14.1) | 137 | 22 (16.1) | 1.17 (0.61, 2.24) | 0.58 | 1.08 (0.54, 2.17) | 0.52 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 34 | 10 (29.4) | 80 | 13 (16.3) | 0.47 (0.18, 1.20) | | 0.42 (0.15, 1.15) | |
| Non-identified | 115 | 11 (9.6) | 57 | 9 (15.8) | 1.77 (0.69, 4.56) | 0.05 | 1.86 (0.63, 5.52) | 0.04 |

* Adjusted for NZ Deprivation Index, ethnicity, maternal age, maternal BMI, smoking.
****** Composite neonatal outcome: defined as neonatal admission >48h and/or Apgar <7 at 5 minutes and/or any ventilation.

*Table 11. Neonatal outcomes (Apgar <7 at 5 min. and any ventilation) pre- and post-GAP (among livebirths)*

| | Pre-GAP | | Post-GAP | | Unadjusted OR (95%CI) | *P interaction* | Adjusted* OR (95%CI) | *P interaction* |
|---|---|---|---|---|---|---|---|---|
| | N | n (%) | N | n (%) | | | | |
| **Apgar <7 at 5 minutes** (n=1 missing Apgar) | | | | | | | | |
| Total | 1098 | 18 (1.6) | 1075 | 20 (1.9) | 1.14 (0.60, 2.16) | | 1.14 (0.60, 2.19) | |
| Non-SGA | 950 | 13 (1.4) | 938 | 16 (1.7) | 1.25 (0.60, 2.62) | | 1.24 (0.59, 2.60) | |
| SGA | 148 | 5 (3.4) | 137 | 4 (2.9) | 0.86 (0.23, 3.27) | 0.63 | 1.07 (0.26, 4.49) | 0.65 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 34 | 1 (2.9) | 80 | 1 (1.3) | 0.42 (0.03, 6.88) | | - | |
| Non-identified | 114 | 4 (3.5) | 57 | 3 (5.3) | 1.53 (0.33, 7.07) | 0.43 | - | - |
| **Any ventilation** | | | | | | | | |
| Total | 1099 | 33 (3.0) | 1075 | 89 (8.3) | 2.92 (1.94, 4.39) | | 2.93 (1.94, 4.43) | |
| Non-SGA | 950 | 25 (2.6) | 938 | 78 (8.3) | 3.36 (2.12, 5.31) | | 3.38 (2.12, 5.37) | |
| SGA | 149 | 8 (5.4) | 137 | 11 (8.0) | 1.54 (0.60, 3.95) | 0.14 | 1.70 (0.63, 4.59) | 0.13 |
| ***SGA subgroup*** | | | | | | | | |
| Identified | 34 | 2 (5.9) | 80 | 5 (6.3) | 1.07 (0.20, 5.79) | | - | |
| Non-identified | 115 | 6 (5.2) | 57 | 6 (10.5) | 2.14 (0.66, 6.95) | 0.51 | - | - |

* Adjusted for NZ Deprivation Index, ethnicity, maternal age, maternal BMI, smoking.

### *5.8 Summary*

Introduction of the GAP program at CMH has been associated with an almost five-fold adjusted odds increase in the antenatal detection of SGA pregnancies. While there was an increase in maternal intervention (induction of labour and caesarean section) during the audit period, the effect was not more pronounced in SGA pregnancies. There was an improvement in composite neonatal outcomes in the post-GAP cohort, and this was more pronounced amongst identified SGA pregnancies. There was a reduction in prolonged admission to the NNU amongst identified SGA babies in the post-GAP epoch.

# Chapter 6: Discussion

## *6.1 Introduction*

This is the first study to evaluate the impact of the GAP programme in a New Zealand setting. Research in the UK (Gardosi et al., 2018) and Australia (Jayawardena & Sheehan, 2018) has shown that introduction of GAP improved detection of SGA, and has been linked to a possible reduction in the incidence of stillbirth (Gardosi, Giddings, et al., 2013). The New Zealand maternity system is unique, with a continuity of care model based on partnership, including a single named lead care provider for each pregnant woman[8] (Guilliland & Pairman, 2010). Whether there is a benefit of GAP in this model of continuity of antenatal care has not been previously assessed. This chapter discusses the interpretation of findings related to introduction of GAP in CMH, which serves an ethnically diverse and predominantly socio-economically deprived population, and the implications for further education, research, and maternity care.

## *6.2 Main findings and interpretation in context with existing literature*

The primary aim of this study was to test the hypothesis that introduction of GAP would increase identification of SGA pregnancies at CMH. The following section will discuss overall detection of SGA pre- and post-introduction of GAP at CMH, in the context of recent evidence, and then detection of SGA in subgroups of women. In the pre-GAP epoch 35 babies (22.9%) were identified as being SGA antenatally, compared to 81 babies (57.9%) in the post-GAP epoch, (aOR=4.81, 95% CI 2.82, 8.18); confirming our primary hypothesis.

Our results compare well with the most recently published observational study on antenatal detection of SGA following GAP in an Australian hospital clinic setting (Jayawardena & Sheehan, 2018). In this study, antenatal SGA detection rates increased significantly following introduction of GAP from 21% to 41%; OR 2.6, 95% CI 1.3, 4.9).

Our post-GAP SGA detection rate of 57.9% in CMH is equivalent to published detection rates in the best performing GAP units in the UK (56%) and considerably better than the average detection rate in UK GAP units (42%) Gardosi et al., 2018). However, while completing this chapter, I was informed that the two top performing

[8] This study was based exclusively on data from hospital employed midwives. Employed midwives provide continuity of antenatal and postnatal care (not intrapartum care) with a named lead care provider for each woman; whereas self-employed midwives usually provide full continuity of antenatal, intrapartum, and postnatal care.

GAP units in the UK now have detection rates of 68% and 70% (S. Turner, personal communication, July 23rd, 2019). Performance appears to be related to leadership, motivation, and full engagement; with the best performing units in the UK implementing GAP well, adhering to the protocol, and learning from auditing of detection rates and missed case analyses (Gardosi et al., 2018). In the UK, appointment of champions effectively strengthened introduction and improved detection rates, as well as being associated with reduced regional stillbirth rates (Turner et al., 2016).

The high detection of SGA in our study is likely due to several factors including a combination of continuity of midwifery care with standardised fundal height measurement. Additionally, all clinicians are provided with the algorithm (see Chapter 2, Figure 6) as a reference for risk factors for SGA at booking; and guide to screening, detection, and management if SGA is detected. Furthermore, there is general agreement between midwifery, obstetric, ultrasound and neonatology clinicians about the value of GAP, and discussion at perinatal meetings when adverse outcomes may have been managed better according to GAP teaching. Regular news about GAP is featured in the electronic newsletter 'Our maternity monthly'.

A concentrated series of multidisciplinary workshops at CMH, led by a recognised national expert in the GAP programme, resulted in a high level of engagement with the programme. While not officially employed as a champion, my presence as a researcher and educator is likely to have raised the profile of GAP at CMH. Funding has now been procured through ACC to appoint local champions for all DHBs, at the time of introduction of GAP, to cascade education, incorporate elements of the programme into local practice, support clinicians, and conduct audits.

With GAP education in New Zealand, scanning is recommended selectively based on presence of risk factors and clinical assessment of fetal growth and appears to have been effective at CMH. Sovio, White, Dacey, Pasupathy, and Smith (2015) reported a tripling of detection of SGA to 57% with routine third trimester ultrasonography (at 36 weeks) compared with 20% with selective (clinically indicated) ultrasonography. While this reported detection of SGA with routine ultrasound is comparable to our findings with selective ultrasound according to GAP, performance of routine late third trimester scanning has not been assessed in a setting like CMH. Furthermore, there are barriers to routine late third trimester ultrasonography, including concern over unnecessary ultrasound in low risk pregnancy and the burden of cost. Additionally, a normal fetal growth scan at 36 weeks may provide false reassurance in a

woman with major risk factors for SGA, as growth velocity may reduce later in pregnancy with increasing risk of stillbirth (Vashevnik, Walker, & Permezel, 2007).

### *6.3 Maternal demographic and clinical characteristics, and identification of SGA*

#### *6.3.1 Maternal age*

Our findings of both fewer and declining numbers of births to women <20, and >40 years at CMH were consistent with national statistics, as is our data showing that most births occurred to women aged 20 to 39 years in both epochs. Figure 26 represents trends in maternal age among births in New Zealand between 2007 and 2016. At the time of writing, the national data on maternal age and births for 2017-2018, the period for our post-GAP audit was not published, but available data (PMMRC, 2017) is a guide to changes during the time between epochs.

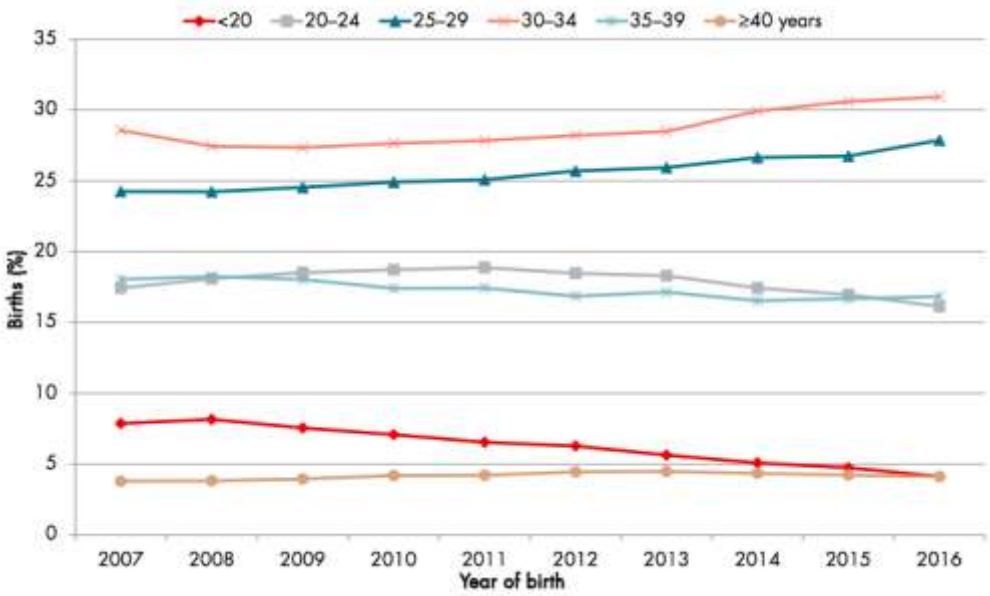



*Figure 26. Trends in maternal age among births in New Zealand 2007-2016 (PMMRC, 2017)*

CMH reported a reduction in births to women < 20 years from 2013 with numbers halving since 2012 (CMH, 2018). During the post-GAP epoch, an increased focus on contraception at CMH has resulted in a report of 100% of women <20yrs booked with hospital employed midwives, having a postnatal contraception discussion with a health professional, and there has also been a free service for insertion of the long acting reversible contraceptive device Jadelle, on the postnatal ward. These measures may have contributed to the reduced numbers of births, particularly for women <20 years.

Our data was underpowered to demonstrate the link between younger and older maternal age and SGA, due to small numbers in these age categories and we did not find a correlation between risk or identification of SGA and maternal age. Teenage pregnancy has been associated with increased risk of SGA although it may be due to lifestyle rather than age as reported by Jones et al. (2010) who demonstrated that fetal size was influenced by maternal weight gain and that teenage mothers who were underweight at booking or who had a low gestational weight gain were more likely to give birth to an SGA infant. Being a tertiary student has also been associated with risk of SGA (McCowan, Roberts, et al., 2009), and this may be a factor influencing the link between SGA and younger maternal age. Nutritional factors such as low intake of fresh fruit and leafy green vegetables have been found to increase risk of SGA (McCowan & Horgan, 2009) and this may be more common in younger mothers, and those with lower incomes. While these factors may offer some explanation, the association between being a young mother and risk of having a growth restricted baby is likely to be multifactorial.

Increasing maternal age is also associated with a higher risk of SGA (Anderson, Sadler, Stewart, Fyfe, & McCowan, 2013; Lean, Derricott, Jones, & Heazell, 2017; McCowan, Roberts, et al., 2009; Monier et al., 2016). The risk of SGA is independent of co-morbidities and fetal anomalies and the mechanism is likely to be associated with placental dysfunction, such as abnormal placental development, accelerated aging and altered nutrient transport (Lean, Heazell, Dilworth, Mills, & Jones, 2017)

### *6.3.2 Maternal ethnicity*

A novel feature of our research is that we have been able to explore the efficacy of GAP on detection of SGA by maternal demographic and clinical characteristics. It is important to know whether the programme is similarly effective across demographic groups and whether there are groups of women who are not receiving the full benefit from GAP.

While GAP was associated with increased detection of SGA amongst all ethnic groups, it was especially pleasing to note the more pronounced effect of GAP on detection of SGA amongst Maaori and Pacific ethnic groups (interaction p=0.049). Improving health equity for Maaori and Pacific people is an important government priority in New Zealand (MoH, 2017), and the GAP programme has been successful in this regard by preferentially increasing detection in those priority groups.

### *6.3.3 NZ deprivation index*

It was reassuring that the GAP programme in CMH was equally effective in increasing detection of SGA in women residing in highest and lower deprivation centiles. Women residing in areas of high deprivation face multiple challenges including communication barriers and difficult access to transport when engaging with care; and the provision of home midwifery antenatal visits by the same midwife may have contributed to early engagement and regular antenatal visits. Early and regular engagement enables stratification of care depending on risk of SGA at booking and as pregnancy progresses, which is a key element of GAP. Women who have high risk of SGA are recommended to be reviewed by a specialist and allocated to a pathway of serial growth scans during pregnancy; whereas those with no known risk factors at booking are managed by routine fundal height measurement from 26-28 weeks, with referral for a growth scan if there is an unsatisfactory pattern of uterine growth. The increased detection of SGA post-GAP across all NZDep. groups may reflect earlier engagement with care by women that has occurred between epochs in CMH amongst women from all deprivation categories, as well as appropriate management according to the GAP pathway.

### *6.3.4 BMI*

We noted a significant difference in distribution of BMI between epochs. Most notable was the reduction in the percentage of women in the underweight BMI group in pre-to post-GAP study groups. In comparing the detection of SGA pre-and post-GAP according to BMI group, detection increased substantially between epochs, and in the women with highest BMI ≥35, post-GAP, the detection of SGA increased from 20.5% pre-GAP to 66.7% post-GAP.

It is important for clinicians to accurately screen for SGA with standardised fundal height measurement if the woman's build is suitable, but the GAP programme in New Zealand recommends a schedule of third trimester growth scans (recommended at 30-32 weeks and 36-38 weeks in the NZMFMN SGA guideline) if the woman has a BMI of ≥35, as maternal habitus is likely to prevent accurate fundal height measurement. The high detection of SGA in women with BMI ≥35 likely reflects that this recommendation has been well incorporated into clinical practice. Of note, the rate of detection of SGA in the subgroup of CMH women with BMI ≥35 is at least as good as the detection of SGA with routine scan at 36 weeks in a population of nulliparous women from Cambridge in the UK (57%), where the majority had a normal BMI (Sovio et al., 2015).

As obesity affects a substantial proportion of the CMH birthing population and is an independent risk factor for both SGA (Anderson et al., 2013) and stillbirth (Flenady et al., 2017), this increase in detection amongst obese women after introduction of GAP is very encouraging. As not all women with BMI ≥35 are likely to have had access to late third trimester ultrasound in CMH, because of limited ultrasound resources, there may be potential for further increments in SGA detection in women with high BMI which could impact on future perinatal mortality.

### *6.3.5 Cigarette smoking*

Cigarette smoking is the individual most modifiable risk factor for SGA. Stopping smoking in pregnancy increases fetal growth and it has been demonstrated that stopping smoking before 16 weeks' gestation is associated with similar rates of SGA as amongst non-smokers (McCowan, Dekker, et al., 2009).

Our data showed that the numbers of women reporting smoking within the last month, at the time of the birth episode, had declined over the time between epochs from 17.6% pre-GAP to 11.9% post-GAP. This coincides with introduction of the incentives-based smoke free programme at CMH in 2013. This programme was considered successful in its first 3 years with twice as many women accessing the programme and three times more women being smoke free by one month after their quit dates (CMH, 2018).

Maaori and Pacific Island women are more at risk of perinatal morbidity and mortality, and it is of concern that smoking rates are still disproportionally higher in these ethnic groups, with smoking rates for Maaori, Pacific Island, Asian and New Zealand European/Other; 43.3%, 13.9%, 5.8%, and 0.9% respectively (CMH, 2018). The ongoing focus on reducing smoking in pregnancy at CMH and the high engagement of Maaori and Pacific women in the incentives-based smoke free programme has potential to reduce smoking in these groups in the future and could impact on SGA rates.

An increase in detection of SGA from 19.4% pre- GAP to 58.3% post-GAP among women who smoked in late pregnancy was also encouraging. The algorithm used for GAP includes a recommendation to perform third trimester growth scans should a woman continue to smoke more than 10 cigarettes daily after 16 weeks of pregnancy. It is likely that this recommendation has contributed to the improved SGA detection for women in the post-GAP cohort who reported continued smoking, as there was no recommendation for scanning in women who continued to smoke prior to the

publication of the NZMFMN SGA guideline (McCowan & Bloomfield, 2014), on which the guidance collated into the GAP algorithm is based.

While it was not possible to collect data on the number of growth scans performed for individual women, the possibility remains that further incremental access to evidence based growth scans for women in CMH, including amongst those who continue to smoke in pregnancy, may further improve SGA detection rates in the future.

### *6.3.6 Pre-eclampsia*

As expected, the detection of SGA in pregnancies with preeclampsia was higher pre-GAP than for pregnancies without preeclampsia. However, detection pre-GAP was disappointing, at 40%, considering that even in the absence of GAP, in pregnancies with pre-eclampsia recommended best practice should have resulted in ultrasound scans for assessment of fetal growth and wellbeing. Notwithstanding, detection of SGA improved post-GAP to 72%. Diagnosis of preeclampsia is an indication for serial growth scans according to the algorithm used in the GAP programme; therefore, an even high detection rate would be expected. Sometimes preeclampsia is diagnosed late in pregnancy or more rarely intra- or post-partum in which case SGA babies at term may not be identified antenatally as induction of labour is offered rather than expectant management.

## *6.4 The influence of GAP on maternal outcomes*

While increased detection of SGA following introduction of GAP is an encouraging outcome, it is important to be aware that any intervention has the potential for unexpected consequences and potential harm; therefore, maternal and neonatal outcomes in our study were assessed for the pre-and post-GAP epochs with adjustments for deprivation, maternal ethnicity, age, current smoking status, and BMI.

### *6.4.1 Induction of labour*

The overall rate of induction increased significantly in both SGA and non-SGA pregnancies between the pre-and post-GAP epochs confirming our hypothesis that introduction of GAP would be associated with an increase in the induction rate amongst SGA (see

Figure 27. Induction of labour as % of all births CMH 2008-2017 (CMH,2018)

for CMH induction rates by year). However, the interaction model showed there was no significant difference in induction rates according to SGA status (interaction p=0.19). In the SGA subgroup, there was also a rise in induction of labour for both

identified and non-identified SGA, with no evidence that the increase in induction of labour differed significantly by identification status.

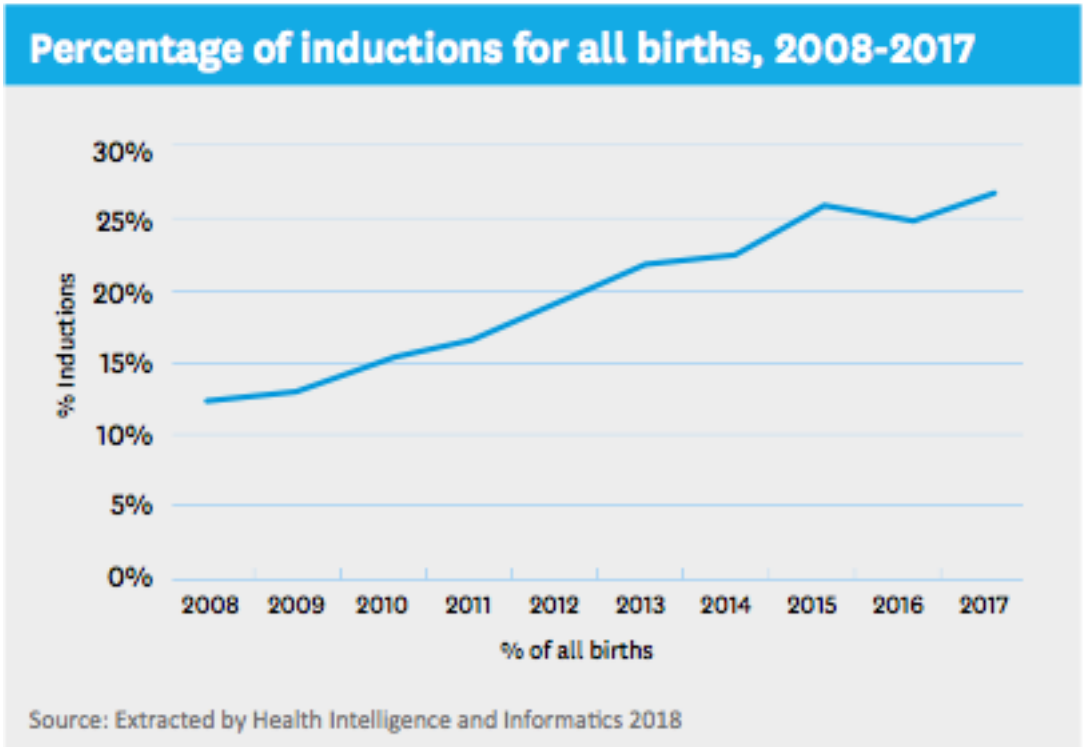



*Figure 27. Induction of labour as % of all births CMH 2008-2017 (CMH,2018)*

The lack of significant interaction in induction between SGA and non-SGA may have been due to limited power as the magnitude of increase was greater amongst SGA compared with non-SGA (31.4 to 45.7% vs 27.7 to 32.3% respectively). An alternative, or additional, explanation is that use of the evidence based NZMFMN SGA guideline limited induction of labour in low risk or constitutionally small SGA babies. The NZMFMN SGA guideline for those pregnancies where SGA has been detected antenatally, but the Doppler findings are normal and the estimated fetal weight is >5$^{th}$ centile, indicates these babies are likely to be constitutionally small and birth is recommended by 40 weeks (McCowan & Bloomfield, 2014). Clinical review is recommended weekly, and growth scans every 2-3 weeks. This New Zealand regime is very similar to that recently evaluated in the UK by (Veglia et al., 2018), which demonstrated a reduction in induction and caesarean section and increase in vaginal birth compared to the previous UK policy of inducing all SGA pregnancies at 37 weeks, regardless of degree of growth restriction and Doppler parameters. The low risk SGA population comprised approximately 50% in the Veglia et al. (2018) study; but similar data, according to constitutional smallness or fetal growth restriction, are not available for our SGA study population.

According to the GAP programme in New Zealand, as informed by the NZMFMN SGA guideline, induction of labour is recommended at 38 weeks if there is evidence from ultrasound scan of estimated fetal weight <5$^{th}$ customized centile, or abnormal uterine, middle cerebral artery, cerebro-placental ratio, or umbilical artery Doppler indices. This is likely to occur in approximately 50% of cases (Veglia et al., 2018) and these women are considered to have babies with FGR (Figueras & Gratacos, 2017). Prior to birth, women are advised regarding prompt reporting of preeclampsia symptoms and any change in fetal movements, as well as being followed up with a holistic assessment including once to twice weekly CTG, liquor volume, umbilical artery, middle cerebral artery, and cerebro-placental ratio Doppler indices, with growth scans every 2-3 weeks. If there is any deterioration in fetal condition prior to 38 weeks, management is reviewed; and, at any time, if there is a finding of absent or reversed end diastolic velocity in the umbilical artery the woman is admitted to hospital urgently for specialist review. The guideline also recognises that ultrasound findings may subsequently indicate that growth has normalised and accordingly recommends a return to low risk care (Lewkowitz, Tuuli, Cahill, Macones, & Dicke, 2019).

### *6.4.2 Caesarean birth*

We hypothesised that there would be no increase in caesarean birth amongst SGA pregnancies after introduction of GAP, and this hypothesis was not confirmed. The overall caesarean birth rates have risen post-GAP at CMH (see **Error! Reference source not found.**) but with similar increases in SGA and non-SGA (38.6 to 47.9% and 30.4 to 34.8% respectively) between epochs. The interaction model showed that the magnitude of the effect did not differ between SGA and non-SGA pregnancies (interaction p=0.58). Importantly, our finding that caesarean birth did not increase in the SGA subgroup identified before birth was pleasing (interaction p=0.86). While the rate of caesarean birth for all women in our study was high (31.5% pre-GAP vs 36.5% post-GAP), compared to the overall rates in CMH (21% in 2012 and 27 % in 2017) (CMH, 2013b, 2018) this may have related to our cohort of women in the care of hospital employed midwives, whose caseloads include more high risk pregnancies compared to caseloads of self-employed midwives.

Timely delivery in identified SGA, according to the management algorithm, may have reduced rates of caesarean birth in the post-GAP epoch as reported by Veglia et al. (2018) and (Jayawardena & Sheehan, 2018), and our findings are also consistent with those from the Disproportionate Intrauterine Growth Restriction Intervention Trial

(DIGITAT), which showed that induction of labour in SGA pregnancies from 36-37 weeks did not lead to an increase in cesarean birth (Boers et al., 2010).

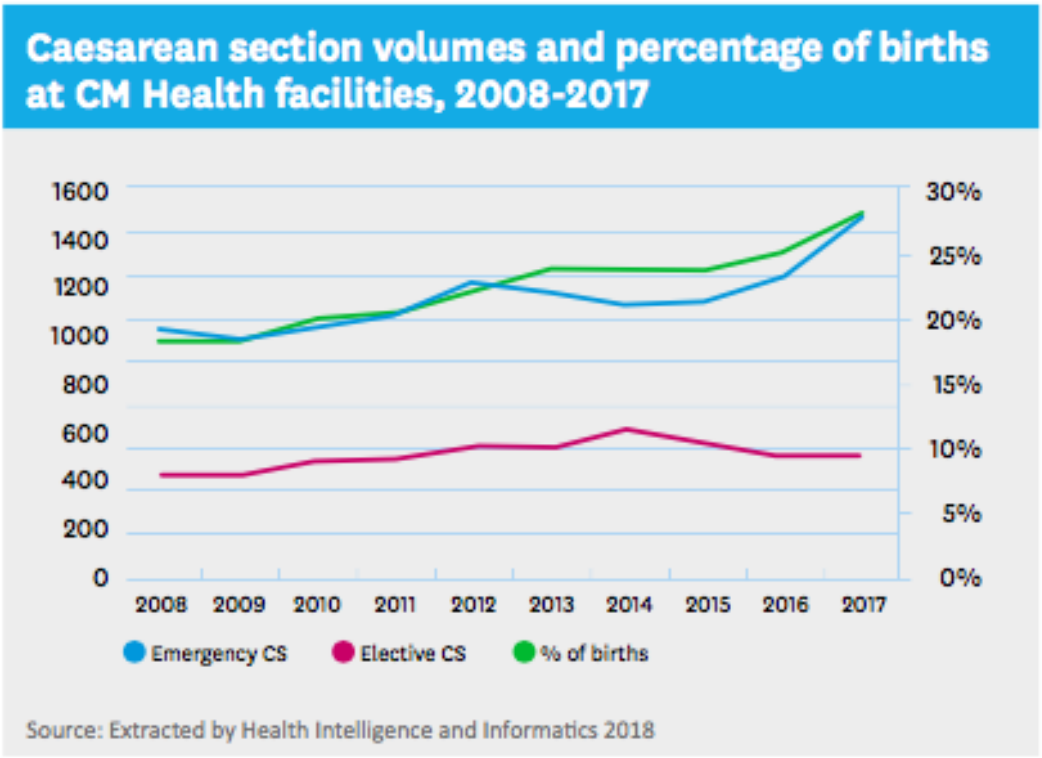



*Figure 28. Caesarean births as % of all births CMH 2008-2017 (CMH,2018)*

### *6.4.3 Preterm birth*

The risks associated with FGR must be balanced against the possible harmful effects of iatrogenic preterm or even early term birth. Every day in utero counts. Preterm babies have difficulties with thermoregulation, respiratory distress, jaundice, infection, and breast feeding (Boyle, 2012). Babies born preterm are at increased risk of mortality (Richter et al., 2019) and reduced cognitive outcomes (Chan, Leong, Malouf, & Quigley, 2016). However, in the context of FGR as a leading cause of stillbirth (Flenady et al., 2017), it is important that timing of birth optimises outcome for each baby. It is, therefore, important to detect any increase in iatrogenic preterm birth, resulting from increased antenatal detection of SGA following introduction of GAP.

The mean gestation at birth reduced by 1.5 days overall between epochs, ($p=0.005$). The pre-term birth rate increased between the pre-GAP and post-GAP epochs, in both non-SGA and SGA, but there was no evidence that this increase in preterm birth differed by SGA versus non-SGA subgroup (interaction $p=0.88$). Of note, preterm birth has not increased amongst detected SGA pregnancies in the post-GAP

epoch and, if anything, there has been a non-significant reduction in preterm birth amongst SGA babies who were identified before birth (see Chapter 5, section 5.6.3).

The fact that pre-term birth did not increase in detected SGA pregnancies may represent appropriate management of identified SGA according to the NZMFMN SGA guideline during the post-GAP epoch. According to post-GAP management, women carrying SGA babies with normal Doppler indices are monitored but not induced until 40 weeks unless indicated; however, women with high-risk FGR pregnancies with an EFW <5$^{th}$ centile or abnormal Doppler findings are induced at 38 weeks if spontaneous labour has not occurred. Conversely, in the pre-GAP epoch, prior to introduction of the NZMFMN SGA guideline, it is possible that women with SGA pregnancies were more likely to be induced prior to term when a fetus was detected as SGA, regardless of degree of risk. While it is important to avoid iatrogenic preterm birth, the stratified induction policy is based on expert opinion and supported by recent research, which has reported benefits of improved neonatal outcome including more births at or after 39 weeks of gestation (Veglia et al., 2018).

### *6.4.4 Post-term birth*

It is also important to minimise post-term birth with SGA pregnancy, due to the increased risk of stillbirth amongst SGA pregnancies with advancing gestation (Vashevnik et al., 2007). We assessed data for pregnancies continuing beyond full term [>40 weeks (280 days)]. Post 40 weeks, births decreased similarly amongst SGA and non-SGA pregnancies between epochs, but we did not observe a significant reduction in post-40 week births by SGA status (interaction p=0.64). This may have been because of the recommended expectant management approach in low risk SGA resulting in induction in some cases after 40 weeks and zero days of gestation, or birth beyond 40 weeks and zero days despite induction at 40 weeks. Future studies should investigate gestation at birth by high and low risk SGA status.

### *6.4.5 Stillbirth*

Observational studies have demonstrated an association between introduction of the GAP and reduced stillbirth (Gardosi et al., 2014); however, our study was under-powered to assess an impact of GAP on stillbirth. Overall, there were 6 stillbirths in the pre-GAP cohort and 7 in the post-GAP cohort, representing rates of 5.4/1000 and 6.5/1000 births respectively. Four of the six stillborn babies in the pre-GAP epoch were SGA (one identified before birth) and two occurred in the second trimester, close to borderline viability. Post-GAP three of seven stillborn babies were SGA (one identified)

with stillbirth occurring between 26 and 29 weeks, when standardised fundal height measurement had only just commenced (recommended to start from 26-28 weeks). We have not reviewed these stillbirths in detail to determine whether major risk factors for SGA were present and whether appropriate care pathways were followed.

With application of the SGA guideline, in the context of GAP education, the women who suffered loss of their SGA babies in the post-GAP epoch would be encouraged to seek early antenatal care in subsequent pregnancies, with obstetric review and offer of prophylactic low dose aspirin to reduce SGA in a future pregnancy (Bujold et al., 2014; Roberge et al., 2017). Ideally, they would also be counselled about lifestyle strategies to improve outcome in a subsequent pregnancy, such as being smoke-free, eating fresh fruit and vegetables daily, engaging in regular exercise, and achieving a healthy weight.

## *6.5 The influence of GAP on neonatal outcomes*

### *6.5.1 Composite morbidity*

Consistent with our study hypothesis, there was evidence that increased detection of SGA in the post-GAP epoch was associated with a two-fold decrease in the likelihood of composite neonatal morbidity among babies where SGA was identified antenatally (see Chapter 5.7.1). This finding is highly clinically significant, given the overall increase in neonatal morbidity in the post-GAP cohort, which is likely to reflect the increasing complexity of pregnancies in the CMH region. Improved recognition of at-risk SGA pregnancies, with evidence-based monitoring and timing of birth, and careful intrapartum surveillance allowing for timely operative vaginal or caesarean birth if necessary, for concern over fetal status, may have contributed to the decrease in composite morbidity. It is unclear why there was an increase in composite morbidity for non-SGA babies between epochs. However, the increase in neonatal unit admission seen in the post-GAP epoch may be related to the overall increased rates of admission between epochs and in particular the significant increase in meconium aspiration syndrome (CMH, 2018).

These findings from our research are consistent with limited international literature that has reported antenatal identification of SGA is associated with reduced severe neonatal morbidity. Lindqvist and Molin (2005) found that a structured programme of identification and surveillance of SGA pregnancies was associated with a four-fold reduced risk of serious fetal complications defined as hypoxic encephalopathy

grade 2 or 3, intracranial haemorrhage, Apgar score <4 at 5 minutes, neonatal convulsions, umbilical artery pH <7.0, cerebral palsy, mental retardation, stillbirth, intrapartum or infant death. In our study, analysis was limited to routinely collected neonatal data; however, analysis of composite morbidity according to the individual components showed that there was an effect of GAP on reduced prolonged neonatal unit admission.

### *6.5.2 Admission to the neonatal unit >48 hours*

Whilst there was an increase in prolonged neonatal admission between epochs, there was no evidence that prolonged NNU admission differed by SGA status (interaction p=0.52); but it was very pleasing to find that increased identification of SGA post-GAP may be associated with a lower incidence of prolonged NNU admission (interaction p=0.04).This confirms findings by Jayawardena and Sheehan (2018) who reported reduced admission of SGA babies to the NNU following introduction of GAP. Larger numbers would be needed to strengthen this finding, but it is encouraging to know that fewer babies needed neonatal care post-GAP and were able to stay with their mothers following the birth. As every day in the NNU costs CMH NZ$1,130 for level 2 care and NZ$2,114 for level 3 (excluding laboratory and radiology costs) (personal communication C. McKinlay, 29th July 2019) this is likely to have reduced costs and has the potential to partially offset any increased costs associated with ultrasound scanning. Currently there is a co-payment of NZ$30-60 for every ultrasound scan, which is met by the DHB for many women at CMH who cannot afford this fee.

Existing literature demonstrates an increased risk of prolonged NNU admission when a baby is growth restricted, including at term gestation (Kalafat, Morales-Rosello, Thilaganathan, Dhother, & Khalil, 2019; Policiano, Fonseca, & Mendes, 2017). Previous studies have not reported neonatal admission by SGA detection status. Our findings suggest that careful surveillance of fetal wellbeing and optimal time of birth amongst detected SGA babies may have been associated with reduced need for prolonged NNU admission. Babies who need admission to the NNU may not be able to have uninterrupted skin to skin contact immediately after the birth, with the associated advantages of enhanced initiation of breastfeeding and bonding. Further, mothers who are separated from their babies may suffer increased anxiety particularly if they have not experienced the kind of birth they were anticipating (Redshaw & Martin, 2013).

In our study, there was an overall increase in prolonged NNU admission between epochs, particularly in non-SGA babies (aOR=1.48, 95% CI 0.84-2.60). This

increase reflects data reported for Counties Manukau, showing an increase in NNU admissions at Middlemore hospital from 2012 to 2017 (See **Error! Reference source not found.**). This is likely to be due to the complexity amongst the women served by CMH, including the increasingly high rates of diabetes and obesity.

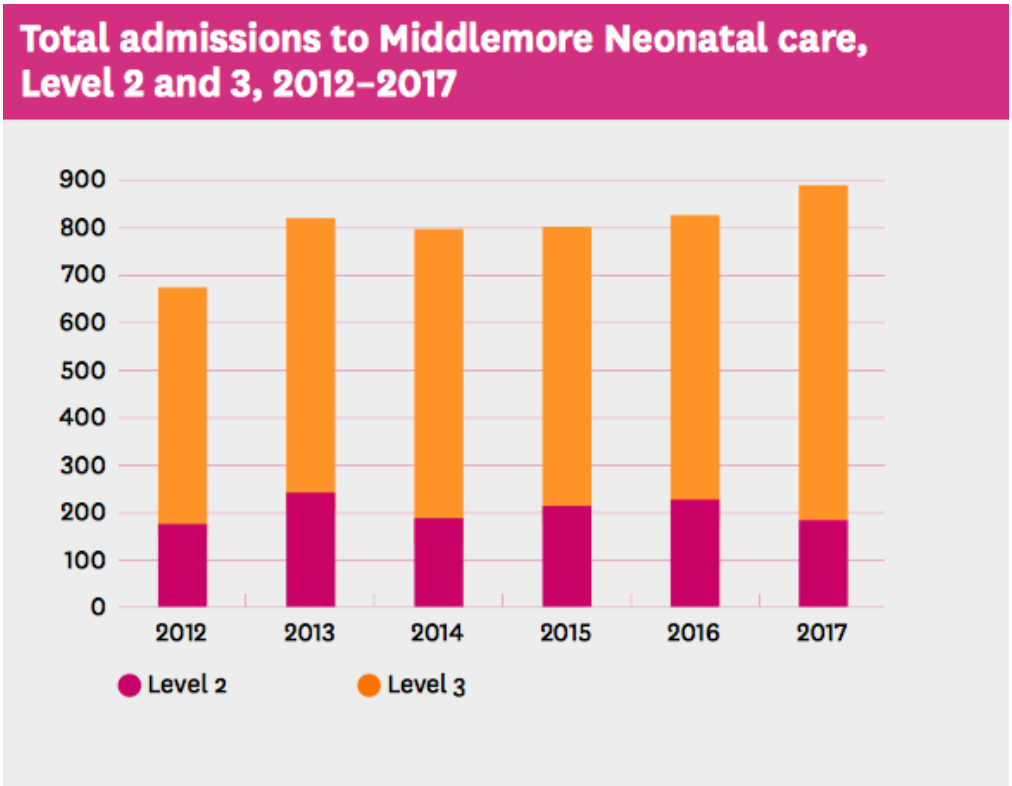



*Figure 29. Admission to NNU level 2 (special care) and level 3 (intensive care) 2012-2017 (CMH,2018)*

For the NNU at Middlemore hospital, which has extremely high occupancy, any reduction in admissions is beneficial. It is crucial that any effect on patient flow is monitored when an intervention such as GAP is introduced. In this context, our finding of reduced prolonged NNU admission is very encouraging, as well as the knowledge that introduction was not associated with an increased clinical burden.

### *6.5.3 Apgar score <7 at 5 minutes*

The Apgar score (Apgar, 1953) provides a numerical assessment of a baby's condition, based on heart rate, respirations, muscle tone, reflex irritability, and colour, routinely estimated at one and five minutes after the birth. An Apgar score <7 at 5 minutes is associated with increased risk of neonatal morbidity, infant mortality, and neurological impairment (Thavarajah, Flatley, & Kumar, 2018).

Our data showed there were very small numbers of babies with Apgar scores <7 at 5 minutes; hence, we have very limited power to investigate this outcome and we did not find any significant difference in Apgar scores <7 across epochs according to SGA non-SGA status or SGA subgroup status. There is potential for a high level of inter-observer variability with calculation of the Apgar score, and setting a level of > or <7 does not distinguish between the intermediate level of 4-6 and the very low levels 0-3 which are more predictive of neurological morbidity (Leionen, 2018; Thorngren-Jerneck & Herbst, 2001). Different Apgar cut-offs and more robust measures of neonatal condition at birth should be incorporated in future studies.

Transition at birth requires complex adaptation to extra-uterine life, more difficult when the infant has suffered intrapartum hypoxia, which predisposes the fetus to neonatal asphyxia, acidosis, short- and long-term morbidity, including hypoxic ischaemic encephalopathy. The umbilical artery lactate test provides an objective assessment of intrapartum hypoxia and is predictive of neonatal and long term outcome. The newborn early warning score (NEWS) (Roland, Madar, & Connolly, 2010), is being implemented in some New Zealand DHBs. This score involves a full assessment at frequencies depending on risk factors, with scores assigned for assessment of 7 vital signs including respiratory rate, breathing effort, heart rate, central colour and perfusion, temperature tone, oxygen saturation and, if indicated, blood glucose and cord lactate. The NEWS could provide a comprehensive measure of neonatal condition in future studies on SGA. Pulse oximetry is assessed as a selective component of NEWS but would also be a useful assessment of neonatal condition in the context of SGA (Tin & Lal, 2015).

### *6.5.4 Ventilatory support*

In this study, we included 2 categories of ventilatory support—Code 569 (continuous ventilatory support, and code 570 (non-invasive ventilatory support). Continuous ventilatory support refers to invasive or mechanical respiratory support via an endotracheal tube (Rocha et al., 2018). Non-invasive respiratory support includes continuous positive airway pressure (CPAP), and heated humidified high flow (HHHF). At the CMH NNU, most late preterm and term babies with persisting respiratory distress receive CPAP. While use of ventilatory support increased two-to three-fold overall in the post-GAP epoch, there was no increase in babies with identified SGA. Given that respiratory support is a key driver of neonatal care costs, this is an important clinical finding, and further supports the ongoing resourcing of the GAP programme.

### *6.5.5 Neonatal death*

A single neonatal death occurred in the pre-GAP cohort of an extremely preterm baby who was not SGA (birthweight centile 22.9%). In the post-GAP cohort, two neonatal deaths occurred, including one baby who was SGA, but not detected antenatally. A detailed review of this case demonstrated potential for intervention had GAP pathways and recommendations been followed. The baby was born at 40 weeks (birthweight centile 1.9%), to a Maaori mother with a previous SGA baby. She had been prescribed low dose aspirin at booking but had only one growth scan at 34 weeks which reported the estimated fetal weight to be on 50$^{th}$ centile. However, the biometry chart showed a 40% discrepancy between the head and abdominal circumference (90$^{th}$/50$^{th}$) suggesting asymmetry in growth. No further growth scans were performed and subsequently the woman presented in strong labour with a prolonged fetal heart deceleration. Following an emergency caesarean, the baby was born in very poor condition and died at 3 days. The outcome could have been different had the GAP pathway of serial growth scans been followed and highlights the need for ongoing education of all clinicians.

## *6.6 Strengths and limitations*

### *6.6.1 Strengths*

This is the first New Zealand study to evaluate introduction of the GAP. Furthermore, the evaluation was carried out in a multi-ethnic high deprivation community with high rates of co-morbidities such as obesity. Multivariable analysis adjusted for confounding variables which are known risk factors for SGA and an interaction model was applied to assess impact of epoch on outcomes. Both datasets for pre- and post-GAP were almost 100% complete after extensive checking of handwritten and electronic records to compete missing fields.

All GAP education at CMH was provided by me, ensuring consistency of education according to generic material used for the programme, and adapted to align with New Zealand guidelines and maternity care.

### *6.6.2 Limitations*

As this study was retrospective and depended on data from records inputted by clinicians, inaccuracies in documentation may have affected accuracy of routine data. However, as clinicians were not aware of this study at the time of data entry it is unlikely that this would have resulted in bias. The pre-GAP audit utilised data from the electronic database, Healthware$_{TM}$ for the entire cohort and all notes for SGA

pregnancies were hand checked; whereas the post-GAP audit data were extracted from the electronic record in the MCIS, in an epoch where handwritten notes were no longer kept. Electronic data may be recorded more systematically than handwritten data, but conversely may contain less detail in the clinical narrative. While challenging, this limitation was addressed in the post-GAP epoch by detailed checking of patient electronic records and the clinical portal for scan reports and correspondence.

Whilst the criteria used for detection of SGA were the same in the pre- and post-GAP epochs, evidence for antenatal SGA detection was less clear in the pre-GAP epoch as clinical notes often lacked definitive information. Evidence of detection was, therefore, obtained directly from ultrasound scan reports, when they had been performed. This could have resulted in some under or over-estimation of SGA detection. However, where there was uncertainty regarding antenatal diagnosis in the pre-GAP epoch, cases were reviewed with a supervisor who is a maternal fetal medicine specialist and expert in SGA diagnosis and management.

Over the four-year time period, between the pre- and post-GAP audits, there were significant demographic and clinical practice changes, and it is possible that increasing awareness of the use of GROW charts and the NZMFMN SGA guideline (first published in 2013) may have resulted in an incremental improvement in SGA detection over the time between epochs. However, we do not have data on the intervening years. A study comparing an epoch devoid of any aspect of GAP with an epoch after introduction would be ideal, but this would have resulted in a much larger time lag between epochs which would present more potential for residual confounding.

While adjustments were made for known confounders, it is possible that some of the effects between epochs are due to residual confounding factors that are not captured in the interaction models. Whilst our study population was broadly representative of the wider population at CMH, with respect to distribution of demographic variables we were not able to include data of women who booked with non-hospital LMCs who provided care for approximately 50% of women at CMH in 2012 (CMH, 2013b) and 71% in 2017. We recommend further study including data from self-employed LMC midwives.

It is acknowledged that a lack of formal introduction science may be a limitation Future scale up of introduction may be assisted by application of theory of change, including strategies to change professional behaviour and formally evaluate “active” ingredients of the GAP package.

We were underpowered to investigate the impact of GAP on stillbirth and neonatal death at CMH, and much larger studies are required to investigate this relationship. While it is important to assess the effect of GAP on scanning resources, this information is not available in our study, as scanning data was not collected prior to 2015. There has been an increase in utilisation of ultrasound services post-GAP, but this has not been confined to the use of growth scans (A. Hicks, personal communication, March 20, 2019). Information about numbers of scans per woman is not available so we are unable to comment on whether the schedule of scanning complied with GAP recommendations.

### *6.7 Recommendations for future education*

The success of GAP depends on the engagement and skill of all clinicians involved with maternity care, and I offer the following recommendations:

- For GAP to be successful in a DHB there needs to be a focus on the educational programme being mandatory for all clinicians engaged in antenatal care.
- Yearly updates with e-learning are recommended by GAP, and it would be beneficial to require this alongside mandatory annual updates on CPR and neonatal resuscitation.
- International midwives are required to undertake specific education when registering in New Zealand. As GAP is being implemented nationally, there would be benefit in adding GAP accreditation to the existing list of educational requirements for international midwives commencing practice in New Zealand.
- GAP accreditation should be required for all access holders of a DHB which has implemented the programme
- Strategies to improve engagement of self-employed community LMC midwives will need to be considered in order to achieve maximum benefit from GAP

### *6.8 Recommendations for future research*

There is immense potential for further research on detection and outcomes amongst SGA pregnancies and babies. Issues to be addressed in future studies could include:

#### *6.8.1 Maternal outcome studies*

- Qualitative exploration of clinician's experience of use of GAP, and women's experience of having a customized growth chart for their pregnancy.
- The effect on ultrasound scanning services and costs associated with education of clinicians. A report on the introduction of the UK based Saving Babies Lives

Care Bundle (O'Connor, 2014), which incorporated GAP alongside initiatives to reduce smoking, manage maternal report of reduced fetal movements, and improve intrapartum fetal monitoring, found that ultrasound service requirements and interventions such as induction of labour and caesarean section were increased (Widdows et al., 2018). Future research needs to address this potential outcome of GAP.

### *6.8.2 Infant outcome studies*

- Investigation of factors contributing to missed cases of SGA, including accuracy of estimated fetal weight on growth scans, and rates of false positive and negative diagnoses of SGA. It is particularly important to address factors associated with false positive SGA diagnoses to minimise unnecessary intervention, and regular auditing of missed cases will inform clinicians of factors involved with false negative diagnoses.
- Include more neonatal outcome variables such as NEWS, cord lactate, oximetry, lower cut-off for Apgar, quality of feeding, hypoglycaemia, and jaundice.
- Compare gestation at birth by high and low risk SGA status.
- Clarification of definition of SGA. Currently there is lack of international consensus on the definition of FGR and the GAP tool reports SGA (customized birthweight <10$^{th}$ centile), which includes constitutionally small babies as well as under-recognising SGA in babies whose weight is >10$^{th}$ centile but still below their individual growth potential. Future work is likely to focus on sensitivity and specificity of diagnosis of FGR and accurately reporting true growth restriction at birth, rather than the surrogate of SGA. Studies on neonatal body composition may lead to a refocussing on body fat and bone growth rather than weight[9].
- The impact of GAP on rare outcomes like stillbirth, neonatal death, and neonatal encephalopathy, which will require large datasets.
- While we have assessed the neonatal outcomes, FGR may affect a child throughout their lifetime. The effect of antenatal detection of SGA could be further evaluated in longitudinal studies to add to existing research on the long-term outcomes of SGA (Baschat, 2011; Bellido-Gonzalez, Diaz-Lopez, Lopez-

[9] The GROW App will be updated shortly to include the 3$^{rd}$ centile, which will assist clinicians to differentiate between constitutionally small and growth restricted infants.

Criado, & Maldonado-Lozano, 2016; Chan et al., 2016; Shah & Kingdom, 2011).

### *6.8.3 Other research*

- It is important to assess the impact of GAP on maternal and neonatal outcomes for women whose maternity care is provided by self-employed midwives as this is the most common model of care in New Zealand

### *6.8.4 Strengthening evaluation of GAP*

As the GAP programme is implemented in other DHBs across New Zealand, it is important to consider which introduction measures are effective and which need further development. While it is important to ensure that intervention fidelity is maintained for accurate interpretation of the effect of the intervention (Gearing et al., 2011), elements of the programme may need to be adjusted for each setting. Elements of fidelity are based on sound design, with a framework comprised of elements essential to the design as well as a plan for structured evaluation and replication. Issues concerned with education such as support and certification of cascade trainers (champions), staffing turnover and resources must be addressed. Throughout the programme intervention delivery should be evaluated and data on intervention receipt such as session attendance, comprehension and barriers to participation should be monitored.
The effectiveness of whether the programme has reached the target population will be monitored by keeping records of clinician education and identification of percentage of employed and access holding clinicians who have competed the education.
It is of utmost importance to monitor programme introduction as there is strong evidence that the level of introduction determines success of outcomes (Wilson, 2009).

## *6.9 Recommendations for practice*

Currently there are challenges for midwives who are following recommended best practice according to the GAP programme. Some issues are already being addressed at CMH but are listed here as they are likely to be generic challenges wherever GAP is introduced.

- Inequities in availability and costs of ultrasound scanning must be urgently addressed in Counties Manukau DHB and across New Zealand.
- Women with a diagnosed SGA pregnancy should be reviewed at recommended times according to the SGA guideline, preferably at a dedicated clinic with availability of ultrasound, a specialist midwife and obstetrician, and not by their

primary care midwife. While it is pleasing to note this has now been achieved at CMH, a similar service is not available at every DHB.

- Women should carry a copy of their own GROW chart, so it is available during review by sonographers and obstetricians.

### *6.10 Conclusion*

In our study, which is the first to evaluate the effect of introduction of GAP in a New Zealand DHB where women receive continuity of midwifery antenatal care, it appeared that introduction of the programme was associated with an almost five-fold increased odds of detection of SGA. While there was an increase in maternal intervention and preterm birth between epochs, the effect was not more pronounced in SGA pregnancies.

Amongst SGA babies who were identified during pregnancy, there was some evidence of reduced composite neonatal morbidity and reduced prolonged neonatal admission. GAP is a safe tool for increasing detection of SGA and suitable for application in an ethnically diverse population with high levels of obesity. This study may inform other DHBs considering introduction of GAP and provide further evidence to guide decisions regarding support for GAP nationally and internationally.

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# Appendices

## *Appendix A: Abbreviations*

| | |
|---|---|
| AC | Abdominal circumference |
| ACC | Accident Compensation Commission |
| AGA | Appropriate for gestational age |
| AOR or aOR | Adjusted odds ratio |
| ARR | Absolute risk reduction |
| AUT | Auckland University of Technology |
| BMI | Body mass index |
| BPD | Bi-parietal diameter |
| CMH | Counties Manukau Health |
| CI | Confidence Interval |
| CPR | Cerebro-placental ratio |
| CTG | Cardio-tocograph |
| CPAP | Continuous positive airway pressure |
| DHB | District Health Board |
| DIGITAT | Disproportionate Intrauterine Growth Intervention Trial at Term |
| EFW | Estimated fetal weight |
| EPPI | Enoxaparin for the prevention of pre-eclampsia and IUGR |
| HHHF | Heated humidified high flow |
| FGR | Fetal growth restriction |
| FL | Femur length |
| GAP | Growth Assessment Protocol |
| GROW | Gestation related optimal weight |
| HC | Head circumference |
| IOL | Induction of labour |
| LGA | Large for gestational age |
| LMC | Lead maternity carer |
| LDA | Low dose aspirin |
| LMWH | Low molecular weight heparin |
| MCIS | Maternity clinical information system |
| MCA | Middle cerebral artery |
| MCGRS | Multicentre Growth Reference Study |
| MMPO | Midwifery and Maternity Providers Organisation |
| MoH | Ministry of Health |
| MoM | Multiples of the mean |
| MQSP | Maternity Quality and Safety Programme |
| NE | Neonatal encephalopathy |
| NHS | National Health Service |
| NICHD | National Institute of Child Health and Human Development |
| NNU | Neonatal unit |
| NEWS | Newborn early warning score |
| NZAPEC | New Zealand Action on Pre-eclampsia |
| NZCOM | New Zealand College of Midwives |
| NZDep | New Zealand deprivation index |
| NZMFMN | New Zealand Maternal Fetal Medicine Network |
| OR | Odds ratio |
| PAPP-A | Pregnancy-associated plasma protein A |
| PE | Pre-eclampsia |

| | |
|---|---|
| PiMS™ | Patient information management system |
| RANZCOG | Royal Australian and New Zealand College of Obstetrics and Gynaecology |
| RCOG | Royal College of Obstetrics and Gynaecology |
| RCT | Randomised controlled trial |
| RR | Relative risk |
| SD | Standard deviation |
| SFH | Symphyseal fundal height |
| SGA | Small for gestational age |
| UA | Umbilical artery |
| UF | Unfractionated heparin |
| UK | United Kingdom |
| US | United States |
| Ut. A | Uterine artery |
| PMMRC | Perinatal and Maternal Mortality Review Committee |
| VON | Vermont Oxford Network Neonatal Encephalopathy Registry |
| WHO | World Health Organisation |

***Appendix B: Neonatal encephalopathy and small for gestational age literature review***

Authors: Joyce Cowan Senior Lecturer Midwifery Auckland University of Technology, Rennae Taylor Research Manager Auckland University and Lesley McCowan, Professor of Obstetrics and Gynaecology University of Auckland.

A structured literature search was conducted to identify publications that had investigated a relationship between Neonatal Encephalopathy (NE) and Small for Gestational Age (SGA) or intrauterine growth restriction (IUGR).

An OVID Medline search was conducted with no date limitation as outlined below.

| Steps | Ovid Medline Search Steps (no limit on years) | 7/06/2017 | Relevant |
|---|---|---|---|
| 1 | Infant, Small for gestational age'/ or 'Fetal Growth Retardation'/ or 'Small for gestational age'. | 18450 | |
| 2 | Neonatal encephalopathy.mp | 744 | |
| 3 | Newborn encephalopathy.mp | 43 | |
| 4 | Hypoxic ischaemic encephalopathy | 485 | |
| 5 | 2 or 3 or 4 | 1246 | |
| 6 | 1 and 5 | 17 | |
| 7 | limit 6 to (English language and humans) | 16 | 6 |
| 8 | risk factors.mp or 'Risk Factors/ | 873182 | |
| 9 | 5 and 8 | 175 | |
| 10 | limit 6 to (English language and humans) | 155 | 6 |
| | **Additional relevant papers added:** | | |
| | Sadler LC 2016 | | 1 |
| | PMMRC Report 2016 | | 1 |
| | **Total in Literature Table** | | **14** |

All abstracts identified by this search (in steps 7, n=16 and 10, n=155), were screened by two reviewers. Reasons for exclusion fell into two main groups: either the subject was not NE or if NE was reported no data were provided on the relationship between NE and SGA. One study was excluded as it was a review article that duplicated data from an original publication. Twelve studies are included in Table 1 that summarises the relationship between NE and SGA

Three recent local reports with data on NE are also included in Table 2: The Tenth and Eleventh Annual Report of the Perinatal and Maternal Mortality Review Committee (PMMRC, 2016 and 2017) and a publication by Sadler et al in 2016 (Sadler 2016).

## Synopsis of Review.

We identified 12 publications that reported the relationship between NE and the infant being born SGA or with IUGR. Nine studies reported a positive association between SGA and risk of NE, two found no association and one was inconclusive (Table 1).

## Why this is important?

The majority of studies included in Table 1 identified that SGA is an important antenatal risk factor for development of NE with odds ratios usually between 3 and 4. Three papers that reported a positive association did not include odds ratios but baseline rates of SGA were higher in NE cases than in the background population. Information on whether the SGA baby was identified before birth was not available but a number of publications commented on the importance of improving antenatal recognition of SGA as an intervention that may reduce the risk of NE.

## What does this mean?

The literature summarised in Table 1 suggests that SGA is an important antenatal risk factor for NE. Table 2 contains data from three recent New Zealand reports. The 2016 and 2017 PMMRC reports demonstrate that SGA is over represented in cases of NE in New Zealand (PMMRC, 2016) and Sadler et al report that failure to assess fetal growth and follow best practice is a theme in avoidable cases of NE in New Zealand (Sadler, 2016).

Currently in routine antenatal care the majority of SGA infants are not recognised before birth and unrecognised SGA babies have increased perinatal mortality (Gardosi, 2014; Stacey, 2012) and adverse neonatal outcomes, including birth asphyxia, which can be an antecedent to NE (Lindqvist, 2005). Many of these unrecognised small babies are therefore not known to be at high risk of fetal compromise in labour. As a consequence, they will not usually receive continuous intrapartum fetal heart rate monitoring (best practice in SGA) which could reduce the secondary complication of asphyxia in labour and later development of NE.

Introduction of the Growth Assessment Protocol (GAP) educational program has been associated with increased antenatal recognition of SGA pregnancies (Turner, 2016). This has likely occurred because of standardised education in fundal height measurement and recommending serial scanning for women with major risk factors for

SGA infants. When SGA infants are detected in pregnancy this should enable appropriate antepartum surveillance and timely delivery to be arranged with careful intrapartum monitoring. The NZ MFM guideline for management of suspected SGA singleton pregnancies after 34 weeks' gestation (http://www.asum.com.au/wp-content/uploads/2015/09/NZMFM-SGA-Guideline-September-2013.pdf) is part of the NZ GAP education program on management of SGA. It recommends continuous fetal heart rate monitoring in labour for SGA pregnancies to facilitate early recognition of fetal compromise enabling operative delivery if necessary. The NZ GAP education program also recommends prescription of low dose aspirin for women with major risk factors for having a SGA baby (Askie, 2006; Bujold, 2010) with potential for a modest reduction in numbers of infants born SGA.

The 2017 PMMRC report identified 77 infants with NE who were SGA from 2010 to 2015. It is likely that these SGA babies were unrecognised before birth. If introduction of GAP resulted in a 20% increase in detection (conservative estimate) and optimum management this number of SGA NE cases could be reduced by 15 or two to three per year. If the GAP program increased detection and optimum management of SGA by 40 % the number of NE cases prevented over 6 years could be as high as 30.

In summary introduction of GAP with the potential for improved detection of SGA, optimum management of SGA before birth and during labour is a package of care that has potential to significantly reduce the burden of NE in New Zealand.

## Table 1: Included Studies

| Authors/Source | Date and Country | Design and Method | Definition of SGA | Study population | Results | Recommendations / Comments |
|---|---|---|---|---|---|---|
| Badawi N et al . BMJ 1998; 317(7172): 1549-53. | 1998, Australia | Aim: to identify antepartum predictors of NE. Population based unmatched; case-control | Birth weight centiles adjusted for gestational age, maternal height and parity, and infant sex. | Western Australian. 164 term infants with moderate or severe NE. 400 randomly selected controls | Prevalence of NE 3.8/1000 births.<br>BWt between 3rd and 9th centile aOR 4.37 (1.43-13.38).<br>BWt< 3rd centile aOR 38.23 (9.44-154.79) | Positive Study: Intrauterine growth restriction the strongest risk factor in this study. Many causal pathways start before birth. Other factors measured were maternal thyroid disease, pre-eclampsia, bleeding, viral illness, alcohol, and gestation at delivery. |
| Westgate JA et al. British Journal of Obstetrics & Gynaecology 1999; 106(8): 774-82 | 1999 New Zealand | Aim: to identify the contribution of antenatal hypoxia, obstetric catastrophe in labour and fetal monitoring practice to the occurrence of NE associated with acidemia at term. | SGA defined as < 10th centile definition not specified. | Tertiary referral hospital in Auckland New Zealand. 22 babies between January and October 1997 with umbilical artery pH ≤ 7.09, 5 min Apgar < 7 and moderate to severe encephalopathy within 5 hours of birth | None of the 22 babies with umbilical artery pH < 7.09, 5 min Apgar < 7 or moderate to severe encephalopathy were reported as SGA | Negative study. Definition of SGA as < 10th centile was likely to based on population standards which may reduce diagnosis in some ethnicities. |
| Bukowski R et al. American Journal of Obstetrics & Gynecology 2003; 188(4): 1011-5 | 2003, USA | Aim: To determine the frequency of growth impairment in neonates with NE. Case controlled study, to determine frequency of growth impairment in neonates with NE | Customized centiles to define SGA. | Texas, USA. 21 neonates with NE compared with 42 healthy controls. | Impairment of fetal growth directly associated with occurrence of NE intrapartum. One third of babies with NE had BWt < 10th centile aOR 20.5 (2.2-114.0) | Positive Study: Large proportion of infants with NE demonstrate signs of antepartum injury reflected in growth impairment |
| Pierrat V et al. Archives of Disease in Childhood Fetal & Neonatal Edition 2005; 90(3): F257-61 | 2005, France | Aim: to determine prevalence of NE in term live births and the underlying diagnosis and outcomes. Population based observational study | < 3rd Centile on French birthweight standards | 90 neonates with moderate or severe NE. North Pas-de-Calais area of France, January to December 2000. No control group. | While most cases of NE were related to perinatal events, IUGR was over-represented and present in 14%.<br>No odds ratios provided. | Positive Study: Intrauterine growth retardation (IUGR) was over represented compared with expected distribution in France. |

| Authors/Source | Date and Country | Design and Method | Definition of SGA | Study population | Results | Recommendations / Comments |
|---|---|---|---|---|---|---|
| West CR et al. Australian & New Zealand Journal of Obstetrics & Gynaecology. 2005; 45(3): 207-10. | 2005, New Zealand | Aim: To review infants with NE to identify antenatal and intrapartum antecedents of NE | <10$^{th}$ percentile for the gestation | New Zealand. 52 cases over 4 years | 17% of the NE babies were SGA. None were induced therefore SGA presumed undetected.<br>No odds ratios provided. | Positive Study:<br>Concerns expressed re poor AN detection of SGA. Advise use of customized growth charts to increase detection of SGA |
| Lindstrom K et al. Acta Obstetricia et Gynecologica Scandinavica 2008; 87(5):503-9 | 2008, Sweden | Aim: to describe prenatal and perinatal data and neurodevelopmental outcomes in children with NE. Population-based birth-cohort study | IUGR diagnosed on ultrasound but standards not stated | From the Swedish Medical Birth Register, sample of 684 children born at term with Apgar score < 7 at 5min of age in 1985. Maternal, delivery, neonatal, and neuropaediatric data were compiled. Neurodevelopmental status was classified according to the presence of 1. cerebral palsy or other major impairments, 2. exclusively cognitive impairments, and 3. no impairments. 42 children with moderate NE selected for study. | Most mothers had experienced an uneventful pregnancy. 2/42 (5%) has BWt <2SD below mean. | Negative study:<br>Data from births over 30 years ago.<br>Children born SGA not over represented in this series. |
| Locatelli A et al. American Journal of Perinatology 2010; 27(8): 649-54 | 2010, Italy | Aim: to investigate antepartum and intrapartum risk factors for NE in term infants. Retrospective case control study | Birth weight <10th centile adjusted for gender and gestational age according to Italian standards | Milan, Italy. 27 term babies. 100 controls | IUGR identified as antenatal risk factor for NE. OR 3 (0.7-12.9) | Inconclusive Study:<br>Future efforts should be directed towards identification of AN risk factors. May be lower threshold for hypoxic or ischaemic events during labour for SGA babies. Timely intervention may reduce occurrence of NE |

| Authors/Source | Date and Country | Design and Method | Definition of SGA | Study population | Results | Recommendations / Comments |
|---|---|---|---|---|---|---|
| Wu YW et al. American Journal of Obstetrics & Gynecology 2011; 204(1): 37. e1-6 | 2011, USA | Aim: to determine the relationship between night time delivery and NE. Retrospective population study. Determined the relationship between night time delivery (7:00 PM to 6:59 AM) and NE and other risk factors. | IUGR was defined as mild (birthweight 10% for gestational age), moderate (5%), or severe (1%), based on ethnicity and sex-specific normative data compiled from the entire study population. | 1,864,766 newborns at a gestation of 36 weeks or more in California, 1999-2002. | 2131 patients had NE (incidence 1.1 per 1000 births). Night- time delivery was an independent risk factor for NE aOR, 1.10 (1.01–1.21), as was severe intrauterine growth retardation aOR, 3.8 (3.1–4.8); no prenatal care, OR 2.0 (1.4 –2.9); primiparity OR 1.5 (1.4 –1.7); advanced maternal age OR (1.16 –1.45); and infant male sex, OR, 1.3 (1.2–1.4). | Positive Study: Intrauterine growth restriction represented the strongest risk factor for NE among the factors examined in this study, confirming similar findings in previous population studies (Badawi et al., 1998) |
| Nelson KB et al. Pediatrics. 2012; 130(5):878-86 | 2012, Vermont, USA | Aim: to identify antecedents in a large registry of infants with NE. Retrospective population study 2006-2010 to determine antecedents of NE in a large NE registry | SGA was defined as birth weight <10$^{th}$ percentile within categories of gender, race, and multiple gestation based on smooth curves from the US Natality data set, 2001 and 2002. | 4165 singleton neonates >=36w gestation, meeting criteria for Vermont Oxford Network NE Registry | An abnormal maternal or fetal condition predated labour in 46%; of which SGA (16%) and maternal hypertension (16%) were the most frequent risk factors. | Positive Study: Most of infants showed marked compromise in delivery room but only ½ of placentas were submitted for examination. |
| Hayes BC et al. American Journal of Obstetrics & Gynecology 2013; 209:29. e1-19 | 2013, Ireland | Aim: To determine risk factors associated with HIE. Case control study of neonates >= 36weeks 0 days to determine risk factors associated with HIE | Not stated | Dublin, Ireland. 237 babies with HIE, 155 with grade 1, 61 with grade 2 and 21 with grade 3. 2 healthy controls for each neonate | IUGR independently associated with HIE. Overall aOR for BWt ≤ 3rd centile 1.85 (0.75-4.54) Grade 1 aOR 1.27 (0.41-3.92) Grade 2 and 3 aOR 5.3 (1.39-20.18) | Positive Study: IUGR associated with severe HIE. Babies with IUGR do not tolerate labour as well as healthy babies. Antenatal recognition guides delivery decision |
| Martinez-Biarge et al. Pediatrics 2013; 132(4): e952-9 | 2013, UK | Aim: to identify antepartum and intrapartum contributions to HIE at term. Retrospective case-control study of infants >= 35 weeks' gestation with HIE | British reference charts according to Cole et al (1998). | Infants with HIE born at or referred to the Hammersmith/Queen Charlotte's Hospitals between 1992 and 2007. 405 infants with HIE, 239 controls. | All cases met criteria for perinatal asphyxia, had neuroimaging findings consistent with acute hypoxia-ischemia, and had no evidence for a non–hypoxic-ischemic cause of their encephalopathy. In univariate analyses, babies < 10th centile had OR 1.7 (1.02-2.7), < 3rd centile 3.5 (1.2-10.4). After inclusion of intrapartum | Positive Study: SGA is an antenatal risk factor. Concluded that intrapartum events are the final and necessary pathway leading to HIE. |

| Authors/Source | Date and Country | Design and Method | Definition of SGA | Study population | Results | Recommendations / Comments |
|---|---|---|---|---|---|---|
| | | | | | factors In MV analyses low BWt was not independently associated with HIE. | |
| McIntyre et al. Obstetrics & Gynecology 2013; 122(4): 869-77. | 2013, Australia | Aim: to examine antecedents of cerebral palsy and perinatal death in a total population case controlled study. | BWt at least 2 std deviations below optimal for gestational age and gender, maternal height and parity or a diagnosis of FGR recorded in notes. | Western Australian births ≥ 35 weeks<br>Neonatal death and cerebral palsy were categorized as without encephalopathy, after neonatal encephalopathy, or after neonatal encephalopathy considered hypoxic-ischemic. | The OR for NND with NE and FGR was 13.1 (5.5-31)<br>The OR for CP with NE and FGR was 9.6 (5.0-18.5) | Positive Study:<br>FGR important factor in neonatal death with NE and CP. |

## Abbreviations

aOR = adjusted Odds Ratio

BWt = Birthweight

CP = Cerebral Palsy

FGR = Fetal Growth Restriction

GAP = Growth Assessment Protocol

HIE =Hypoxic Ischemic Encephalopathy

NE = Neonatal encephalopathy

NND = Neonatal Death

SGA = Small for gestational age

Std = Standard deviation

IUGR = Intrauterine growth restriction

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## Table 2: Recent New Zealand reports on Neonatal Encephalopathy

| Authors/Source | Date and Country | Design and Method | Definition of SGA | Study population | Results | Recommendations / Comments |
|---|---|---|---|---|---|---|
| New Zealand Perinatal and Maternal Mortality Review Committee (PMMRC) 2016. | 2016, NZ | Review of neonatal and maternal mortality and neonatal encephalopathy | SGA defined as < 10th centile customized | Review of all NZ neonatal clinical data for 2010-2014 (353 babies). | The New Zealand Perinatal & Maternal Mortality Review Committee report summarised clinical data for 353 babies with moderate and severe neonatal encephalopathy (NE), over the 5-year period from 2010 to 2014. Of these babies with NE 67/353 (19%) were small for gestational age (SGA) at birth which is 58% higher than the background risk of SGA in a general obstetric population (12%) | SGA was over-represented in the population of NE neonates reported in 2016 for 5-year period 2010 to 2014. |
| New Zealand Perinatal and Maternal Mortality Review Committee (PMMRC) 2017. | 2017, NZ<br>Reports on births up to 2015 | Review of neonatal and maternal mortality and neonatal encephalopathy | SGA defined as < 10th centile customized | Review of all NZ neonatal clinical data for 2010-2015. 70 additional cases added from 2016 report<br>(total 423 babies with NE) | The New Zealand Perinatal & Maternal Mortality Review Committee report summarised clinical data for 423 babies with moderate and severe neonatal encephalopathy (NE), over the 6-year period from 2010 to 2015. Of these babies with NE 77/423 (18.2%) were small for gestational age (SGA) at birth. This is higher than the expected background risk of SGA in a general obstetric population (12%). | SGA was again over-represented in the population of NE neonates reported in 2016 for the 6-year period 2010 to 2015.<br>These NZ findings are consistent with the international literature. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Sadler LC et al. American Journal of Obstetrics & Gynecology 2016; 1. e1-8. | 2016, NZ | Aim: The objective of the study was to undertake a multi-disciplinary structured review of all cases of NE that arose following the onset of labour in the absence of acute peripartum events in 2010-2011 to determine the frequency of contributory factors, the proportion of potentially avoidable morbidity and mortality and to identify themes for quality improvement. | SGA defined as < 10th centile customized | NE cases occurring after the onset of labour in the absence of an acute peripartum event, excluding those at 1 minute with normal gases and normal Apgar scores, among all cases of moderate and severe neonatal encephalopathy at term in New Zealand in 2010 and 2011. | Eighty-three babies fulfilled the inclusion criteria for the review, 56 moderate (67%) and 27 severe (33%), 21 (25%) of whom were deceased prior to hospital discharge. Contributory factors were identified in 84% of 83 cases, most commonly personnel factors (76%). Fifty-five percent of cases with morbidity or mortality were considered to be potentially avoidable, and 52% of cases were considered potentially avoidable because of personnel factors. The most frequently identified theme related to the use and interpretation of cardiotocography in labor. | Of all reviewers' comments relating to failure to follow best practice, failure to assess fetal growth and recognise small for gestational age was the most common. |

## References Table 2:


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2. Bujold E; Roberge S; Lacasse Y; Bureau M; Audibert F; Marcoux S; Forest JC; Giguere Y. (2010). Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. Obstetrics & Gynecology, 116(2 Pt 1):402-14.
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4. Lindqvist, P. G., & Molin, J. (2005). Does identification of small-for-gestational-age fetuses significantly improve their outcome? *Ultrasound in Obstetrics and Gynecology, 25*, 258-264.
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## *Appendix C: NE taskforce overview*

NE TASKFORCE | Working to prevent Neonatal Encephalopathy

April 2018

# NE Taskforce Overview

## Background

Neonatal Encephalopathy (NE) is a major cause of brain injury in newborn babies. With 1.15/1000 reported cases per registered birth, NE does not occur often. However, when NE does occur, the effects are long-lasting with very high impact.

ACC is working with the maternity sector to achieve a 25% reduction in the incidence and severity of preventable NE by at least 25% by 2022.

Achieving this challenging target requires a comprehensive, collaborative, sector-wide approach over five years to maximise the best outcomes for babies, their families.

## The size of the problem

There are many reasons why babies are born with NE. The Perinatal and Maternal Mortality Review Committee (PMMRC) reports annually and has identified 423 cases of NE that occurred between 2010 and 2015 in New Zealand. For every 1000 births registered between 2010 and 2015, 1.15 cases of NE were reported. There has been no statistically significant change in rate over this time

When NE is caused by treatment, ACC covers the injury for the life of the child. The number of NE treatment injury claims ACC receives is about 12 per annum. The severity of the cases is reflected by the substantial costs they generate.

**Predicted outstanding claims liability for the 148 NE treatment injury claims as of 31st December 2016**

| Type of ACC Claim | Number of claims | Mean lifetime | Outstanding claims liability |
|---|---|---|---|
| Serious injury | 34 | $56m | $12m |
| Moderate injury | 25 | $36m | $7m |
| Non-serious injury | 83 | N/A | N/A |

## It's possible to reduce the incidence and severity of NE cases

Evidence indicates it is possible to reduce the incidence and severity of NE injury.

In 2014, PMMRC undertook a multidisciplinary review funded by ACC of 83 NE cases of babies born in 2010-12 where there was no identifiable acute event[1]. The review found that the death or severity of morbidity of these NE cases was potentially avoidable in 55% of cases.

Another review funded by ACC and conducted by PMMRC in 2016 of 47 NE cases with known acute intra partum events found an even higher rate of preventability at 66%.

An ACC supported DHB review of 31 NE cases that occurred between 2010 and 2014, found that 52% of these injuries were potentially avoidable.

[1] Sadler LC, Farquhar CM2, Masson VL, Bettin MR. Contributory factors and potentially avoidable neonatal encephalopathy associated with perinatal asphyxia Am J Obstet Gynecol. 2016 Jun; 214(6):747.e1-8. doi: 10.1016/j.ajog.2015.12.037

In the UK, the story is similar. In 2015 the Royal College of Obstetricians and Gynaecologists undertook a multidisciplinary review of 727 babies who suffered brain injuries, stillbirth, and neonatal death. This review found that in 76% of the cases, the baby might have had a different outcome if different care had been given.

While the UK data is not directly comparable as it includes cases other than NE, it does add to the evidence base indicating that changes can be made to reduce the incidence and severity of NE.

## NE Taskforce

ACC convened an expert NE Taskforce in late 2015. The Taskforce comprises of; expert health care providers, clinicians, professional bodies, relevant government agencies, and family representatives to ensure high-level expertise in designing maternity safety improvement initiatives.

The NE Taskforce is designed to function over several years. It works collaboratively with health care providers, clinicians, professional bodies, and advocacy groups related to NE, to design and establish an evidence-based improvement programme by:

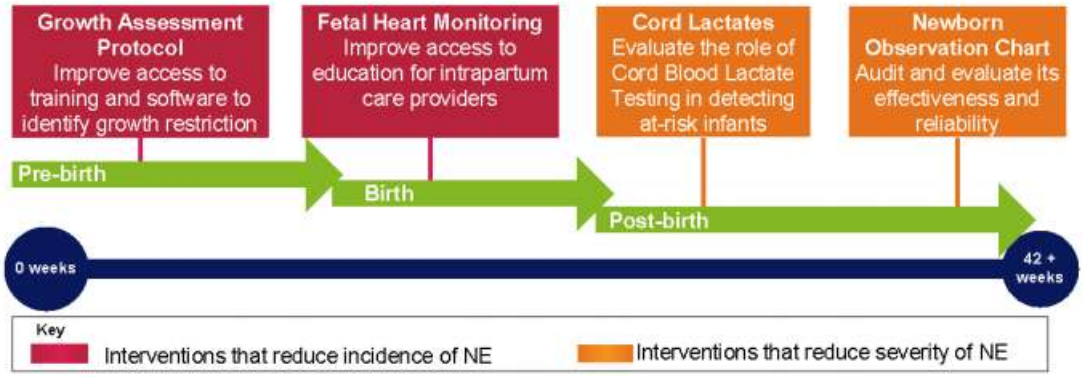
- Investigating, identifying and describing the size and scope of the problem
- Researching, prioritising, and implementing solutions based on national and international best practice
- Coordinating, delivering and evaluating evidence-based initiatives to reduce the incidence and severity of NE

## Next Steps

Reducing the incidence and severity of NE cases requires a comprehensive and collaborative sector-wide approach lasting a number of years.

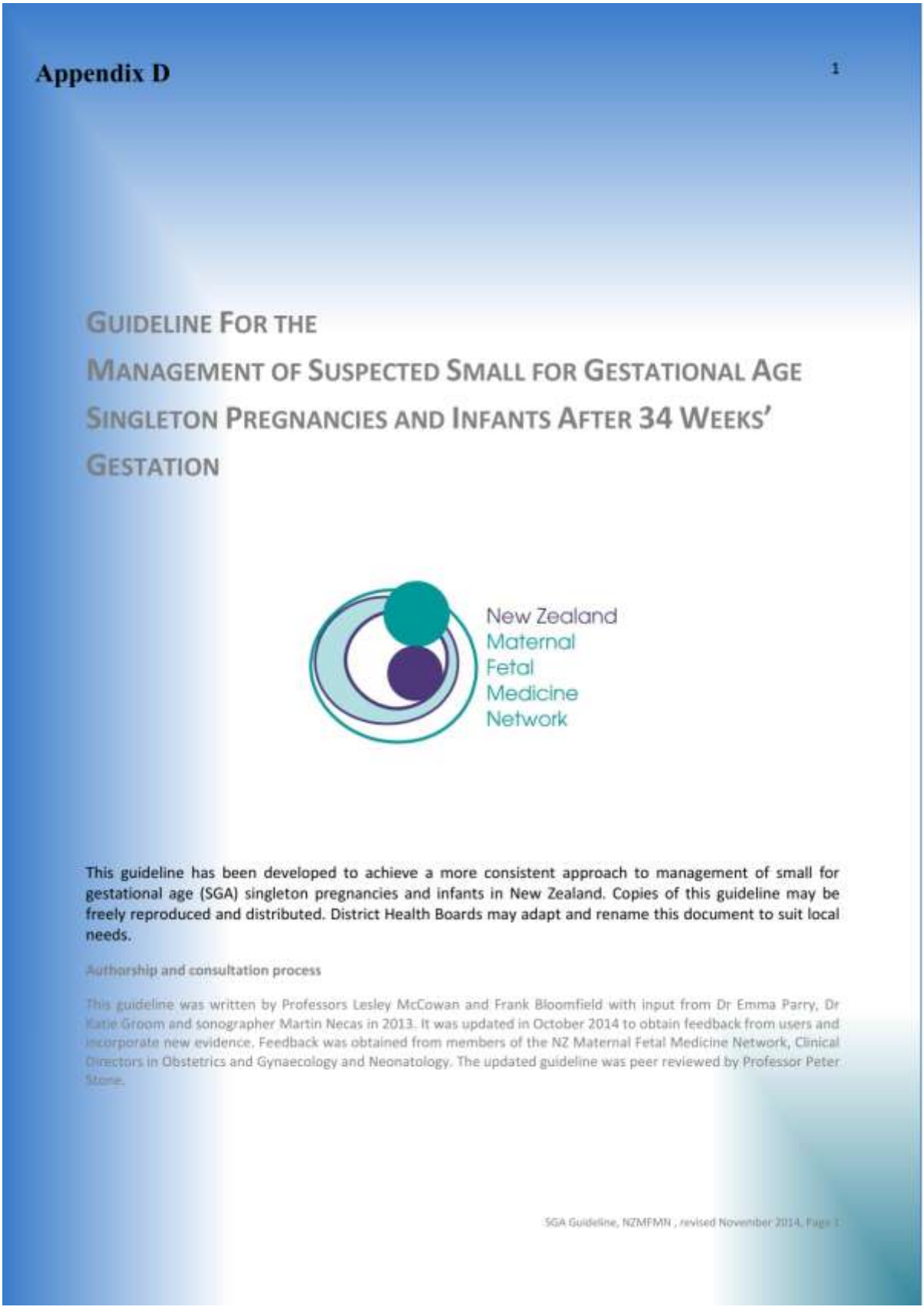
The evidence has been collated and evaluated by ACC's NE Taskforce, resulting in four succinct recommendations for proactive national interventions.

**Four interventions to reduce the incidence and severity of NE in relation to the pregnancy timeline**




A similar project to investigate prevention has been running in the UK over the last 2 to 3 years under the auspices of the Royal College of Obstetricians and Gynaecologists (RCOG) called Each Baby Counts. It is reassuring that this parallel project has reached very similar conclusions to ACC's NE Taskforce.

***Appendix D: Guideline for the management of suspected small for gestational age singleton pregnancies and infants after 34 weeks' gestation***



**Appendix D**

1

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

New Zealand Maternal Fetal Medicine Network

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.

SGA Guideline, NZMFMN , revised November 2014. Page 1

## TABLE OF CONTENTS

## 1. EXECUTIVE SUMMARY AND GRADES OF RECOMMENDATIONS

| | Level of Evidence |
|---|---|
| • SGA infants comprise approximately 40% of non-anomalous stillbirths born after 34 weeks | B |
| • A minority of these SGA infants are currently detected before birth in New Zealand | B |
| • Improved detection accompanied by careful management and timely delivery is associated with reduced morbidity and mortality | C |
| • Risk assessment for major risk factors for SGA should be undertaken at the booking visit | ☑ |
| • Utilisation of a GROW chart, associated with structured education, can increase antenatal detection of SGA pregnancies and may be associated with reduced perinatal mortality | C |
| • Routine growth scans in women at low risk of SGA do not improve perinatal outcomes | A |
| • Women with major risk factors for SGA are recommended to have fetal growth assessed by ultrasound | B |
| • 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 | ☑ |
| • 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 | C |
| • Fetal abdominal circumference <=5$^{th}$ centile or EFW <10$^{th}$ centile can be used to diagnose the suspected SGA fetus | A |
| • As >80% of SGA infants are born after 37 weeks' serial growth scans should continue until delivery in high risk women | ☑ |
| • All women in whom SGA is suspected on ultrasound scan should have umbilical artery Doppler performed | A |
| • 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 | ☑ |
| • Management algorithms describe recommended fetal surveillance depending on Doppler indices and severity of the suspected fetal growth restriction | C |
| • Cardiotocography or biophysical profile should not be the only surveillance in the SGA pregnancy | C |
| • Delivery of the fetus suspected to be SGA at approximately 38 weeks is associated with reduced perinatal morbidity compared with earlier or later delivery, is cost effective and is not associated with increased Caesarean section rates | B |
| • 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 SGA fetuses | B |
| • Infants who are confirmed to be SGA or IUGR at birth are at increased risk of morbidity and, in particular, require monitoring for hypoglycaemia | B |
| • Infants with a birthweight that is disproportionately low compared with other growth 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 | B |
| • Treatment of neonatal hypoglycaemia with buccal dextrose gel reduces neonatal unit admission for hypoglycaemia and increases breastfeeding post- hospital discharge | A |

## 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 <3$^{rd}$ 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 normally-formed stillborn infants born at ≥24 weeks' have a birth weight < 10$^{th}$ customised centile [5] . In the Auckland Stillbirth Study 37% of late stillbirths (≥ 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 ≤ 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%20Antenatal%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 not discontinued earlier in the third trimester if growth is normal at this time.

In women assessed to be at high risk of severe or early 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 current 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: http://www.ranzcog.edu.au/college-statements-guidelines.html#obstetrics
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.
http://www.asum.com.au/newsite/files/documents/policies/PS/D7_policy.pdf

**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 $\leq 5^{th}$ centile
- Discrepancy between head and abdominal circumferences (e.g. HC $75^{th}$ centile and AC $20^{th}$ 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 $<10^{th}$ centile
- EFW on the GROW chart is crossing centiles with $\geq$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 $5^{th}$ or $10^{th}$ 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)

**Figure 1a : Estimated fetal weight patterns on GROW charts that suggest suboptimal fetal growth**

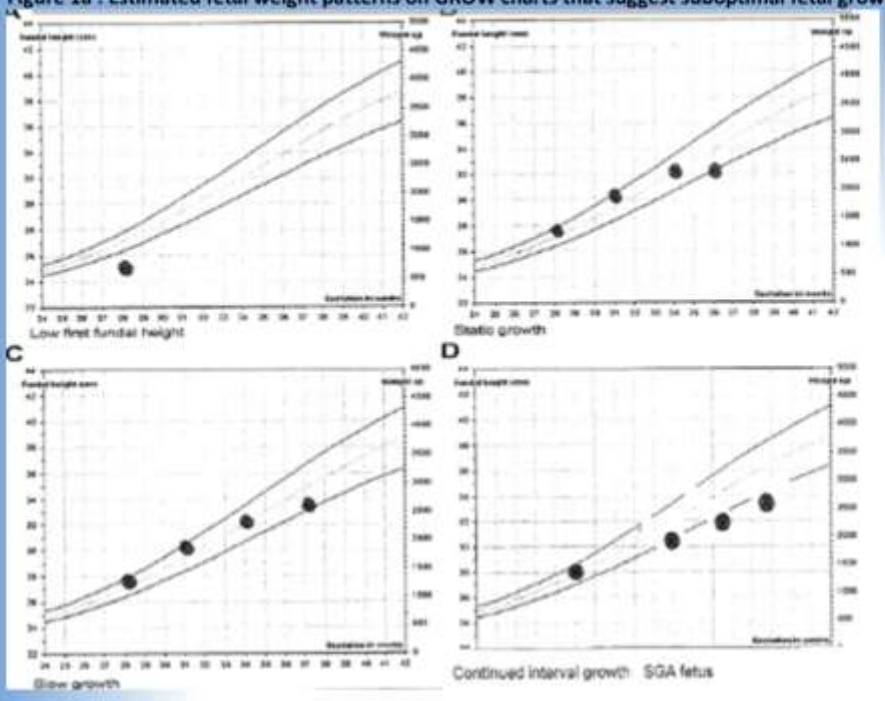
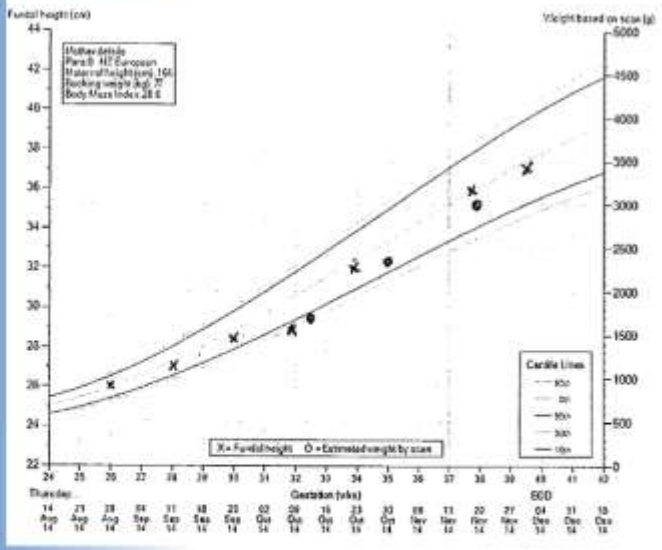



**Figure 1b: Estimated fetal weight pattern on GROW chart that suggests normal fetal growth trajectory**




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

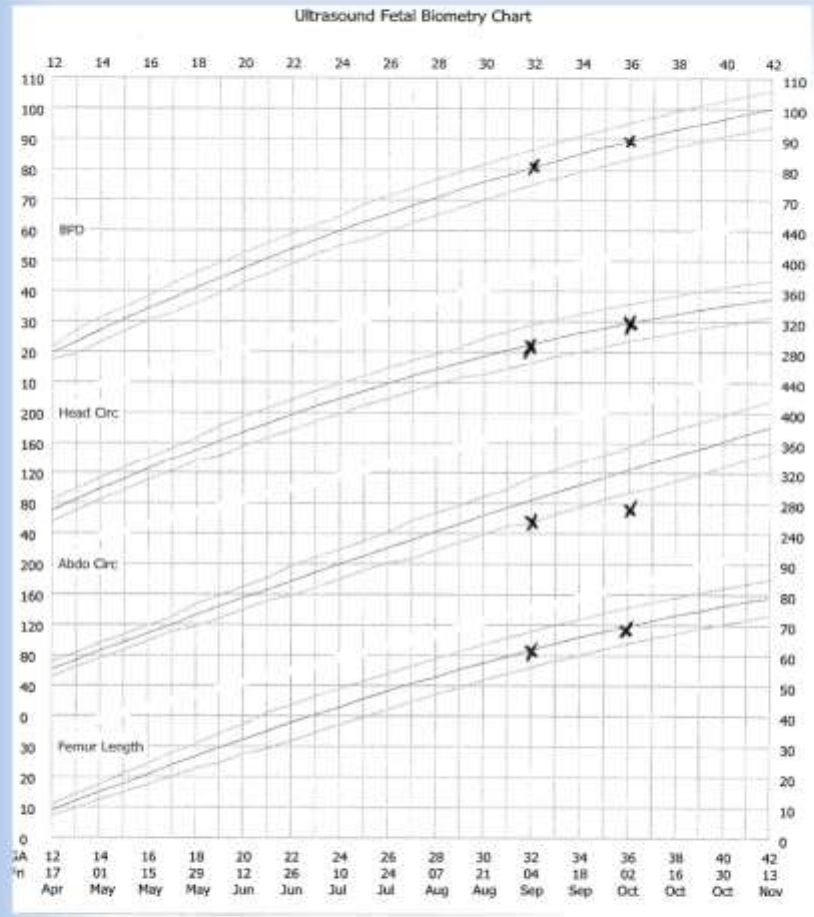


**Figure 2b: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound chart**

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.

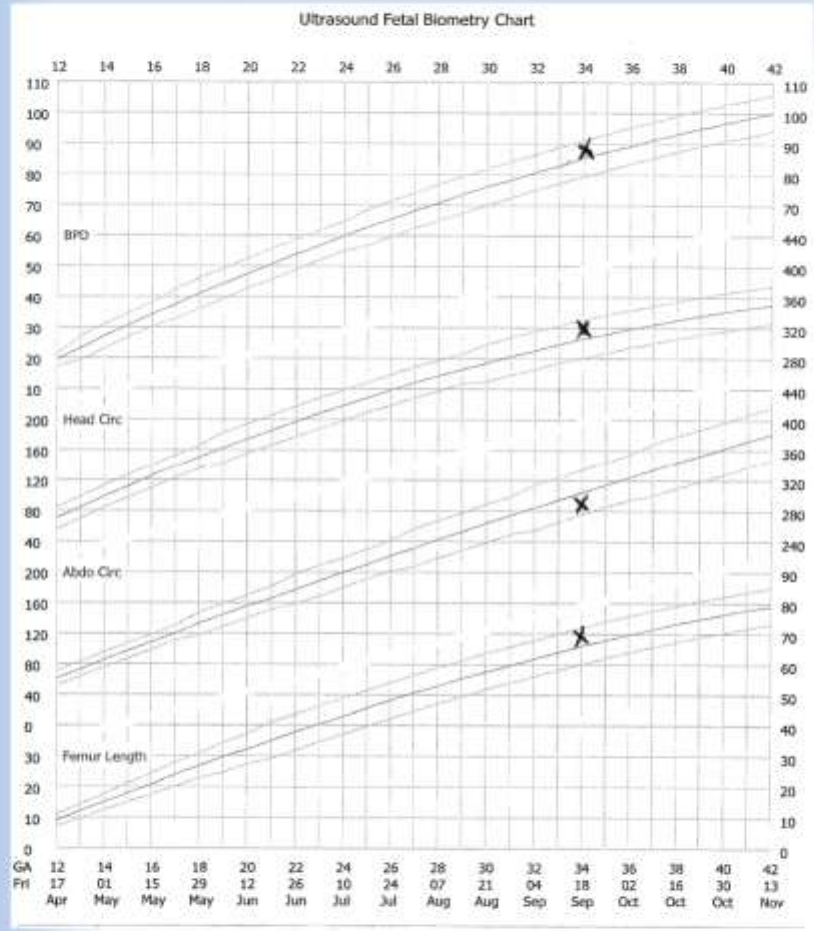
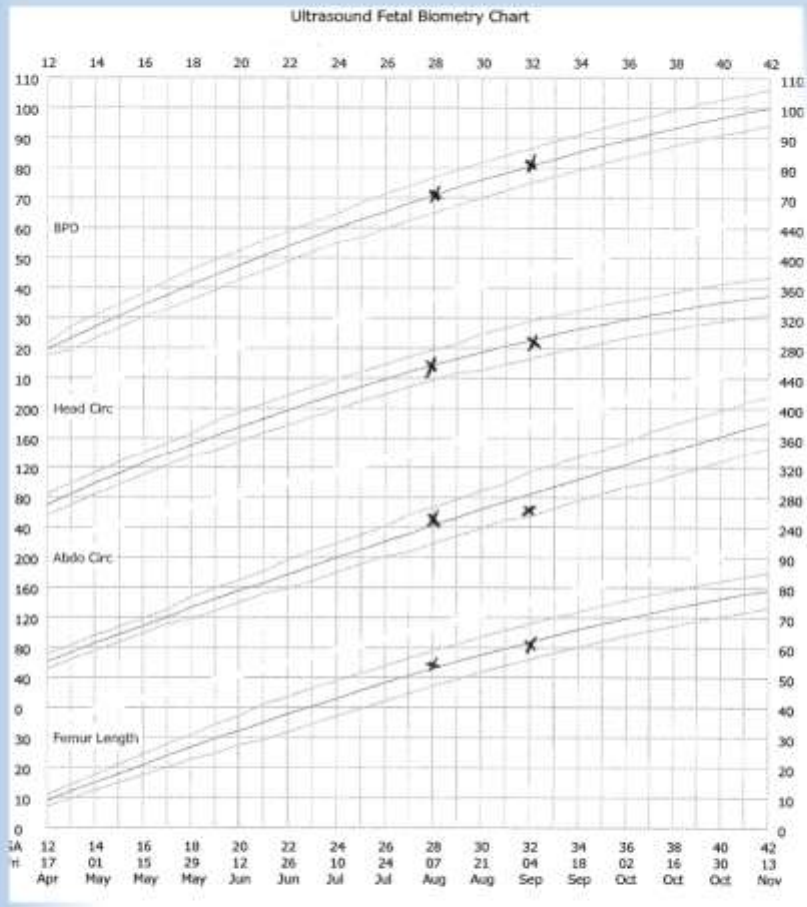


**Figure 2c: Examples of suspected sub-optimal fetal growth on ASUM population ultrasound chart**

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 ante-grade 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 (≤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 increased risk of Caesarean section [40]. Expectant management was 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 well-being.**
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 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.

| | 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 |

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 pre-feed 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-threshold-graphs

  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.

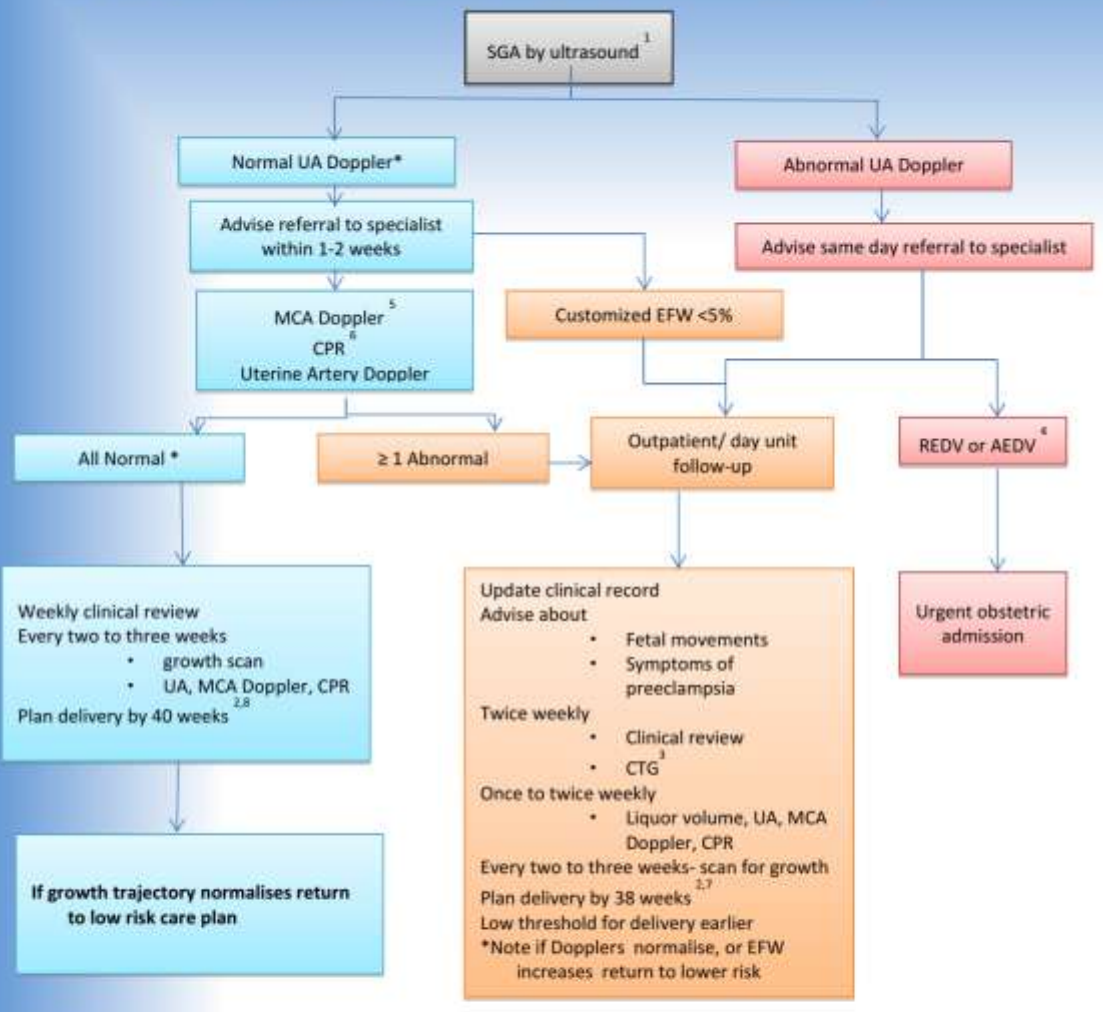
## 10. MATERNAL FOLLOW-UP/ADVICE FOR FUTURE PREGNANCIES

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

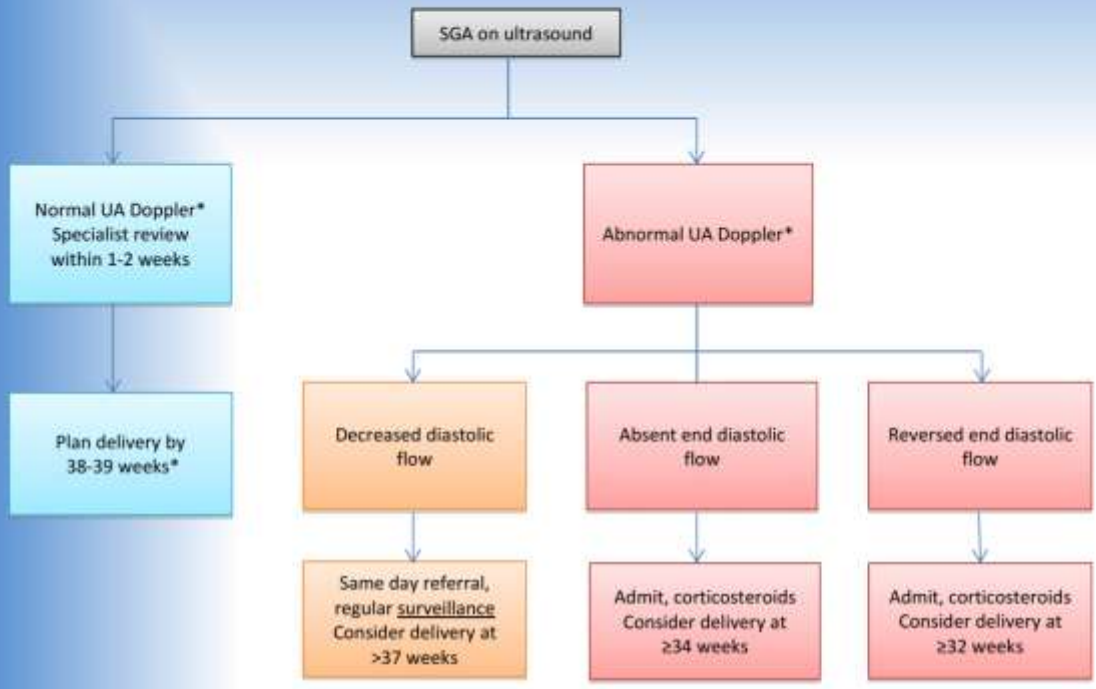
- Rates of antenatal detection of SGA infants
- Proportion of women with suspected SGA who have umbilical artery doppler studies performed
- Proportion of women with major risk factors for SGA infants who have serial growth scans
- Proportion of women with suspected SGA pregnancies with abnormal Doppler 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
[4] Reversed or absent end diastolic velocity
[5] Middle cerebral artery,
[6] Cerebro-placental ratio
[7] Continuous fetal heart rate monitoring from onset of contractions
[8] Continuous fetal heart rate monitoring in established labour
* see appendix for reference ranges

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




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

† In 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 ◆ >95th percentile is abnormal | | MCA PI ◆ <5th percentile is abnormal | | Cerebroplacental Ratio (CPR) ◆ CPR = MCA PI/UA PI <5th percentile is abnormal | | Mean Uterine Artery PI ◆ Mean PI=(RT PI + LT PI)/2 >95th percentile is abnormal | |
|---|---|---|---|---|---|---|---|---|
| Gestation Weeks | 50th percentile | 95th percentile | 50th percentile | 5th percentile | 50th percentile | 5th percentile | 50th percentile | 95th 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 |

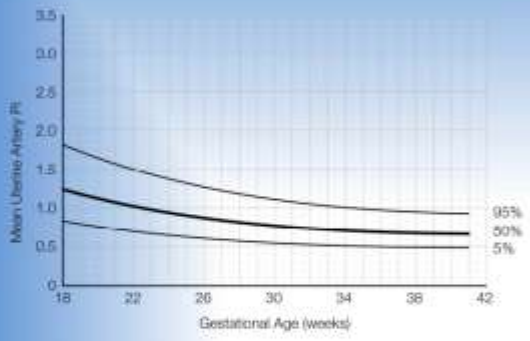
References:
* Acharya G, et al. Reference ranges for serial measurements of blood velocity and pulsatility index at the intra-abdominal portion, and fetal and placental ends of umbilical artery. Ultrasound Obstet Gynecol 2005; 26:162-169.
* Ebbing, C., Rasmussen, S., & Kiserud, T. Middle cerebral artery 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.

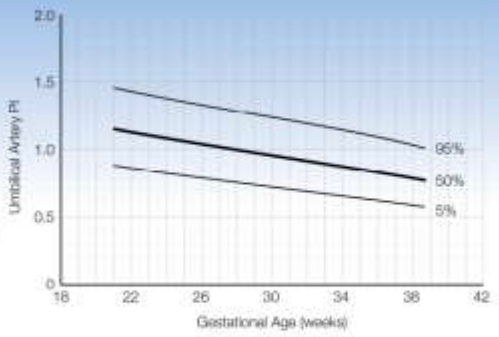
Note to ultrasound practitioners:

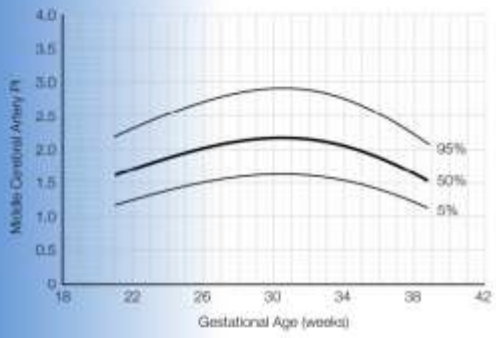
Further information about the standards of performance and reference ranges of obstetric Doppler examinations is available in the NZMFMN Obstetric Doppler Guideline 2014 from the following web link.

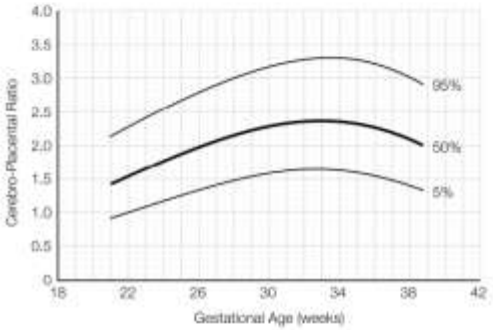
http://www.healthpoint.co.nz/public/new-zealand-maternal-fetal-medicine-network/?solo=otherList&index=1

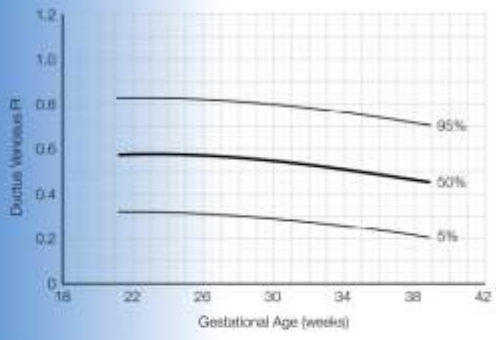
## 2. Doppler reference range charts




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., Hinson, 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 (≥ 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 ≤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 breast-feeding 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:
http://www.nice.org.uk/guidance/cg98/chapter/appendix-d-the-treatment-threshold-graphs

"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 |
| 1- | 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 high-quality 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**

| | |
|---|---|
| A | At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; or<br>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 |
| B | A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or<br>Extrapolated evidence from studies rated as 1++ or 1+ |
| C | A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or<br>Extrapolated evidence from studies rated as 2++ |
| D | Evidence level 3 or 4; or<br>Extrapolated evidence from studies rated as 2+ |

**Good practice point**

| | |
|---|---|
| ✓ | Recommended best practice based on the clinical experience of the guideline development group |

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## *Appendix E: MoH Communication re GROW June 2015*

MINISTRY OF HEALTH
MANATŪ HAUORA

19 June 2015

No. 1 The Terrace
PO Box 5013
Wellington 6145
New Zealand
T +64 4 496 2000

Attention: Clinical Directors

Dear Colleague

**GROW system of detecting Intrauterine Growth Restriction/Small for Gestational Age**

The Ministry has been investigating the use of the GROW system for the measurement of fetal growth during pregnancy to detect intrauterine growth restriction (IUGR) or small for gestational age (SGA) babies. The GROW system was developed by the Perinatal Institute in the United Kingdom and has shown encouraging results in the use of customised growth charts for the detection of IUGR/SGA babies during pregnancy leading to a fall in the stillbirth rate amongst such babies.

The GROW system has been in New Zealand for some time being used by a number of DHBs. The 2012 Guidelines for Consultation with Obstetric and Related Medical Services (Referral Guidelines) require the use of a customised growth chart when referring a woman to the obstetric service for suspected IUGR/SGA. The Perinatal and Maternal Mortality Review Committee has also recommended the use of a customised growth chart and the DHB Clinical Directors of Obstetrics made a decision in 2014 that a woman needed to have a customised growth chart when being referred for a consultation for IUGR/SGA.

Many DHBs already use the GROW system and the Midwifery and Maternity Provider Organisation has had access to the customised charts free of charge for some time and has provided access to their members. In 2013, the Perinatal Institute in the UK lost its NHS funding and the GROW system became a proprietary IT product that now attracts an annual licence fee.

There was a multidisciplinary meeting held in May 2014 between the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, the New Zealand College of Midwives to determine a path for the provision of the GROW system in New Zealand. It was agreed that GROW is the customised growth chart that is currently used and is based on New Zealand data provided to the GROW system.

The issue has been one of deciding how it becomes available for clinicians in both the DHBs and the community (primary maternity care) and how it is funded.

Through discussions with the stakeholders, the Ministry has developed the view that the GROW system that produces a customised growth chart is the agreed tool for use in New Zealand and is already in use in a number of DHBs. As the DHB Clinical Directors have decided a customised growth chart is necessary for an obstetric referral for suspected IUGR/SGA, the tool needs to be available to referring clinicians.

It is each DHB's responsibility to ensure the GROW tool is available and to pay any licence fees required. They also need to ensure that all the clinicians who will be using the tool have the necessary education to use it correctly as this is an essential component of the GROW system's efficacy – that clinicians are taking the measurements in the same way.

The roll-out of the Maternity Clinical Information System (MCIS) is DHB by DHB and is still in the early implementation phase. Once it is established in a DHB, the MCIS has the capability of embedding the GROW system so it becomes part of the electronic maternity record.

Each DHB has a Maternity Quality and Safety Programme operating to put a quality improvement focus onto maternity care. The provision of the GROW tool fits neatly within its scope to ensure that all women have access to appropriate maternity care as required under Standard 1 of the New Zealand Maternity Standards.

Yours sincerely

Dr Don Mackie
**Chief Medical Officer**
**Clinical Leadership, Protection and Regulation Business Unit**

## *Appendix F: AUTEC approval*

**AUTEC Secretariat**

Auckland University of Technology
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E: ethics@aut.ac.nz
www.aut.ac.nz/researchethics

6 December 2016

Judith McAra-Couper
Faculty of Health and Environmental Sciences

Dear Judith

Re Ethics Application: **16/68 Does application of the Growth Assessment Protocol (GAP) at Counties Manukau District Health Board improve detection of fetal growth restriction?**

Thank you for providing evidence as requested, which satisfies the points raised by the Auckland University of Technology Ethics Committee (AUTEC).

Your ethics application has been approved for three years until 6 December 2019.

As part of the ethics approval process, you are required to submit the following to AUTEC:

- A brief annual progress report using form EA2, which is available online through http://www.aut.ac.nz/researchethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 6 December 2019;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/researchethics. This report is to be submitted either when the approval expires on 6 December 2019 or on completion of the project.

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to participants. You are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to obtain this.

To enable us to provide you with efficient service, please use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

All the very best with your research,

Kate O'Connor
Executive Secretary
**Auckland University of Technology Ethics Committee**

Cc: Joyce Cowan; Alain Vandal

## *Appendix G: Counties Manukau Health approval*

COUNTIES MANUKAU HEALTH

CMH Research Office
Counties Manukau Health
Clinical Support Building
Room 124, Level 1
Middlemore Hospital

For the attention of:
Joyce Cowan, Principal Investigator
Kathy Ogilvy, CMH Facilitator

19 September 2016

Dear Joyce and Kathy,

Thank you for the information you supplied to the CMH Research Office regarding your research proposal:

Research Registration Number: **07**

Ethics Reference Number: **AUTEC 16/68**

Research Project Title: **Does accredited training in the Growth Assessment Protocol (GAP) at CMDHB increase detention of fetal growth restriction?**

I am pleased to inform you that the CMH Research Committee and Director of Hospital Services have approved this research with Joyce named as Principal Investigator and Kathy as the CM Health Co-ordinating Investigator.

Your study is approved as specified on your AUTEC ethics approval dated 17 March 2016.

**Amendments:**

- All amendments to your study must be submitted to the Research Office for review.
- Any substantial amendment must also be submitted to the Ethics Committee for approval.

All external reporting requirements must be adhered to.

Please note that failure to submit amendments and external reports may result in the withdrawal of Ethical and CMH Organisational approval.

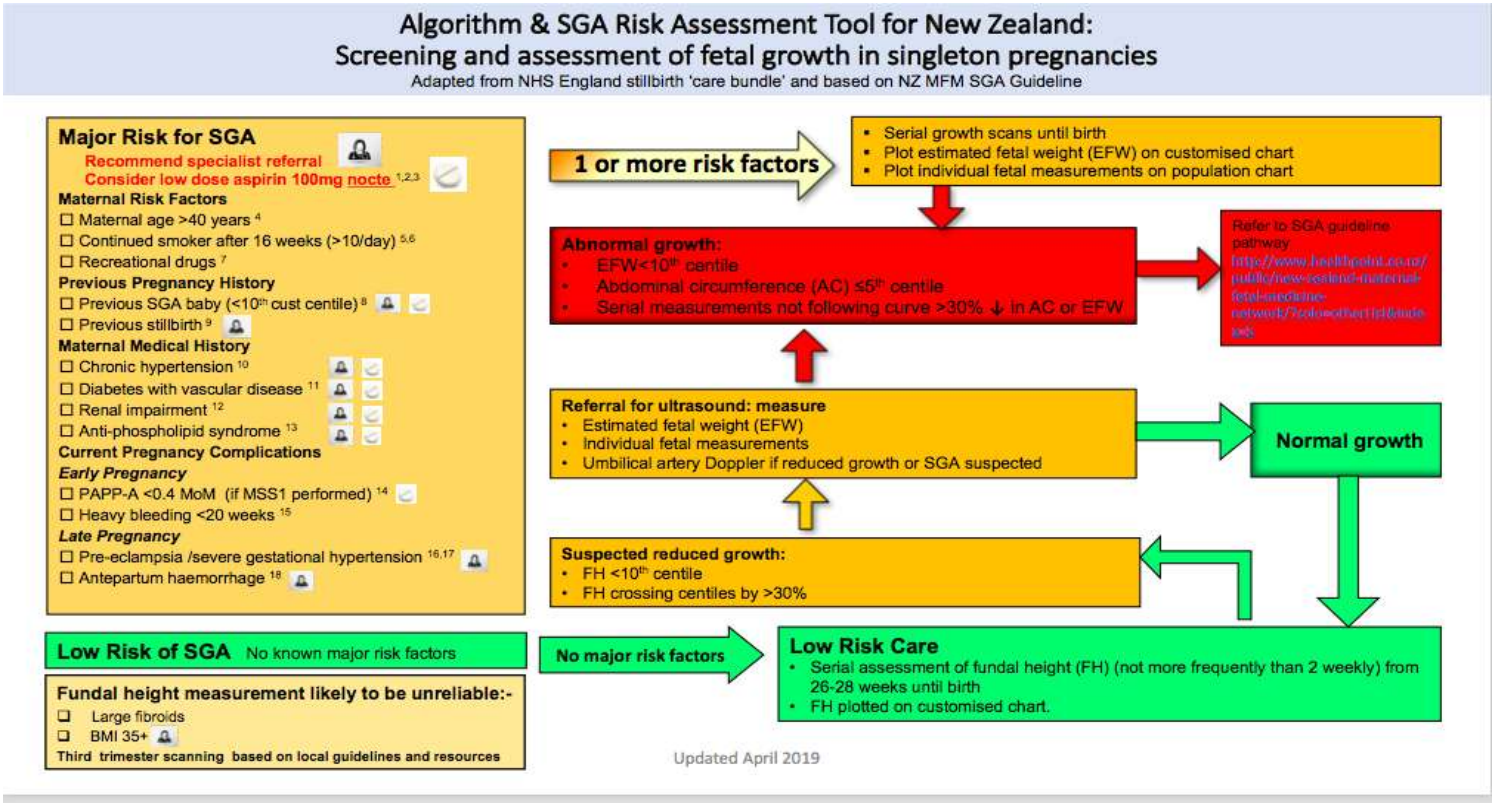
We wish you well in your project. Please inform the Research Office when you have completed your study (including when a study is terminated early) and provide us with a brief final report (1-2 pages) which we will disseminate locally.

Yours sincerely

S Karatela

Dr Shamshad Karatela
**Research Advisor**
Counties Manukau Health
*Under delegated authority from CMH Research Committee and Director of Hospital Services*

## *Appendix H: Algorithm and SGA risk assessment tool for New Zealand*



**Algorithm & SGA Risk Assessment Tool for New Zealand: Screening and assessment of fetal growth in singleton pregnancies-References**

| Low Dose Aspirin Evidence (1,2,3) | Estimate Measure | Point estimate and 95% CI |
|---|---|---|
| Maternal Age > 40 yrs. (4) | OR | 3.2 (1.9-5.4) |
| Smoker ≥ 11 cigarettes /day (5,6) | OR | 2.2 (2.0-2.4) |
| Recreational drug use (7) | OR | 3.2 (2.4-4.3) |
| Prev. SGA (< 10$^{th}$% customised) (8) | OR | 3.9 (2.1-7.1) |
| Previous stillbirth (9) | OR | 6.4 (0.8-52.6) |
| Chronic hypertension (10) | ARR | 2.5 (2.1-2.9) |
| Diabetes with vascular disease (11) | OR | 6.0 (1.5-2.3) |
| Renal Impairment (12) | AOR | 5.3 (2.8-10) |
| Antiphospholipid syndrome (13) | RR | 6.2 (2.4-16.0) |
| PAPP-A <0.4 MoM (14) | AOR | 2.5 (2.2-2.8) |
| Heavy bleeding early pregnancy (15) | AOR | 2.6 (1.2-5.6) |
| Preeclampsia (16) | AOR | 2.6 (1.2-4.2) |
| Severe Gestational Hypertension (17) | RR | 2.5 (2.3-2.8) |
| Unexplained Antepartum haemorrhage (18) | OR | 5.6 (2.5-12.2) |

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