THE UNIVERSITY OF QUEENSLAND

AUSTRALIA

Preventing stillbirths: Better data to inform interventions in Australia

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BAppSc (Medical Radiation Technology), MIPH

A thesis submitted for the degree of Doctor of Philosophy at

The University of Queensland in 2016

School of Public Health

Abstract

Background

In Australia, one in every 139 women reaching 20 weeks gestation will have a stillborn baby. There is significant disparity in stillbirth rates within subgroups of the Australian population. Among Aboriginal and Torres Strait Islander (Indigenous) women, the stillbirth rate is one in every 93 women reaching 20 weeks gestation. Unfortunately, there has been no reduction in the national stillbirth rates over the past two decades and nearly a third are 'unexplained'. The ability to identify women at increased risk of stillbirth is an important and challenging priority. At present in Australia, there is a paucity of high quality data on causes and contributing factors to stillbirth. Furthermore, inconsistent approaches to investigation and classification affect the quality of data on causes of death and hamper the development of effective interventions to prevent stillbirth.

Aims

The primary aim of this Thesis is to describe the epidemiology of stillbirth within the Australian context. This aim was addressed by:

- Examining trends in stillbirth by clinical classification of cause of death, Indigenous status and gestational age, to identify focal areas for preventive efforts
- Assessing gestational age specific risk of stillbirth associated with four important contributors (diabetes, hypertension, antepartum haemorrhage and small-for-gestational age) to higher stillbirth rates among Indigenous women in order to identify periods of increased risk
- Developing and validating a statistical model to predict the risk of antepartum stillbirth at term (≥37 weeks) using maternal and pregnancy factors as a potential decision-making aid for clinicians and women
- Assessing consistency in application of the Perinatal Society of Australia and New Zealand Perinatal Death Classification system between hospital committees and an independent expert panel, to identify areas for quality improvement
- Determining maternal and pregnancy factors associated with parental consent to autopsy following stillbirth and explore parents' views and experiences of the autopsy consent process to inform clinical practice

Methods and Results

Data for 1995-2011 (n=881,211 singleton births) from the Queensland Perinatal Data Collection was analysed to address the first three aims. Stillbirth trends analysis found consistently higher rates of stillbirth among Indigenous women, however, the gap in stillbirth rates had narrowed. Gestational age specific stillbirth risk analysis found disparity in the magnitude of stillbirth risk for pre-existing diabetes and small-for-gestational age between Indigenous and non-Indigenous women. Despite strong association between maternal clinical factors and antepartum stillbirth risk, the prediction model had a poor ability to predict stillbirth risk at term.

Consistency in application of the perinatal death classification system was assessed by calculating agreement. A substantial level of agreement was found between hospital committee and expert panel review of a cohort of 217 stillbirth cases, however, low levels of agreement were found for the categories of antepartum haemorrhage and fetal growth restriction.

Parents' lived experiences were explored using mixed methods. The study identified maternal and pregnancy characteristics associated with consent or decline of autopsy following stillbirth; likewise the in-depth interviews revealed that the autopsy consenting process was part of a larger bereavement journey for parents. Parents expected healthcare professionals to have an appreciation for their loss and provide bereavement care in a sensitive and respectful manner.

Conclusions

These studies highlight the need for early detection and management of pre-existing medical conditions as well as improving equitable access to high quality antenatal care. Of continued concern are stillbirths which remain unexplained after investigation. Numerous factors influence parents' decision making around stillbirth autopsy and sensitivity and respectfulness in particular on the part of healthcare providers is essential.

Declaration by author

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my research higher degree candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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Publications during candidature

Peer Reviewed papers

Ibiebele I, Coory M, Boyle FM, Humphrey M, Vlack S & V Flenady. Stillbirth rates among Indigenous and non-Indigenous women in Queensland, Australia: is the gap closing? *BJOG: An International Journal of Obstetrics and Gynaecology*, 2015. **122**(11): p. 1476-1483. DOI: 10.111/1471-0528.13047

Ibiebele I, Flenady V, Coory M, Boyle FM, Vlack S, Middleton P, Roe Y, Smith G. Gestational age specific stillbirth risk among Indigenous and non-Indigenous women in Queensland, Australia: a population based study. *BMC Pregnancy and Childbirth*, 2016. **16**(1): p.159. DOI: 10.1186/s12884-016-0943-7.

Additional publications by the candidate during candidacy not forming part of the Thesis

Mahomed K, **Ibiebele I**, Buchanan J for the Betadine Study Group. The Betadine Trial – Povidone-Iodine wound irrigation prior to skin closure at caesarean section to prevent surgical site infection: a randomised controlled trial. *Australia and New Zealand Journal of Obstetrics and Gynaecology,* 2016. 56(3):301-306. DOI: 10.1111/ajo.12437

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(Published abstract: Journal of Paediatrics and Child Health, 2015. **51 (Suppl. 1)**: p. 28)

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(Published abstract: Journal of Paediatrics and Child Health, 2015. **51 (Suppl. 1)**: p. 126)

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(Published abstract: Journal of Paediatrics and Child Health, 2015. **51 (Suppl. 1)**: p. 72)

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Publications included in this thesis

Ibiebele I, Coory M, Boyle FM, Humphrey M, Vlack S & V Flenady. Stillbirth rates among Indigenous and non-Indigenous women in Queensland, Australia: is the gap closing? *BJOG: An International Journal of Obstetrics and Gynaecology*, 2014; published online September 3. DOI: 10.111/1471-0528.13047 - incorporated as Chapter 3 (see Appendix E for final submitted manuscript)

Contributor	Statement of contribution
Ibinabo Ibiebele (Candidate)	Concept of the study (10%) Data management and analysis (100%) Interpretation of results (40%) Wrote the paper (50%)
Michael Coory	Concept of the study (20%) Technical assistance with data analysis (50%) Interpretation of results (20%) Wrote and edited paper (10%)
Frances Boyle	Concept of the study (5%) Interpretation of results (5%) Wrote and edited paper (10%)
Michael Humphrey	Interpretation of results (5%) Wrote and edited paper (5%)
Susan Vlack	Interpretation of results (10%) Wrote and edited paper (10%)
Vicki Flenady	Concept of the study (65%) Technical assistance with data analysis (50%) Interpretation of results (20%) Wrote and edited paper (15%)

All authors reviewed and approved the final version of the manuscript prior to submission

Ibiebele I, Coory M, Smith GS, Boyle F, Vlack S, Middleton P, Roe Y, Flenady V Gestational age specific stillbirth risk among Indigenous and non-Indigenous women in Queensland, Australia: a population based study. *BMC Pregnancy and Childbirth*, 2015. **16**(1): p.159. DOI: 10.1186/s12884-016-0943-7 – incorporated as Chapter 4 (see Appendix F for final submitted manuscript)

Contributor	Statement of contribution
Ibinabo Ibiebele (Candidate)	Concept of the study (20%) Data management and analysis (100%) Interpretation of results (30%) Wrote the paper (65%)
Michael Coory	Concept of the study (20%) Technical assistance with data analysis (30%) Interpretation of results (10%) Wrote and edited paper (5%)
Gordon Smith	Technical assistance with data analysis (30%) Interpretation of results (10%) Wrote and edited paper (5%)
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Susan Vlack	Interpretation of results (10%) Wrote and edited paper (5%)
Philippa Middleton	Interpretation of results (10%) Wrote and edited paper (5%)
Yvette Roe	Interpretation of results (10%) Wrote and edited paper (5%)
Vicki Flenady	Concept of the study (50%) Technical assistance with data analysis (40%) Interpretation of results (10%) Wrote and edited paper (5%)

All authors reviewed and approved the final version of the manuscript prior to submission

Contributions by others to the thesis

Associate Professors Vicki Flenady, Frances Boyle and Michael Coory (PhD advisors) provided extensive input into the concept and content of this Thesis. They critically reviewed and provided considerable feedback on multiple occasions.

Statement of parts of the thesis submitted to qualify for the award of another degree

None

Acknowledgements

This Thesis would not have been possible without the support of so many people. I would firstly like to thank my advisors: Associate Professor Vicki Flenady, Associate Professor Fran Boyle and Associate Professor Michael Coory. I am especially grateful for their guidance and generosity with their time and expertise.

Special thanks to Viviana Rodriguez, Courtney Nathan, Aleena Wojcieszek, Dr Hannah Reinbrandt and Dr Paul Gardiner at the Translating Research into Practice Centre, Mater Research Institute for their assistance with preparing documentation for ethics and governance submissions. I would like to acknowledge the Queensland Health Statistics Unit for access to perinatal data for the population based studies and the members of the Perinatal Mortality Sub-Committee of the Queensland Maternal and Perinatal Quality Council for stillbirth classification of the population data.

My gratitude to members of the expert review panel (Professor David Tudehope, Dr Rohan Lourie, Professor David Ellwood, Dr Diane Payton, Dr Glenn Gardener and Associate Professor Vicki Flenady) for their assistance with stillbirth classification for the agreement study; and the assistance of Dr Jane Fox with preparing case reports for the expert review panel meetings.

I would like to thank my fellow PhD students at the Mater Research Institute and School of Public Health, especially Lisa Daly for her words of encouragement.

I am thankful to Joanne Hoey, Patricia Wilson, Liana Kuhne, Deborah Birthisel, Dr Yogesh Chadha and Associate Professor Fran Boyle for their assistance with study coordination, recruitment and data collection for the *Parental Consent to Stillbirth Autopsy Study*.

I would especially like to thank the parents who willingly shared their experiences with us in the *Parental Consent to Stillbirth Autopsy Study*.

I would like to acknowledge the financial support of the National Health and Medical Research Council (GNT 1038070) and the University of Queensland (41373800) in the form of postgraduate research scholarships. I would also like to acknowledge project funding from the following organisations: Stillbirth Foundation (*Parental Consent to*

Stillbirth Autopsy Study), Mater Foundation (*Parental Consent to Stillbirth Autopsy Study*) and the National Health and Medical Research Council (Stillbirth Investigations Study).

I would like to thank my mother for her continual support, love and encouragement. It has finally come to pass.

Finally, I would like to thank God who has made all of this possible.

Keywords

stillbirth, fetal death, Aboriginal and Torres Strait Islander, Indigenous, trends, risk, prediction, autopsy, stillbirth classification

Australian and New Zealand Standard Research Classifications (ANZSRC)

ANZSRC code: 111706, Epidemiology, 60%

ANZSRC code: 111402, Obstetrics and Gynaecology, 25%

ANZSRC code: 111701, Aboriginal and Torres Strait Islander Health, 15%

Fields of Research (FoR) Classification

FoR code: 1117, Public Health and Health Services, 60%

FoR code: 1114, Paediatrics and Reproductive Medicine, 40%

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List of Abbreviations

ABS	Australian Bureau of Statistics
ANZACPM	Australia and New Zealand Antecedent Classification of Perinatal Death
APH	Antepartum haemorrhage
ARIA	Accessibility/Remoteness Index of Australia
ASGC	Australian Standard Geographic Classification
FGR	Fetal growth restriction
ICD 10 AM	International Classification of Disease 10th Edition Australian Modification
ICD 9	International Classification of Disease 9th Edition
IRSD	Index of Relative Socio Economic Disadvantage
LGA	Large-for-gestational age
MR63D	Queensland Perinatal Data Collection form
NPDCAT	National Perinatal Death Clinical Audit Tool
POA	Postal Area
PSANZ PDC	Perinatal Society of Australia and New Zealand Perinatal Death Classification
QCOPMM	Queensland Council of Perinatal Mortality and Morbidity
QCPMC	Queensland Council Perinatal Mortality Classification
QPDC	Queensland Perinatal Data Collection
SEIFA	Socio Economic Index for Areas
SES	Socioeconomic status
SGA	Small-for-gestational age
WHO	World Health Organisation

Chapter 1

Literature Review

1.1 Definition

Stillbirth within Australia is widely defined across birth registration and perinatal death collections as "*a fetal death prior to the complete expulsion or extraction from its mother of a product of conception of 20 or more completed weeks of gestation or of 400 grams or more birthweight. The death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles*" [1]. However, the statutory definition of stillbirth in South Australia excludes induced terminations of pregnancy [2]. Furthermore, where information is missing on gestational age and birthweight, there are slight differences in application of the rules in relation to reporting across states and territories [3]. In Australian reports pertaining to perinatal deaths, the terms *fetal death* and *stillbirth* are used synonymously. However, the term *fetal death* is a broader term encompassing fetal deaths at earlier gestational ages than stillbirth, where the birth is not recognised [4]. Stillbirth is the preferred term [5].

Stillbirths can be further classified into antepartum stillbirths, which are deaths occurring before the onset of labour, and intrapartum stillbirths, which are deaths occurring after the onset of labour but before birth [6]. Stillbirths can also be classified by gestational age. Early gestation stillbirths refer to deaths occurring at less than 28 weeks gestation and late gestation stillbirths refer to deaths at 28 weeks gestation or more [7, 8]. The legal requirements for registration and reporting of stillbirth vary widely within and between countries [9]. Nevertheless, the World Health Organisation (WHO) recommends a definition of at least 500g birthweight or 22 weeks gestation for national reporting and at least 1000g or 28 weeks gestation for international comparisons [10]. For the purposes of these studies, the Australian legal definition of stillbirth (at least 400g or at least 20 weeks gestation) will be used.

1.2 Stillbirth: the global picture

Stillbirth is a significant but under-appreciated public health issue globally. It is estimated that nearly 3 million stillbirths occur during the third trimester of pregnancy each year [11]. In 2012, compared with the leading global causes of death in all age categories, stillbirth during the third trimester ranked 5th ahead of lung cancer related deaths (1.6 million each year), HIV/AIDS-related deaths (1.5 million each year) and diarrhoeal disease (1.5 million each year) [12]. The majority (98%) of stillbirths occur in low and middle income countries, and nearly three quarters occur in South Asia and Sub-Saharan Africa [11]. Underreporting of stillbirths is an important issue in many developing countries as nearly half of all births occur at home [11]. Therefore, assessments of the number of stillbirths in the most affected countries are likely to be an underestimate.

Despite the magnitude of this issue, there had been little political impetus for preventive action. Stillbirths were severely under-represented in the global health policy agenda. This is evidenced by the lack of its inclusion in the Millennium Development Goals (MDGs), or as an indicator in the Countdown to 2015 monitoring process or in the Global Burden of Disease estimates [11, 13]. There was very little research, programmatic or policy attention devoted to stillbirth prevention in low and middle income countries [14] and most government departments in these countries did not count stillbirths [13]. The Lancet Series on Stillbirths published in 2011 focussed global attention on stillbirths; and the Every Newborn action plan was launched in May 2014 to prioritise newborn deaths and stillbirths by strengthening the newborn health components in existing health sector strategies relating to reproductive, maternal and child health [15]. A goal within the action plan is to reduce all national stillbirth rates to 10 or less per 1000 by 2035 and close equity gaps within countries [15].

1.2.1 Stillbirth rates in low and middle income countries (LMICs)

Comparison of stillbirth rate estimates between 1995 and 2008 suggest there have been decreases in the rate of stillbirth in many low and middle income countries but the rate of decrease has not been uniform across countries or regions [16]. Cuba, Sri Lanka, Malaysia and Mexico made substantial reductions in national stillbirth rates and China achieved a two-thirds reduction in national stillbirth rates [11]. There has been limited information on how these reductions were achieved. Family planning and increased inter-

pregnancy interval have been implicated in the reductions seen in China [17] and anti-helminthic interventions and its impact on maternal nutrition have been suggested for reductions in Sri Lanka [18].

Variations in stillbirth rates were observed between rural and urban populations within many low and middle income countries. In South Asia and Sub-Saharan Africa, with predominantly rural populations, two-thirds of stillbirths occur in rural areas [11]. Disparities in stillbirth rates between urban and rural populations also mirror disparities in rates of skilled attendance at birth and caesarean section delivery [11]. In Africa and South Asia, women living in rural areas had 50% lower rates of skilled attendance at birth compared with women living in urban areas. Similarly, there were higher rates of birth by caesarean section in urban areas in South Asia and Africa, 14% and 5% respectively compared with rural areas which had rates of 5% and 1%, respectively [11]. Up to a reported 70% of stillbirths occurring in low and middle income countries are intrapartum deaths associated with obstetric emergencies [13]. This suggests that improved care around the time of delivery may have a significant effect on stillbirth rates in LMIC settings.

1.2.2 Stillbirth rates in high income countries (HICs)

Despite the lack of attention to stillbirth prevention in policies and programs, there have been significant declines in the rate of stillbirths in high income countries (HICs) [13]. In a study of stillbirth rates in eleven European countries, a similar pattern of decline was observed between the countries [19]. This decline in stillbirth rates has been attributed to antenatal care, admission to hospital for delivery, use of caesarean section for fetal distress – all of which were introduced after 1935-40 [13]. However, the rate of decline in stillbirth rates in many HICs has slowed or stalled over the past two decades [13].

Historical trends in type of stillbirth

There have been variations in the rate of reduction of different types of stillbirth. In high income countries, stillbirths at term or during birth (intrapartum) have been significantly reduced to less than 15% of all stillbirths [13, 19]. Reductions in intrapartum stillbirth rates were achieved as a result of effective birth attendants supported by skilled obstetricians, advancements in medical technology and the advent of specialised neonatal intensive care units (NICU) [19]. The recent slow decline in stillbirth rates has been attributed to little

or no reduction in the rate of antepartum stillbirths. There has been an increase in the proportion of preterm births as a result of increased induction of labour in pregnancies thought to be at increased risk of antepartum death [20]. Antepartum and preterm-related stillbirths now make up the majority of stillbirths in high income countries [13], suggesting the need for increased attention to understanding the aetiologies of antepartum and preterm-related stillbirth.

International comparison of national stillbirth rates

Using the WHO stillbirth definition for international comparison (≥1000g or 28 weeks gestation), 193 countries were ranked by national stillbirth rates (see Table 1.1). Finland had the lowest stillbirth rate (2.0 per 1000 total births) and Pakistan had the highest estimated stillbirth rates with 46.1 per 1000 total births. Australia was ranked 15th with 2.9 per 1000 total births [21]. However, within countries there is wide variation in stillbirth rates. In Australia, stillbirth rates among Indigenous Australians were nearly twice that of non-Indigenous Australians. Using the WHO definition for international comparison, Indigenous Australians would be ranked 56th after Malaysia with a rate of 6.0/1000 total births [22] (see Table 1.1).

Table 1.1: Selected country stillbirth rate estimates per 1000 total births, 2009

Rank	Country	Total births	Total stillbirths	Stillbirth rate per 1000 births
1	Finland	59,540	120	2.0
15	Australia	270,360	780	2.9
17	USA	4,425,800	13,070	3.0
26	Canada	359,280	1,180	3.3
33	United Kingdom	751,370	2,630	3.5
34	New Zealand	58,790	210	3.5
55	Malaysia	553,410	3,290	5.9
82	China	18,500,000	182,150	9.8
154	India	27,400,000	605,230	22.1
193	Pakistan	5,667,980	264,550	46.7

Source: World Health Organization, Save the Children. Stillbirths: The Invisible Public Health Problem (press release). 2011. http://www.who.int/pmnch/media/news/2011/20110414_stillbirths_pressrelease.pdf. (accessed 24/02/2013)

1.3 Stillbirth: the Australian picture

1.3.1 Rates and trends

There were significant reductions in stillbirth rates during the 1970s and 1980s, however, this reduction has slowed over the past 20 years and rates may be slowly increasing (Figure 1.1). Reductions in stillbirth rates have been more modest than those seen in perinatal mortality rates and over the past two decades have remained steady at about 7.4/1000 total births [23]. This equates to more than 2000 stillbirths each year. Data from the National Perinatal Data Collection indicate that during the 1970s to 1980s there was a higher rate of decline in intrapartum deaths compared with antepartum deaths with a trough in 1994 (see Figure 1.2). From 1991 to 2009 there were increases in the rate of extremely preterm stillbirths [4].

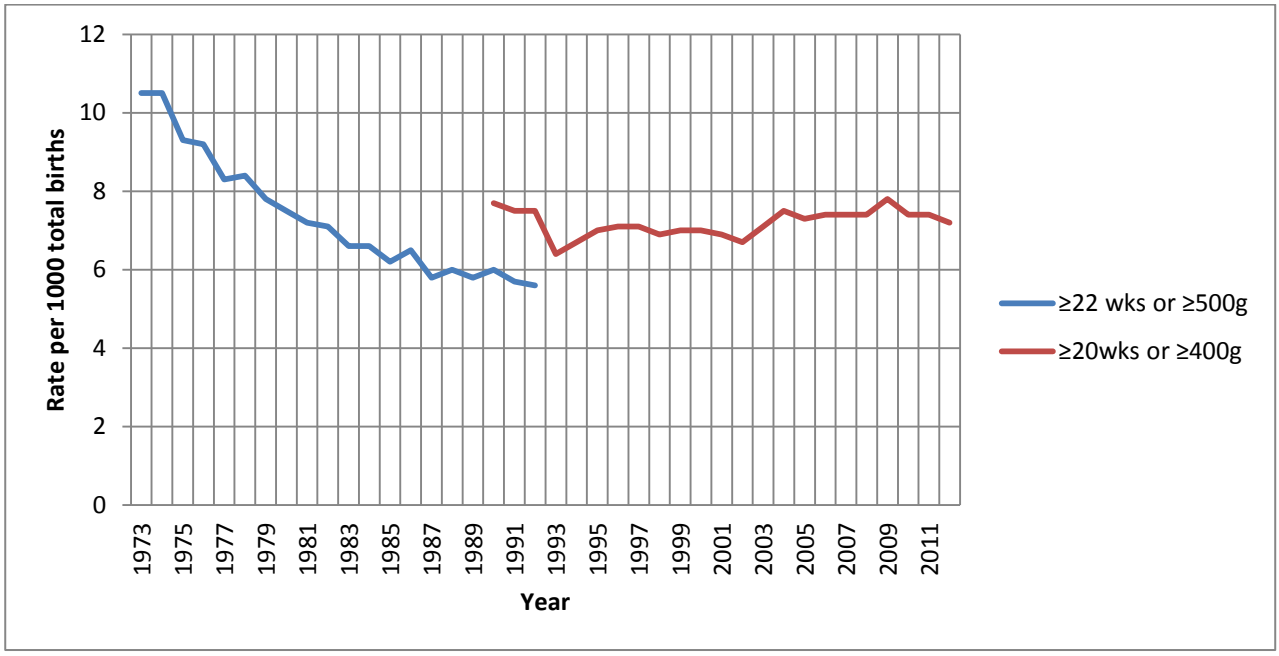


Figure 1.1: Trends in national stillbirth rate, Australia, 1973-2012

Data for the years 1973-1989 were from the Australian Bureau of Statistics (ABS) using the definition of fetal death of at least 22 weeks gestation or birthweight of at least 500g. Data for the years 1990 and onwards were from the National Perinatal Statistics Unit using the definition of fetal death of at least 20 weeks gestation or birthweight of at least 400g. Source: Australia's mothers and babies report 1992 to 2012

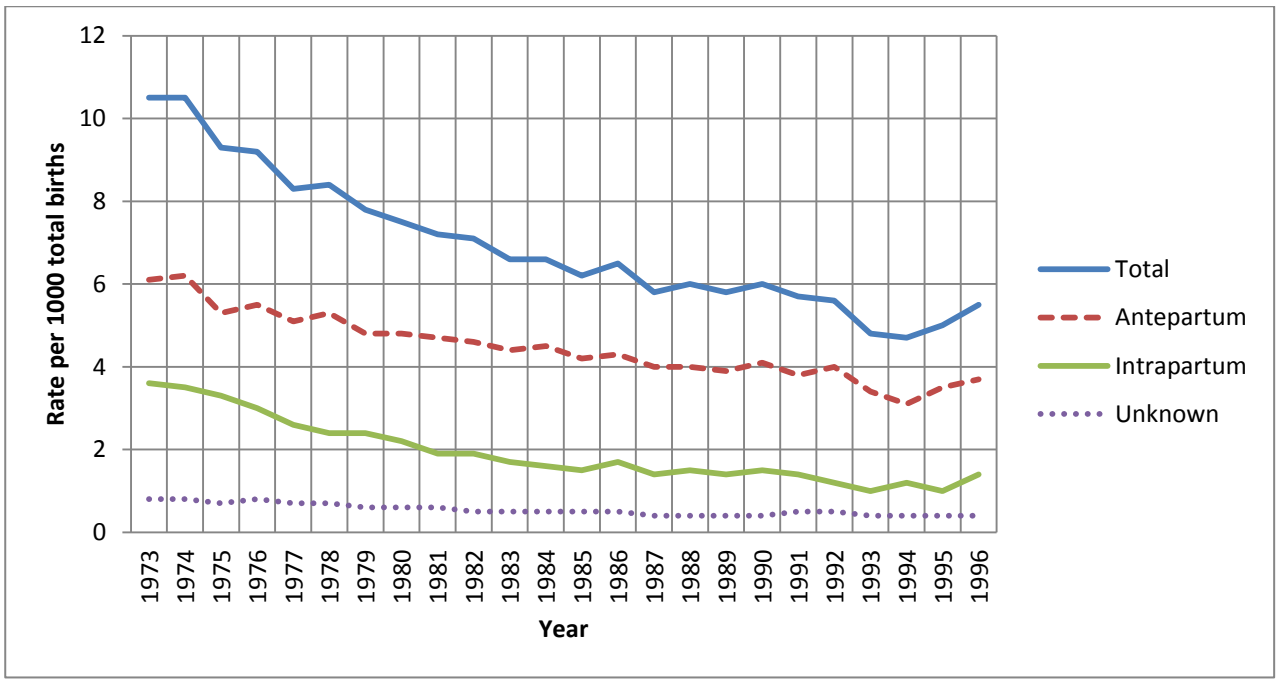


Figure 1.2: Trends in type of stillbirth, Australia, 1973-1996

Data is from the Australian Bureau of Statistics using the definition of fetal death of at least 22 weeks gestation or at least 500g birthweight. Source: Australia's mothers and babies reports 1992 to1996

1.3.2 Disparity in stillbirth rates

In the Australian obstetric population, disparity in stillbirth rates has been reported for a number of subgroups including teenage women [24] and women born in South Asia [25]. However, the focus of this Thesis is on disparity between Indigenous and non-Indigenous women in Australia. There is continued disproportionate disadvantage among Indigenous Australians in relation to education attainment, employment and ill health [26]. Life expectancy for Indigenous Australian men and women is lower than values for indigenous populations in New Zealand (Māori), Hawai'i (Kanaka Maoli) and Micronesia [27]. Furthermore, worse reproductive health outcomes have been reported for Indigenous women, for example higher rates of low birthweight (11.8% versus 6.0%), preterm birth (14.3% vs 8.3%) and perinatal mortality (14.9 vs 9.4 per 1000 births) compared to their non-Indigenous counterparts [24].

In 2012, Indigenous women made up 4.0% of women giving birth in Australia [24]. The stillbirth rates for Indigenous and non-Indigenous women in Australia were 10.8/1000 births and 7.1/1000 births, respectively [24]. Examining historical trends, it appears the gap is reducing somewhat between Indigenous and non-Indigenous stillbirth rates (see Figure 1.3). Indigenous women also have higher rates of risk factors known to be

associated with stillbirth, including maternal obesity, smoking and alcohol consumption, diabetes and lower rates of adequate antenatal care [23]. It is suggested that maternal behaviours, genetics, physical and social environment, access to and quality of health care may be at the core of this disparity [28]. The excess mortality in Indigenous births may be due mainly to low birthweight and preterm birth and these should be priority areas for primary health care [29].

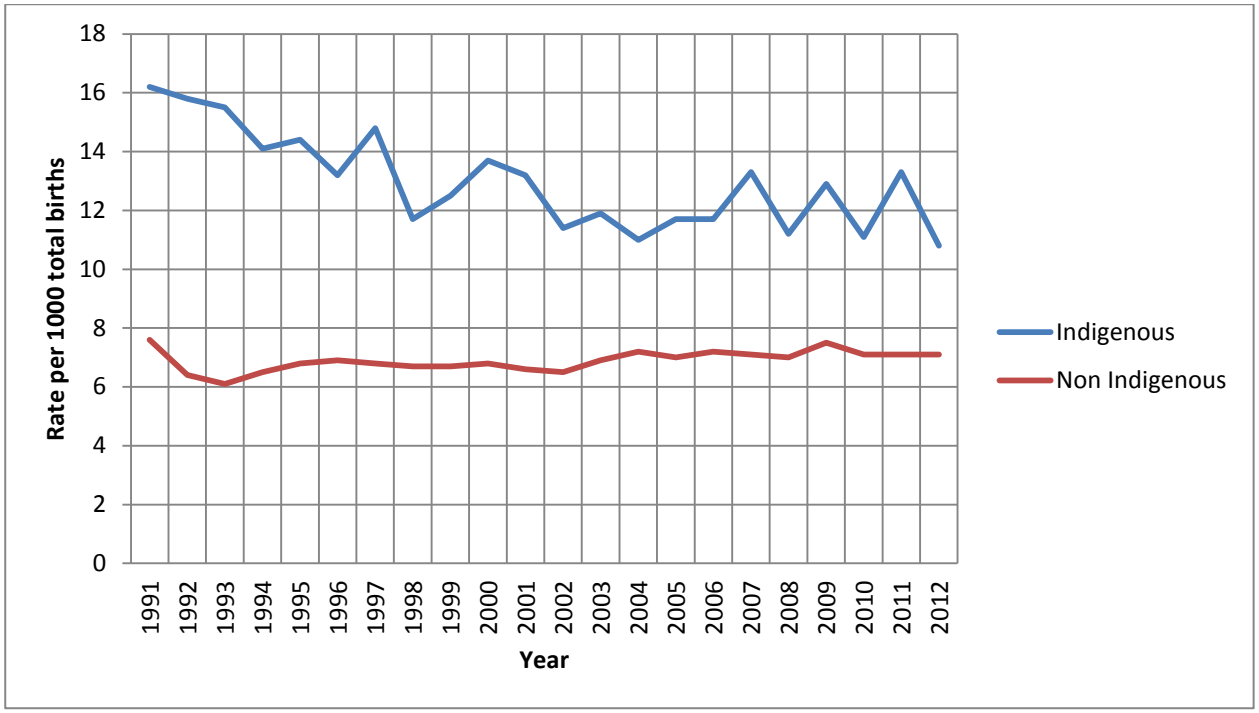


Figure 1.3: Trends in stillbirth rate by maternal race, Australia, 1991-2012

Data are from the National Perinatal Statistics Unit using the definition of fetal death of at least 20 weeks gestation or at least 400g birthweight. Source: Australia's mothers and babies report 1992 to 2012.

1.3.3 Risk Factors for stillbirth

Several factors have been identified to be associated with increased risk of stillbirth. Scientific inquiry into risk factors for stillbirth is important for uncovering possible aetiologic pathways as well as suggesting areas for primary prevention. In this review, discussion will be limited to potentially modifiable risk factors and factors for which data are available in the state perinatal data collections.

The risk factors to be examined include maternal (age, overweight and obesity, maternal place of birth, socioeconomic status, geographic location, smoking, alcohol and substance use), medical and obstetric factors (diabetes, hypertension, antenatal care, parity and assisted reproductive technology).

1.3.3.1 Maternal Factors

Maternal age

Women at the extremes of reproductive age are at increased risk of stillbirth and other adverse pregnancy outcomes [30]. From 1991 to 2010, the mean age of women giving birth in Australia increased 7.5% [23]. The proportion of teenage mothers (aged less than 20 years old) was stable around 3.9%, a slight decrease from 5.0% in 2001 [23]. In 2012, the rate of stillbirth among women younger than 20 years and women aged 40 years or older was 12.6/1000 and 11.7/1000 respectively compared with the overall rate of 7.2/1000 total births [24].

Data from the National Perinatal Data Collection indicate differences in the age profile of Indigenous compared with non-Indigenous mothers. More Indigenous mothers birthed at a younger age; mean maternal age for Indigenous mothers in 2012 was 25.2 years compared with non-Indigenous (30.3 years) [24]. A higher proportion of Indigenous mothers were teenagers compared with non-Indigenous mothers – 18.6% versus 3.0% and conversely, 8.9% of Indigenous mothers were aged 35 years or older compared with 23.0% of non-Indigenous mothers [24].

There is conflicting evidence on the association between young maternal age (defined as less than 20 years old) and stillbirth. Bateman and Simpson reported an increased risk of stillbirth after adjusting for medical and obstetric predisposing factors (adjusted OR 1.11, 95% CI 1.08-1.14)[30] while Chandra reported no effect of maternal age on perinatal mortality for teenage mothers; however, there was an increased risk of low birth weight and growth restriction [31]. A meta-analysis of six studies on young maternal age found no association with stillbirth [32].

However, two studies on very young maternal age (defined as less than 15 years old) reported significantly increased risk of stillbirth. Salihu and colleagues reported adjusted odds ratio of 1.57 (95% CI 1.49 – 1.66) [33] and Wilson et al reported adjusted hazard ratio of 2.6 (95% CI 2.1 – 3.3) [34]. It has been hypothesised that the increased risk of stillbirth in young mothers is due to biological immaturity [34, 35] and social disadvantage [34]. This hypothesis is supported by findings that compared to women aged 20-24 years old, there was a higher risk of intrapartum stillbirth in mothers aged less than 15 years (adjusted HR 4.3, 95% CI 4.0-4.7) and 15-19 years (adjusted HR 1.5, 95% CI 1.2-1.8) [34].

In Australia, there has been a trend towards delayed childbearing. The proportion of mothers aged over 35 years increased from 16.3% in 1999 to 22.4% in 2012 [23, 24]. The proportion of women aged 40 years or older giving birth increased from 2.9% in 2001 to 4.3% in 2012 [23, 24]. Women aged 45 years or older made up 0.2% of women giving birth in Australia in 2012 [24].

Advanced maternal age (older than 35 years) is associated with a 65% increase in odds of stillbirth and the risk increases with increasing age. Compared with women aged less than 35 years, the odds of stillbirth were: 35-39 years (adjusted OR 1.46, 95% CI 1.22-1.73), 40-44 years (adjusted OR 1.82 95% CI 1.43-2.31), older than 45 years (adjusted OR 2.85 95% CI 1.86-4.36) and older than 50 years (adjusted OR 2.20 95% CI 1.01-4.75)[32]. While higher stillbirth rates are reported for women aged 40 years or older in Australia, between 1991 and 2009, the stillbirth rate among these women decreased from 12.7/1000 to 10.6/1000 [4].

It has been suggested that the mechanism behind the increased risk of stillbirth may be related to the direct effect of maternal aging which manifests as low utero-placental perfusion as a result of poor uterine vasculature [35, 36]. It has also been suggested that the association between older maternal age and the increased risk of chronic disease (such as diabetes and hypertensive disorders) and other medical or obstetric complications may be another pathway ultimately leading to stillbirth [36].

Overweight and obesity

Obesity is a significant health issue during pregnancy and is associated with increased risk of maternal, antenatal, peripartum and neonatal complications [23, 37]. Overweight and obesity is measured using the Body Mass Index (BMI), which is a ratio of body weight to height and is classified according to World Health Organisation (WHO) recommendations outlined in Table 1.2 [38].

It is estimated that up to one third of pregnant women in Australia are overweight or obese [24, 39]. Data from the National Perinatal Data Collection indicates that 22.4% of mothers were classified as obese at the time of conception, and a higher proportion of Indigenous mothers were obese compared to non-Indigenous mothers (29.1% versus 21.8%) [23, 37].

Table 1.2: BMI classification according to World Health Organisation (WHO)

Classification	BMI cut points
Underweight	Less than 18.5 kg/m^2
Normal range	18.5 – 24.9 kg/m^2
Overweight	25 – 29.9 kg/m^2
Obese I	30 – 34.9 kg/m^2
Obese II	35 – 39.9 kg/m^2
Obese III	≥ 40 kg/m^2

Source: World Health Organization. Obesity and overweight. Fact sheet No. 311. 2012. www.who.int/topics/obesity (accessed 24/02/2013)

Women who are obese are at increased risk of thromboembolism, gestational diabetes, pre-eclampsia, post partum haemorrhage, wound infection and caesarean section delivery [23]. Outcomes for babies born to mothers who are obese include increased risk of congenital anomalies, stillbirth and neonatal death [23]. Pregnancy complications of maternal obesity are related to pre-conception obesity and excessive weight gain during pregnancy.

Maternal pre-conception obesity is associated with an increased risk of stillbirth [40]. A recent meta-analysis reported a 23% increase in the odds of stillbirth (OR 1.23 95%CI 1.09-1.38) associated with a maternal BMI of 25-30 kg/m^2; and a 63% increase in the odds of stillbirth (OR 1.63 95% CI 1.35-1.95) associated with a BMI of >30 kg/m^2 [32]. Similarly, a population-based retrospective cohort study found increasing risk of stillbirth with increasing BMI and attributed about 25% of stillbirths between 37 and 42 weeks to maternal obesity [41]. Furthermore, an interpregnancy weight gain of 4 units in body mass index is associated with a 55% increase in risk of stillbirth [42].While maternal obesity has been identified as a leading modifiable risk factor for stillbirth, the mechanism to explain the association is not clear [40]. Inadequate placental function has been implicated as a possible mechanism [43].

Guidelines issued in 2009 by the Institute of Medicine recommend total weight gain according to pre-pregnancy BMI as follows: Underweight 12.7-18.1kg, Normal 11.3-15.9kg, Overweight 6.8-11.3kg, and Obese (all classes) 5.0-9.1kg [44]. Using these recommendations, inadequate gestational weight gain is associated with increased risk of preterm birth and small-for-gestational age, while excessive gestational weight gain is associated with increased risk of pregnancy-induced hypertension, caesarean section delivery, large-for-gestational age and macrosomia [45]. However, there is uncertainty around appropriate gestational weight gain targets for women who are obese pre-

pregnancy [46]. Evidence shows that diet or exercise or both can reduce the risk of excessive weight gain, but more studies are needed to establish safe levels of exercise during pregnancy [47] and it is unclear how best to implement guidelines on gestational weight gain, physical activity and nutrition [48]. There is little high level evidence for best practice management of obesity (BMI > 30 kg/m^2) during pregnancy and current clinical practice guidelines are based on consensus [37].

Maternal place of birth

There is some indication that there might be differences in the rate of stillbirth between Australian born and overseas born mothers. Data from the National Perinatal Data Collection from 2006 to 2012 indicate that the rate among overseas born mothers may be higher (see Figure 1.4). In 2010, 28.1% of mothers birthing in Australia were born overseas and one in ten (12.7%) was born in an Asian country [23]. Overseas born women birthing in Australia have a 13% increased risk of stillbirth [49]. In a recent Victorian study, Drysdale and colleagues reported an increased risk of late antepartum stillbirth among women born in South Asia (adjusted OR 2.5, 95% CI 1.3-5.1) [25]. This population had lower rates of smoking, hypertension and mean BMI but higher rates of diabetes and low birthweight; however, these risk factors did not fully explain the difference in stillbirth risk suggesting that different aetiological factors may be at work in this population [25].

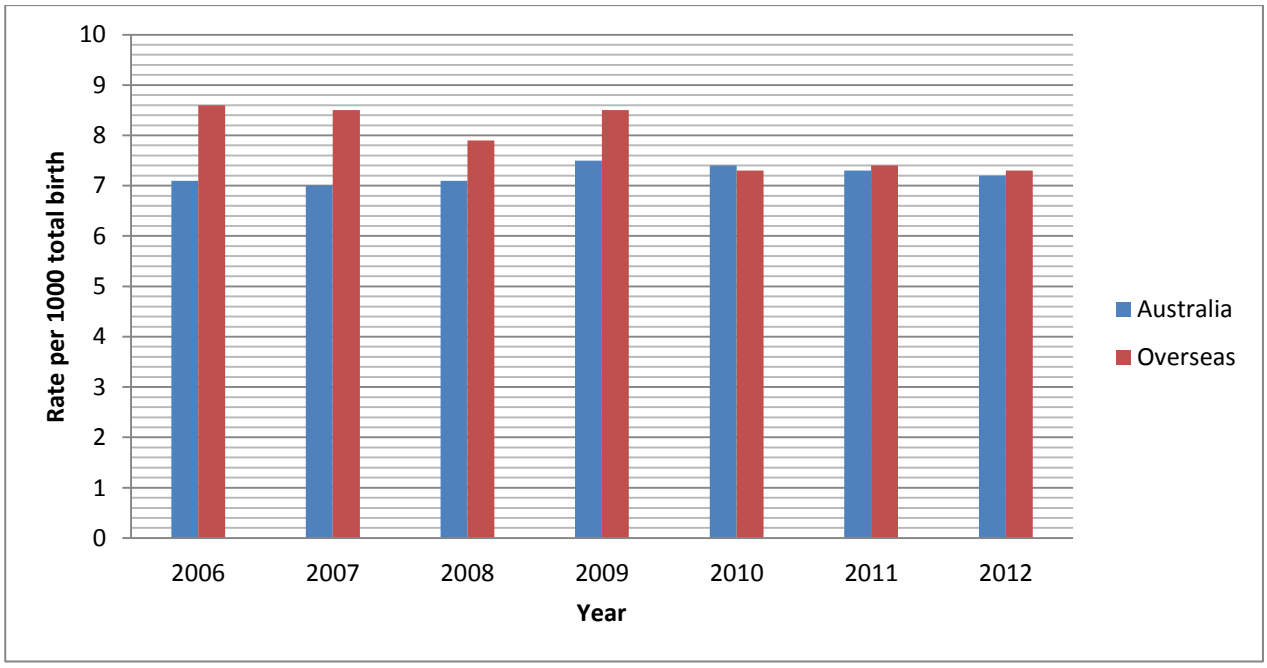


Figure 1.4: Fetal death rates by maternal place of birth, Australia, 2006-2012

Source: Australia's mothers and babies reports 2006-2012

Socioeconomic status (SES)

Socioeconomic status is a combined measure based on income, education and occupation. It can be defined at the individual or community level. Observational studies have demonstrated an association between stillbirth and socioeconomic status. In a meta-analysis by Flenady and colleagues, low socioeconomic status was associated with a 20% increased risk of stillbirth, with an associated population attributable fraction of 9% in high income countries [32].

In a number of studies assessing the relationship between low socioeconomic status and adverse pregnancy outcomes, individual level factors relating to socioeconomic status (such as maternal education, household income) were found to be stronger and independent predictors of stillbirth than community level SES indicators (eg neighbourhood SES) [50, 51].

It has been hypothesised that low socioeconomic status affects stillbirth through health risk behaviour associated with low socioeconomic status such as smoking or pre pregnancy obesity [50]. In a Canadian study that reported an increased risk of stillbirth with low socioeconomic status after controlling for individual SES factors; there was an 18.5% reduction in the estimate of odds ratio (from adjusted OR 3.31 to 2.79) for low SES and stillbirth when adjustment was made for smoking [50].

Geographic location (Remoteness)

In Australia, remoteness is a measure classifying the distance of a geographic location to the nearest urban centre [52]. The distribution of remoteness varies with states and territories. In 2012, overall 71.5% of women birthing in Australia resided in major cities (ranging from 61.5% in Queensland to 99.8% in Australian Capital Territory); 27.9% resided in regional areas (ranging from 0.2% in Australian Capital Territory to 98.1% in Tasmania) and 2.6% in remote or very remote areas (ranging from 0.1% in Victoria to 46.2% in Northern Territory) [24]. Furthermore, there are differences in the residential distribution of women giving birth by Indigenous status. In 2012, the majority (73.3%) of non-Indigenous mothers resided in major cities compared with 30.6% of Indigenous mothers. Conversely, 24.1% of Indigenous mothers lived in remote or very remote areas compared with 1.8% of non-Indigenous mothers [24].

Two studies from NSW have found increased risk of stillbirth with rural or regional residence compared with residence in urban areas [53, 54]. Abdel-Latif and colleagues reported an unadjusted odds ratio of 1.20 (95% CI 1.09-1.32)[54]. Roberts et al found a not statistically significant association between stillbirth and remote residence (crude OR 1.55) for Indigenous women and an increased risk of stillbirth for non-Indigenous women living in remote areas (crude OR 1.66, p <0.001) [53]. Whereas both analyses did not adjust for maternal and pregnancy factors; the descriptive characteristics of the populations indicate relative socioeconomic disadvantage and suboptimal maternity services.

Maternal smoking

Maternal smoking is an important modifiable risk factors for adverse pregnancy outcomes, and is associated with maternal, fetal and infant morbidity and mortality [55]. Smoking during pregnancy is associated with intrauterine growth restriction, placenta praevia, placental abruption, decreased maternal thyroid function, preterm premature rupture of membrane, low birthweight, preterm birth, babies that are small for gestational age and perinatal mortality [55-57]. Infants born to mothers who smoke are at increased risk of sudden infant death syndrome (SIDS), asthma, infantile colic and childhood obesity [55, 58].

Maternal smoking is associated with an increased risk of stillbirth, and the risk increases in a dose-dependent fashion [59]. Recent meta-analyses have estimated increased odds of 36-47% for stillbirth associated with any smoking [32, 60]; and there may be a dose-response effect with odds of stillbirth increasing with higher daily cigarette consumption [60]. It has been suggested that maternal cigarette smoking increases the risk of fetal death through fetal growth restriction and placental abruption [20]. Interestingly, there have been reports that smoking has a protective effect on pregnancy-induced hypertension [61].

In 2012, it is estimated that 12.5% of women smoked during pregnancy, a 14% decrease from rates in 2009 [24]. Smoking rates are particularly high among teenage and Indigenous mothers. Teenage mothers made up 10.2% of mothers who smoked and 34.9% of teenage mothers smoked during pregnancy [24]. An estimated 48.1% of Indigenous mothers smoked during pregnancy compared with 10.7% of non-Indigenous mothers [24] . The proportion of mothers who smoked increased with increasing levels of socioeconomic disadvantage but there was little variation in smoking rates across age

groups of Indigenous women [56]. It has been estimated that 6.2% of stillbirths in Australia could be averted by prevention of smoking during pregnancy, and among Indigenous women this proportion is estimated at 20% [32].

There is evidence of stillbirth risk reduction with smoking cessation during pregnancy. A UK study found similar rates of stillbirth among non-smokers and women who quit smoking by four months gestation [62], and more recently smoking cessation by 15 weeks gestation was associated with reduced risk of small-for-gestational age and spontaneous preterm birth [63]. Smoking cessation prior to the third trimester has been reported to reduce much of the reduction in birthweight associated with smoking [55] and there is high level evidence to support the effectiveness of smoking cessation interventions for pregnant women in reducing smoking, preterm birth and low birthweight rates [64-66]. Nevertheless, there are high rates of relapse during pregnancy and post-delivery [66]. In 2012, 21.1% of women quit smoking during pregnancy, however, the quit rate was lower among Indigenous women (11.6% versus 22.9%) [24]. This highlights the need for policy and guidelines to incorporate smoking cessation interventions tailored and targeted at Indigenous women into routine antenatal care. Smoke-free legislation was associated with reduced risk of preterm birth which could impact perinatal mortality [67]

Alcohol Use

Alcohol is considered a teratogen and fetal exposure to alcohol is associated with placental dysfunction, decreased placental size, impaired blood flow and nutrient transport, endocrine changes, increased rates of stillbirth and abruption, umbilical cord vasoconstriction and low birthweight [68]. Maternal alcohol consumption increases the risk of placental abruption as well as the toxic effects on the fetus, including birth defects and neurodevelopmental disorders [20]. High level and frequent intake of alcohol during pregnancy has been associated with increased risk of miscarriage, stillbirth and preterm birth [10].

Although there is evidence that women reduce alcohol consumption once they become aware of their pregnancy [69], a national survey on alcohol consumption during pregnancy estimated that up to 47% of women drank during pregnancy [70]. A Western Australian study found that 59% of women drank during pregnancy, and of these women 15% drank above the NHMRC recommended guidelines (no more than 7 standard drinks per week or no more than 2 standard drinks per day) during the first trimester [70]. A further 14%

reported drinking more than 5 standard drinks on a typical occasion prior to pregnancy [70]. This is particularly significant for possible fetal alcohol exposure during early pregnancy, before the mother is aware of her pregnancy. Among Indigenous women, it has been reported that 19-44% consume alcohol during pregnancy and a further 10-19% consumed alcohol at harmful levels [70].

At present, there is uncertainty about whether the effects of fetal alcohol exposure is dose dependent and if there is a threshold above which adverse effects occur [70]. Systematic reviews have found inconclusive evidence of the adverse effects of antenatal alcohol exposure at low to moderate levels (up to 83g per week) [71, 72]. Some studies have reported adverse effects on fetal neurodevelopmental outcomes [73] and increased risk of stillbirth with antenatal binge drinking [74]. A review of the adverse effects of smoking and drinking during pregnancy found a synergistic effect of these two factors on adverse pregnancy outcomes such as preterm labour, low birthweight and growth restriction [75]. As a result, Australian national guidelines are based on the safest option of no drinking during pregnancy [70, 76]. However, it has been shown that up to 72% of pregnant women do not comply with these guidelines [77].

Substance Use

Substance use includes the use of illicit substances such as heroin, methamphetamines, marijuana and the abuse of licit substances such as paint or petrol. Reports from the National Drug Strategy Household Survey indicate that 7% of pregnant women used marijuana/cannabis, 8% used any illicit drug and 4% used an illicit drug other than cannabis in 2001 [78]. Polydrug use is common among women with substance abuse issues [79]. Data on prevalence of substance use is based on self-report and it has been shown that pregnant women are particularly reluctant to disclose a history of substance use [79, 80].

Studies have shown that women with substance use issues also had increased risk of other risk factors for adverse pregnancy outcomes such as later presentation to antenatal care, fewer antenatal visits, one or more sexually transmitted infections during pregnancy [81], lower education level and lower household income [82].

Researchers have proposed that adverse pregnancy outcomes associated with substance use may be due to a number of factors including the teratogenic effect on the developing

fetus, drug withdrawal or toxicity or the associated maternal lifestyle and health issues [79].

Many reports on the association with stillbirth have looked at illicit drug or substance use as a group. In a meta-analysis by Flenady and colleagues, there was a nearly two fold increase in odds of stillbirth associated with illicit drug use (adjusted OR 1.9, 95% CI 1.2-3.0) and it was estimated that 2.1% of stillbirths in high income countries could be averted by addressing maternal illicit drug use [32]. However, attempts to assess the effect of specific drugs or class of drugs on stillbirth have been challenged by difficulties in separating the role of the drug from that of the lifestyle associated with abusive behaviour [81, 83].

An interesting finding by Pinto and colleagues was the low incidence of pre-eclampsia among drug users after controlling for parity and smoking [84]. This is a similar finding to the low incidence of pregnancy induced hypertension observed among smokers, and may suggest some common aetiologic effect between illicit drug use and smoking.

1.3.3.2 Medical and Obstetric Factors

Diabetes

Diabetes is a metabolic disorder of multiple aetiology which results in chronic hyperglycaemia and disturbances in the metabolism of carbohydrates, fats and protein from insulin secretion, insulin action or both [85]. The effects of diabetes are long term damage, dysfunction and failure of various organs (including effects on the developing baby) [85]. Glucose intolerance is determined by measuring plasma or blood glucose concentration (see Table 1.3 and 1.4).

Table 1.3: WHO recommended diagnostic criteria for diabetes and other categories of hyperglycaemia

	Glucose Concentration (mmol/l)			
	Whole blood		**Plasma**	
	Venous	**Capillary**	**Venous**	**Capillary**
Diabetes Mellitus				
Fasting or	≥ 6.1	≥ 6.1	≥ 7.0	≥ 7.0
2 hour post glucose load or both	≥ 10.0	≥ 11.1	≥ 11.1	≥ 12.2
Impaired glucose tolerance				
Fasting and	< 6.1	< 6.1	< 7.0	< 7.0
2 hour post glucose load	≥6.7 to <10.0	≥7.8 to <11.1	≥7.8 to <11.1	≥ 8.9 to <12.2
Impaired fasting glycaemia				
Fasting	≥5.6 to <6.1	≥5.6 to <6.1	≥ 6.1 to <7.0	≥6.1 to <7.0
2 hour	< 6.7	< 7.8	< 7.8	< 8.9

Source: Alberti K, Zimmet P, for the WHO consultation. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complication - Part 1: Diagnosis and Classification of Diabetes Mellitus Provisional Report of a WHO Consultation. *Diabetic Medicine* 1998; **15**: 539-53.

Table 1.4: Australasian Diabetes in Pregnancy Society (ADIPS) revised diagnostic criteria for gestational diabetes mellitus

Capillary plasma glucose levels
Fasting glucose ≥ 5.1 mmol/l
1 hour glucose ≥ 10.0 mmol/l
2 hour glucose ≥ 8.5 mmol/l
Glycated haemoglobin (HbA1c) ≥ 6.5%*

* Glycated or glycosylated haemoglobin reflects average plasma glucose levels over an extended period of time

Source: Nankervis A, McIntyre HD, Moses R, Ross GP, Callaway L, Porter C, et al. Australasian Diabetes In Pregnancy Society (ADIPS) Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia. 2013.

Gestational diabetes (GDM) is carbohydrate intolerance resulting in hyperglycaemia of variable severity which is first recognised during pregnancy [9]. It was estimated that gestational diabetes affected 4.8-10.3% of pregnancies across various states and territories in Australia in 2012 [24]; and that GDM rates are higher among Indigenous women [86, 87]. Risk factors for gestational diabetes include previous GDM, ethnicity (Asian including Indian, Aboriginal, Pacific Islander, Maori, Middle Eastern, non-white African), maternal age ≥ 40 years, family history of diabetes, obesity (BMI > 35kg/m^2), previous macrosomia (defined as birthweight > 4500g), polycystic ovarian syndrome and medications including corticosteroids and antipsychotics [9].

The incidence of stillbirth among women with diabetes has decreased dramatically with improved care [88]. However, pre-existing diabetes is associated with a three-fold increase in the odds of stillbirth [32]. An increase in risk was not found for gestational diabetes [32]. Pre-existing diabetes complicated 0.6-1.7% of pregnancies across Australian states and

territories in 2012 [24]; and pregnant Indigenous women have been reported to have higher rates of pre-existing diabetes than their non-Indigenous counterparts [89] . Obesity is associated with Type 2 diabetes and gestational diabetes and the prevalence of these conditions is increasing [90]. In diabetes-associated stillbirths, it has been proposed that the mechanism leading to mortality begins with hyperglycaemia which leads to fetal anaerobic metabolism with hypoxia and acidosis [88]. There is evidence of differences in pregnancy outcomes by ethnicity among women with gestational diabetes, for example, compared to Caucasian women, African American women had higher risk of caesarean delivery and intrauterine fetal death, while Asian women had decreased risk of macrosomia (birthweight >4000g) [91].

Many national guidelines on the screening, diagnosis and management of gestational diabetes were updated since publication of results from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study which found strong correlation between increasing maternal glucose levels at 24-32 weeks gestation and adverse maternal and fetal outcomes [92]. However, there is controversy around the screening and management of women with diabetes during pregnancy. Pre-pregnancy counselling has been found to significantly lower the risk of major congenital anomalies associated with diabetes during pregnancy (RR 0.36, 95% CI 0.22-0.59; absolute risk 2.1% versus 6.5%) [9]. Interventions to reduce adverse pregnancy outcomes associated with diabetes during pregnancy include folate supplementation, ceasing of oral hypoglycaemics and moving women onto insulin and screening for diabetes complications. Glycaemic control is a major objective of antenatal care for women with diabetes during pregnancy [93].

Hypertension

Hypertension is one of the most common medical conditions occurring during pregnancy [94]. It is defined as a systolic blood pressure of ≥ 140 mmHg and/or a diastolic blood pressure of ≥ 90mmHg. Severe hypertension in pregnancy is defined as a systolic blood pressure of ≥ 170mmHg and/or a diastolic BP of ≥ 110 mmHg [94]. Hypertension in pregnancy is classified as pre-eclampsia/eclampsia, gestational hypertension, chronic hypertension and pre-eclampsia superimposed on chronic hypertension (see Table 1.5)

Table 1.5: Classification and definitions of hypertensive conditions during pregnancy

Classification	Definition
Pre-eclampsia / Eclampsia	Hypertension + Involvement of one or more organ systems and/or the fetus Renal, haematological, liver, neurological, pulmonary oedema, Intrauterine growth restriction, placental abruption
Gestational hypertension	New onset of hypertension After 20 weeks gestation No additional features of pre-eclampsia Resolves within 3 months post-partum
Chronic Hypertension **Essential** **Secondary**	Pre-existing hypertension BP ≥ 140/90 pre conception or prior to 20 weeks gestation without underlying cause BP < 140/90 entering pregnancy on antihypertensives Hypertension due to chronic kidney disease, renal artery stenosis, systemic disease with renal involvement, endocrine disorders, coarctation of the aorta
Pre-eclampsia superimposed on chronic hypertension	Pre-existing hypertension With systemic features of pre-eclampsia After 20 weeks gestation

Source: Queensland Maternity and Neonatal Clinical Guidelines Program. Hypertensive disorders of pregnancy. Document No. MN10.13-V3-R15: Queensland Health, 2010.

The risk factors for pre-eclampsia include: a history of pre-eclampsia (either family history or in a previous pregnancy), adverse pregnancy outcome in a previous pregnancy (placental abruption, fetal growth restriction, fetal death), nulliparity, interdelivery interval > 10 years, pre-exisiting medical condition (chronic hypertension, pre-existing or gestational diabetes, renal disease or thrombophilia), maternal age ≥ 40 years, BMI > 35kg/m^2, multiple pregnancy and gestational trophoblastic disease [94-96]. In 2012, pregnancy induced hypertension complicated 2-7% of pregnancies; while pre-existing hypertension affected 0.6-1.3% of pregnancies across the various states and territories [24].

Hypertension is associated with increased odds of stillbirth. A recent systematic review and meta-analysis by Flenady and colleagues found the risk of stillbirth varied with classification of hypertensive disorder. The reported odds ratios were gestational hypertension (OR 1.33, 95% CI 1.14-1.58), pre-existing hypertension (OR 2.58, 95% CI 2.13-3.13), pre-eclampsia (OR 1.6, 95% CI 1.1-2.2), severe pre-eclampsia (OR 3.10, 95% CI 2.40-4.0) and eclampsia (OR 2.2 95%, CI 1.5-3.2)[32]. It should be noted that the estimate for severe pre-eclampsia was based on one study and so the result should be interpreted cautiously.

Studies have shown that the risk of hypertension and pre-eclampsia vary with ethnic background [96] and pregnant women from ethnic minority groups in the US, UK and Netherlands had higher blood pressure than Caucasian women [97]. Women of African descent appear to have an excess risk of stillbirth due to pre-eclampsia [96, 98]. However, little is known about the underlying mechanism explaining these differences [97]. It has been suggested that socioeconomic factors may play a role, however, recent studies have found that education and lifestyle factors did not explain these differences [97]. Paradoxically, smoking has been found to decrease the risk of pre-eclampsia, however, smokers with pre-eclampsia have increased risk of adverse pregnancy outcomes [61, 99].

Major objectives of antenatal care for women with hypertensive disorder during pregnancy are: to control blood pressure, diagnose pre-eclampsia early, prevent eclampsia and optimise birth outcomes for the mother and infant [94].

Antenatal Care

Antenatal care involves the monitoring and management of women during pregnancy to prevent complications and optimise healthy outcomes for the mother and infant [20]. The World Health Organisation recommends at least four antenatal care visits. Studies have shown that antenatal care attendance is associated with improved perinatal and maternal outcomes [9], however it is unclear what specific components of antenatal care are associated with decreased risk of stillbirth [100].

Data on antenatal visit from six Australian states and territories indicates that at least 99.1% of women in these areas had one visit; 94.9% had five or more visits and 0.1% had no visits [24]. There were differences between Indigenous and non-Indigenous women with regards to attending antenatal care. Eighty five per cent of Indigenous women who birthed at 32 weeks or more had at least five antenatal care visits compared with 95.9% of non-Indigenous mothers [24].

Inadequate antenatal care has been associated with increased risk of preterm birth [101] and stillbirth [32]. National estimates indicate that nearly 12% of pregnant women in 2010 did not begin antenatal care until after 20 weeks gestation [23]. A case control study from New Zealand reported a two-fold increase in the odds of late stillbirth with attendance of less than 50% of the recommended number of antenatal care visits (adjusted OR 2.68,

95% CI 1.04-6.90) after adjusting for maternal age, BMI, ethnicity, smoking, parity, SES and medical and obstetric history [100].

No antenatal care is associated with a three-fold increase in the odds of stillbirth (adjusted OR 3.30 95% CI 3.10-3.60) [32]. Women not accessing antenatal care were more likely to be from the most disadvantaged and marginalised groups in society. Studies indicate that these women were more likely to be highly parous [102, 103]; less highly educated [103], more likely to have used alcohol [102], tobacco [103] or abuse substances [103]. Preterm labour, preterm birth, babies with low birthweight, babies with low apgar score and post-partum haemorrhage were more common among this group of women [102, 103].

Gravidity and Parity

Gravidity refers to the number of times a woman has been pregnant, while parity refers to the number of times a woman has given birth at a specified gestational age, regardless of birth outcome and counting multiple births (for example twin or triplets) as one birth. Nulligravidity is associated with preterm birth [104]; while stillbirth, small-for-gestational age and caesarean section delivery in a previous pregnancy is associated with stillbirth in a subsequent pregnancy [105-107]. Primiparity is associated with increased risk of stillbirth compared with multiparity (having at least one previous pregnancy) [9]. Primiparity is associated with a 42% increase in odds of stillbirth (OR 1.42, 95% CI 1.33-1.51), and it was estimated that 14.5% of stillbirths in Australia were associated with primiparity [32]. In Australia, as in other high income countries, there is a trend towards delayed childbearing and the proportion of older primiparous women is increasing. Of all first time mothers, 13.9% were aged 35 years or older in 2008, compared with 10.7% in 2001 [91]. Evidence indicates that stillbirth risk among older primiparous women is greater than that in primiparous women less than 35 years [32], with reported adjusted OR for older primiparous women ranging from 1.68 to 3.60 [32]. Grandmultiparous women (having 5 or more previous births) reportedly have higher rates of anaemia, malpresentation, obstructed labour, placenta praevia and abruption [108-111]. However, there are mixed results on the effect of high parity on perinatal outcomes [112].

Assisted Reproductive Technology (ART)

Assisted reproductive technology is defined as a range of procedures carried out to circumvent infertility including in vitro fertilisation (IVF), embryo transfer (ET), gamete intrafallopian transfer (GIFT) and artificial insemination (AI) [113]. The number of ART procedures performed in Australia has increased at a rate of over 10% per year [114]. In Australia, it is estimated that 3.3% of children were conceived through ART [114].

Studies have shown that ART is associated with low birthweight, preterm birth, small for gestational age and birth defects [115-118]; and a two-fold risk in perinatal mortality has been reported for singleton births conceived by ART compared with spontaneously conceived singleton births [115]. With the trend towards delayed childbearing a considerable proportion of older mothers are conceiving through ART. In 2012, the average age of women undergoing ART was 34.3 years compared with 29.8 years for women not undergoing ART [24]; similarly, 58.1% of women undergoing ART were having their first baby [24]. Also, the proportion of women undergoing autologous cycles who were aged 40 years or more increased from 22.8% in 2007 to 26.5% in 2011 [119]. In recent years there has been a decrease in multiple births among women undergoing ART as a result of clinical shift towards single embryo transfers [119].

A number of studies have proposed that the increased risk of stillbirth observed in women undergoing ART may be due to factors related to infertility [118] or fertility treatment [120].

1.3.4 Data for Stillbirth Prevention

Accurate cause of death information is important not only for developing effective prevention strategies for stillbirth [121], but it is vital for parents faced with the loss of a baby. Having an accurate cause of death helps parents understand the circumstances surrounding the death of their baby; and aids in counselling regarding the risk of recurrence in future pregnancies [122, 123]. The quality of data for stillbirth prevention strategies is influenced by the quality and comprehensiveness of investigations undertaken to uncover cause of death, the characteristics of the classification system and its ability to retain useful information and consistent application of the classification system over time.

1.3.4.1 Investigation of stillbirth

Autopsy is currently the gold standard investigation for determining cause of death following perinatal death [124, 125]. Autopsy findings have been shown to change the primary diagnosis of cause of death in 9-34% of stillbirth cases and confirm diagnosis in 49-58% of cases, while placental histology alone or maternal blood tests provide information for classification of stillbirth in 47% and less than 15% of stillbirth cases, respectively [126]. However, perinatal and stillbirth autopsy rates have been decreasing in many high income countries [127]. Perinatal autopsy rates in Queensland have decreased by 50% over the period 1997 to 2003 and are currently around 30% [128]. This is well below the recommendation of 75% by the Royal College of Pathologists [129]. In this atmosphere of declining perinatal autopsy rates, a substantial proportion of stillbirths (about 30%) are 'unexplained' [130]; and at gestational ages approaching term this proportion increases to around 60% [131]. It has been argued that many of these stillbirths are under-investigated rather than unexplained [126].

The reasons for the decline in perinatal and stillbirth autopsy rates are varied and multifaceted, however parental consent has been identified as a major factor [132]. The process of counselling and consent for autopsy is a difficult and intrusive process for clinicians and parents. It requires parents to gain an understanding of detailed consent procedures in a state of acute grief. Reasons identified for parents declining autopsy have been given as: 1) fear of additional suffering and mutilation of the baby, 2) belief that the pre-delivery ultrasound provides sufficient information, 3) health professionals not providing an adequate explanation for the need for autopsy, 4) failure by health professionals to offer options to autopsy in post mortem examination, and 5) lack of understanding of cultural and religious influences on parent's decisions [133]. The most common reasons for parents to request an autopsy was to find the cause of the baby's death; altruism was also highly ranked [126, 134].

Studies have shown that the attitude of staff towards perinatal autopsy has an important influence on parental decision-making regarding consent for autopsy. Typically, the medical consultant approaches parents for consent, but midwives, nurses, social workers and pathologists often can provide information to parents to assist in decision making. A study found that while perinatal pathologist were the most knowledgeable about the autopsy procedure and its efficacy in determining the cause of death, they were less likely to meet the bereaved parents [126]. One Australian study showed that while midwives and neonatal nurses were reluctant to seek consent, obstetricians and neonatologists viewed

nurses and midwives as influential on parent's decisions around autopsy [135]. Studies from USA, UK and Japan reported that nurses and midwives felt ill-equipped to deal with grieving parents and highlighted lack of experience, communication skills, confidence and competence to provide sensitive care [136]. Studies examining staff attitude towards perinatal autopsy have highlighted that clinicians feel inadequate talking to parents about autopsy, and they may avoid discussing about autopsy to spare parents additional distress [137, 138].

Other factors that have been identified which affect clinicians' willingness to approach parents for autopsy consent include: low gestational age at death [135, 139], the professional discipline of the clinician and their level of seniority [140], ambivalence about the value of autopsy [141], and lack of technical understanding of autopsy procedures [142]. Parents may regret their decision about autopsy as a result of poor communication or inadequate information [143]. A study found that 52% of bereaved parents reported a poor understanding of events surrounding the stillbirth and 71% were dissatisfied with information they were given [144]. Twice as many parents who declined an autopsy later regretted their decision compared to those who agreed to an autopsy (34.4% versus 17.4%) [134]. Numerous studies have highlighted the need for specific training around communication with bereaved parents following a perinatal death [145, 146]. Furthermore, studies have demonstrated that the role of health professionals in handling the death and the interaction with bereaved persons can influence the intensity of grief; and skilled, sensitive and caring treatment in the time around the death of the unborn baby can positively impact the grief experience for parents [124].

There is guidance within the PSANZ Clinical Practice Guideline for Perinatal Mortality for clinicians in communicating with parents regarding the autopsy consent process, including a brochure for parents explaining perinatal autopsy and also to guide health care professionals in counselling about autopsy [124]. However, there is limited understanding about how the interactions between health care providers and parents impact on parent's perception of care and the decision making process about investigation into the cause of death [144].

1.3.4.2 Classification of cause of death

The value of a death classification system is using available information to establish the likely cause of death which is important for developing strategies for prevention and for monitoring the impact of such strategies [121, 147, 148]. More specifically, classification of stillbirth helps to identify groups for closer investigation and ongoing monitoring, policy development for prevention and health service utilisation [148]. Currently there are more than 81 classification systems in use for stillbirth but none is universally accepted [149]. Furthermore, there is no agreement on the features of an ideal classification system, although there has been work towards consensus on some important elements of a good classification system [150, 151]. Some of these elements include: ease of use, uniform definitions, clear guidelines and a well-defined structure to ensure that the system is applied unambiguously and consistently [147, 150], good inter-rater agreement, reproducibility, and the ability to amend the system for future research developments [147, 150]. The ability to explain the underlying cause of death is another important element [152]. However, assigning a cause of stillbirth is a complex undertaking that involves processes and interactions between the mother, baby and placenta. Therefore, complete evaluation is needed to provide pathologic, clinical and diagnostic data. There is a degree of uncertainty about what specific condition caused death due to a lack of sufficient knowledge about disease states and normal fetal physiology [147]. At present, efforts are underway to identify features of an international classification system to be used in low, middle and high income settings which will be aligned with the International Classification of Disease (ICD) [149].

The ICD is used internationally to classify health conditions and diseases for epidemiology, health management and clinical purposes [153], however it does not consistently treat the baby, umbilical cord, placenta and membranes as separate entities for which codes can be assigned [151]. The result is significant loss of information requiring supplementation to retain important information [151, 154]. Furthermore, the ICD contains a large number of categories that are not relevant to stillbirth [155]. As a result of these deficiencies, a number of classification systems have been developed. There is currently work being undertaken to apply the current ICD10 to perinatal mortality (ICD-Perinatal Mortality); and concurrently, the 11th revisions to ICD are underway [156]. This presents an opportunity to provide feedback to alter existing ICD codes.

1.3.4.3 PSANZ-PDC

The classification system for stillbirth currently used across much of Australia is the Perinatal Society of Australia and New Zealand (PSANZ) Perinatal Death Classification (PDC). The major categories are outlined in Table 2.7. The PSANZ-PDC system was developed following the PSANZ annual conference in 2000, as Australian states were using different systems at that point [157], making monitoring of trends difficult. As will be outlined below, PSANZ-PDC has many of the elements described in the preceding section.

The PSANZ-PDC is similar to the Aberdeen system in that it identifies antecedent obstetric factors that initiated the chain of events leading to perinatal death. It is based on clinical and autopsy findings, including placental pathology [147, 157]. It uses a hierarchical structure in descending order for the major categories; whereby primary conditions are assigned based on the order of categories, with categories closer to the top of the list taking precedence. It has been argued that hierarchical systems are easier to use because of the structured and consistent approach to classification, especially where there are competing conditions [154]; however, it has also been argued that erroneous results are produced when classification to a less important condition occurs because of the relatively higher position of that condition on the list of conditions [151].

PSANZ-PDC has been shown to be relatively easy to use, has specific definitions and guidelines which are linked to the Australian national birthweight/gestation percentile charts [157]. It has the provision to expand classifications and it considers the obstetric and fetal/neonatal factors and can be used to classify stillbirths and neonatal deaths [157].

PSANZ-PDC has been validated with high reliability when used with the PSANZ perinatal mortality audit guidelines. A national study found 83% agreement for stillbirths and 87% agreement for neonatal deaths with three classifiers using the PSANZ-PDC; reported kappas ranged from 0.83-0.95, $p<0.01$ [64]. An international study evaluating the performance of six classification systems (Amended Aberdeen, Extended Wigglesworth, PSANZ-PDC, ReCoDe, Tulip and CODAC) according to: ability to retain important information, ease of use, inter-observer agreement and proportion of unexplained stillbirths found PSANZ-PDC achieved the second highest score for retention of information and ease of use [155]. Both Aberdeen and Wigglesworth had unsatisfactory scores for retention of information. PSANZ-PDC had good inter-observer agreement with an overall kappa of 0.63. CODAC and ReCoDe also had good agreement with overall kappas of

0.65 and 0.51, respectively. Aberdeen and Wigglesworth had poor inter-observer agreement with reported kappas of 0.35 and 0.25, respectively [155]. The rates of unexplained stillbirth obtained using the six classification systems ranged from 9.5% to 50.2%. Aberdeen and Wigglesworth had unexplained rates of 44.3% and 50.2%, CODAC and Tulip had rates of 9.5% and 10.2%, PSANZ-PDC and ReCoDe had rates of 15.4% and 13.8% [155].

The PSANZ PDC has been highlighted as being useful for surveillance of cause of perinatal death, identifying the main cause of death for preventative strategies, investigating cause of death by gestational age or birthweight groups including aetiology and for facilitating studies on specific causes of death [157].

1.3.4.4 Application of the PSANZ PDC system

The PSANZ Clinical Practice Guideline for Perinatal Mortality was developed with the aim of ensuring a systematic and high quality approach to investigation and classification of stillbirth [124]. However, uptake of the guidelines has been poor [158]. Limited evidence base for the stillbirth investigation protocol and lack of an adequate implementation plan at the initial release of the guidelines may have played a role in the poor uptake [158]. To address the issue of implementation, an education program (IMPROVE) was developed by the Australia and New Zealand Stillbirth Alliance and PSANZ Perinatal Mortality Group to assist with implementation [159].

While the PSANZ Clinical Practice Guideline for Perinatal Mortality provides detailed guidance on classifying perinatal death, variations in the reported categories of PSANZ-PDC across Australia has raised concerns about the quality of data on causes of stillbirth. Data from six Australian states and territories show wide variation in the leading causes of stillbirth by jurisdiction (see Table 1.6). Variations in reported cause of death may be due to jurisdictional differences in the application of the PSANZ-PDC system [24].

Table 1.6: Variation in leading categories of stillbirth using PSANZ-PDC from six Australian states and territories, 2012

PSANZ PDC Category	Mean (%)	Range (%)
Congenital abnormality	29.1	17.4 – 36.4
Spontaneous preterm	16.5	7.2 – 23.6
Unexplained antepartum death	15.2	8.0 – 25.3

Source: Hilder, L., Z. Zhichao, M. Parker, S. Jahan, and G. Chambers, Australia's mothers and babies 2012. Perinatal statistics series no. 30. Cat. no. PER 69. 2014, AIHW: Canberra.

Currently, a number of models are employed in the multidisciplinary review and classification of stillbirths including hospital-based and centralised state-wide reviews [124, 160]. It has been argued that reviews should be hospital-based as there is potentially increased access to clinical information than review at statewide level [160]. However, there may be limited expertise in perinatal mortality audit at smaller maternity centres requiring aggregation of cases between maternity centres. A study carried out in New South Wales assessed agreement between hospital review and expert panel review and found the level of agreement to be low [131]. The low level of agreement was attributed to lack of familiarity on the part of the hospital review panels with the PSANZ perinatal mortality audit guidelines [131]. To our knowledge, no assessments in consistency of application of the PSANZ PDC system have been undertaken since the introduction of the IMPROVE education program.

1.4 Research aims and specific objectives

In high income countries such as Australia, it has been highlighted that further improvements in stillbirth rates can be achieved. Addressing inequity and lifestyle factors, the need for high quality data on stillbirths and detection and management of women at increased risk of stillbirth have been suggested as ways of accomplishing this [28]. This Thesis aims to describe the epidemiology of stillbirth within the Australian context and contribute to improving the quality of data through appropriate investigation of stillbirths.

The specific objectives are to:

1. Examine trends in stillbirth by clinical classification of cause of death, Indigenous status and gestational age, to identify focal areas for preventive efforts (Chapter 3)

2. Assess gestational age specific risk of stillbirth associated with four important contributors (diabetes, hypertension, antepartum haemorrhage and small-for-gestational age) to higher stillbirth rates among Indigenous women in order to identify periods of increased risk (Chapter 4)
3. Develop and validate a statistical model to predict the risk of antepartum stillbirth at term (≥37 weeks) using maternal and pregnancy factors as a potential decision-making aid for clinicians and women (Chapter 5)
4. Assess consistency in application of the Perinatal Society of Australia and New Zealand Perinatal Death Classification system between hospital committees and an independent expert panel, to identify areas for quality improvement (Chapter 6)
5. Determine maternal and pregnancy factors associated with parental consent to autopsy following stillbirth and explore parents' views and experiences of the autopsy consent process to inform clinical practice (Chapter 7)

Chapter 2

Data Management for Queensland perinatal data

This chapter describes the data management procedures carried out on the Queensland perinatal data utilised in various investigations within this Thesis. Queensland perinatal data was utilised for the following investigations:

- Stillbirth trends analysis (Chapter 3)
- Gestational age specific stillbirth risk analysis (Chapter 4)
- Term antepartum stillbirth risk prediction (Chapter 5)
- Predictors of autopsy following stillbirth (Chapter 7)

The data management procedures are described here to avoid repetition within the respective chapters. Section 2.1 of this chapter describes the data source and range of variables obtained while Section 2.2 outlines the data cleaning and management procedures. Section 2.3 concludes this chapter with some reflections on the quality of the Queensland perinatal data.

2.1 Data Source and Variables

Data was obtained from the Queensland Perinatal Data Collection (QPDC). The QPDC was started in November 1986 under state legislation Part II of the Health Act 1937 requiring perinatal data to be provided to the Chief Executive of Queensland Health for every baby born in Queensland. This data source was particularly useful for as it was the most extensive collection of maternal demographic, pregnancy outcomes and clinical classification of cause of death data available on a population level within Queensland. Data was requested for births in Queensland during the period 1994 to 2011. The study period was chosen to maximise the number of years with consistent data collection; and 2011 was the most recent year of data available at the time of data request. Analysis was restricted to singleton births because of the differences in the type and distribution of causes of death between singleton and multiple pregnancies [3].

Data was collected via the Queensland Perinatal Data Collection form (MR63D), the Perinatal Online Application or via electronic extracts from the hospital electronic records.

Data was provided to the QPDC by all public and private hospitals, private midwives and medical practitioners involved in the delivery of babies outside hospital. However, the completeness of data from births outside hospital is unknown. The scope of information requested included maternal demographic, medical, obstetric and birth outcome information. Data checks were performed by the Queensland Health Statistics Unit to validate information received by the QPDC and queries were directed back to the hospital or independent healthcare practitioner who submitted the data [161]. Although validation studies are yet to be performed on the perinatal data from Queensland, data audits completed in other Australian states using state-based perinatal data collections show that misclassification (i.e. false positive and false negatives) are generally <5% for coding of conditions such as diabetes, hypertensive disorders and antepartum haemorrhage [162].

Birth outcome information requested included maternal, fetal and underlying cause of perinatal death using ICD codes as well as the antecedent causes of perinatal mortality using the Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ-PDC). Antecedent cause of perinatal death available from the QPDC dataset was assigned by the Perinatal Mortality sub-committee of the Queensland Maternal and Perinatal Quality Council. This was a multidisciplinary perinatal mortality review committee which systematically assigned clinical classification of cause of death as part of routine procedure. The sub-committee undertook review of all perinatal death in the state using confidential case summaries, autopsy, placental and other pathology reports, medical certificates of cause of perinatal death, and QPDC data forms [163].

2.1.1 Ethics and Data Custodian approvals

Non-identifiable routinely collected data from the QPDC were utilised for this study. Ethics approval was obtained from the Queensland Health Central Office (Ref: HREC/05/QHC/009) and University of Queensland School of Population Health Human Research Ethics Committees (Ref: II180313). In addition, approval was obtained from the Director General for access to and use of confidential information under Section 284 of the *Public Health Act 2005* (Ref: RD004800) (See Appendix A).

2.2 Data Management

Data were obtained on maternal, medical and obstetric and birth outcome variables from the QPDC. Data were supplied in five separate zipped and password protected ASCII comma delimited text files (see Table 2.1 below). Outlined in this section are the data management procedures undertaken for each group of variables.

Table 2.1: Details of data files from the Queensland Perinatal Data Collection, 1994-2011

Filename	File Type	n	Comments
peri9411	.dat	928,313	Main dataset, one observation per pregnancy
medic_cond	.dat	255,516	Pre-existing maternal medical conditions, multiple entries relating to a pregnancy permitted
deliv_cmplc	.dat	1,071,431	Delivery complications, multiple entries relating to a pregnancy permitted
preg_cmplc	.dat	820,706	Maternal conditions arising as a result of pregnancy, multiple entries relating to a pregnancy permitted
cong_anom	.dat	51,511	Congenital anomalies, multiple entries relating to a pregnancy permitted

2.2.1 Maternal Variables

Maternal variables included:

- Age
- Maternal Indigenous status
- Marital status
- Smoking status
- Alcohol and substance use status
- Postcode of usual residence
- Socioeconomic status
- Geographic location
- Maternal region of birth

Maternal age

Data on maternal age were provided in categories starting with “Less than 18 years” and increasing in two year blocks up to “45 years or older”. These were re-categorised as: “Less than 18 years”, “19-24 years”, “25-30 years”, “31-34 years” and “35+ years”. This was to adequately separate lower and higher risk maternal age groups and for comparability with other studies.

Maternal Indigenous status

Maternal Indigenous status was based on maternal self-identification as Aboriginal and/or Torres Strait Islander during clinical interview. Classification as 'non-Indigenous' referred to women who identified as neither Aboriginal nor Torres Strait Islander. A national assessment of the quality of reporting of Indigenous status in perinatal data over the period 1991-2004 found data from the QPDC to be suitable for trend analyses from 1991 onwards [56].

Marital status

Marital status was categorised as "Married/defacto", "Never married", "Divorced", "Separated" or "Widowed". These categories were collapsed into two groups: "Domestic partner" (married/defacto) and "No domestic partner" (never married, divorced or widowed).

Smoking status

Smoking status was based on maternal self-report and referred to any smoking during pregnancy (yes or no). Consistent data collection commenced in July 2005.

Alcohol and Substance Use

Alcohol use was based on the presence of the diagnostic codes 291, 303, 305.0 (ICD9) or F10 (ICD10AM) in maternal hospital records while substance use was based on the presence of the diagnostic codes 291-292 or 303-305 (ICD9) or F10-F19 (ICD10AM). It should be noted that the coding for substance use status includes alcohol use. The prevalence of alcohol use within this population was 0.05%, well below national reports which ranged from 47% to 59% [70]. Whereas the prevalence of substance use was 0.6% compared with reports of around 8% nationally [78]; furthermore a prevalence of 0.8% has been reported among the obstetric population in South Australia using hospital records [164]. While it has been reported that pregnant women are reluctant to disclose a history of substance use [80, 164], the magnitude of difference in prevalence of alcohol use between

this population and national reports led us to conclude that the data on alcohol use were not reliable and it was not used in subsequent analyses.

Postcode of maternal usual residence

Postcode of usual residence was used to derive measures of socioeconomic status and geographic location.

Socioeconomic status

Socioeconomic status was derived from the postcode of maternal usual place of residence. The postcode was mapped to the Australian Bureau of Statistics' Index of Relative Socio-economic Disadvantage (IRSD), which is a summary measure allowing the ranking of geographic areas in Australia according to social and economic wellbeing [165]. The IRSD was derived from census data on income, educational attainment, employment, measures of material and social resources and the ability to participate in society [165]. This index was chosen specifically because of the interest in the effect of socioeconomic disadvantage on stillbirth and the need for a broad measure of disadvantage rather than a specific measure such as income alone.

Data on IRSD were published every five years from 1991. Publications between 1991 and 2001 did not include explicit listings of deciles of IRSD by postcode, therefore, this measure was calculated from the data provided. Contained in these publications were listings of: absolute disadvantage scores for each census collection district, population size within each collection district, and listing of the collection districts within each postcode area. Collection districts were the smallest unit of census data collection and were roughly equivalent to 250 households in an urban setting or a group of suburban blocks [165]. Postcode areas were developed by the ABS and matched to postcodes as closely as possible [165].

To obtain decile ranks for each postcode, the population-weighted average disadvantage score and percentile rank were calculated (see below). Data from 1991 and 1996 were manipulated using Steps 1 and 2. Data from 2001 were manipulated using Step 2 only. Decile ranks were applied to the corresponding study periods, eg decile ranks calculated from the 2001 publication were applied to study data from 2001 to 2005. IRSD could not

be determined for 80 unique postcodes. The reasons for this were: few (10 or less) people living or working in the area, low response rates to census questions on occupation, labour and education, and classification of the area as prison, offshore, shipping or migratory area [165].

For the purpose of this study, decile ranks were coded into three categories: lowest ranked 20%, middle 60% and top ranked 20%. Socioeconomic disadvantage was defined as residing in an area with a postcode classified in the lowest ranked 20%.

Figure 2.1: Calculation of decile rankings for IRSD data published between 1991 and 2001

Step 1: Calculation of population-weighted disadvantage score for each collection district

$$\frac{\textit{Score for each collection district in postcode} \times \textit{population in collection district}}{\textit{population in each postcode}}$$

Step 2: Calculation of decile rank for each postal area

Geographic location

Geographic location, in terms of remoteness, was derived by mapping postal areas (POA) from postcode of maternal usual place of residence to the Australian Standard Geographical Classification (ASGC) Remoteness Areas. This allowed for the classification of geographic areas by their physical road distance to the nearest urban centre using the Accessibility/Remoteness Index of Australia (ARIA) [52].

Geographic areas were classified as: major cities (ARIA 0 to 0.2), inner regional (ARIA >0.2 to ≤2.4), outer regional (ARIA >2.4 to ≤5.92), remote (>5.92 to ≤10.53) and very remote (ARIA >10.53). In the event of a postal area falling within two or more geographic area classifications, the classification applied was the one with the largest proportion of that postcode. For example: The postal area 4133 is listed as 87.3% major cities and 12.7% inner regional and would be classified as major cities. For the analyses, the five

categories of geographic areas were collapsed to three: Urban (major cities), Regional (inner and outer regional) and Remote (remote and very remote).

Remoteness data linked to postal areas were available from the ABS for 2006 only; data available for earlier time periods were linked to other measures such as SLA but not postal areas. As a result, data from 2006 were applied to the entirety of the study period. A potential consequence of this may be misclassification of urban and regional areas in earlier parts of the study period, if there has been increased urbanisation over the study period. It is unlikely to affect classification of remoteness in later parts of the study period.

Issue was raised about the analyses of variables derived from the ABS remoteness structure and socioeconomic index for areas (which includes IRSD) – as these are derived from similar census data items. This issue was explored in the course of the *Gestational age specific stillbirth risk analysis* (Chapter 4) as it was important to assess the effect of geographic location on the risk of stillbirth; and socioeconomic status (as defined using the IRSD) was an important potential confounder. The association between these variables and with stillbirth was explored using multivariate analysis. It was found that the standard errors in the models were not particularly larger with either or neither of the variables "socioeconomic status" and "geographic location" in the models; as well the effect estimates for stillbirth were stable in terms of magnitude and direction of effect with either or neither of these variables in the multivariate models. It was also noted that the measure IRSD published in 2006 was derived from data that included Indigenous status. This was another reason for stratification of the analysis in the *Gestational age specific stillbirth risk analysis* (Chapter 4) by Indigenous status.

Maternal region of birth

Maternal region of birth was derived from maternal country of birth. Country of birth classification was based on the Australian Bureau of Statistics' Standard classification of countries, which underwent a number of revisions over the study period (Table 2.2). Countries were grouped using the United Nations Geographic regions. These groups were further collapsed based on frequency into the following nine categories: Africa, Americas and Caribbean, East Asia, South East Asia, Asia (Other), Europe, Australia and New Zealand, Oceania (excluding Australia and New Zealand) and Other.

Table 2.2: Details of classification of maternal region of birth, 1994-2011

Study Period	Classification	Comments
Jan 1986 - June 1994	Country of birth code list	Country and region level coding, 90 codes
July 1994 – June 2001	Australian Standard Classification of Countries for Social Statistics (ASCCSS)	Country level coding, 280 codes
July 2001 – June 2004	Standard Australian Classification of countries - Version 1 (V1_SACC)	Country level coding, 249 codes
July 2004 – current	Standard Australian Classification of countries - Version 2 (V2_SACC)	Country level coding, 253 codes

2.2.2 Medical and Obstetric Variables

Medical and obstetric variables included:

- Accommodation status
- Primigravidity
- Use of assisted conception techniques
- Number of antenatal care visits
- Congenital anomalies
- Pre-existing diabetes
- Pre-existing hypertension
- Antepartum haemorrhage, Gestational Diabetes, Pregnancy Induced Hypertension and Pre-eclampsia/Eclampsia

Hospital accommodation Status

Hospital accommodation status was defined as the type of ward accommodation elected regardless of method of payment for admission. Hospital accommodation status was classified as ‘Public’ or ‘Private’.

Primigravidity

Primigravidity was defined as having no previous pregnancy (excluding the current pregnancy).

Use of assisted conception techniques

Use of assisted conception techniques referred to whether pregnancy was achieved using any of the following methods: artificial insemination (AIH/AID), ovulation induction, in-vitro fertilisation (IVF), gamete intra fallopian transfer (GIFT), intracytoplasmic sperm injection (ICSI) or other methods such as assisted hatching or blastocyst culture.

Number of antenatal care visits

Number of antenatal care visits was collected in two categories: “Less than 2 visits” and “2 or more visits” prior to mid-1998. This was changed from July 1998 and data was collected in four categories: “Less than 2”, “2 to 4”, “5 to 7” and “8 or more” visits. Data were not available on the gestational age at initiation of antenatal care visits prior to July 2009, therefore, adequacy of antenatal care index could not be derived for the majority of the study period. However, attending less than 2 antenatal care visits was used as a proxy for inadequate antenatal care in models adjusted for gestational age. This was to ensure that bias was not introduced for stillbirths occurring at very young gestational ages where the mother may have only had an opportunity to attend one antenatal care visit.

Congenital anomalies

Data on congenital anomalies were extracted from the supplementary dataset **‘cong_anom.dat’**. This dataset allowed for multiple entries relating to a specific pregnancy. Congenital anomalies were coded using the British Paediatric Association Classification of Disease extension to the International Classification of Disease (ICD) codes 740-759 (9^{th} edition) and Q00-Q99 (10^{th} edition Australian modification).

Antepartum haemorrhage, Gestational Diabetes, Pregnancy Induced Hypertension and Pre-eclampsia/Eclampsia

Data on antepartum haemorrhage, diabetes (pre-existing and gestational) and hypertension (essential, pregnancy induced and pre-eclampsia/eclampsia) were extracted from supplementary datasets **‘medic_cond.dat’** and ‘**preg_cmplc.dat’**. These supplementary datasets were set up to allow multiple entries for each pregnancy. Data extraction involved extracting all occurrences of the ICD9 and ICD10 codes associated

with each condition of interest (see Table 2.3) and using each woman's unique study number (duplicate entries were dropped) to merge the data with the main dataset. Within the main dataset, entries with missing data for the maternal condition/pregnancy complication were coded as not having the condition/complication. The proportion of women with antepartum haemorrhage or hypertensive disorders was consistent throughout the data collection period. However, the ascertainment of pre-existing and gestational diabetes increased dramatically to coincide with the introduction of ICD10AM for classification of maternal conditions and pregnancy complication.

Table 2.3: International Classification of Disease (ICD) codes for selected maternal conditions and pregnancy complications

Condition	Sub-categories	ICD9 codes	ICD10 AM codes	Data Collection period
Antepartum haemorrhage	Placenta praevia with haemorrhage, placental abruption, antepartum haemorrhage not elsewhere classified	641.1, 641.2, 641.3, 641.8, 641.9	O44.1 O45 O46	1994-2011
Gestational diabetes*	Gestational diabetes	648.0	O24.4	July 1999 - 2011
	Unspecified		O24.9	July 1999 - 2011
Pre-existing diabetes*	Type I	250	O24.0, E10	July 1999 - 2011
	Type II		E11, O24.1	July 1999 - 2011
	Unspecified		E14, O24.3	July 1999 - 2011
	Other specified (malnutrition related)		O24.2, E13	July 1999 - 2011
Essential hypertension	Pre-existing hypertension complicating pregnancy	401.0 401.1 642.0 642.00 642.01	O10.0 O10.1 O10.2 O10.3 I10 I11 I12 I13	1994-2011
	Secondary hypertension	642.1	O10.4 I15	1994-2011
	Unspecified/Other	401.9 642.2	O10.9	1994-2011
	Superimposed with pre-eclampsia	642.7	O11	1994-2011
Pregnancy Induced hypertension	Gestational hypertension or transient hypertension of pregnancy or other unspecified hypertension complicating pregnancy	642.3 642.9	O13 O16	1994-2011
Pre-eclampsia and Eclampsia	Pre-eclampsia	642.4 642.5	O14.0 O14.1 O14.9	1994-2011
	Eclampsia	642.6	O15.0 O15.1 O15.2 O15.9	1994-2011

* Level of detail provided for ICD9 codes did not allow for identification of type of diabetes mellitus (ie whether Type I or II). ^ British Paediatric Association Classification of Disease extension to ICD9 and ICD10 used

2.2.3 Birth Outcome Variables

Birth outcome variables included:

- Gestational age at birth
- Birthweight
- Baby's sex
- Small for gestational age (SGA) and large for gestational age (LGA)
- Birth status (stillbirth or livebirth)
- Type of perinatal death (antepartum, intrapartum, unknown stillbirth, neonatal)
- Clinical classification of stillbirth
- Post-mortem/autopsy

Gestational age at birth

Gestational age was determined by clinical assessment after birth and given in completed weeks. Births eligible for registration in the QPDC were all livebirths and stillbirths of at least 20 weeks gestation and/or 400 grams birthweight. The QPDC also included livebirths that were less than 20 weeks gestation and also less than 400 grams birthweight. However, these were excluded from analyses, as they were not within the population of interest.

Birthweight

Birthweight was measured after birth and given to the nearest gram. Births eligible for registration in the QPDC were all livebirths and stillbirths of at least 20 weeks gestation and/or 400 grams birthweight. The QPDC also included livebirths that were less than 400 grams birthweight and also less than 20 weeks gestation. However, these were excluded from analyses, as they were not within the population of interest.

Baby's sex

Baby's sex was classified as "Male", "Female" and "Indeterminate".

Small for gestational age (SGA) and Large for gestational age (LGA)

Small for gestational age was defined as having a birthweight less than the 10th population centile by gestational age, plurality and gender of the infant (Table 2.4). The population birthweight percentiles used were those published by Dobbins and colleagues [166] as

they were derived from population data arising from a similar period as our data (1998-2007). Large for gestational age was defined as having a birthweight more than the 90th population centile by gestational age, plurality and gender of the baby (Table 2.4).

Table 2.4: Birthweight percentile values (grams) for live singleton births (female and male), 1998-2007

Gestational age (weeks)	Birthweight percentile (grams)					
	Female			Male		
	3rd	10th	90th	3rd	10th	90th
20	210	265	410	248	273	430
21	250	300	470	290	335	500
22	325	400	560	370	410	600
23	375	445	660	450	500	700
24	430	520	754	470	550	810
25	470	559	884	505	620	944
26	490	594	1026	576	680	1078
27	568	675	1175	605	752	1250
28	622	764	1347	680	844	1395
29	712	870	1494	782	964	1620
30	870	1030	1715	900	1091	1800
31	1000	1190	1948	1055	1270	2028
32	1140	1348	2170	1214	1430	2270
33	1330	1560	2450	1381	1638	2560
34	1525	1764	2705	1580	1860	2810
35	1710	1980	2995	1795	2080	3095
36	1940	2198	3250	2015	2295	3360
37	2175	2430	3545	2265	2540	3670
38	2440	2690	3770	2540	2800	3910
39	2600	2830	3890	2700	2950	4040
40	2740	2975	4030	2840	3090	4195
41	2855	3090	4170	2970	3220	4340
42	2850	3110	4240	2980	3250	4430
43	2800	3010	4210	2782	3085	4470
44	-	3070	4230	-	3110	4415

Source: Dobbins TA, Sullivan EA, Roberts CL, Simpson JM. Australian national birthweight percentiles by sex and gestational age, 1998-2007. Med J Aust. 2012; **197**(5): 291-4.

Birth Status

Birth status was defined as whether the baby was born alive or not. Stillbirth was defined as a baby born with no evidence of life (for example: does not breathe, no heartbeat, no pulsing of umbilical cord or movement of voluntary muscles) at 20 weeks gestation or older or 400grams birthweight or more.

Type of perinatal death

The type of perinatal death was indicated using one of five categories and these were coded accordingly (see Table 2.5 below).

Table 2.5: Categories and coding for type of perinatal death

Categories	Coding 1	Coding 2
Before labour commenced	Antepartum stillbirth	stillbirth
During labour, before delivery	Intrapartum stillbirth	stillbirth
Before delivery, but not known if before or during labour	Unknown stillbirth	stillbirth
After delivery	Neonatal death	neonatal death
Not known if before or after delivery	Perinatal death	perinatal death

Clinical Classification of stillbirth

Stillbirth was classified according to the Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ-PDC) [124], which has been in use since 2004. Over the study period, there were four predecessors to the PSANZ-PDC in use. The classification system in use in Queensland around the start of the study period was the Queensland Council on Obstetric and Paediatric Mortality and Morbidity (QCOPMM) based on the Whitfield classification system [167] with the category “Other Specific Obstetric conditions”. This additional category included fetomaternal haemorrhage and idiopathic hydrops, which would have been classified as “Other” under the Whitfield system. The aim of the QCOPMM was to identify the primary maternal and/or fetal factors leading to perinatal death [157]. The QCOPMM system was further refined to identify important sub-categories obscured by the Whitfield classification system. The new system was developed by the QCOPMM was renamed the Queensland Council Perinatal Mortality Classification (QCPMC). In 2000, following the Perinatal Society of Australia and New Zealand annual conference, there was consensus to develop uniform classification system for use across Australia and New Zealand. Developed by representatives from South Australia and Queensland, this system was named ANZACPM and was the immediate predecessor of the PSANZ-PDC.

The PSANZ-PDC system aims to identify the single most important maternal or fetal factor which initiated the chain of events leading to perinatal death [124]. The classification system consists of eleven main categories and 67 major subcategories and is meant to be

applied using a hierarchical approach although this can be overridden depending on the scenario. These classification systems were mapped to the current PSANZ-PDC [124]. In mapping categories across the classification systems, most major categories were mapped without problems. However, there were differences in the definition of sub-categories within the major categories of idiopathic preterm birth and unexplained antepartum fetal death. This did not allow sub-categories to be mapped across the entire time period, so wider categories were used. Table 2.6 shows the distribution of stillbirths across the main categories of the classification systems in use over the study period. Table 2.7 shows the detailed categories and descriptions of the PSANZ PDC.

Table 2.6: Classification systems and their main categories in use in Queensland, 1995-2011

Category	PSANZ-PDC (2004-2011)	ANZACPM (2000-2003)	QCPMC (1997-1999)	QCOPMM (1994-1996)
1 Congenital abnormality	718 (25.3)	231 (20.0)	159 (20.7)	105 (18.4)
2 Perinatal infection	75 (2.6)	31 (2.7)	38 (4.9)	39 (6.8)
3 Hypertension	81 (2.9)	30 (2.6)	70 (9.1)	25 (4.4)
4 Antepartum haemorrhage	196 (6.9)	89 (7.7)	90 (11.7)	55 (9.6)
5 Maternal conditions	81 (2.9)	49 (4.2)	20 (2.6)	30 (5.3)
6 Specific perinatal conditions	140 (4.9)	80 (6.9)	37 (4.8)	20 (3.5)
7 Hypoxic peripartum death	54 (1.9)	27 (2.3)	16 (2.1)	12 (2.1)
8 Fetal Growth Restriction	146 (5.1)	61 (5.3)	25 (3.3)	19 (3.3)
9 Spontaneous preterm	395 (13.9)	149 (12.9)	100 (13.0)	67 (11.8)
10 Unexplained antepartum death	896 (31.6)	405 (35.0)	206 (26.8)	194 (34.0)
11 No obstetric antecedent	54 (1.9)	4 (0.3)	7 (0.9)	4 (0.7)
Total	**2836 (100.0)**	**1156 (100.0)**	**768 (100.0)**	**570 (100.0)**

QCOPMM = Queensland Council on Obstetric and Paediatric Morbidity and Mortality; QCPMC = Queensland Council Perinatal Mortality Classification; ANZACPM = Australia and New Zealand Antecedent Classification of Perinatal Death; PSANZ-PDC = Perinatal Society of Australia and New Zealand Perinatal Death Classification

Table 2.7: Categories and description of the Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ-PDC)

Main Category	Description and main sub-categories
1 Congenital abnormality (including terminations for congenital abnormality)	Includes all major fetal abnormalities and is the only category which strictly overrides all other categories. Major subcategories: central nervous system, cardiovascular system, urinary system, gastrointestinal system, chromosomal, metabolic, multiple/non-chromosomal syndromes, other congenital abnormality (musculoskeletal, respiratory, diaphragmatic hernia, haematological, tumours, other specified congenital abnormality) and unspecified congenital abnormality.
2 Perinatal Infection	Identifies all primary infections preterm and secondary infections in term births based on laboratory evidence. Major subcategories: bacterial, viral, protozoal, fungal, other specified organism, other unspecified organism
3 Hypertension	Includes deaths where hypertensive disorder is considered the initiating factor in the events leading to perinatal death. Major subcategories: chronic hypertension (essential, secondary, unspecified), gestational hypertension, pre-eclampsia, pre-eclampsia superimposed on chronic hypertension, unspecified hypertension
4 Antepartum haemorrhage (APH)	Identifies all perinatal deaths where the primary factor leading to death was an antepartum haemorrhage. Major subcategories: placental abruption, placenta praevia, vasa praevia, other APH, APH of undetermined origin
5 Maternal conditions	Identifies all perinatal deaths attributed to any medical or surgical disorder in the mother, its complications or treatment, excluding hypertension. Major subcategories: Termination of pregnancy for maternal psychosocial indications, Diabetes / Gestational Diabetes, Maternal injury, Maternal sepsis, Antiphospholipid syndrome, Obstetric cholestasis, Other specified maternal conditions
6 Specified perinatal conditions	Includes deaths of normally formed, appropriately grown babies in which the specific perinatal condition was a major contributing factor to perinatal death. Major subcategories: Twin-twin transfusion, Fetomaternal haemorrhage, Antepartum cord complications, Uterine abnormalities (including cervical incompetence), Birth trauma, Alloimmune disease, Idiopathic hydrops, Other specific perinatal conditions, Unspecified perinatal conditions
7 Hypoxic peripartum death (typically infants of >24 weeks gestation or >600g birthweight)	Identifies perinatal deaths, usually of > 24 weeks gestation or 600g birthweight, due to intrapartum events. Major subcategories: With intrapartum complications, Evidence of non-reassuring fetal status in a normally grown infant, No intrapartum complications and no evidence of non-reassuring fetal status, Unspecified hypoxic peripartum death
8 Fetal Growth Restriction (FGR)	Includes all death of babies with birthweight less than 10th percentile for gestational age for livebirths or non-macerated stillbirths, or all perinatal deaths with antenatal evidence of fetal growth restriction or growth arrest before death or FGR determined at autopsy. Major subcategories: With evidence of reduced vascular perfusion on Doppler studies and/or placental histopathology, With chronic villitis, No placental pathology, No examination of placenta, Other specified placental pathology, Unspecified or not known whether placenta examined.
9 Spontaneous preterm (<37 weeks gestation)*	Identifies perinatal deaths of normally formed, appropriately grown babies born before 37 weeks' gestation, following spontaneous onset of preterm labour or rupture of membranes, irrespective of mode of delivery. Major subcategories: Spontaneous preterm with intact

Main Category	Description and main sub-categories
	membranes or membrane rupture <24 hours before delivery, Spontaneous preterm with membrane rupture ≥24 hours before delivery, Spontaneous preterm with membrane rupture of unknown duration before delivery. Further subdivisions within major subcategories: with chorioamnionitis on placental histopathology, without chorioamnionitis on placental histopathology, with clinical evidence of chorioamnionitis - no examination of placenta, No clinical signs of chorioamnionitis – no examination of placenta, Unspecified or not known whether placenta examined.*
10 Unexplained antepartum death	Identifies normally formed babies who died before the onset of labour without any predisposing conditions which were likely to have caused death. Perinatal autopsy is not required for this category. Major subcategories: With evidence if reduced vascular perfusion on Doppler studies and/or placental histopathology, With chronic villitis, No placental pathology, No examination of placenta, Other specified placental pathology, Unspecified or not known whether placenta examined.
11 No obstetric antecedent	Stillbirths with no obstetric contributing factors and other unknown or unspecified causes of death. Major subcategories: Sudden Infant Death Syndrome (SIDS), Postnatally acquired infection, Accidental asphyxiation, Other accident, poisoning or violence (postnatal), Other specified, Unknown/Undetermined

***** The duration of membrane rupture with or without secondary chorioamnionitis was only consistently captured as subcategory from 2000 onwards. PSANZ Clinical Practice Guidelines for Perinatal Mortality including the PSANZ PDC is available at: www.stillbirthalliance.org.au/guideline1.htm

Terminations of pregnancy

Data on stillbirths as a result of termination of pregnancy for maternal psychosocial reasons was systematically collected over the data collection period. Data was not available on stillbirths resulting from terminations of pregnancy for maternal and fetal reasons other than maternal psychosocial reasons within the QPDC.

Provision was made for classification of stillbirths as a result of termination of pregnancy due to congenital anomaly from 2009 [124], however, data was available only for 2009 (partial) and 2010 (complete). Data from 2010 indicated that 6.7% and 14.4% of stillbirths among Indigenous and non-Indigenous women were terminations of pregnancy for congenital anomalies, respectively. Among Indigenous women, this consisted of urinary (3.3%) and central nervous system (3.3%) anomalies. Among non-Indigenous, terminations for congenital anomaly included: central nervous system (4.2%), chromosomal (3.9%), cardiovascular system (3.6%), urinary system (1.2%), multiple/non-chromosomal (0.6%), unspecified anomaly (0.6%) and musculoskeletal (0.3%). Available details of terminations of pregnancy due to congenital anomaly for 2009 are shown in Table 2.8 below.

Table 2.8: Trends in stillbirths as a result of termination of pregnancy due to congenital anomaly, by Indigenous status, Queensland, 2009-2011

Type of congenital anomaly	Indigenous			Non-Indigenous		
	Percentage of all stillbirths					
	2009 (n=34)	2010 (n=30)	2011 (n=34)	2009 (n=377)	2010 (n=333)	2011 (n=329)
Central nervous system	0.0	3.3	-	0.8	4.2	-
Cardiovascular system	0.0	0.0	-	0.3	3.6	-
Urinary system	0.0	3.3	-	0.0	1.2	-
Chromosomal	0.0	0.0	-	0.5	3.9	-
Multiple/non-chromosomal	0.0	0.0	-	0.0	0.6	-
Musculoskeletal	0.0	0.0	-	0.0	0.3	-
Unspecified congenital anomaly	0.0	0.0	-	0.0	0.6	-

- no reports of stillbirths as a result of termination of pregnancy due to congenital anomaly for 2011

Autopsy

Data was obtained on whether or not an autopsy was conducted. Data was classified as "No", "Yes", "Under Investigation" or "unknown". The category "Under Investigation" was re-classified as "Yes". Complete ascertainment of autopsy status was available from mid 2000. Prior to this time, the rate of missing data ranged from 30.4% in 1994 decreasing to 6.9% in 1999.

2.3 Reflection on data quality

Data from the QPDC was utilised for the population based studies within this Thesis instead of data from the Australian Bureau of Statistics (ABS) for a number of reasons relating to data accuracy and completeness.

Data Accuracy

In Australia, perinatal data from the ABS is obtained from death certificates. Typically, death certificates are completed before many stillbirth investigations are performed, as a result, the cause of death given on the death certificate may not reflect the cause of death found after investigation. It is estimated that up to 40% of cause of death information on stillbirth death certificates are incorrect [168]. In contrast, the QPDC contains clinical classification of cause of death obtained through expert review of each stillbirth.

Data completeness

The QPDC is the most comprehensive collection of population based perinatal data available in Queensland; and data from the QPDC is provided to the Australian Institute of Health and Welfare for national reporting of perinatal statistics [169]. There is around 2.7% underreporting of births in ABS data compared with the QPDC [170]. The QPDC also compares favourably with perinatal data collections used for reporting in other high income countries. In USA, there was evidence of underreporting of fetal deaths particularly around the lower limits of gestational age [171], while in England, up to 8% of stillbirths were missing from CEMACE data compared with death registration data [172].

In relation to missing data, the QPDC was again comparable to data collections used in other high income countries. As shown in Table 2.9, the proportion of missing data for a number of important variables such as gestational age, birthweight and maternal ethnicity/Indigenous status was comparatively low during the data collection period (1994-2011). Although the proportion of missing data has subsequently reduced for USA [171]. It was also interesting to note that the proportion of missing data was higher among stillbirths than live births for both the QPDC and National Centre for Health Statistics (NCHS).

Table 2.9: Proportion of missing data for population based perinatal data collections in Australia, England and USA.

Characteristics	Australia (QPDC) 1994-2011	England CMACE 2011	USA NCHS Vital Statistics 2006
Gestational age	0.01% (all births) 0.15% (stillbirth) 0.01% (live births)	3% (all births)	 2.09% (stillbirth) 0.60% (live births)
Birthweight	0.01% (all births) 0.71% (stillbirth) 0.01% (livebirths)	19% (all births)	 9.88% (stillbirth) 0.03% (live births)
Ethnicity/ Indigenous status	0.03% (all births) 1.6% (stillbirths) 0.02% (live births)	6% (all births)	 5.22% (stillbirth) 0.71% (live births)

Source: Australian estimates from QPDC (Queensland Perinatal Data Collection. Estimates for England from Healthcare Quality Improvement Partnership (HQIP). *Report on the Data for Perinatal Deaths which occurred in England 2010, 2011 and 2012*. 2013 10/09/2015]; Available from: www.hqip.org.uk/assets/Downloads/Report-on-2010-2011-2012-perinatal-mortality-data-FINAL.pdf. Estimates for USA from MacDorman, M.F., S. Kirmeyer, E.C. Wilson, and et al., *Fetal and perinatal mortality, United States, 2006. .* National Vital Statistics Reports, 2012. **60**(8).

Data quality issues relating to the individual variables used for analyses in this Thesis are outlined in Section 2.2. However, some key issues and their implications are highlighted here.

- Within the population dataset supplied, it was not possible to identify women who had subsequent pregnancies over the data period of 1994-2011; as a result, adjustments could not be made in the multivariate analyses for correlations between pregnancies at different periods. This may result in overly optimistic estimates of the true associations between maternal factors and stillbirth. However, the magnitudes of associations found in our results have been comparable to estimates from other studies.
- Maternal age was provided as categorical data in two year intervals with truncation of categories at the extremes of maternal age (e.g. Less than 18 years, and 45 years and older). As a result, nuanced assessment of the effects of maternal age was limited.
- Ascertainment of alcohol use during pregnancy was unreliable and as a result could not be used in analyses
- Number of antenatal care visits was provided as categorical data (e.g. Less than 2, 2-4, 5-7 and 8 or more), and gestational age at initiation of first antenatal care visit was unavailable at the time of data request. As a result, the composite measure of adequacy of antenatal care utilisation could not be derived nor its effects on stillbirth risk adequately assessed. However, the number of antenatal care visits was always adjusted for gestational age in multivariate analyses.
- Over the data collection period, increases in the ascertainment rate of characteristics such as smoking (data collection commenced mid 2005) and diabetes (improved ascertainment with introduction of ICD10-AM in mid 2000) were observed. As a result, analyses were restricted to study periods after mid 2005 to reduce bias from missing data.

Data from the QPDC was comparable to data from other Australian states and territories. Presented in Table 2.10 are data on selected maternal and pregnancy factors for 2011. Queensland had the second highest proportion of Indigenous mother giving birth after the Northern Territory. The stillbirth rate for Queensland was comparable to other Australian jurisdictions; however, it should be noted that the majority of terminations for maternal psychosocial reasons were performed in Victoria and the rate for Western Australia included late terminations of pregnancy [3].

Table 2.10: Selected maternal characteristics showing similarity across data sources

Characteristics	New South Wales	Victoria	Queensland	Western Australia	South Australia	Tasmania	Australian Capital Territory	Northern Territory	National
Maternal age less than 20 years (%)	3.2	2.5	5.1	4.3	4.0	6.1	2.3	9.3	3.7
Maternal age of 35 years or older (%)	23.7	24.8	19.9	20.9	20.6	18.6	25.6	16.1	22.6
Public patient (%)	74.3	71.8	70.1	59.1	74.1	66.0	70.4	80.4	71.0
Indigenous (%)	3.1	1.3	6.0	5.3	3.5	4.7	1.8	36.5	3.9
Smoker (%)	11.2	12.2	16.1	12.1	17.0	18.4	10.0	26.0	13.2
Pre-existing hypertension (rate per 1000 women)	8.2	-	5.8	11.5	11.8	14.5	14.3	13.9	-
Pregnancy induced hypertension (rate per 1000 women)	64.1	-	46.9	9.1	72.6	62.2	54.4	37.2	-
Pre-existing diabetes (rate per 1000 women)	6.4	-	6.0	7.2	6.9	10.9	8.4	18.1	-
Gestational diabetes (rate per 1000 women)	63.6	-	64.7	69.4	69.5	44.5	59.3	69.2	-
Antepartum haemorrhage (rate per 1000 women)	-	-	25.5	35.2	32.9	21.7	55.5	13.4	-
Stillbirth (rate per 1000 births)	5.9	9.8	6.4	8.4	7.4	5.4	7.7	7.1	7.4

Source: Li, Z., R. Zeki, L. Hilder, and A.E. Sullivan, *Australia's mothers and babies 2011. Perinatal statistics series no. 28. Cat. no. Per 59.* 2013, AIHW National Perinatal Epidemiology and Statistics Unit: Canberra.

Chapter 3

Trends in stillbirth rates and causes by gestational age, geographic location and Indigenous status

3.1 Introduction

Stillbirth is devastating to families and remains a challenging problem globally, with an estimated 3 million deaths occurring during the third trimester of pregnancy each year [11]. Applying the standard lower gestational age definition used in many high income countries, the numbers of stillbirths are likely to be at least double this estimate [32].

Despite significant reductions in stillbirth rates in high income countries over the past 50 years, reduction has slowed in recent times [28]. National reports from Canada [173] and Australia [23, 174] indicate that stillbirth rates may be increasing. In comparison, neonatal death rates in many of these countries have continued to decline. Globally, between 1990 and 2012, neonatal death rates fell by 2.0% while stillbirth rates fell by 1.0% [175]. In Australia [174] and USA [176], neonatal death rates declined at a faster pace than stillbirths. Between 1990 and 2000, the fetal and neonatal death rates in USA declined by an average of 1.3% and 2.4% per year, respectively [176]. Likewise in Australia during the same period, fetal and neonatal death rates declined by an annual average rate of 1.0% and 4.5%, respectively [174, 177]. In Queensland during this period, fetal death rates increased by 0.14% per year while neonatal death rates decreased by 2.5% per year [178]. National reports on trends in stillbirth rates by gestational age group indicate that reductions in late gestation (≥28 weeks) stillbirth rates combined with increases in early gestation stillbirth rates may explain the relatively unchanged overall stillbirth rates observed in some high income countries [4, 179].

The need to address disparities that exist across different population groups was recently highlighted as a priority in high income countries [13]. In Australia, as in other high income countries, marked disparity in adverse pregnancy outcomes such as stillbirth between Indigenous and non-Indigenous populations are evident [23, 180]. A number of factors including genetics, physical and social environment, maternal behaviour and access to and quality of health care have been suggested as contributing to this disparity [28, 181]. Geographic location (regional or remote residence) has been identified as an important risk factor for stillbirth in the Australian context [54, 182].

The study of temporal trends in rates and underlying causes of death is important to gaining an understanding of the scope for further reductions in stillbirth rates and to direct further clinical and research efforts [183, 184]. The objective of this study was to assess the differences in stillbirth rates over time among Indigenous and non- Indigenous women based on their geographic location and gestational age to determine whether the gap was closing. Additionally, this study aimed to assess cause-specific stillbirth rates to determine where the greatest disparities lie in order to identify focal areas for preventive efforts.

Presented in this chapter are findings from the *Stillbirth trends* analysis, a large population based study (n=881,211 births) assessing trends and disparity in stillbirth rates and causes among Indigenous and non-Indigenous women birthing in Queensland. Also presented are trends in a number of maternal, medical and obstetric factors. The analyses were stratified by geographic location and gestational age groups and two methods of gestational age-specific stillbirth rate calculation were utilised.

Findings from this study were presented at the following conferences in 2014: Perinatal Society of Australia and New Zealand (PSANZ), International Stillbirth Alliance (ISA)/International Society for Prevention of Infant Death (ISPID) and Australian Society for Medical Research (ASMR) postgraduate student conference (Appendix G4, G5 and G6). In addition, the study was published in *BJOG: An International Journal of Obstetrics and Gynaecology* in September 2014 (Appendix E).

3.2 Methods

Study Population

The *Stillbirth trends analysis* was a population-based retrospective cohort study involving all singleton livebirths and stillbirths of at least 20 weeks gestation and/or at least 400 grams birthweight occurring in Queensland between January 1995 and December 2011. During the study period, 881 654 singleton births were registered in Queensland. Four hundred and forty three births were excluded from this study. Of these, 148 births were excluded from the analyses as these were terminations of pregnancy for maternal psychosocial reasons; maternal Indigenous status was unknown for 270 births and a further 25 births occurred at less than 20 weeks gestation and were also less than 400g birthweight (see Figure 3.1).

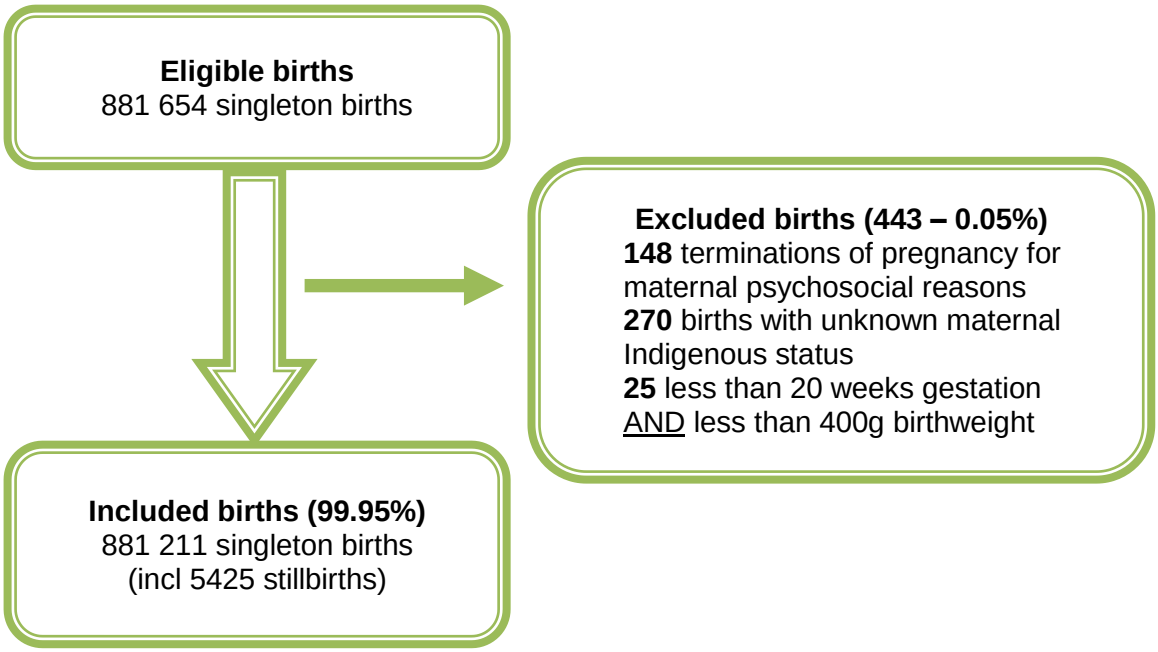


Figure 3.1: Flowchart showing study population, Stillbirth trends analysis, 1995-2011

Power calculations

Post-hoc power calculations were undertaken separately for the population of Indigenous and non-Indigenous women. For Indigenous women, a sample size of 49,450 provided over 90% power to detect an odds ratio of 0.90 with confidence interval of 95% and an

overall event proportion of 10.7/1000 ongoing pregnancies. For non-Indigenous women, a sample size of 831 761 had over 99% power to detect an odds ratio of 1.04 with 96% confidence interval, with an overall event proportion of 5.9/1000 ongoing pregnancies.

Statistical Analysis

Data for this study was obtained from the Queensland Perinatal Data Collection (QPDC). Maternal demographic data included age, marital status, socioeconomic status and geographic location. Pregnancy data included primigravidity, hospital accommodation, smoking, substance use, pregnancy complications, assisted conception and number of antenatal care visits. Pregnancy complications were defined as any conditions in the period immediately preceeding labour and delivery that were directly attributable to pregnancy and may have affected care and outcomes during the current pregnancy (ICD9 codes 630-679 and ICD10AM codes O00-O99). Birth outcome data included baby's sex, gestational age at birth, birthweight and stillbirth. Data management was carried out as described in section 2.2. All variables measured on a continuous scale were classified into categories and Chi square and Fisher's exact tests were used to assess differences in proportions between Indigenous and non-Indigenous women.

The primary outcome measure was crude stillbirth risk per 1000 ongoing pregnancies by gestational age and classification of stillbirth. Two methods were employed in the calculation of stillbirth risk (Figure 3.2). The first method described by Feldman produced prospective stillbirth risk which is an indication risk at the gestational age window of interest and beyond [185]. The second method described by Yudkin gave an indication of stillbirth risk at the gestational age window of interest only [186]. There has been debate about the appropriateness of each of these methods for the calculation of stillbirth risk; with some researchers arguing that no one method is superior and the choice of method depends on the research question being addressed or the particular situation being studied [187]. For the purpose of this analysis, both methods were used as they are both commonly used methods and the results tell distinct but complementary stories.

Figure 3.2 Comparison of stillbirth risk calculation methods

Prospective Stillbirth Risk

Gestational age specific prospective stillbirth risk

$$\frac{Number\ of\ stillbirths\ occurring\ at\ given\ gestational\ age\ \ and\ older}{Number\ of\ ongoing\ pregnancies\ at\ start\ of\ gestational\ age\ window} \times 1000$$

Cause and gestational age specific prospective stillbirth risk

$$\frac{Number\ of\ stillbirths\ attributed\ to\ specific\ cause\ occurring\ at\ given\ gestational\ age\ and\ older}{Number\ of\ ongoing\ pregnancies\ at\ start\ of\ gestational\ age\ window} \times 1000$$

Stillbirth Risk

Gestational age specific stillbirth risk

$$\frac{Number\ of\ stillbirths\ occurring\ within\ given\ gestational\ age\ window}{Number\ of\ ongoing\ pregnancies\ at\ start\ of\ gestational\ age\ window} \times 1000$$

Cause and gestational age specific stillbirth risk

$$\frac{Number\ of\ stillbirths\ attributed\ to\ specific\ cause\ occurring\ within\ given\ gestational\ age}{Number\ of\ ongoing\ pregnancies\ at\ start\ of\ gestational\ age\ window} \times 1000$$

To assess changes in all-cause and gestational age-specific stillbirth risk, percentage differences were calculated in 2-3 year groupings and over the whole study period. Univariate Poisson regression involving time period was used to assess trends in rates of stillbirth and other sociodemographic and maternal characteristics. Disparity in stillbirth risk was determined by calculating relative risk and 95% confidence intervals for Indigenous women compared with non-Indigenous women by geographic location, cause of stillbirth and gestational age grouping.

Autopsy rates were calculated using the number of autopsies performed within a particular subgroup divided by the total number of stillbirths within that subgroup. Autopsy rates were presented as percentages. Relative risk and 95% confidence intervals for having an autopsy performed following a stillbirth were also estimated for Indigenous women compared with non-Indigenous women.

Geographic location was classified as urban, regional or remote. Cut points for gestational age groups were 24 weeks, 28 weeks and 37 weeks. These groups were chosen to reflect the commencement of active clinical management (≥24 weeks), for international comparison (≥28 weeks) and to distinguish between preterm and term births (≥37 weeks).

All statistical analyses were performed using Stata 11.2 (StataCorp LP 2009, Texas, USA). Statistical significance was set at $p<0.05$.

3.3 Results

Characteristics of Indigenous and non-Indigenous women

A total of 881,211 births (including 5425 stillbirths) were included in these analyses. Of these, 49,450 births were to Indigenous women and 831,761 births were to non-Indigenous women. The characteristics of the women by Indigenous status are presented in Table 3.1.

There were significant differences between Indigenous and non-Indigenous women birthing in Queensland between 1995 and 2011. There was a higher proportion of Indigenous women aged 20 years or less (26.1% vs 8.0%, *p<0.001*) and conversely a higher proportion of non-Indigenous women aged 35 years or older (17.1% vs 8.1%, *p<0.001*). The rate of primigravidity was higher among non-Indigenous women (30.2% vs 23.5%, *p<0.001*) while Indigenous women were more likely to have a preterm (<37 weeks gestation) birth (11.4% vs 6.4%, *p<0.001*). A higher proportion of Indigenous women were in the lowest ranked quintile of socioeconomic disadvantage index (39.3% vs 16.1%, *p<0.001*) and Indigenous women were underrepresented among women who birthed as private patients (2.3% vs 30.7%, *p<0.001*). There were higher rates of smoking (53.0% vs 16.8%, *p<0.001*) and substance use (1.6% vs 0.5%, *p<0.001*) among Indigenous women compared with non-Indigenous women. Non-Indigenous women were less likely to reside in regional or remote areas (39.5% vs 79.2%, *p<0.001*) and there were higher rates of pregnancy complications among non-Indigenous women (63.4% vs 61.6%, p<0.001). The most frequently coded pregnancy complications included: uterine scar from previous surgery, premature rupture of membranes, late/prolonged pregnancy and breech presentation. There was no difference in the proportion of male babies (51.7% vs 51.5%, *p=0.40*).

Table 3.1: Characteristics of Indigenous and non-Indigenous women and babies, Queensland, 1995-2011

Characteristics	Indigenous n(%)	Non-Indigenous n(%)	p value
All births	**49 450**	**831 761**	
Maternal age (years)			
≤ 20	12 888 (26.1)	66 171 (8.0)	
21-34	32 577 (65.9)	623 301 (74.9)	<0.001
≥ 35	3 985 (8.1)	142 289 (17.1)	
Marital status			
Partner	30 887 (62.5)	735 936 (88.5)	<0.001
No Partner	18 545 (37.5)	95 727 (11.5)	
Primigravid			
Yes	11 624 (23.5)	250 877 (30.2)	<0.001
Baby sex[a]			
Male	25 548 (51.7)	428 092 (51.5)	0.38
Gestational age at birth (weeks)			
<24 weeks	355 (0.7)	2 646 (0.3)	
24-27 weeks	386 (0.8)	2 701 (0.3)	
28-36 weeks	4 913 (9.9)	48 605 (5.8)	<0.001
37-41 weeks	43 044 (87.1)	767 101 (92.2)	
42+ weeks	723 (1.5)	10 654 (1.3)	
Birthweight			
Less than 10th centile[b]	7 995 (16.2)	76 024 (9.1)	<0.001
Socioeconomic status			
Highest 20%	1 110 (2.3)	110 013 (13.3)	
Middle 60%	28 727 (58.4)	585 074 (70.6)	<0.001
Lowest 20%	19 340 (39.3)	133 460 (16.1)	
Accommodation status			
Private	1 127 (2.3)	255 685 (30.7)	
Public	48 322 (97.7)	576 056 (69.3)	<0.001
Smoker[c]			
Yes	11 140 (53.0)	59 680 (16.8)	<0.001
Substance Use			
Yes	785 (1.6)	4 514 (0.5)	<0.001
Pregnancy complications[d]			
Yes	19 903 (61.6)	344 075 (63.4)	<0.001
Remoteness			
Urban	10 281 (20.8)	503 085 (60.5)	
Regional	28 820 (58.3)	306 402 (36.8)	<0.001
Remote	10 347 (20.9)	22 255 (2.7)	
Stillbirth			
Yes	527 (1.1)	4 898 (0.6)	<0.001

[a] Data was missing for 4 births and sex was indeterminate for 108 births (97 non-Indigenous and 11 Indigenous). [b] Data on smoking was collected from July 2005, smoking status was unknown for 504 307 births (28 404 Indigenous and 475 903 non-Indigenous births). [c] Australian population birthweight centile. [d] pregnancy complication data consistently collected from July 2001

Temporal trends in characteristics of women by Indigenous status

Indigenous women

Between 1995 and 2011, stillbirth rates among Indigenous women decreased from 13.3 to 9.1 per 1000 ongoing pregnancies ($p_{trend}=0.014$). Concurrent with this trend of decreasing stillbirth rates were changes in a number of maternal sociodemographic and pregnancy factors (Table 3.2). There were significant increases in the proportion of older mothers (aged 35 years or older) from 5.5% to 10.1% ($p_{trend}<0.001$), while the proportion of younger mothers (aged 20 years or younger) was stable around 26.1% ($p_{trend}=0.402$). Decreases were observed in the proportion of Indigenous women who reported any smoking during pregnancy (from 54.2% to 51.9%, $p_{trend}=0.015$). In contrast, there was a two-fold increase in the proportion of women who reported substance use during pregnancy (0.9% to 1.8%, $p_{trend}<0.001$). There was evidence of increased affluence among Indigenous women during this period; there was an 8.6% increase in the proportion of women living in the highest ranked quintile (i.e. least disadvantaged) neighbourhoods and similarly an 82.4% decrease in the proportion of women living in the lowest ranked quintile (i.e. most disadvantaged) neighbourhoods.

There was an increase in the rate of primigravidity among Indigenous women from 23.6% to 24.7% ($p_{trend}=0.030$), as well as an increase in the proportion of Indigenous women birthing as public patients ($p_{trend}<0.001$). There was a 48.7% decline in the rate of inadequate antenatal care (defined as attending less than two antenatal care visits during pregnancy) from 7.8% in 1995-1997 to 4.0% in 2010-2011 ($p_{trend}<0.001$). There was no change in the proportion of Indigenous women using assisted conception technology ($p_{trend}=0.066$).

There was an increase in the proportion of women with pregnancy complications from 61.4% to 63.2% ($p_{trend}<0.001$). There was no change in the proportion of male infants born ($p_{trend}=0.416$) or the proportion of preterm births ($p_{trend}=0.973$). There was no change in the proportion of low or extremely low birthweight infants; but there was a decrease in the proportion of growth restricted infants (defined as birthweight less than the 10th population centile) (Table 3.2).

Table 3.2: Temporal trends in sociodemographic characteristics of Indigenous women and babies, Queensland, 1995-2011

Characteristics	1995-97 %	1998-00 %	2001-03 %	2004-06 %	2007-09 %	2010-11 %	Total %	% difference	p_{trend}
Total births	**n=7498**	**n=8273**	**n=8182**	**n=8678**	**n=9758**	**n=7061**	**n=49450**		
Maternal age									
20 years or younger	27.2	25.1	26.4	25.8	25.8	26.2	26.1	-3.7	0.402
35 years or older	5.5	6.6	7.8	8.7	9.5	10.1	8.1	+83.6	<0.001
Smoker	-	-	-	54.2	53.2	51.9	53.0	-4.2	0.015
Substance Use	0.9	1.1	2.3	1.6	1.8	1.8	1.6	+100.0	<0.001
Socioeconomic status									
Lowest ranked 20%	39.6	38.4	44.3	41.4	36.2	36.2	39.3	-8.6	<0.001
Highest ranked 20%	1.7	2.1	1.6	2.4	2.6	3.1	2.3	+82.4	<0.001
Primigravidity	23.6	23.0	23.1	22.6	24.1	24.7	23.5	+4.7	0.030
Assisted conception	0.8	0.4	0.4	0.4	0.4	0.6	0.5	-25.0	0.066
Public patient	97.5	96.9	97.9	98.2	97.8	98.1	97.7	+0.6	<0.001
Number of antenatal care visits									
Less than 2	7.8	6.9	6.9	7.2	5.8	4.0	6.5	-48.7	<0.001
8 or more	-	47.0	48.5	46.2	47.9	51.5	48.1	+9.6	<0.001
Pregnancy complication	-	-	61.4	60.9	61.1	63.2	61.6	+2.9	<0.001
Male babies	51.5	51.2	51.9	51.5	51.9	52.0	51.7	+1.0	0.416
Preterm birth	11.3	11.4	11.7	12.0	10.9	11.6	11.4	+2.7	0.973
Birthweight									
Extremely low (<1500g)	2.5	2.3	2.7	2.6	2.4	2.5	2.5	0.0	0.944
Low (<2500g)	10.8	10.5	11.2	11.0	10.3	10.8	10.8	0.0	0.636
Less than 10th population centile	17.0	16.1	17.3	16.5	15.2	15.1	16.2	-11.2	<0.001
Stilbirth (rate per 1000 ongoing pregnancies)	13.3	10.9	10.8	10.0	10.0	9.1	10.7	-31.6	0.014

% difference = (rate (2010-11) minus rate (1995-97)) x 100 / rate (1995-97) - Data unavailable

Non-Indigenous women

Stillbirth rates among non-Indigenous women in Queensland remained steady at 5.9 per 1000 ongoing pregnancies over the period 1995 to 2011. There was a decrease in the proportion of younger mothers (aged 20 years or younger) from 9.0% to 6.9% ($p_{trend}<0.001$); concurrent with an increase in the proportion of older mothers (12.9% to 20.4%, $p_{trend}<0.001$). A decrease in the proportion of women who reported smoking during pregnancy was also observed ($p_{trend}<0.001$). There was evidence of increased affluence among non-Indigenous women with an increase in the proportion of women who lived in the highest ranked quintile (least disadvantaged) neighbourhoods (9.5% to 16.8%, $p_{trend}<0.001$) and a decrease in the proportion of women who lived in the lowest ranked quintile (most disadvantaged) neighbourhoods (20.7% to 12.1%, $p_{trend}<0.001$). There was no change in the proportion of women who reported substance use during this period ($p_{trend}=0.879$). There was no change in the proportion of primigravid women ($p_{trend}=0.310$) or the proportion of male babies born ($p_{trend}=0.878$). However, there was an increase in the proportion of women who used assisted conception technologies (2.5% to 4.3%, $p_{trend}<0.001$). There was also an increase in the proportion of women with preterm births (6.2% to 6.7%, $p_{trend}<0.001$). There was no change in the proportion of low or very low birthweight infants; however, there was a decrease in the proportion of growth restricted infants (defined as birthweight less than the 10th population centile) from 10.2% to 8.5% ($p_{trend}<0.001$) (Table 3.3).

Table 3.3: Temporal trends in sociodemographic characteristics of non-Indigenous women and babies, Queensland, 1995-2011

Characteristics	1995-97 %	1998-00 %	2001-03 %	2004-06 %	2007-09 %	2010-11 %	Total %	% difference	p_{trend}
Total births	**n=13282**	**n=13349**	**n=13606**	**n=14867**	**n=16765**	**n=11304**	**n=83176**		
Maternal age									
20 years or younger	9.0	8.5	8.4	7.6	7.3	6.9	8.0	-23.3	<0.001
35 years or older	12.9	14.6	16.1	18.3	20.1	20.4	17.1	+58.1	<0.001
Smoker~	-	-	-	18.6	17.4	14.6	16.8	-21.5	<0.001
Substance Use	0.4	0.6	0.8	0.5	0.5	0.5	0.5	+25.0	0.88
Socioeconomic status									
Lowest ranked 20%	20.7	19.9	18.5	15.7	10.7	12.1	16.1	-41.6	<0.001
Highest ranked 20%	9.5	11.1	11.5	13.5	16.8	16.8	13.3	+76.8	<0.001
Primigravidity	30.3	30.2	30.2	30.1	30.0	30.3	30.2	0.0	0.31
Assisted conception	2.5	2.2	2.7	3.2	3.6	4.3	3.1	+72.0	<0.001
Public patient	72.0	72.8	67.3	67.2	68.1	68.6	69.3	-4.7	<0.001
Number of antenatal care visits									
Less than 2	1.5	1.1	1.0	0.9	0.8	0.5	1.0	-66.7	<0.001
8 or more*	-	65.4	74.2	75.4	74.6	76.3	73.6	+16.7	<0.001
Pregnancy complication	-	-	62.9	62.8	63.9	63.9	63.4	+1.6	<0.001
Male babies	51.3	51.4	51.4	51.7	51.8	50.9	51.5	-0.8	0.88
Preterm birth	6.2	6.3	6.4	6.7	6.7	6.7	6.5	+8.1	<0.001
Birthweight									
Extremely low (<1500g)	1.1	1.1	1.1	1.2	1.1	1.1	1.1	0.0	0.35
Low (<2500g)	5.0	5.1	5.0	5.2	5.0	5.0	5.0	0.0	0.59
Less than 10th population centile	10.2	9.6	9.1	8.9	8.6	8.5	9.1	-16.7	<0.001
Stillbirth (per 1000 births)^	5.8	5.7	5.7	6.1	6.1	5.9	5.9	+1.7	0.26

% difference = (rate (2010-11) minus rate (1995-97)) x 100 / rate (1995-97)

Maternal characteristics by Indigenous status and geographic location

Table 3.4 shows the distribution of maternal characteristics by Indigenous status and geographic location and Table 3.5 shows the relative risk of each of these maternal characteristics for Indigenous women relative to non-Indigenous women. Stillbirth rates among Indigenous women varied significantly with geographic location. Indigenous women living in urban areas had the lowest stillbirth rate (8.5/1000 ongoing pregnancies) compared with Indigenous women living in regional (10.8/1000) and remote areas (12.5/1000)(*p=0.019*). In contrast, stillbirth rates among non-Indigenous women were not significantly different (p=0.070). Stillbirth rates among non-Indigenous women living in urban, regional and remote areas were 5.8/1000, 6.1/1000 and 5.3/1000, respectively (Table 3.4). Analyses of the distribution of sociodemographic characteristics for these women showed significant differences by geographic location.

Among Indigenous and non-Indigenous women, there were higher proportions of younger (20 years or younger) mothers living in regional and remote areas and conversely, higher proportions of older (35 years or older) mothers living in urban areas. Indigenous women were more than three-fold more likely to smoke during pregnancy (53.0% vs 16.8%, RR 3.16, 95% CI 3.11-3.21). For both groups of women, smoking rates were lowest for women living in urban areas (46.6% and 14.5% for Indigenous and non-Indigenous women, respectively) and highest for women living in regional areas (54.8% and 20.7%) (Table 3.4). Disparity in smoking rates was greatest for women living in urban areas (RR 3.22, 95% CI 3.11-3.33) and smallest for women living in regional areas (RR 2.65, 95% CI 2.60-2.70) (Table 3.5).

Substance use rates for Indigenous and non-Indigenous women were highest in urban areas (3.3% and 0.6%, respectively), followed by regional areas (1.3% and 0.5%) and then remote areas (0.7% and 0.2%)(Table 3.4). Disparity in substance use rates was greatest for women living in urban areas (RR 5.32, 95% CI 4.76-5.95) and least for women living in regional areas (RR 2.85, 95% CI 2.54-3.19)(Table 3.5).

Overall Indigenous women were more than twice as likely to be classified in the lowest quintile of socioeconomic disadvantage index. Disparity was least marked for women living in regional areas (RR 1.83, 95% CI 1.79-1.86) and most marked for women living in remote areas (RR 3.31, 95% CI 3.22-3.42) (Table 3.5). Both Indigenous and non-Indigenous women living in urban areas were more likely to be primigravid than their

regional and remote dwelling counterparts. Disparity in rates of primigravidity was greatest in remote areas (25.2% vs 31.0%, RR 0.75, 95% CI 0.72-0.78) (Table 3.5).

Rates of assisted conception technology use were highest in urban areas, followed by regional and remote areas (Table 3.4); overall, Indigenous women were less likely to use these technologies (RR 0.16, 95% CI 0.14-0.18). Disparity in rates of assisted conception technology use between Indigenous and non-Indigenous women was greatest in remote areas (0.3% vs 2.2%, RR 0.13, 95% CI 0.09-0.18) (Table 3.5).

Inadequate antenatal care (assessed using less than 2 visits) was higher among Indigenous than non-Indigenous women (6.5% vs 1.0%, RR 6.73 95% CI 6.46-7.00). Disparity in rates of inadequate antenatal care was greatest for women living in regional areas, followed by urban and then remote areas (Table 3.5).

Overall there was a slightly lower rate of pregnancy complications among Indigenous women (61.6% vs 63.4%, RR 0.97, 95% CI 0.96-0.98). Rates of pregnancy complications among women living in urban areas were marginally higher for Indigenous women; and marginally higher for non-Indigenous women among women living in regional areas (Table 3.5).

Overall Indigenous women had higher rates of preterm birth (11.4% vs 6.5%, RR 1.76, 95%CI 1.72-1.81), the disparity in rates was larger with regional and remote residence than urban residence.

Disparity in rates of low birthweight (assessed using WHO cut points of <1500g and <2500g for extremely low and low birthweight, respectively), showed the greatest disparity in rates of low and extremely low birthweight in remote areas, followed by regional and then urban areas. However, when small-for-gestational age was assessed (defined as birthweight less than 10th Australian population birthweight percentile for sex and gestational age), disparity was greatest for women living in regional areas (RR 1.82, 95% CI 1.77-1.87), followed by remote (RR 1.76, 95% CI 1.65-1.87) and then urban areas (RR 1.59 95% CI 1.52-1.67) (Table 3.5).

Table 3.4: Distribution of maternal characteristics by Indigenous status and geographic location, Queensland, 1995-2011

Characteristics	Indigenous					Non-Indigenous				
	Urban %	Regional %	Remote %	Total %	p value	Urban %	Regional %	Remote %	Total %	p value
Total births	n=1028	n=28820	n=1034	n=4944		n=50308	n=30640	n=2225	n=8317	
Maternal age										
20 years or less	24.0	26.6	26.6	26.1	<0.001	7.0	9.6	8.0	8.0	<0.001
35 years or older	8.7	8.0	7.5	8.1	0.003	18.6	14.9	13.4	17.1	<0.001
Smoker	46.6	54.8	54.3	53.0	<0.001	14.5	20.7	18.2	16.8	<0.001
Substance Use	3.3	1.3	0.7	1.6	<0.001	0.6	0.5	0.2	0.5	<0.001
Socioeconomic status										
Lowest ranked 20%	33.0	32.2	65.8	39.3	<0.001	15.0	17.7	19.8	16.1	<0.001
Highest ranked 20%	9.1	0.6	0.1	2.3	<0.001	20.3	2.5	3.0	13.3	<0.001
Primigravidity	25.2	23.4	22.0	23.5	<0.001	31.0	28.9	29.4	30.2	<0.001
Assisted conception	1.1	0.4	0.3	0.5	<0.001	3.6	2.3	2.2	3.1	<0.001
Public patient	94.2	98.2	99.7	97.7	<0.001	66.2	73.7	77.3	69.3	<0.001
Number of antenatal care visits										
Less than 2	5.5	6.9	6.0	6.5	<0.001	0.9	1.1	1.0	1.0	<0.001
8 or more	50.6	45.7	52.5	48.1	<0.001	74.8	71.9	69.2	73.6	<0.001
Pregnancy complications	61.2	57.6	59.4	58.7	<0.001	60.6	56.7	56.6	59.0	<0.001
Male babies	51.9	51.6	51.6	51.7	0.85	51.4	51.6	51.6	51.5	0.45
Preterm birth	10.0	11.9	11.6	11.4	<0.001	6.6	6.4	5.8	6.5	<0.001
Birthweight										
Extremely low (<1500g)	2.1	2.6	2.7	2.5	0.005	1.1	1.2	1.0	1.1	0.01
Low (<2500g)	9.2	11.5	10.3	10.8	<0.001	5.0	5.1	4.4	5.0	<0.001
Less than 10th population centile	14.2	17.3	14.9	16.2	<0.001	8.9	9.5	8.5	9.1	<0.001
Stillbirth (per 1000 births)	8.5	10.8	12.5	10.7	0.02	5.8	6.1	5.3	5.9	0.07

*remoteness status unavailable for 2 women

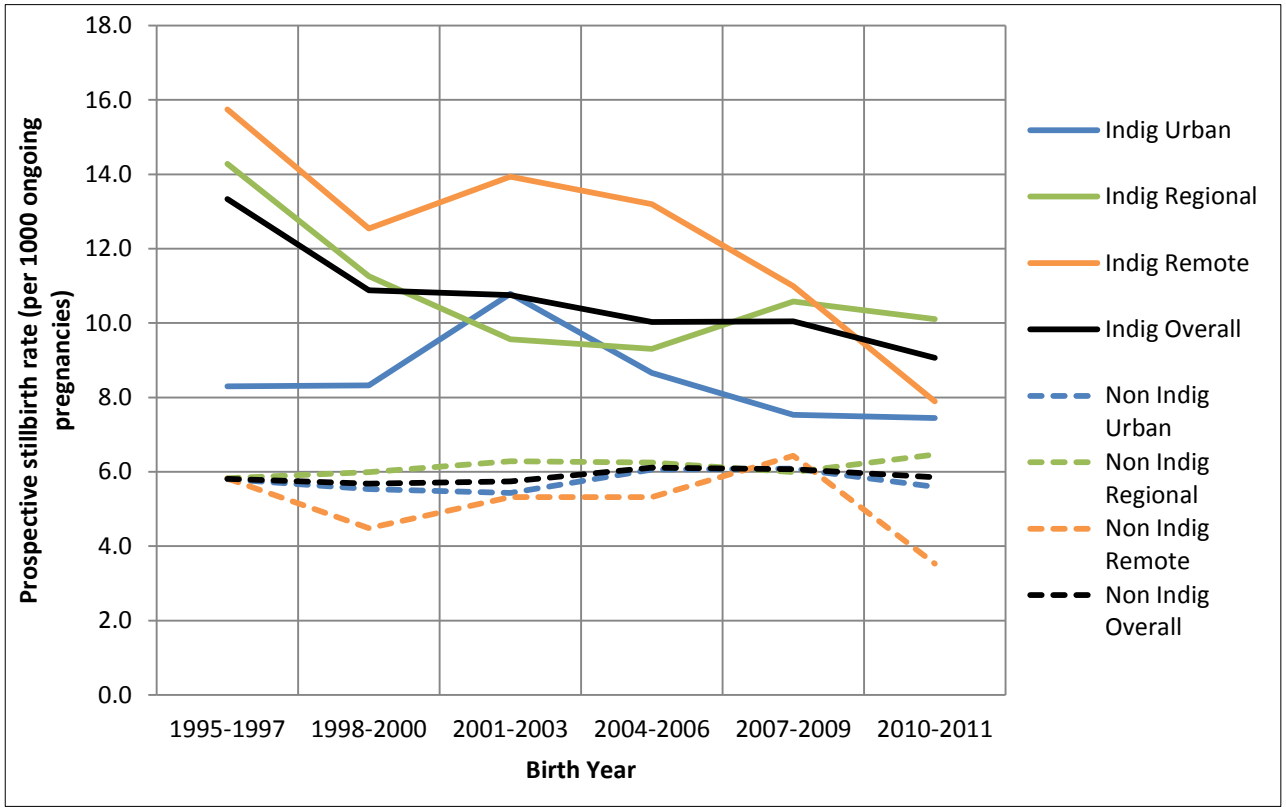
Table 3.5: Comparison of maternal characteristics (Indigenous versus non-Indigenous) by geographic location, Queensland, 1995-2011

Characteristics	Relative Risk (95% Confidence Interval)			
	Urban	Regional	Remote	Total
Maternal age				
20 years or younger	3.44 (3.32-3.56)	2.78 (2.72-2.84)	3.33 (3.15-3.52)	3.28 (3.22-3.33)
35 years or older	0.47 (0.44-0.50)	0.54 (0.52-0.56)	0.56 (0.52-0.60)	0.47 (0.46-0.49)
Smoker	3.22 (3.11-3.33)	2.65 (2.60-2.70)	2.98 (2.83-3.14)	3.16 (3.11-3.21)
Substance Use	5.32 (4.76-5.95)	2.85 (2.54-3.19)	3.52 (2.45-5.06)	2.93 (2.71-3.16)
Socioeconomic status				
Lowest ranked 20%	2.20 (2.14-2.26)	1.83 (1.79-1.86)	3.31 (3.22-3.42)	2.44 (2.41-2.47)
Highest ranked 20%	0.45 (0.42-0.48)	0.22 (0.19-0.26)	0.04 (0.03-0.07)	0.17 (0.16-0.18)
Primigravidity	0.82 (0.79-0.84)	0.81 (0.79-0.83)	0.75 (0.72-0.78)	0.78 (0.77-0.79)
Assisted conception	0.29 (0.24-0.35)	0.16 (0.13-0.19)	0.13 (0.09-0.18)	0.16 (0.14-0.18)
Public patient	1.42 (1.42-1.43)	1.33 (1.33-1.34)	1.29 (1.28-1.30)	1.41 (1.41-1.41)
Number of antenatal care visits				
Less than 2	6.15 (5.65-6.70)	6.52 (6.17-6.88)	5.78 (4.98-6.71)	6.73 (6.46-7.00)
8 or more	0.68 (0.66-0.69)	0.64 (0.63-0.64)	0.76 (0.74-0.78)	0.65 (0.65-0.66)
Pregnancy complications	1.02 (1.00-1.04)	0.98 (0.97-0.99)	1.00 (0.98-1.03)	0.97 (0.96-0.98)
Male babies	1.01 (0.99-1.03)	1.00 (0.99-1.00)	1.00 (0.98-1.02)	1.00 (1.00-1.01)
Preterm birth	1.52 (1.44-1.62)	1.85 (1.79-1.91)	2.02 (1.87-2.17)	1.76 (1.72-1.81)
Birthweight				
Extremely low (<1500g)	1.86 (1.63-2.14)	2.26 (2.09-2.44)	2.77 (2.32-3.31)	2.24 (2.11-2.37)
Low (<2500g)	1.83 (1.72-1.95)	2.25 (2.17-2.33)	2.34 (2.16-2.55)	2.14 (2.09-2.20)
Less than 10^{th} population centile	1.59 (1.52-1.67)	1.82 (1.77-1.87)	1.76 (1.65-1.87)	1.77 (1.73-1.81)
Stillbirth	1.47 (1.18-1.81)	1.76 (1.56-1.98)	2.37 (1.84-3.04)	1.81 (1.66-1.98)

Stillbirth rate trends by Indigenous status and geographic location

Figure 3.3 shows trends in stillbirth rates by Indigenous status and geographic location over 17 years. Over the period 1995 to 2011, the stillbirth rate for all women birthing in Queensland was steady around 6.2/1000 ongoing pregnancies. Among Indigenous women, stillbirth rates decreased 31.9% from 13.3 to 9.1/1000 ongoing pregnancies (p_{trend}=0.014); while stillbirth rates among non-Indigenous women was steady around 5.9/1000 ongoing pregnancies. The difference in overall stillbirth rates between Indigenous and non-Indigenous women reduced by 57.3% from 7.5 to 3.2/1000 ongoing pregnancies over this period (Figure 3.1). Stillbirth rates among Indigenous women decreased by 10.2%, 29.2% and 49.9% for women living in urban, regional and remote areas, respectively. In contrast, stillbirth rates among non-Indigenous women increased by 0.9% and 11.4% for women living in urban and regional areas and decreased by 39.2% among non-Indigenous women living in remote areas (Figure 3.3).

Figure 3.3: Stillbirth rates by Indigenous status and geographic location, singleton births, Queensland, 1995-2011



The difference in stillbirth rates between Indigenous and non-Indigenous women decreased by 25.7%, 57.0% and 56.1% for urban, regional and remote areas, respectively.

Stillbirth rate trends by Indigenous status and gestational age

Figures 3.4a and 3.4b show stillbirth rates by Indigenous status and gestational age groupings using the Feldman (prospective) and Yudkin ('instantaneous') methods, respectively.

Using the Feldman method, stillbirth rates among Indigenous women decreased by 31.9%, 42.9%, 48.0% and 7.1% for births at ≥20, ≥24, ≥28 and ≥37 weeks, respectively (Figure 3.4a). Similarly, using the Yudkin method, the corresponding stillbirth rates among Indigenous women decreased by 9.5%, 29.3%, 69.1% and 7.1% for births at <24 weeks, 24-27 weeks, 28-36 weeks and ≥37 weeks, respectively (Figure 3.4b).

Among non-Indigenous women, using the Feldman method, stillbirth rates increased by 0.9% at ≥20 weeks and decreased by 14.9%, 16.8% and 21.7% at ≥24, ≥28 and ≥37 weeks, respectively (Figure 3.4a). Using the Yudkin method, there was a 36.3% increase in stillbirth rates at <24 weeks and decreases in the remaining groups of 9.0%, 12.4% and 21.7%, respectively (Figure 3.4b). Results from both methods showed reductions in the difference in stillbirth rates between Indigenous and non-Indigenous women at all gestational age groupings except ≥37 weeks. The difference in stillbirth rates at ≥37 weeks between Indigenous and non-Indigenous women increased by 18.0% (0.9/1000 to 1.1/1000 ongoing pregnancies) and between 2001 and 2011, the difference was steady around 1.2/1000 ongoing pregnancies.

Figure 3.4a: Prospective stillbirth rates by Indigenous status and gestational age grouping, singleton births, Queensland, 1995-2011 (Feldman method)

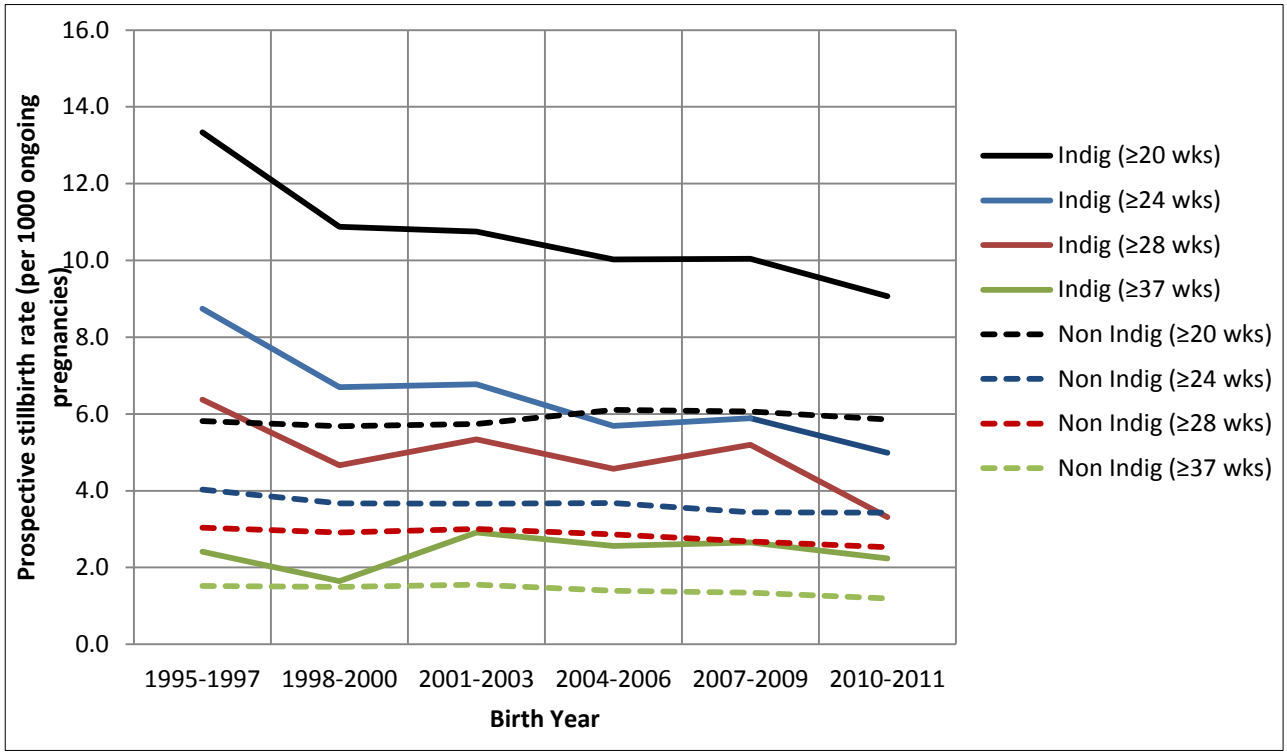
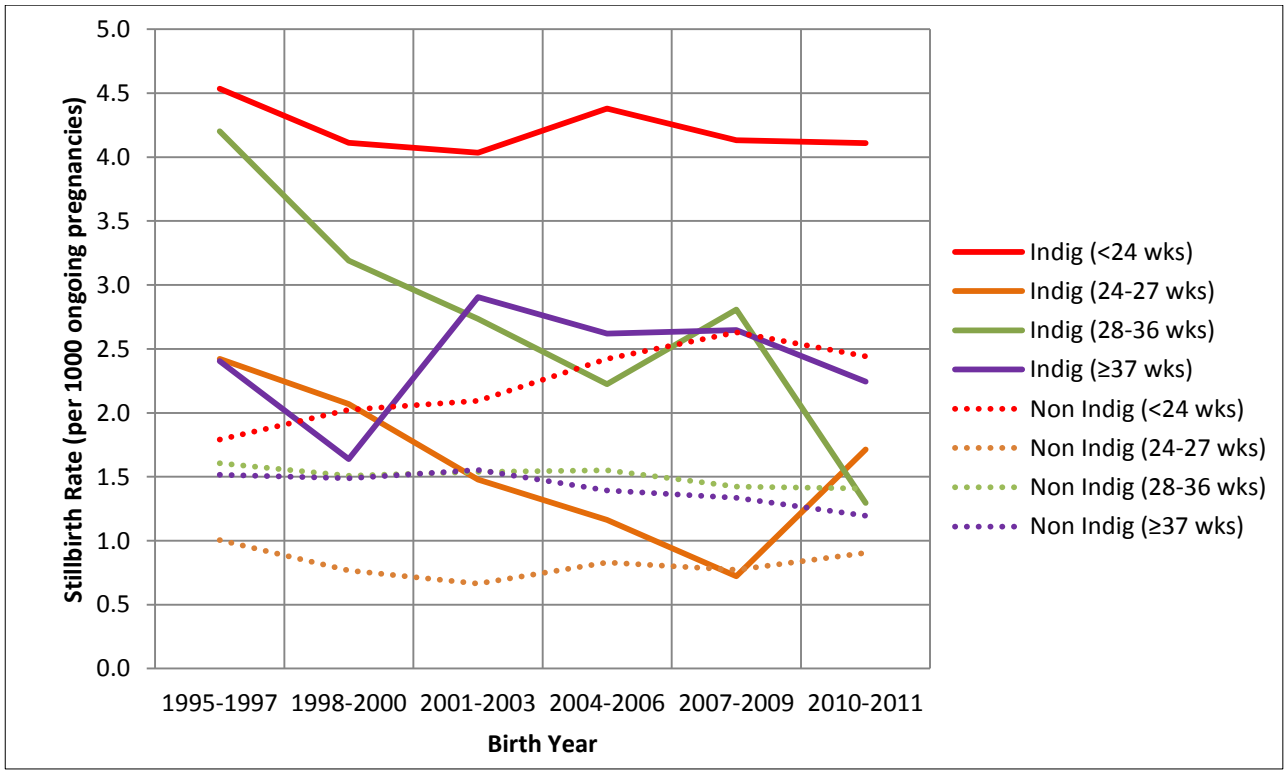


Figure 3.4b: Stillbirth rates by Indigenous status and gestational age grouping, singleton births, Queensland, 1995-2011 (Yudkin method)



Overall stillbirth rates by Indigenous status and gestational age

Tables 3.6a and 3.6b present overall stillbirth rates by gestational age grouping for Indigenous and non-Indigenous women. Stillbirth rates were higher among Indigenous women for all gestational age groupings assessed and all methods used. The gestational age specific stillbirth rates were not statistically different from each other.

Table 3.6a: Overall stillbirth rates by Indigenous status and gestational age grouping using Feldman method, Queensland, 1995-2011

	≥20 weeks	≥24 weeks	≥28 weeks	≥37 weeks
Indigenous	10.60	6.44	4.93	2.42
Non-Indigenous	5.88	3.65	2.84	1.42
Relative Risk	1.80	1.77	1.74	1.71
(95% CI)[a]	(1.65-1.97)	(1.57-1.98)	(1.52-1.98)	(1.40-2.09)

[a] Relative risk = Indigenous relative to non-Indigenous rates

Table 3.6b: Overall stillbirth rates by Indigenous status and gestational age grouping using Yudkin method, Queensland, 1995-2011

Yudkin method	<24 weeks	24-27 weeks	28-36 weeks	37-42+ weeks
Indigenous	4.21	1.55	2.75	2.42
Non-Indigenous	2.25	0.82	1.51	1.42
Relative Risk	1.87	1.89	1.83	1.71
(95% CI)[a]	(1.62-2.16)	(1.49-2.40)	(1.53-2.18)	(1.40-2.09)

[a] Relative risk = Indigenous relative to non-Indigenous rates

Comparison of cause-specific stillbirth rates

The overall stillbirth rate among Indigenous women was higher than for non-Indigenous women (10.7 vs 5.9/1000 ongoing pregnancies, RR 1.81, 95%CI 1.66-1.98)(Tables 3.4 and 3.5). The major PSANZ-PDC categories contributing to the disparity were: maternal conditions, perinatal infection, no obstetric antecedent, spontaneous preterm, hypertension, fetal growth restriction, unexplained antepartum fetal death and antepartum haemorrhage (Table 3.7).

Overall, Indigenous women had a nearly four-fold increased risk of stillbirth due to maternal conditions (RR 3.78, 95%CI 2.59-5.51) and perinatal infection (RR 3.70, 95% CI 2.54-5.39). Pre-existing and gestational diabetes constituted a large component (42.2%) of maternal conditions; and Indigenous women had over a six-fold increased risk of stillbirth due to diabetes (RR 6.42, 95% 3.89-10.6). Perinatal infections were comprised of

bacterial infections (53.0%), viral and other (fungal and protozoal) infections. While numbers are small, there was a significantly increased risk of stillbirth due to syphilis infection among Indigenous women (Table 3.7).

More than half (56.3%; 56.0% Indigenous and 56.3% non-Indigenous) of all stillbirths assigned to the category of spontaneous preterm had evidence of placental chorioamnionitis and a further 7.6% (6.7% Indigenous and 7.8% non-Indigenous) had clinical chorioamnionitis. Indigenous women had a three-fold increased risk of stillbirth due to spontaneous preterm birth (RR 3.08, 95% CI 2.51-3.77).

The majority of stillbirths (65.5%) attributed to hypertension were due to chronic hypertension with or without superimposed pre-eclampsia. The risk of stillbirth due to hypertension was significantly higher for Indigenous compared to non-Indigenous women (RR 2.22, 95% CI 1.45-3.39). Indigenous women had an increased risk of stillbirth due to fetal growth restriction (RR 1.78, 95% CI 1.17-2.71) and antepartum haemorrhage (RR 1.58, 95% CI 1.13-2.22). Placental abruption accounted for 86.0% of all stillbirths attributed to antepartum haemorrhage.

The risk of unexplained antepartum fetal death was higher for Indigenous women (RR 1.61, 95% CI 1.37-1.90), further, there were 69 stillbirths classified as having no obstetric antecedent identified and births to Indigenous women were over-represented within this category (RR 3.19, 95% CI 1.67-6.08).

No increased risk of stillbirth was evident for the main categories of congenital abnormality, hypoxic peripartum death or stillbirth due to specific perinatal conditions (including antenatal cord complication and feto-maternal haemorrhage) among Indigenous women compared with non-Indigenous women (Table 3.7). However, within subgroups an increased risk of stillbirth due to central nervous system (CNS) abnormality (RR 1.84, 95% CI 1.27-2.66) and uterine abnormalities (including cervical incompetence) (RR 2.59, 95% CI 1.10-6.11) was observed.

Table 3.7: Comparison of cause specific prospective stillbirth rates by Indigenous status, singleton births, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Indigenous n=49,450		Non-Indigenous n=831,761		Total n=881,211		
	n	rate[b]	n	rate[b]	n	rate[b]	RR (95% CI)
All cause[a]	**527**	**10.7**	**4898**	**5.9**	**5425**	**6.2**	**1.81 (1.66-1.98)**
Congenital Abnormality	**75**	**1.5**	**1138**	**1.4**	**1213**	**1.4**	**1.11 (0.88-1.40)**
Central nervous system	31	0.6	284	0.3	315	0.4	1.84 (1.27-2.66)
Cardiovascular system	5	0.1	122	0.1	127	0.1	0.69 (0.28-1.69)
Chromosomal	13	0.3	352	0.4	365	0.4	0.62 (0.36-1.08)
Multiple	13	0.3	161	0.2	174	0.2	1.36 (0.77-2.39)
Other	13	0.3	219	0.3	232	0.3	1.00 (0.57-1.75)
Perinatal Infection	**33**	**0.7**	**150**	**0.2**	**183**	**0.2**	**3.70 (2.54-5.39)**
GBS	3	0.1	30	0.0	33	0.0	1.68 (0.51-5.51)
Syphilis	15	0.3	1	0.0	16	0.0	252 (33-1910)
Other bacterial	7	0.1	41	0.0	48	0.1	2.87 (1.29-6.40)
Viral	1	0.0	43	0.1	44	0.0	0.39 (0.05-2.84)
Fungal/Protozoal/other	7	0.1	35	0.0	42	0.0	3.36 (1.49-7.57)
Hypertension	**24**	**0.5**	**182**	**0.2**	**206**	**0.2**	**2.22 (1.45-3.39)**
Pre-existing	9	0.2	53	0.1	62	0.1	2.86 (1.41-5.79)
Pregnancy induced/Pre-eclampsia	14	0.3	127	0.2	141	0.2	1.85 (1.07-3.22)
Unspecified	1	0.0	2	0.0	3	0.0	8.41 (0.76-92.7)
Antepartum Haemorrhage	**37**	**0.7**	**393**	**0.5**	**430**	**0.5**	**1.58 (1.13-2.22)**
Abruption	31	0.6	339	0.4	370	0.4	1.54 (1.06-2.22)
Other	6	0.1	54	0.1	60	0.1	1.87 (0.80-4.34)
Maternal conditions	**33**	**0.7**	**147**	**0.2**	**180**	**0.2**	**3.78 (2.59-5.51)**
Diabetes	21	0.4	55	0.1	76	0.1	6.42 (3.88-10.6)
Autoimmune (lupus)	3	0.1	7	0.0	10	0.0	7.21 (1.86-27.9)
Other	9	0.2	85	0.1	94	0.1	1.78 (0.90-3.54)
Specific perinatal conditions	**16**	**0.3**	**261**	**0.3**	**277**	**0.3**	**1.03 (0.62-1.71)**
Fetomaternal haemorrhage	4	0.1	49	0.1	53	0.1	1.37 (0.50-3.80)
Antenatal cord complication	3	0.1	83	0.1	86	0.1	0.61 (0.19-1.92)
Uterine abnormalities	6	0.1	39	0.0	45	0.1	2.59 (1.10-6.11)
Other	3	0.1	90	0.1	93	0.1	0.56 (0.18-1.77)
Hypoxic peripartum death	**6**	**0.1**	**103**	**0.1**	**109**	**0.1**	**0.98 (0.43-2.23)**
With intrapartum complications	2	0.0	49	0.1	51	0.1	0.69 (0.17-2.82)
No/Unspecified intrapartum complications	4	0.1	54	0.1	58	0.1	1.25 (0.45-3.44)
Fetal growth restriction	**24**	**0.5**	**227**	**0.3**	**251**	**0.3**	**1.78 (1.17-2.71)**
Reduced vascular perfusion	13	0.3	128	0.2	141	0.2	1.71 (0.97-3.02)
Other	11	0.2	99	0.1	110	0.1	1.87 (1.00-3.48)
Spontaneous preterm	**110**	**2.2**	**601**	**0.7**	**711**	**0.8**	**3.08 (2.51-3.77)**
Unexplained antepartum fetal death	**157**	**3.2**	**1638**	**2.0**	**1795**	**2.0**	**1.61 (1.37-1.90)**
No obstetric antecedent	**11**	**0.2**	**58**	**0.1**	**69**	**0.1**	**3.19 (1.67-6.08)**

[a] Clinical classification data missing for 1 stillbirth (Indigenous). "Other" category consists of combinations of subcategories. [b]Rate per 1000 ongoing pregnancies ≥20 weeks or ≥ 400g birthweight

Temporal trends in cause-specific stillbirth rates by Indigenous status

Tables 3.8 and 3.9 show the temporal trends in cause-specific stillbirth rates among Indigenous (Table 3.8) and non-Indigenous women (Table 3.9). Among Indigenous women, decreasing rates of stillbirth due to perinatal infection ($p_{trend}<0.001$) and conversely, increasing rates of stillbirth due to fetal growth restriction ($p_{trend}=0.040$) were shown over the study period. (Table 3.8). Among non-Indigenous women, significant increases in the rates of stillbirth due to congenital abnormality ($p_{trend}<0.001$) and spontaneous preterm birth ($p_{trend}=0.013$) were shown concurrent with decreases in the rates of stillbirth due to hypertension ($p_{trend}<0.001$), antepartum haemorrhage ($p_{trend}<0.001$), perinatal infection ($p_{trend}=0.029$), maternal conditions ($p_{trend}=0.044$) and unexplained antepartum fetal death ($p_{trend}=0.011$) (Table 3.9).

Table 3.10 shows trends in the cause specific relative risk of stillbirth for Indigenous relative to non-Indigenous women. The magnitude of disparity in all-cause rates did not vary significantly over the study period. In addition, there were significantly higher rates of stillbirth due to maternal conditions and spontaneous preterm birth, with no evidence of significant variation in disparity of the 17 years assessed (Table 3.10).

Table 3.8: Temporal trends in cause-specific stillbirth rates, Indigenous women, singleton births, Queensland, 1995-2011

PSANZ-PDC category	1995-97	1998-00	2001-03	2004-06	2007-09	2010-11	Total	% difference	p_{trend}
Congenital abnormality	1.9	1.7	0.4	1.4	2.2	1.6	1.5	-15.8	0.170
Central nervous system	0.7	0.8	0.1	0.6	0.7	0.8	0.6	14.3	0.319
Cardiovascular system	0.1	0.0	0.1	0.0	0.3	0.0	0.1	-100.0	0.550
Chromosomal	0.3	0.1	0.1	0.3	0.4	0.3	0.3	0	0.215
Multiple/non-chromosomal	0.4	0.4	0.0	0.1	0.3	0.4	0.3	0	0.688
Perinatal Infection	2.4	0.5	0.6	0.1	0.3	0.3	0.7	-87.5	<0.001
Syphilis	1.2	0.2	0.2	0.0	0.0	0.3	0.3	-75.0	0.003
Other bacterial	0.4	0.0	0.2	0.0	0.2	0.0	0.1	-100.0	0.310
Hypertension	0.7	0.8	0.4	0.3	0.3	0.4	0.5	-42.9	0.351
Pregnancy Induced/Pre-eclampsia	0.4	0.5	0.4	0.1	0.1	0.3	0.3	-25.0	0.337
Antepartum haemorrhage	1.1	0.7	1.1	0.8	0.6	0.1	0.7	-90.9	0.184
Placental abruption	0.8	0.6	1.0	0.8	0.5	0.0	0.6	-100.0	0.226
Maternal conditions	0.7	0.6	1.2	0.6	0.5	0.4	0.7	-42.9	0.775
Diabetes	0.3	0.4	1.0	0.2	0.4	0.3	0.4	0	0.835
Specific perinatal conditions	0.3	0.5	0.7	0.1	0.2	0.1	0.3	-66.7	0.392
Antepartum cord complications	0.1	0.0	0.1	0.0	0.1	0.0	0.1	-100	0.714
Hypoxic peripartum death	0.1	0.0	0.1	0.1	0.2	0.1	0.1	0	0.343
Fetal growth restriction	0.1	0.5	0.4	0.6	0.7	0.6	0.5	500.0	0.040
Reduced vascular perfusion +/- placental histopathology	0.0	0.2	0.1	0.2	0.4	0.6	0.3	-	0.010
Spontaneous preterm	2.7	1.8	2.7	2.2	2.2	1.8	2.2	-33.3	0.697
Unexplained antepartum fetal death	3.3	3.5	3.2	3.0	2.7	3.5	3.2	6.1	0.294
No obstetric antecedent	0.1	0.1	0.0	0.8	0.2	0.0	0.2	-100.0	0.455
All cause	13.3	10.8	10.8	10.0	10.0	9.1	10.6	-31.6	0.015
Autopsy rate (per 100 SBs)	36.0	48.3	25.0	42.5	40.8	32.8	37.8	8.9	

% difference = (rate (2010-11) minus rate (1995-97)) x 100 / rate (1995-97)

Table 3.9: Temporal trends in cause-specific stillbirth rates, non-Indigenous women, singleton births, Queensland, 1995-2011

PSANZ-PDC category	1995-97	1998-00	2001-03	2004-06	2007-09	2010-11	Total	% difference	p_{trend}
Congenital abnormality	1.0	1.2	1.2	1.4	1.7	1.6	1.4	60.0	<0.001
Central nervous system	0.3	0.2	0.3	0.4	0.4	0.5	0.3	66.7	0.003
Cardiovascular system	0.1	0.1	0.1	0.1	0.2	0.2	0.1	100.0	0.001
Chromosomal	0.3	0.4	0.4	0.4	0.4	0.5	0.4	66.7	0.047
Multiple/non-chromosomal	0.2	0.1	0.2	0.2	0.3	0.1	0.2	-50.0	0.639
Perinatal Infection	0.2	0.2	0.1	0.2	0.2	0.2	0.2	0	0.029
Syphilis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0	0.746
Other bacterial	0.1	0.0	0.1	0.0	0.0	0.1	0.0	0	0.185
Hypertension	0.5	0.2	0.1	0.2	0.2	0.1	0.2	-80.0	<0.001
Pregnancy Induced/Pre-	0.2	0.1	0.1	0.2	0.2	0.1	0.2	-50.0	0.126
Antepartum haemorrhage	0.6	0.6	0.4	0.5	0.4	0.4	0.5	-33.3	<0.001
Placental abruption	0.6	0.4	0.3	0.4	0.4	0.3	0.4	-50.0	0.003
Maternal conditions	0.2	0.1	0.2	0.2	0.1	0.1	0.2	-50.0	0.044
Diabetes	0.1	0.1	0.1	0.1	0.1	0.0	0.1	-100.0	0.389
Specific perinatal conditions	0.3	0.3	0.4	0.3	0.4	0.3	0.3	0	0.463
Antepartum cord	0.0	0.1	0.1	0.1	0.1	0.1	0.1	-	0.021
Hypoxic peripartum death	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0	0.426
Fetal growth restriction	0.2	0.2	0.3	0.3	0.3	0.3	0.3	50.0	0.068
Reduced vascular perfusion +/- placental histopathology	0.1	0.1	0.2	0.2	0.2	0.2	0.2	100.0	0.029
Spontaneous preterm	0.5	0.7	0.7	0.8	0.8	0.7	0.7	40.0	0.013
Unexplained antepartum fetal	2.1	2.0	2.1	2.0	1.8	1.9	2.0	-9.5	0.011
No obstetric antecedent	0.0	0.1	0.0	0.1	0.1	0.2	0.1	-	<0.001
All cause	5.8	5.7	5.7	6.1	6.1	5.9	5.9	1.72	0.263
Autopsy rate (per 100 SBs)	56.1	70.8	45.7	41.3	53.7	51.4	52.8	-8.4	

% difference = (rate (2010-11) minus rate (1995-97)) x 100 / rate (1995-97)

Table 3.10: Trends in cause specific relative risk of stillbirth for Indigenous relative to non-Indigenous women, Queensland, 1995-2011

PSANZ-PDC category	1995-1997	1998-2000	2001-2003	2004-2006	2007-2009	2010-2011	Total
Congenital abnormality	1.81 (1.05-3.14)	1.44 (0.83-2.48)	0.29 (0.09-0.92)	0.96 (0.53-1.71)	1.30 (0.84-2.03)	0.97 (0.53-1.78)	1.11 (0.88-1.40)
Central nervous system	2.11 (0.83-5.33)	3.64 (1.61-8.27)	0.44 (0.06-3.19)	1.62 (0.65-4.04)	1.82 (0.84-3.97)	1.78 (0.77-4.13)	1.84 (1.27-2.66)
Cardiovascular system	1.27 (0.17-9.62)	-	1.11 (0.15-8.39)	-	1.36 (0.42-4.39)	-	0.69 (0.28-1.69)
Chromosomal	0.84 (0.20-3.48)	0.28 (0.04-2.04)	0.30 (0.04-2.18)	0.79 (0.25-2.52)	0.92 (0.34-2.50)	0.55 (0.13-2.26)	0.62 (0.36-1.08)
Multiple/non-chromosomal	2.13 (0.64-7.04)	2.42 (0.72-8.14)	-	0.49 (0.07-3.57)	1.20 (0.37-3.86)	3.20 (0.93-11.1)	1.36 (0.77-2.39)
Perinatal Infection	9.96 (5.60-17.7)	2.15 (0.76-6.11)	4.38 (1.63-11.7)	0.69 (0.09-5.06)	1.98 (0.60-6.55)	1.78 (0.41-7.66)	3.70 (2.54-5.39)
Syphilis	-	-	33.3 (3.02-367)	-	-	-	252 (33.3-1910)
Other bacterial	3.80 (1.09-13.2)	-	4.75 (0.99-22.9)	-	4.30 (0.91-20.2)	-	2.87 (1.29-6.40)
Hypertension	1.27 (0.51-3.13)	4.91 (2.11-11.4)	2.93 (0.86-10.0)	1.90 (0.58-6.27)	1.78 (0.54-5.83)	3.00 (0.87-10.3)	2.22 (1.45-3.39)
Pre-eclampsia/ Eclampsia	1.90 (0.58-6.24)	3.23 (1.10-9.44)	3.33 (0.96-11.5)	0.71 (0.10-5.28)	0.61 (0.08-4.51)	2.67 (0.60-11.9)	1.85 (1.07-3.22)
Antepartum haemorrhage	1.69 (0.82-3.48)	1.31 (0.57-3.01)	2.82 (1.39-5.72)	1.69 (0.78-3.67)	1.45 (0.63-3.34)	0.40 (0.06-2.91)	1.58 (1.13-2.22)
Placental abruption	1.40 (0.61-3.21)	1.42 (0.57-3.53)	3.09 (1.46-6.58)	2.00 (0.91-4.37)	1.34 (0.54-3.33)	-	1.54 (1.07-2.22)
Maternal conditions	3.05 (1.18-7.89)	4.25 (1.59-11.4)	5.36 (2.63-10.9)	2.68 (1.04-6.87)	3.58 (1.37-9.38)	4.00 (1.13-14.2)	3.78 (2.59-5.51)
Diabetes	5.06 (1.05-24.4)	4.84 (1.33-17.6)	13.3 (5.25-33.7)	2.28 (0.52-9.99)	6.25 (1.99-19.6)	16.01 (2.26-	6.42 (3.89-10.6)
Specific perinatal conditions	1.01 (0.24-4.21)	1.66 (0.59-4.63)	1.96 (0.84-4.56)	0.44 (0.06-3.20)	0.55 (0.14-2.27)	0.46 (0.06-3.34)	1.03 (0.62-1.71)
Antepartum cord	5.91 (0.61-56.8)	-	0.88 (0.12-6.54)	-	1.07 (0.14-8.10)	-	
Hypoxic peripartum death	1.11 (0.15-8.35)	-	0.92 (0.12-6.92)	1.01 (0.13-7.57)	1.49 (0.35-6.34)	1.60 (0.21-12.5)	0.98 (0.43-2.23)
Fetal growth restriction	0.74 (0.10-5.46)	2.08 (0.74-5.90)	1.19 (0.37-3.83)	1.82 (0.73-4.58)	2.36 (1.07-5.19)	2.00 (0.71-5.66)	1.78 (1.17-2.71)
Reduced vascular perfusion +/- placental histopathology	-	1.79 (0.42-7.73)	0.69 (0.09-5.12)	1.31 (0.31-5.55)	2.37 (0.83-6.74)	3.05 (1.05-8.88)	1.71 (0.97-3.02)
Spontaneous preterm	5.13 (3.12-8.44)	2.50 (1.45-4.30)	3.93 (2.47-6.26)	2.78 (1.71-4.52)	2.56 (1.62-4.05)	2.48 (1.38-4.44)	3.08 (2.51-3.77)
Unexplained antepartum	1.62 (1.08-2.44)	1.79 (1.22-2.63)	1.52 (1.02-2.27)	1.47 (0.98-2.19)	1.47 (0.99-2.20)	1.89 (1.25-2.86)	1.61 (1.37-1.90)
No obstetric antecedent	5.91 (0.61-56.8)	2.02 (0.25-16.1)	-	8.57 (3.46-21.2)	3.44 (0.75-15.7)	-	3.19 (1.67-6.08)
All cause	2.29 (1.87-2.82)	1.89 (1.52-2.36)	1.87 (1.50-2.33)	1.64 (1.32-2.04)	1.66 (1.35-2.04)	1.55 (1.20-2.00)	1.81 (1.65-1.98)
Autopsy rate (per 100 SBs)	0.64 (0.49-0.84)	0.68 (0.55-0.85)	0.55 (0.38-0.79)	1.03 (0.80-1.33)	0.76 (0.60-0.97)	0.64 (0.45-0.91)	0.72 (0.64-0.80)

Cause-specific stillbirth rates by geographic location

In urban areas, Indigenous women had increased risk of stillbirth due to perinatal infection and spontaneous preterm birth; while Indigenous women living in remote areas had increased risk of stillbirth due to central nervous system abnormality (RR 3.38, 95% CI 1.31-8.72), maternal conditions, spontaneous preterm birth and unexplained antepartum fetal death. Indigenous women living in regional areas had increased risk of stillbirth due to perinatal infection [particularly syphilis and non GBS bacterial infection], hypertension including gestational hypertension and pre-eclampsia with or without chronic hypertension (RR 2.26, 95% CI 1.14-4.48), maternal conditions including diabetes (RR 6.38, 95% CI 3.12-13.05), fetal growth restriction, spontaneous preterm birth and unexplained antepartum fetal death (Table 3.11).

Table 3.11: Relative risk of stillbirth for Indigenous versus non-Indigenous women by geographic location, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Relative Risk Indigenous versus Non Indigenous			
	Urban	Regional	Remote	Total
Congenital abnormality	1.02 (0.60-1.73)	1.06 (0.78-1.45)	1.11 (0.63-1.95)	1.11 (0.88-1.40)
Perinatal Infection	3.09 (1.35-7.05)	3.67 (2.18-6.19)	-	3.70 (2.54-5.39)
Hypertension	0.81 (0.20-3.27)	3.17 (1.85-5.45)	2.69 (0.72-10.01)	2.22 (1.45-3.39)
Antepartum haemorrhage	1.75 (0.82-3.71)	1.31 (0.85-2.03)	1.37 (0.53-3.52)	1.58 (1.13-2.22)
Maternal conditions	2.15 (0.79-5.85)	4.38 (2.63-7.28)	3.44 (1.13-10.52)	3.78 (2.59-5.51)
Diabetes	2.80 (0.67-11.6)	6.38 (3.12-13.1)	-	6.42 (3.88-10.6)
Specific perinatal conditions	0.63 (0.16-2.53)	0.87 (0.42-1.78)	1.84 (0.62-5.48)	1.03 (0.62-1.71)
Hypoxic peripartum death	0.78 (0.11-5.60)	1.22 (0.43-3.42)	0.43 (0.05-3.68)	0.98 (0.43-2.23)
Fetal growth restriction	1.31 (0.49-3.55)	2.70 (1.61-4.52)	0.61 (0.13-2.96)	1.78 (1.17-2.71)
Spontaneous preterm	2.45 (1.54-3.88)	2.99 (2.24-3.99)	6.26 (3.16-12.41)	3.08 (2.51-3.77)
Unexplained antepartum fetal death	1.39 (0.95-2.03)	1.50 (1.20-1.86)	2.64 (1.64-4.23)	1.61 (1.37-1.90)
No obstetric antecedent	1.69 (0.23-12.39)	2.28 (0.94-5.50)	8.60 (0.96-76.96)	3.19 (1.67-6.08)
All cause	1.47 (1.18-1.81)	1.76 (1.56-1.98)	2.37 (1.84-3.04)	1.81 (1.66-1.98)
Autopsy rate (Indigenous, Non-Indigenous)	28.7%, 40.0%	27.4%, 36.9%	18.6%, 42.7%	25.5%, 38.9%
Relative Risk (95% CI)	0.72 (0.51-1.00)	0.74 (0.61-0.90)	0.44 (0.29-0.66)	0.65 (0.56-0.76)

Cause-specific stillbirth rates by gestational age

No change was shown in all-cause stillbirth risk for Indigenous women relative to non-Indigenous women as gestational age increased (Table 3.12a and Table 3.13b). Similarly, there were no statistically significant differences in cause-specific stillbirth risk by gestational age group.

Table 3.12a: Cause-specific relative risk of stillbirth for Indigenous relative to non-Indigenous women by gestational age grouping, Feldman method, singleton births, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Relative Risk (95% Confidence Intervals) Indigenous versus Non Indigenous			
	≥ 20 weeks	≥ 24 weeks	≥ 28 weeks	≥ 37 weeks
Congenital abnormality	1.11 (0.88-1.41)	1.27 (0.87-1.87)	1.41 (0.91-2.21)	0.83 (0.26-2.65)
Perinatal Infection	**3.61 (2.47-5.29)**	**4.52 (2.85-7.16)**	**4.68 (2.69-8.14)**	**3.23 (1.35-7.71)**
Hypertension	**2.22 (1.45-3.40)**	**1.97 (1.18-3.31)**	1.74 (0.87-3.45)	2.09 (0.48-9.04)
Antepartum haemorrhage	**1.58 (1.13-2.22)**	1.30 (0.83-2.02)	1.16 (0.69-1.96)	1.91 (0.88-4.17)
Maternal conditions	**3.66 (2.50-5.37)**	**3.46 (2.27-5.27)**	**4.02 (2.55-6.34)**	**5.78 (3.16-10.6)**
Specific perinatal conditions	1.03 (0.62-1.71)	0.82 (0.42-1.60)	1.02 (0.52-2.00)	0.21 (0.03-1.54)
Hypoxic peripartum death	0.98 (0.43-2.23)	0.99 (0.44-2.26)	1.04 (0.46-2.37)	1.07 (0.43-2.64)
Fetal growth restriction	**1.78 (1.17-2.71)**	**2.20 (1.44-3.37)**	**2.36 (1.48-3.76)**	**2.85 (1.41-5.77)**
Spontaneous preterm	**3.06 (2.49-3.75)**	**3.35 (2.16-5.19)**	**3.60 (1.59-8.14)**	-
Unexplained antepartum fetal death	**1.60 (1.36-1.89)**	**1.63 (1.37-1.95)**	**1.61 (1.32-1.95)**	**1.66 (1.28-2.17)**
No obstetric antecedent	**2.90 (1.48-5.67)**	2.41 (0.95-6.16)	3.03 (1.17-7.85)	1.04 (0.14-7.85)
All cause	**1.79 (1.64-1.96)**	**1.77 (1.58-1.99)**	**1.76 (1.54-2.00)**	**1.75 (1.44-2.13)**
Autopsy rates (Indigenous, Non-Indigenous)	25.4%, 38.9%	29.2%, 43.7%	31.3%, 44.0%	31.2%, 45.0%
Relative Risk (95% CI)	0.65 (0.56-0.76)	0.67 (0.56-0.80)	0.71 (0.59-0.86)	0.69 (0.52-0.92)

Table 3.12b: Cause-specific relative risk of stillbirth for Indigenous relative to non-Indigenous women by gestational age grouping, Yudkin method, singleton births, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Relative Risk (95% CI) Indigenous versus Non Indigenous				
	< 24 weeks	**24 - 27 weeks**	**28 – 36 weeks**	**≥ 37 weeks**	**Total[a]**
Congenital abnormality	1.03 (0.77-1.38)	0.99 (0.46-2.13)	**1.63 (1.00-2.64)**	0.85 (0.27-2.69)	1.11 (0.88-1.40)
Perinatal Infection	**2.63 (1.35-5.12)**	**4.22 (1.85-9.67)**	**6.79 (3.26-14.1)**	**3.23 (1.35-7.71)**	**3.70 (2.54-5.40)**
Hypertension	**2.99 (1.41-6.35)**	**2.41 (1.09-5.33)**	1.67 (0.77-3.64)	1.05 (0.14-7.85)	**2.22 (1.45-3.40)**
Antepartum haemorrhage	**2.24 (1.33-3.78)**	1.88 (0.81-4.36)	0.88 (0.43-1.79)	1.64 (0.71-3.79)	**1.58 (1.13-2.22)**
Maternal conditions	**5.89 (2.49-13.9)**	1.69 (0.52-5.54)	**2.83 (1.40-5.73)**	**5.79 (3.17-10.6)**	**3.78 (2.59-5.51)**
Specific perinatal conditions	1.55 (0.71-3.36)	-	2.06 (0.99-4.29)	0.21 (0.03-1.54)	1.03 (0.62-1.71)
Hypoxic peripartum death	-	-	1.13 (0.15-8.57)	1.08 (0.44-2.67)	0.98 (0.43-2.23)
Fetal growth restriction	-	1.69 (0.60-4.72)	**2.12 (1.13-3.97)**	**2.86 (1.41-5.77)**	**1.78 (1.17-2.71)**
Spontaneous preterm	**3.01 (2.40-3.79)**	**3.26 (1.94-5.49)**	**3.40 (1.41-8.16)**	-	**3.08 (2.51-3.77)**
Unexplained antepartum fetal death	1.53 (0.98-2.39)	**1.81 (1.19-2.76)**	**1.63 (1.23-2.16)**	1.67 (1.28-2.17)	**1.61 (1.37-1.90)**
No obstetric antecedent	**4.39 (1.79-10.78)**	-	**6.17 (1.97-19.4)**	1.11 (0.15-8.37)	**3.19 (1.68-6.08)**
All cause	**1.87 (1.62-2.16)**	**1.87 (1.47-2.37)**	**1.83 (1.53-2.18)**	**1.71 (1.40-2.09)**	**1.81 (1.65-1.98)**
Autopsy rates (Indigenous, Non-Indigenous)	19.7%, 31.1%	22.7%, 42.7%	31.3%, 43.1%	30.2%, 45.1%	25.5%, 38.9%
Relative Risk (95% CI)	0.63 (0.48-0.84)	0.53 (0.35-0.81)	0.73 (0.56-0.94)	0.67 (0.50-0.90)	0.66 (0.56-0.76)

[a] includes all birth ≥ 20 weeks

3.4 Discussion

Main Findings

The objective of this study was to examine the differences in stillbirth rates between Indigenous and non-Indigenous women birthing in Queensland over the period 1995-2011 with a particular emphasis on variation by geographic location, gestational age and clinical classification of cause of stillbirth.

We found that although Indigenous stillbirth rates were consistently higher than non-Indigenous stillbirth rates, the gap had narrowed. These findings mirror national reports of declining Indigenous stillbirth rates over the period 1991-2004 [56] and US reports among American Indian and Alaskan Native women (7.5 to 6.2/1000 births between 1990 and 2005)[188]. However, our study found that these reductions were not uniform across sub-groups of Indigenous women. Indigenous women living in regional and remote areas experienced greater reductions in stillbirth rates than their urban counterparts, and the stillbirth rate among Indigenous women varied significantly with geographic location. These findings are in contrast to two population-based studies carried out in Queensland [189] and nationally [190] that reported similar risk of stillbirth among Indigenous women regardless of urban or rural/remote residence. The incongruence in findings may be due to confounding factors controlled for by Coory et al and Graham et al, as confounders were not adjusted for at this stage.

In some high income countries, reports of increasing stillbirth rates have been attributed to inclusion of terminations for congenital abnormality in national counts of stillbirths [191]. In this study, we were unable to adequately quantify the contribution of terminations of pregnancy for congenital abnormality to the trends in stillbirth rates. This was because such terminations were not systematically identified within the Queensland Perinatal Data Collection. Provision was made in 2009 for identification of such terminations [124] however the data from that time period were incomplete. Analysis of the available data suggested higher rates of terminations among non-Indigenous women compared with Indigenous women (14.4% versus 6.7%), further suggesting that disparity between Indigenous and non-Indigenous women may be underestimated. Our study also found that there was little narrowing of the stillbirth rate gap in gestational ages of 37 weeks or more. At these gestational ages, there was increased risk of stillbirth for Indigenous women due to maternal conditions (mainly diabetes), perinatal infection, fetal growth restriction. Similar findings were reported among Inuit and First Nation women in Canada,

where excess stillbirths compared with non-Aboriginal women were attributed to fetal growth restriction, placental disorders and congenital anomalies among Inuit women and diabetes and hypertension among First Nation women [180]. In New Zealand, Māori women had increased risk for all PSANZ-PDC categories compared with New Zealand European women except hypoxic peripartum death and specific perinatal conditions, although the differences were not statistically significant [192]. Unexplained antepartum fetal death was also higher for Indigenous women at term. These findings highlight the opportunity for further reductions in term stillbirths among the Indigenous population.

Overall, we found an increased risk of stillbirth due to maternal conditions, perinatal infection, spontaneous preterm birth, hypertension, fetal growth restriction, antepartum haemorrhage and unexplained antepartum fetal death among Indigenous women compared with non-Indigenous women. Most of these categories of stillbirth are potentially amenable to interventions in the pre-pregnancy and antenatal periods. Flenady and colleagues highlighted strategies and interventions to address priority areas for stillbirth prevention in high income countries [28]. These strategies involve addressing risk factors for adverse pregnancy outcomes.

Interpretation of findings

Antenatal Care

Inadequate antenatal care has been associated with increased risk of stillbirth [32] and Indigenous women in our study population had a six-fold higher rate of inadequate antenatal care (defined as less than two antenatal care visits). Detection of fetal growth restriction, though challenging, is a key component of antenatal care. There is limited evidence from randomised controlled trials to inform best practice surveillance for pregnancies with growth restriction [193]. There is low level evidence for the use of Doppler ultrasound in high risk pregnancies to reduce the risk of perinatal death [194], however there is no conclusive evidence for the routine use of Doppler ultrasound in low risk or unselected populations [195]. Serial fundal height measurements with customised charts and clinical practice guidelines have been shown to increase antenatal detection of growth restriction [196]. Differentials in the rates of attendance and early initiation of antenatal care have been reported between Indigenous and non-Indigenous women [23]. In addition, significant variation in the quality of antenatal care received by Indigenous

women has been reported including low rates of morphology ultrasound and screening for gestational diabetes and infection [197]. A number of maternal and child health programs and service delivery models aimed at improving outcomes for women within Indigenous communities in various states and territories have shown varying levels of success [198, 199]. Features common to many successful programs are: community-based or controlled services, respect for Indigenous people and culture, continuity of care and an integrated spectrum of services, and consideration of logistic issues (e.g. transportation and child care) [198].

Maternal smoking

Maternal smoking during pregnancy has been associated with fetal growth restriction, placenta praevia, placental abruption, low birthweight, preterm birth and stillbirth [32, 57, 200, 201]. The smoking rates among Indigenous women in our study were high (53.0%), similar to national rates (49.3% in 2010) [23], furthermore, smoking quit rates among Indigenous women are lower than for non-Indigenous women [23, 202]. There is evidence to show that psychosocial interventions can increase smoking cessation rates in late pregnancy and decrease rates of preterm birth and low birthweight [203]; however, there is insufficient evidence to show the safety or effectiveness of nicotine replacement therapy for smoking cessation in pregnancy [204]. Incentive-based programs look promising in increasing quit rates post-pregnancy, however further research is needed to investigate the endurance of such programs [205]. This highlights a need for effective policy and guidelines for smoking cessation interventions tailored and targeted to Indigenous women.

Diabetes

There was a six-fold increased risk of stillbirth due to diabetes among Indigenous mothers. These findings are consistent with reports that Indigenous women have disproportionally higher rates of pre-existing and gestational diabetes in pregnancy than non-Indigenous women [89]. At present there is little evidence for or against pre-conception care for women with pre-existing diabetes [206], although lower rates of congenital abnormalities have been reported among women with Type 1 diabetes receiving preconception care compared to those who did not [207]. Likewise, lifestyle modifications in combination with insulin were found to improve birth outcomes for women with mild gestational diabetes

[208]. However, interventions to prevent or manage diabetes have not had the same magnitude of impact within the Indigenous population and not enough clinical focus on women at risk or women with diabetes has been given as a possible explanation for this[198]. Gestational diabetes is strongly linked with high body mass index (BMI>35kg/m^2) [9]. High BMI is also independently associated with stillbirth [32]. With increasing prevalence of high BMI in women of childbearing age and higher rates of obesity among Indigenous women of childbearing age [209], efforts to ensure that women enter pregnancy with a normal BMI is critically important to optimise outcomes for both the woman and her offspring [32].

Congenital abnormalities

Our study found an increased risk of stillbirth due to CNS abnormalities among Indigenous women, especially those living in remote areas. These findings are supported by national reports of higher rates of neural tube defects (NTDs), the most common CNS abnormalities, among Indigenous women and women living in remote areas [210]. The association between folate and reduced risk of NTDs has been well established. Lifestyle factors such as fruit and vegetable intake, smoking and high levels of alcohol consumption have been associated with folate deficiency [211]. It has been suggested that for some remote Aboriginal and Torres Strait Islander communities, micronutrient deficiency may be a direct result of limited availability and high costs of healthy food such as fruit and vegetables [212, 213]. A number of strategies were employed to reduce the prevalence of folate deficiency among women of childbearing age including promotion of peri-conceptual folic acid supplementation (1992), voluntary fortification of specified food products (1996) and mandatory folic acid fortification of wheat flour (2009) [214]. Reductions in rates of NTD were observed following voluntary fortification but these reductions were limited mainly to the non-Indigenous population [214, 215]. At present, there is limited information on the impact of mandatory fortification on folate levels among women of childbearing age or Indigenous women [216].

Perinatal Infection

We found a disproportionately high burden of stillbirth due to perinatal infection among Indigenous women, particularly syphilis. This finding is supported by several studies that

found high rates of sexually transmitted infections (STIs) among Indigenous women of reproductive age living in rural communities [217, 218] and pregnant Indigenous women living in urban areas [219]. Similarly, a population based study in Western Australia found infection to be an important cause of death for Indigenous infants [220]. Early diagnosis and treatment of syphilis has been shown to be associated with similar risk of stillbirth as general uninfected population [221]. A number of programs which demonstrated sustained reductions in rates of STIs in Aboriginal and Torres Strait Islander communities have highlighted the need for STI screening to be incorporated into antenatal care protocols for Indigenous women [198].

Preterm birth

We found higher rates of preterm birth and higher risk of stillbirth due to spontaneous preterm birth among Indigenous compared with non-Indigenous women. While preterm birth may be as a result of early induction of labour for medical or non-medical indications, most occur spontaneously and have been associated with infection, chronic diseases (diabetes and hypertension), socioeconomic disadvantage and genetic influence, however many are idiopathic [222]. Evidence for strategies to reduce preterm birth is limited and a better understanding of the mechanisms and causes of preterm to enable focused intervention studies is required [222].

Summary of findings

The key findings in this study were that the gap in stillbirth rates between Indigenous and non-Indigenous women is decreasing; however Indigenous women remain at increased risk of stillbirth due to a number of potentially preventable conditions. There has been no reduction in the gap for term stillbirths; and Indigenous women have higher rates of stillbirth at term due to diabetes, perinatal infection, fetal growth restriction and unexplained antepartum fetal death. In addition, during the study period we found decreasing rates of maternal smoking, inadequate antenatal care and fetal growth restriction among Indigenous women. It is possible that decreasing rates of maternal smoking may play a role in the decreasing rates of fetal growth restriction observed. However, without trends data on maternal body mass index, it is difficult to comment on the role of maternal obesity on fetal growth restriction rates among Indigenous women.

We observed increasing rates of women birthing at 35 years or older, substance use and evidence of socioeconomic affluence. Among non-Indigenous women, there were increasing proportions of women birthing at 35 years or older, women utilising assisted conception technology and increasing rates of preterm birth. There was also evidence of decreasing rates of maternal smoking, fetal growth restriction and increased affluence. There was no change in the rates of substance use or primigravidity.

Analysis of trends in maternal sociodemographic characteristics suggest that there may be an association with stillbirth risk and highlights the need to evaluate the effect of these characteristics on gestational age-specific prospective stillbirth risk. This will be the main focus of the fetal death risk analysis study presented in Chapter 4 and 5.

3.5 Conclusion

The gap in stillbirth rates between Indigenous and non-Indigenous women is narrowing, but Indigenous women continue to be at increased risk of stillbirth due to a number of potentially preventable causes. There has been no reduction in the gap between Indigenous and non-Indigenous women in relation to term stillbirth rates and this presents an area of focus for further preventive efforts. At term, Indigenous women had increased risk of stillbirth due to maternal conditions (mainly diabetes), perinatal infection, fetal growth restriction and unexplained antepartum fetal death. High quality antenatal care at all levels using culturally appropriate service delivery models which incorporate diabetes management, smoking cessation, STI screening and treatment, folic acid and fetal growth monitoring hold some promise of helping to improve pregnancy outcomes for Indigenous women.

Chapter 4

Gestational age specific risk of stillbirth among Indigenous and non-Indigenous women

4.1 Introduction

In Australia, stillbirth rates have failed to improve over the past two decades and reports indicate rates may be slowly increasing [3]. Marked variation in stillbirth rates within population subgroups indicate that further reductions may be achievable [3, 28]. There persists marked disparity in stillbirth rates between Aboriginal and Torres Strait Islander (Indigenous) and non-Indigenous women [24, 223]. In 2012, national stillbirth rates among Indigenous women were one and a half times higher (10.8 vs 7.1 per 1000) than among non-Indigenous women [24]. Moreover, this disparity persists in the rate of term stillbirths (RR 1.71, 95% CI 1.40-2.09) with little change in the disparity over time [223].

Diabetes, hypertension, antepartum haemorrhage and small-for-gestational age are important contributors to the higher stillbirth rates observed among Indigenous women [223]. In Queensland, pre-existing and gestational diabetes affected around 0.6% and 6.7% of pregnancies [24]; while Australian national estimates are 0.6% and 4.7%, respectively [89]. There is evidence of increasing prevalence of pre-existing and gestational diabetes within Queensland [24, 49]; with consistently higher rates of diabetes reported for Indigenous women [86]. Also of concern are reports of larger increases in the prevalence of gestational diabetes among non-Indigenous women [87]. Hypertensive disorders of pregnancy (including pre-existing and pregnancy induced hypertension) affect around 0.6% and 4.4% of pregnancies in Queensland [24]. Antepartum haemorrhage (including placenta praevia and abruption) is associated with up to 20% of very preterm births [224] and affects 2.4% of pregnancies in Queensland [24]. Indigenous women have higher rates of small-for-gestational age births than non-Indigenous women [225].

Given the contribution of these conditions to the rates of stillbirth and the disproportionate burden among Indigenous women, determining the periods of increased risk of stillbirth associated with these conditions is important for clinical management and potential further reductions in stillbirth rates. The specific objectives of this study were to: 1) describe the all-cause gestational age specific risk of stillbirth among Indigenous and non-Indigenous

women, 2) examine the gestational age-specific risk of stillbirth associated with diabetes, hypertension, antepartum haemorrhage and small-for-gestational age among Indigenous and non-Indigenous women, and 3) examine the influence of geographic location on these gestational age specific risks among Indigenous and non-Indigenous women.

Presented in this chapter are findings from a large population based study (n=360,987 births) assessing gestational age specific risk of stillbirth among Indigenous and non-Indigenous women birthing in Queensland. Findings from this study were presented at the Perinatal Society of Australia and New Zealand conference in April 2015 (Appendix G3) and a manuscript was published in *BMC Pregnancy and Childbirth* in July 2016 (Appendix F).

4.2 Methods

Study Population

This was a population based retrospective database study involving all singleton livebirths and stillbirths of at least 20 weeks gestational age or at least 400g birthweight occurring in Queensland between July 2005 and December 2011. There were 379,107 singleton births registered in the Queensland Perinatal Data Collection for the period July 2005 to December 2011. Among these 18,119 births were excluded for the following reasons: congenital anomalies (99.2%), unknown maternal Indigenous status (0.7%), gestational age less than 20 weeks and birthweight less than 400g (0.1%) and terminations of pregnancy for maternal psychosocial reasons (0.0%) (Figure 4.1). Births with congenital anomalies were excluded from analyses because of the association between diabetes and congenital anomalies [226].

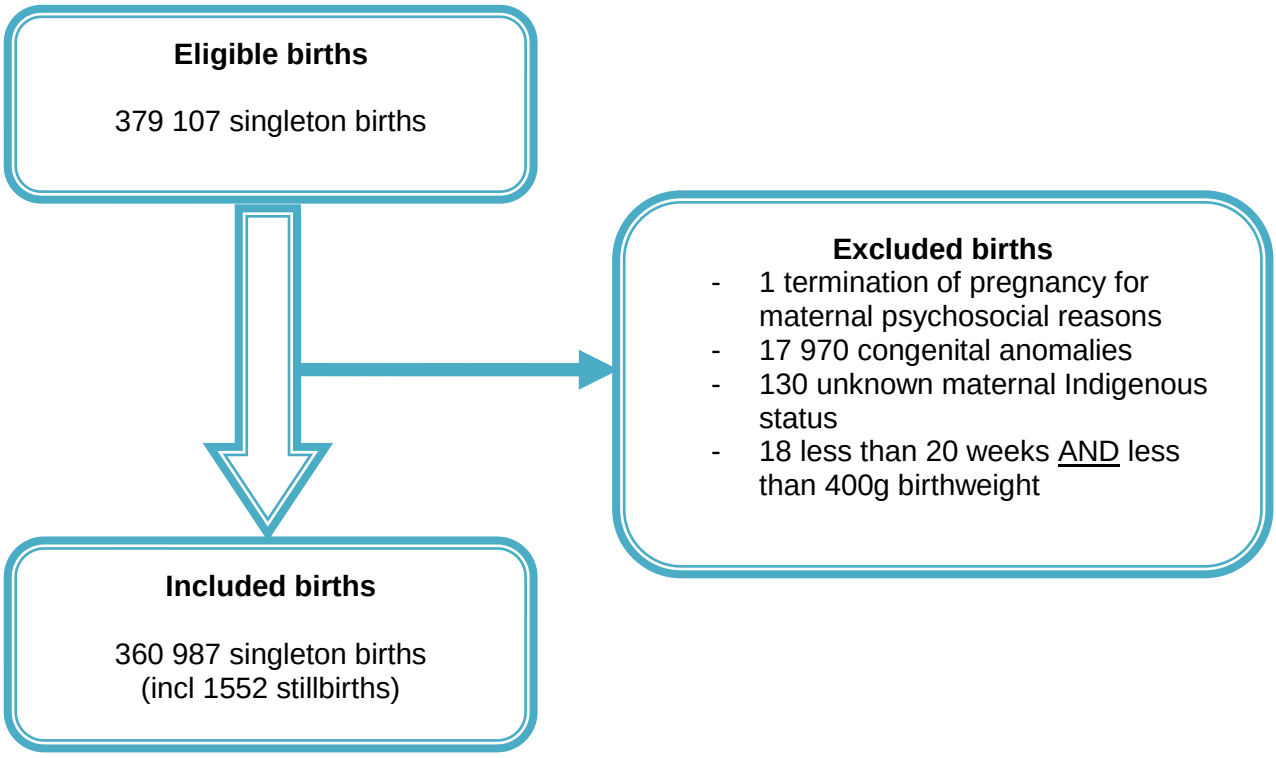


Figure 4.1: Flowchart showing study population, Gestational age specific stillbirth risk analysis, mid 2005-2011

Statistical Analysis

Data from the Queensland Perinatal Data Collection (QPDC) was utilised for this study and data management was undertaken as outlined in Section 2.2. Maternal demographic data included age, marital status, socioeconomic status and geographic location. Pregnancy data included primigravidity, hospital accommodation, smoking, substance use, pregnancy complications, assisted conception and number of antenatal care visits. Birth outcome data included baby's sex, gestational age at birth, birthweight, small-for-gestational age and stillbirth. All variables measured on a continuous scale were classified into categories and Chi square or Fisher's exact test used to explore differences in maternal and pregnancy factors between women with a stillbirth and women with a livebirth. Statistical significance was set at $p<0.05$. Analysis was carried out for the population as a whole and also stratified by Indigenous status as Indigenous women differed significantly on a number of maternal and pregnancy factors.

The main outcome of interest was stillbirth risk by gestational age group and Indigenous status. The conditional probability of stillbirth for each week gestation between 20 and 42 weeks was calculated using lifetable approach [227]. This method was preferred over the Yudkin method (described in Chapter 3) because of overestimation of the denominator with the Yudkin method [227].

Gestational age specific risk of stillbirth associated with diabetes, hypertension, antepartum haemorrhage and small-for-gestational age was assessed using time-to-event analysis. This method is particularly appropriate for addressing the study objectives because it uses the appropriate population (i.e. number of ongoing pregnancies) as its denominator, allows for assessment of cumulative risk, simultaneous adjustment for multiple covariates, correction for duration of pregnancy and enables formal testing of the assumption that the risk associated with predictors varies over the duration of pregnancy [6] which were particularly useful for this study.

The association between stillbirth and various predictors was explored using univariate Cox Proportional Hazard model. In the model, stillbirth was the event, gestational age was the timescale and all livebirths were censored. A *p=0.25* cutoff was used to select potential candidates for multivariate analysis [228]. To enable comparisons across Indigenous and non-Indigenous women, the same predictors were retained in the multivariate model if the p value was less than 0.25 for one or both populations. Multivariate Cox Proportional Hazard models were built for each condition of interest. Models were tested for violation of

assumption of proportionality using methods described by Grambsh and Therneau [229]. This involved testing for a non-zero slope in a linear regression of the scaled Shoenfeld residuals for each predictor against time. This test was run for each predictor within the model as well as a global test of the model. A resulting p value of less than 0.05 was taken as an indication that the association between stillbirth and the predictor varied with gestational age. In addition, for each model the Shoenfeld residuals were graphed against the scaled time vector and the graph was inspected for deviation from zero-slope. The graphical method was used in addition to hypothesis testing to detect any cases of violation of proportionality where there was a nonlinear relationship between time and the residuals, which may not have been detected using hypothesis testing alone.

Checking for Interactions between characteristics

In exploring the associations between maternal/pregnancy characteristics and stillbirth as potential candidates for multivariate analysis, interactions between these characteristics were also explored. Exploration of interactions was guided by previous knowledge from published literature. Significant interactions were found between maternal age and smoking status, and maternal age and marital status among Indigenous women; additionally among non-Indigenous women there was a significant interaction between smoking status and small-for-gestational age (Appendix B1). Interaction terms were included in the multivariate regression models. Care was taken with derived variables such as socioeconomic status and geographic location and other related variables which may have shared common factors in their derivation (eg accommodation status and maternal age). Some of these factors produced unstable estimates.

Assessment and management of violation of assumption of proportionality

Univariate analysis indicated the stillbirth hazard varied with gestational age for all conditions except antepartum haemorrhage for non-Indigenous women and pre-existing diabetes for Indigenous women (Appendix B2). As a result, the violation of the proportionality assumption was handled by assessing gestational age specific risk using logistic regression and assessing risk in five gestational age groupings. The groups used were: 20-23 weeks, 24-27 weeks, 28-32 weeks, 33-36 weeks and 37-42 weeks. These groups were used to allow comparison with literature [230]. Within each gestational age

grouping, the denominator was adjusted to reflect the population at risk. This was achieved by dropping all births prior to the gestational age interval of interest and recoding all stillbirths occurring after the gestational age interval of interest as livebirths. The logistic regression model for each condition was adjusted for the same predictors as the corresponding multivariate Cox model. Where numbers in each gestational age group were small, exact logistic regression was used.

To assess the proportion of stillbirths that would be eliminated if each of the factors associated with stillbirth was eliminated, population attributable risk or fractions (PAR/PAF) were calculated using the adjusted effect estimates. In the literature, the terms population attributable risk (PAR) and fraction (PAF) are used interchangeably.

Results are presented from the logistic regression models in Section 4.3. Results from preliminary steps involving univariate and multivariate Cox regression models are shown in Appendix B1-B7. Analyses were also carried out using Poisson regression with no material difference in results compared with logistic regression. Statistical analysis was performed using Stata/SE for Windows 13.1 (StataCorp LP, College Station, TX, USA) and SAS version 9.3 (SAS Institute, Cary, NC, USA.) for exact logistic regression.

4.3 Results

A total of 360,987 births were included in the analyses. Of these, 20,273 (5.6%) births were to Indigenous women and 340,714 (94.4%) were to non-Indigenous women. The stillbirth rates were 7.9 (95% CI 6.8-9.2) and 4.1 (95% CI 3.9-4.3) per 1000 births, respectively. There were differences in the prevalence of the conditions of interest between Indigenous and non-Indigenous women as follows: pre-existing diabetes (1.3% vs 0.5%, Rate Ratio 2.54, 95% CI 2.23-2.89), gestational diabetes (6.6% vs 5.3%, Rate Ratio 1.23, 95% CI 1.16-1.29), pre-existing hypertension (1.0% vs 0.7%, Rate Ratio 1.49, 95% CI 1.29-1.72), pregnancy induced hypertension (2.4% vs 2.9%, Rate Ratio 0.83, 95% CI 0.76-0.91), pre-eclampsia/eclampsia (2.9% vs 2.2%, Rate Ratio 1.31, 95% CI 1.20-1.42), antepartum haemorrhage (2.3% vs 2.7%, Rate Ratio 0.83, 95% CI 0.75-0.91) and small-for-gestational age (15.2% vs 8.4%, Rate Ratio 1.81, 95% CI 1.75-1.87).

Although pregnancies with a congenital abnormality were excluded from the main analysis because of the association between diabetes and congenital abnormality, secondary analysis showed that there was little difference in the proportion of stillbirths due to congenital abnormality between Indigenous and non-Indigenous women (0.19% versus 0.16%).

Characteristics by birth outcome and Indigenous status

Table 4.1 shows the maternal, medical and obstetric characteristics of the study population by birth outcome (stillbirth or livebirth) for Indigenous and non-Indigenous women. For Indigenous and non-Indigenous women, there were higher rates of smoking, substance use, preterm birth and fewer than 8 antenatal care visits among women with a stillbirth compared to women who had a livebirth (Table 4.1). Among non-Indigenous women, there were higher rates of socioeconomic disadvantage, not having a domestic partner and public hospital accommodation among women who had a stillbirth compared with those who did not.

Table 4.1: Maternal and pregnancy characteristics by birth outcome and Indigenous status, singleton births, Queensland, mid 2005-2011

Characteristics	Indigenous (n=20273)			Non-Indigenous (n=340714)		
	Stillbirth (n=160)	Livebirth (n=20113)	Odds Ratio (95% CI)	Stillbirth (n=1392)	Livebirth (n=339322)	Odds Ratio (95% CI)
Maternal age (years)						
≤18 years	10 (6.3)	1 444 (7.2)	0.81 (0.41-1.61)	42 (3.0)	4 360 (1.3)	2.62 (1.91-3.60)
19-24 years	67 (41.9)	8 698 (43.3)	0.91 (0.62-1.31)	313 (22.5)	67 583 (19.9)	1.26 (1.09-1.46)
25-30 years	48 (30.0)	5 645 (28.1)	Ref (1.00)	437 (31.4)	118 816 (35.0)	Ref (1.00)
31-34 years	14 (8.8)	2 413 (12.0)	0.68 (0.38-1.24)	290 (20.8)	81 032 (23.9)	0.97 (0.84-1.13)
≥35 years	21 (13.1)	1 913 (9.5)	1.29 (0.77-2.16)	310 (22.3)	67 531 (19.9)	1.25 (1.08-1.44)
Geographic Location						
Major City	26 (16.3)	4 143 (20.6)	Ref (1.00)	835 (60.0)	208 943 (61.6)	Ref (1.00)
Regional area	95 (59.4)	11 825 (58.8)	1.28 (0.83-1.98)	525 (37.7)	122 065 (36.0)	1.08 (0.96-1.20)
Remote area	39 (24.4)	4 145 (20.6)	1.50 (0.91-2.47)	31 (2.2)	8 303 (2.5)	0.93 (0.65-1.34)
missing	*0 (0.0)*	*0 (0.0)*		*1 (0.1)*	*11 (0.0)*	
Marital Status						
Domestic partner	102 (63.8)	12 931 (64.3)	Reference	1 148 (82.5)	301 064 (88.7)	Reference
No domestic partner	58 (36.3)	7 174 (35.7)	1.02 (0.74-1.42)	241 (17.3)	38 211 (11.3)	1.65 (1.44-1.90)
missing	*0 (0.0)*	*8 (0.0)*		*3 (0.2)*	*47 (0.0)*	
Relative socioeconomic disadvantage						
Highest 20%	4 (2.5)	549 (2.7)	Reference	201 (14.4)	55 422 (16.3)	Reference
Middle 60%	97 (60.6)	12 164 (60.6)	1.09 (0.40-2.99)	997 (71.6)	244 228 (72.0)	1.13 (0.97-1.31)
Lowest 20%	59 (36.9)	7 363 (36.6)	1.10 (0.40-3.04)	190 (13.6)	39 313 (11.6)	1.33 (1.09-1.63)
missing	*0 (0.0)*	*37 (0.2)*		*4 (0.3)*	*359 (0.1)*	
Any smoking during pregnancy						
No	58 (36.3)	9 389	Reference	1016 (73.0)	281 286 (82.9)	Reference
Yes	95 (59.4)	10 597 (52.7)	1.45 (1.05-2.01)	332 (23.9)	56 388 (16.6)	1.63 (1.44-1.85)
missing	*7 (4.4)*	*127 (0.6)*		*44 (3.2)*	*1 648 (0.5)*	
Substance Use during pregnancy						
No	149 (93.1)	19 781 (98.4)	Reference	1377 (98.9)	337 632 (99.5)	Reference
Yes	11 (6.9)	332 (1.7)	4.40 (2.36-8.19)	15 (1.1)	1 690 (0.5)	2.18 (1.31-3.63)

Characteristics	Indigenous (n=20273)			Non-Indigenous (n=340714)		
	Stillbirth (n=160)	Livebirth (n=20113)	Odds Ratio (95% CI)	Stillbirth (n=1392)	Livebirth (n=339322)	Odds Ratio (95% CI)
Hospital accommodation status						
Private	3 (1.8)	417 (2.1)	Reference	305 (21.9)	110 687 (32.6)	Reference
Public	157 (98.1)	19 696 (97.9)	1.11 (0.35-3.49)	1 084 (77.9)	228 633 (67.4)	1.72 (1.52-1.95)
missing	*0 (0.0)*	*0 (0.0)*		*3 (0.2)*	*2 (0.0)*	
Assisted Conception						
No	159 (99.4)	20 022 (99.6)	Reference	1 321 (94.9)	326 459 (96.2)	Reference
Yes	1 (0.6)	91 (0.5)	1.38 (0.19-9.99)	66 (4.7)	12 843 (3.8)	1.27 (0.99-1.63)
missing	*0 (0.0)*	*0 (0.0)*		*5 (0.4)*	*20 (0.0)*	
Primigravidity						
No	123 (76.8)	15 316 (76.2)	Reference	973 (69.9)	237 647 (70.0)	Reference
Yes	37 (23.1)	4 797 (23.9)	0.96 (0.90-1.13)	418 (30.0)	101 673 (30.0)	1.00 (0.90-1.13)
missing	*0 (0.0)*	*0 (0.0)*		*1 (0.1)*	*2 (0.0)*	
Number of antenatal care visits						
Less than 2	47 (29.4)	1 055 (5.2)	14.2 (8.98-22.4)	147 (10.6)	2 144 (0.6)	43.3 (35.7-52.5)
2 – 4	57 (35.6)	3 348 (16.6)	5.43 (3.50-8.42)	459 (33.0)	16 890 (5.0)	17.2 (15.0-19.6)
5 – 7	23 (14.4)	5 805 (28.9)	1.26 (0.74-2.17)	367 (26.4)	63 019 (18.6)	3.68 (3.19-4.24)
8 or more	31 (19.4)	9 880 (49.1)	Reference	407 (29.2)	257 089 (75.8)	Reference
missing	*2 (1.3)*	*25 (0.1)*		*12 (0.9)*	*180 (0.1)*	
Gestational age at birth (weeks)						
< 37 weeks	117 (73.1)	2 073 (10.3)	23.5 (16.5-33.4)	1030 (74.0)	20 426 (6.0)	44.8 (39.7-50.5)
≥37 weeks	43 (26.9)	18 029 (89.6)	Reference	359 (25.8)	318 877 (94.0)	Reference
missing	*0 (0.0)*	*11 (0.1)*		*3 (0.2)*	*19 (0.0)*	
Baby's gender						
Female	*66 (41.5)*	*9 782 (48.6)*	Reference	*675 (48.5)*	*165 084 (48.7)*	Reference
Male	93 (58.1)	10 331 (51.4)	1.33 (0.97-1.83)	715 (51.4)	174 237 (51.4)	1.00 (0.90-1.12)
missing	*1 (0.6)*	*0 (0.0)*		*2 (0.1)*	*1 (0.0)*	

Percentages may add up to greater than 100% due to rounding. Missing values omitted from calculation of odds ratios (ORs)

Table 4.2 shows the differences in prevalence of diabetes, hypertension, antepartum haemorrhage and small-for-gestational age by birth outcome (stillbirth or livebirth) for Indigenous and non-Indigenous women. Relative to women who had a livebirth, there were higher rates of pre-existing diabetes, pre-existing hypertension, antepartum haemorrhage and small-for-gestational age among women who had a stillbirth for both Indigenous and non-Indigenous women. Furthermore, among non-Indigenous women, the rate of pre-eclampsia and eclampsia was higher among women who had a stillbirth. Conversely, the rate of gestational diabetes was lower among women who had a stillbirth, and the rate of pregnancy-induced hypertension was lower among non-Indigenous women who had a stillbirth.

Univariate associations from Cox proportional hazard models are shown in Appendix B3 and B4. The magnitude of association was similar between univariate hazard ratios and univariate odds ratios.

Table 4.2: Maternal and pregnancy conditions by birth outcome and Indigenous status, singleton births, Queensland, mid 2005-2011

Characteristics	Indigenous (n=20273)			Non-Indigenous (n=340714)		
	Stillbirth (n=160)	Livebirth (n=20113)	Odds Ratio (95% CI)	Stillbirth (n=1392)	Livebirth (n=339322)	Odds Ratio (95% CI)
Pre-existing diabetes*						
No	148 (92.5)	19 865 (98.8)	Reference	1 371 (98.5)	337 620 (99.5)	Reference
Yes	12 (7.5)	248 (1.2)	6.49 (3.56-11.9)	21 (1.5)	1 702 (0.5)	3.04 (1.97-4.69)
Gestational diabetes						
No	156 (97.5)	18 789 (93.4)	Reference	1 334 (95.8)	321 187 (94.7)	Reference
Yes	4 (2.5)	1 324 (6.6)	0.36 (0.13-0.98)	58 (4.2)	18 135 (5.3)	0.77 (0.59-1.00)
Pre-existing hypertension						
No	153 (95.6)	19 923 (99.1)	Reference	1 361 (97.8)	337 133 (99.4)	Reference
Yes	7 (4.4)	190 (0.9)	4.80 (2.22-10.4)	31 (2.2)	2 189 (0.7)	3.51 (2.45-5.02)
Pre-eclampsia/Eclampsia						
No	155 (96.9)	19 539 (97.2)	Reference	1 315 (94.5)	331 963 (97.8)	Reference
Yes	5 (3.1)	574 (2.9)	1.10 (0.45-2.69)	77 (5.5)	7 359 (2.2)	2.64 (2.10-3.33)
Pregnancy Induced hypertension						
No	159 (99.4)	19 625 (97.6)	Reference	1 365 (98.1)	329 425 (97.1)	Reference
Yes	1 (0.6)	488 (2.4)	0.25 (0.04-1.81)	27 (1.9)	9 897 (2.9)	0.66 (0.45-0.96)
Antepartum haemorrhage						
No	116 (72.5)	19 701 (98.0)	Reference	1 055 (75.8)	330 374 (97.4)	Reference
Yes	44 (27.5)	412 (2.0)	18.1 (12.6-26.0)	337 (24.2)	8 948 (2.6)	11.8 (10.4-13.4)
Small for gestational age**						
No	99 (61.9)	17 079 (84.9)	Reference	967 (69.5)	311 059 (91.7)	Reference
Yes	58 (36.3)	3 021 (15.0)	3.31 (2.39-4.59)	410 (29.5)	28 214 (8.3)	4.67 (4.16-5.25)
missing	3 (1.9)	13 (0.1)		15 (1.1)	49 (0.0)	

ICD10-AM codes: Antepartum haemorrhage (O44.1, O45-O46), Essential hypertension (O10.0, O10.2-10.4, O10.9, O11), Pregnancy Induced hypertension (O13), Pre-eclampsia/Eclampsia (O14, O15), Pre-existing diabetes (O24.0, O24.1, O24.3, O24.8), Gestational diabetes (O24.4, O24.9). *Insufficient detail in codes to differentiate types of pre-existing diabetes mellitus. **Small for gestational age = less than 10th Australian population percentile for gestational age, sex and plurality.

Description of all-cause gestational age specific risk of stillbirth

The all-cause gestational age specific risk of stillbirth is characterised in Figure 4.2. For Indigenous and non-Indigenous women, the probability of stillbirth is initially low; averaging around 0.6/1000 and 0.3/1000 ongoing pregnancies between 20 and 24 weeks, respectively. The probability of stillbirth between 25 and 37 weeks is about 0.2/1000 and 0.1/1000 for Indigenous and non-Indigenous women. A sharp increase in the probability of stillbirth is observed around term (≥37 weeks); reaching 30/1000 and 6/1000 ongoing pregnancies at 42+ weeks among Indigenous and non-Indigenous women, respectively. The ratio of probability steadily increases from 38 weeks onwards as shown in Figure 4.3

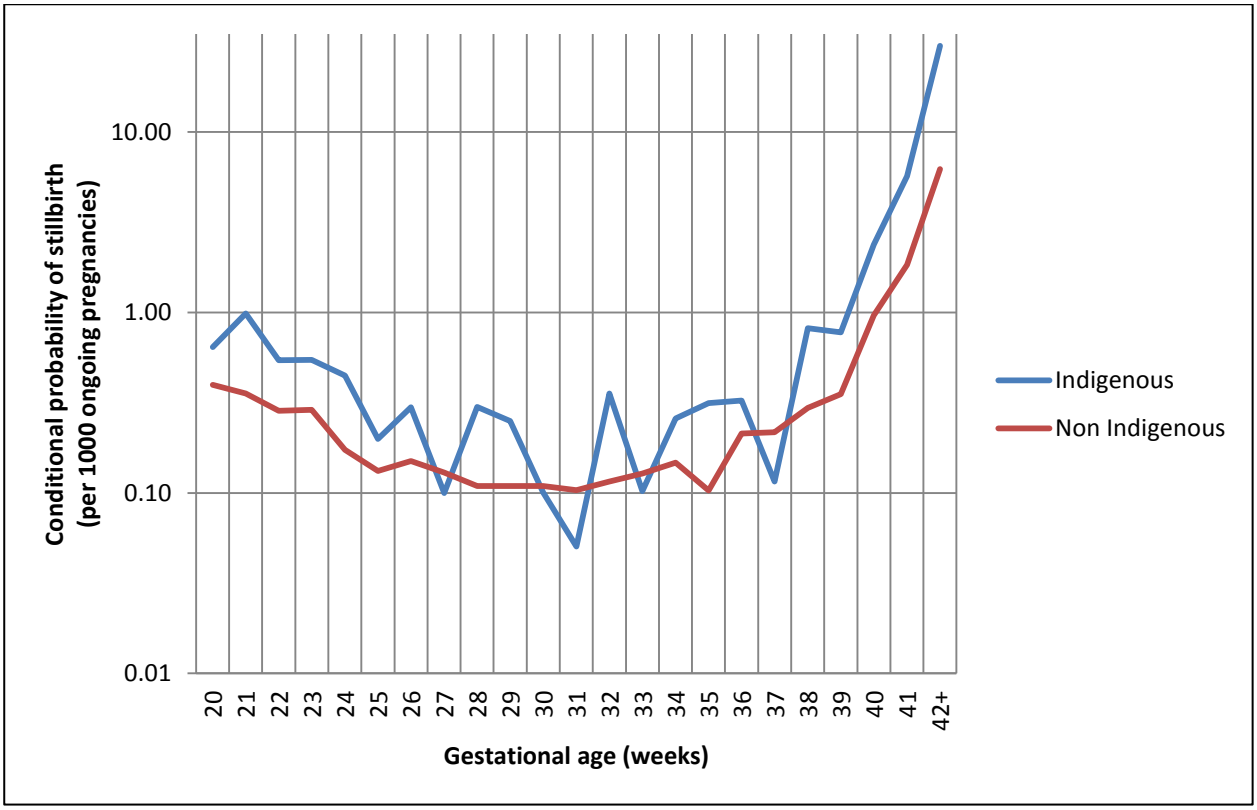


Figure 4.2: Gestational age specific risk of stillbirth by Indigenous status, singleton births, Queensland, mid 2005-2011

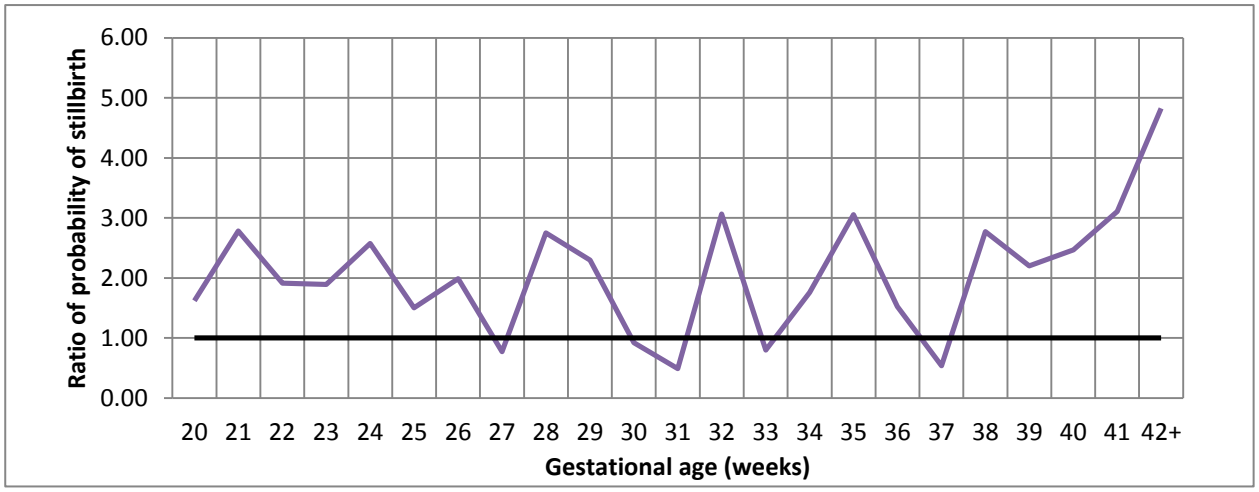
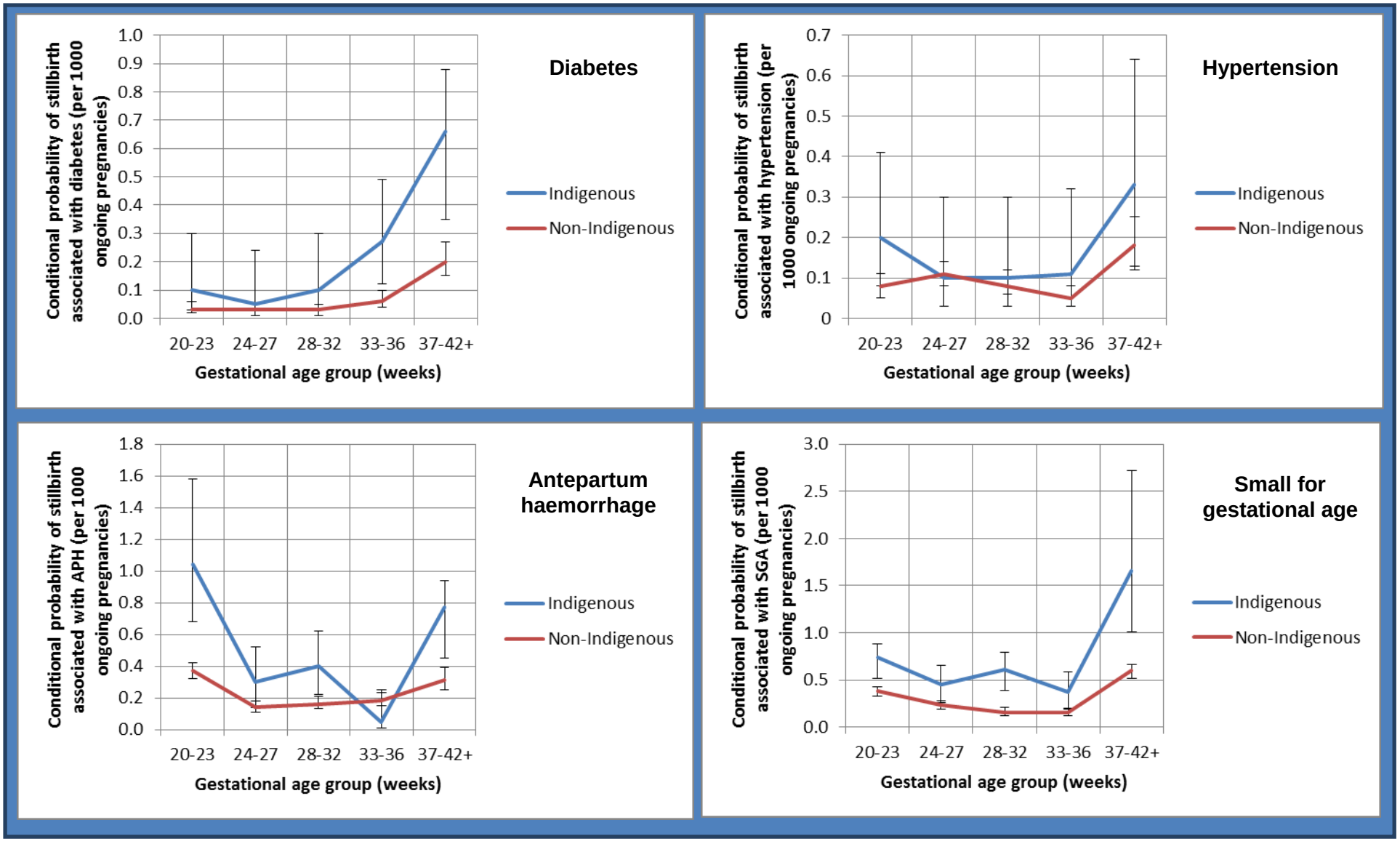


Figure 4.3: Ratio of stillbirth risk, Indigenous relative to non-Indigenous

The gestational age specific risk of stillbirth associated with diabetes, hypertension, antepartum haemorrhage and small-for-gestational age is shown in Figure 4.4. The risk was generally higher for Indigenous women, particularly at 37-42+ weeks.

Figure 4.4: Gestational age specific risk of stillbirth by maternal/pregnancy condition of interest for Indigenous and non-Indigenous women, singleton births, Queensland, mid 2005 – 2011



Adjusted gestational age specific stillbirth risk associated with diabetes, hypertension, antepartum haemorrhage and small-for-gestational age

The gestational age specific risk of stillbirth associated with diabetes, hypertension, antepartum haemorrhage and small-for-gestational age for the total population (Indigenous and non-Indigenous women) is shown in Table 4.3 and the effect of Indigenous status (relative to non-Indigenous status) is shown in Table 4.3a. For all conditions of interest, an increased risk of stillbirth from 37 weeks onwards was observed for Indigenous women (Table 4.3a). Gestational age specific risk for each condition of interest is given for Indigenous and non-Indigenous women separately in Table 4.4.

Table 4.3: Gestational age-specific odds of stillbirth associated with diabetes, hypertension, antepartum haemorrhage and SGA, combined Indigenous and non-Indigenous women, Queensland, mid 2005-2011

Conditions	All births (n=360 987)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Pre-existing diabetes^	1.02 (0.31-3.37)	3.34 (1.17-9.57)	3.00 (0.92-9.78)	7.28 (3.35-15.8)	8.26 (4.70-14.5)
Gestational diabetes^	0.41 (0.18-0.91)	0.68 (0.28-1.67)	1.12 (0.55-2.28)	1.80 (1.07-3.02)	1.24 (0.82-1.87)
Pre-existing hypertension*	6.30 (3.70-10.7)	6.29 (2.97-13.3)	4.39 (1.75-11.0)	2.76 (1.00-7.64)	1.36 (0.50-3.70)
Pre-Eclampsia/Eclampsia	0.92 (0.49-1.73)	5.50 (3.57-8.46)	4.47 (2.76-7.26)	2.10 (1.03-4.27)	2.63 (1.61-4.30)
Antepartum haemorrhage^	9.68 (7.85-12.0)	8.49 (6.14-11.7)	13.8 (10.1-18.6)	16.4 (12.1-22.2)	8.44 (6.32-11.3)
Small-for-gestational age[a]	3.26 (2.64-4.02)	5.95 (4.47-7.93)	3.98 (2.93-5.40)	3.51 (2.56-4.81)	3.35 (2.66-4.22)
Smoker	1.76 (1.21-2.57)	3.51 (2.07-5.95)	3.08 (1.85-5.12)	2.82 (1.64-4.84)	2.80 (1.89-4.15)
Non smoker	4.45 (3.48-5.69)	7.42 (5.32-10.3)	4.65 (3.19-6.77)	3.93 (2.68-5.77)	3.65 (2.75-4.83)

Table 4.3a: Effect of Indigenous status on gestational age specific odds of stillbirth (Indigenous relative to non-Indigenous)

Conditions	All births (n=360 987)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Pre-existing diabetes^	**0.71 (0.51-0.98)**	**0.51 (0.30-0.86)**	0.66 (0.39-1.11)	0.86 (0.51-1.46)	**1.45 (1.01-2.09)**
Gestational diabetes^	**0.71 (0.51-0.99)**	**0.53 (0.31-0.89)**	0.67 (0.40-1.12)	0.89 (0.52-1.51)	**1.49 (1.04-2.15)**
Pre-existing hypertension*	**0.71 (0.51-0.98)**	**0.51 (0.30-0.86)**	0.66 (0.39-1.11)	0.86 (0.51-1.46)	**1.45 (1.01-2.09)**
Pre-Eclampsia/Eclampsia	0.72 (0.52-1.00)	**0.53 (0.31-0.89)**	0.67 (0.40-1.12)	0.90 (0.53-1.53)	**1.50 (1.04-2.15)**
Antepartum haemorrhage^	0.77 (0.55-1.08)	**0.56 (0.33-0.96)**	0.73 (0.43-1.23)	0.99 (0.58-1.69)	**1.53 (1.07-2.21)**
Small-for-gestational age[a]	**0.68 (0.49-0.95)**	**0.49 (0.29-0.83)**	0.58 (0.34-0.99)	0.85 (0.50-1.45)	1.42 (0.98-2.04)
Smoker	0.73 (0.46-1.16)	**0.36 (0.16-0.80)**	0.69 (0.34-1.38)	0.68 (0.32-1.43)	1.60 (0.99-2.58)
Non smoker	0.65 (0.39-1.07)	0.68 (0.33-1.38)	0.46 (0.19-1.12)	1.13 (0.54-2.37)	1.06 (0.57-1.97)

All models adjusted for maternal age, smoking status, gravidity, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. [a]Models include the following interaction term: smoke*FGR10 (analysis stratified by smoking). ^These models additionally adjusted for pre-existing hypertension. *These models additionally adjusted for pre-existing diabetes.
Bold estimates indicate statistically significant effect of Indigenous status.

Table 4.4: Gestational age-specific odds of stillbirth associated with medical/pregnancy conditions, by Indigenous status, Queensland, mid 2005-2011

Conditions	Indigenous (n=20,273 births)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Pre-existing diabetes^~	1.21 (0.14-10.3)	2.55 (0.21-31.5)	5.80 (0.86-39.2)	18.8 (5.04-69.7)	16.5 (5.20-52.1)
Gestational diabetes^~	-	-	-	0.61 (0.08-4.81)	0.90 (0.21-3.92)
Pre-existing hypertension*~	2.18 (0.25-18.7)	4.23 (0.35-50.8)	15.0 (2.17-104)	1.27 (0.12-13.0)	2.66 (0.31-22.9)
Pre-Eclampsia/Eclampsia~	0.70 (0.09-5.18)	1.19 (0.15-9.52)	-	2.88 (0.37-22.4)	2.67 (0.62-11.5)
Antepartum haemorrhage^	18.1 (9.86-33.3)	15.4 (5.44-43.6)	38.1 (14.1-102)	2.34 (0.29-19.2)	18.2 (7.61-43.4)
Small-for-gestational age	1.30 (0.67-2.54)	3.03 (1.17-7.85)	7.47 (2.86-19.6)	3.10 (1.18-8.17)	1.97 (1.02-3.83)
Conditions	**Non-Indigenous (n=340,714 births)**				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Pre-existing diabetes^	0.87 (0.18-4.17)	3.29 (0.94-11.6)	1.35 (0.18-10.1)	8.79 (3.83-20.2)	7.66 (3.92-15.0)
Gestational diabetes^	0.50 (0.22-1.12)	0.84 (0.34-2.05)	1.30 (0.63-2.66)	1.87 (1.08-3.25)	1.32 (0.86-2.02)
Pre-existing hypertension*	6.24 (3.54-11.0)	5.28 (2.33-12.0)	2.95 (0.92-9.50)	2.42 (0.76-7.75)	1.26 (0.40-3.97)
Pre-eclampsia/Eclampsia	0.77 (0.39-1.51)	4.63 (2.96-7.24)	4.36 (2.67-7.12)	1.75 (0.82-3.75)	2.39 (1.42-4.02)
Antepartum haemorrhage^	9.63 (7.65-12.1)	8.61 (6.08-12.2)	13.1 (9.41-18.2)	18.1 (13.3-24.8)	7.81 (5.73-10.6)
Small-for-gestational age					
Smoker	1.89 (1.23-2.91)	3.79 (2.14-6.71)	2.51 (1.39-4.53)	2.93 (1.62-5.32)	3.49 (2.21-5.52)
Non Smoker	4.84 (3.76-6.22)	7.74 (5.49-10.9)	4.57 (3.10-6.73)	3.90 (2.62-5.81)	3.66 (2.74-4.88)

Models adjusted for maternal age, smoking status, remoteness, substance use, gender, gravidity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. ^ These models additionally adjusted for pre-existing hypertension. * These models additionally adjusted for pre-existing diabetes. ~Exact logistic regression model

Diabetes

In the population as a whole, increased odds of stillbirth associated with pre-existing diabetes was found at 24-27 weeks (adjusted OR 3.34, 95% CI 1.17-9.57) and from 33 weeks onwards [adjusted OR 33-36 weeks (7.28 95% CI 3.35-15.8) and adjusted OR 37-42+ weeks (8.26 95% CI 4.70-14.5)] (Table 4.3). Among Indigenous women, increased risk of stillbirth associated with pre-existing diabetes was found from 33 weeks onwards [adjusted OR 33-36 weeks (18.8 95% CI 5.04-69.7) and adjusted OR 37-42+ weeks (16.5 95% CI 5.20-52.1)] (Table 4.4). However, these risk estimates were not significantly different from each other. While among non-Indigenous women, increased risk of stillbirth associated with pre-existing diabetes was found from 33 weeks gestation onwards [adjusted OR 33-36 weeks (8.79 95% CI 3.83-20.2) and adjusted OR 37-42+ weeks (7.66 95% CI 3.92-15.0)] (Table 4.4). The effect estimates for non-Indigenous women were around half those of Indigenous women from around 28 weeks gestation onwards.

In the whole population, increased odds of stillbirth associated with gestational diabetes were observed at 33-36 weeks (adjusted OR 1.80, 95% CI 1.07-3.02) but no association was found at other gestational age intervals. Risk estimates suggest stillbirth was less common among Indigenous women with gestational diabetes, however, no significant association was found (Table 4.4). Among non-Indigenous women, a nearly two fold increased risk of stillbirth associated with gestational diabetes was found for births at 33-36 weeks gestation (adjusted OR 1.87 95% CI 1.08-3.25).

Hypertension

In the whole population, increased odds of stillbirth associated with pre-existing hypertension was found at gestational ages less than 37 weeks [adjusted OR 20-23 weeks (6.30 95% CI 3.70-10.7), adjusted OR 24-27 weeks (6.29 95% CI 2.97-13.3), adjusted OR 28-32 weeks (4.39 95% CI 1.75-11.0) and adjusted OR 33-36 weeks (2.76 95% CI 1.00-7.64)] (Table 4.3). Increased risk of stillbirth associated with pre-existing hypertension was found among Indigenous women at 28-32 weeks gestation (adjusted OR 15.0 95% CI 2.17-104). The estimates suggest increasing risk with gestational age with a peak at 28-32 weeks followed by decreasing risk from late preterm to term gestational ages, however, the numbers are small and the results did not reach statistical significance (Table 4.4). A different pattern was shown among non-Indigenous women, with decreasing risk as

gestational age increased, with an initial peak at 20-23 weeks (adjusted OR 6.24 95% CI 3.54-11.0). However, the risk estimates for the first three groups are not significantly different from each other.

Increased odds of stillbirth associated with pre-eclampsia and eclampsia was found from 24 weeks onwards in the whole population (Table 4.3). Among Indigenous women, no significant association was found between stillbirth and pre-eclampsia at any of the gestational ages examined. However, the risk estimates suggest decreasing risk of stillbirth with increasing gestational age. In contrast, among non-Indigenous women, there was increased risk of stillbirth at 24-27 weeks (adjusted OR 4.63 95% CI 2.96-7.24), 28-32 weeks (adjusted OR 4.36 95% CI 2.67-7.12) and at term (adjusted OR 2.39 95% CI 1.42-4.02). The results suggest the risk of stillbirth may be higher in preterm gestational ages, however, the estimates were not significantly different from each other.

Antepartum haemorrhage

Antepartum haemorrhage was associated with increased odds of stillbirth at all gestational ages examined in the whole population [adjusted OR range 8.44-16.4] (Table 4.3). Antepartum haemorrhage was associated with increased risk of stillbirth among Indigenous women at all gestational ages examined, although estimate for 33-36 weeks (adjusted OR 2.34 95% CI 0.29-19.2) did not reach statistical significance. The adjusted odds ratios suggest the risk may be highest at 28-32 weeks (adjusted OR 38.1 95% CI 14.1-102), however, numbers were small and this result was not significantly different from the estimates at the other gestational ages (Table 4.4). In contrast, among non-Indigenous women the magnitude of the risk estimates were around half those for Indigenous women. Increased risk of stillbirth was associated with the presence of antepartum haemorrhage for all gestational age groups assessed; with the risk of stillbirth significantly higher at 33-36 weeks (adjusted OR 18.1 95% CI 13.3-24.8).

Small-for-gestational age

Increased odds of stillbirth associated with small-for-gestational age were found at all gestational age intervals examined with a peak at 24-27 weeks (adjusted OR 5.95 95% CI 4.47-7.93) which was significantly higher than the risk estimate for 20-23 weeks (adjusted

OR 3.26 95% CI 2.64-4.02) and term (adjusted OR 3.35 95% CI 2.66-4.22) (Table 4.3). Moreover, an interaction between smoking and small for gestational age was found among non-Indigenous women (Table 4.3 and 4.4); with effect modification of the risk of stillbirth at 20-23 weeks (higher odds of stillbirth for non-smokers compared with smokers) but this effect was not observed at older gestational ages. Among Indigenous women, increased risk of stillbirth was observed from 24 weeks onwards. The risk estimates suggest there may be an inverted "V" shaped relationship between small-for-gestational age and stillbirth among Indigenous women with a peak at 28-32 weeks (adjusted OR 7.47 95% CI 2.86-19.6), however, the risk estimates were not significantly different from each other from 24 weeks gestation onwards.

Table 4.5: Population attributable fraction associated with conditions of interest

Condition	Indigenous			Non Indigenous		
	P	Adjusted HR	PAF (%)	P	Adjusted HR	PAF (%)
Pre-existing diabetes	1.28	7.28 (3.70-14.3)	7.44	0.51	4.20 (2.70-6.56)	1.61
Pre-existing hypertension	0.97	2.82 (1.11-7.19)	1.73	0.65	3.67 (2.54-5.31)	0.17
Pre eclampsia/ Eclampsia	-	-	-	2.18	2.67 (2.11-3.39)	3.51
Antepartum haemorrhage	2.25	18.7 (12.9-27.3)	28.5	2.73	11.6 (10.2-13.2)	22.4
Small-for gestational age	15.2	2.34 (1.65-3.30)	16.9	8.40	3.97 (3.51-4.47)	20.0

P = Prevalence (%) PAF(%) = Population attributable fraction

Presented in Table 4.5 are the population attributable fractions associated with the conditions of interest. Antepartum haemorrhage had the highest values for both Indigenous and non-Indigenous women (28.5% and 22.4%, respectively), followed by small-for-gestational age with 16.9% and 20.0% for Indigenous and non-Indigenous women, respectively.

Maternal characteristics by geographic location and Indigenous status

Table 4.6 shows the distribution of maternal, medical and obstetric factors by geographic location and birth outcome for Indigenous women. Indigenous women with a stillbirth, regardless of where they lived, were more likely to: attend fewer antenatal care visits, have

a preterm infant, have a growth restricted infant, have antepartum haemorrhage and pre-existing diabetes. A higher proportion of Indigenous women with a stillbirth who lived in major city or regional areas were more likely to have substance use issues; while Indigenous women with a stillbirth who lived in a remote area were more likely to have a male infant.

Table 4.6: Maternal and pregnancy characteristics by birth outcome and geographic location, Indigenous women, Queensland, mid 2005-2011

Characteristics	Indigenous (n=20273)					
	Major City (n=4169)		Regional (n=11920)		Remote (n=4184)	
	Stillbirth (n=26)	Livebirth (n=4143)	Stillbirth (n=95)	Livebirth (n=11825)	Stillbirth (n=39)	Livebirth (n=4145)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Maternal age (years)						
≤18 years	2 (7.7)	233 (5.6)	5 (5.3)	907 (7.7)	3 (7.7)	304 (7.3)
19-24 years	11 (42.3)	1684 (40.7)	38 (40.0)	5191 (43.9)	18 (46.2)	1823 (44.0)
25-30 years	6 (23.1)	1263 (30.5)	28 (29.5)	3211 (27.2)	14 (35.9)	1171 (28.3)
31-34 years	3 (11.5)	527 (12.7)	9 (9.5)	1393 (11.8)	2 (5.1)	493 (11.9)
≥35 years	4 (15.4)	436 (10.5)	15 (15.8)	1123 (9.5)	2 (5.1)	354 (8.5)
p value	0.779*		0.280*		0.630*	
Marital Status						
Partner	14 (53.9)	2474 (59.7)	62 (65.3)	7668 (64.9)	26 (66.7)	2789 (67.3)
No partner	12 (46.2)	1667 (40.3)	33 (34.7)	4153 (35.1)	13 (33.3)	1354 (32.7)
p value	0.541		0.936		0.931	
missing	0 (0.0)	2 (0.0)	0 (0.0)	4 (0.0)	0 (0.0)	2 (0.0)
Relative socioeconomic disadvantage						
Highest 20% (least disadvantaged)	3 (11.5)	426 (10.3)	1 (1.1)	114 (1.0)	0 (0.0)	9 (0.2)
Lowest 20% (most disadvantaged)	8 (30.8)	1123 (27.1)	26 (27.4)	3413 (28.9)	25 (64.1)	2827 (68.4)
p value	0.792*		0.795*		0.636*	
missing	0 (0.0)	0 (0.0)	0 (0.0)	25 (0.2)	0 (0.0)	12 (0.3)
Any smoking during pregnancy						
Yes	13 (56.5)	1903 (45.9)	59 (62.1)	6447 (54.5)	23 (59.0)	2247 (54.2)
p value	0.342		0.054		0.575	
missing	3 (11.5)	60 (1.4)	4 (4.2)	46 (0.4)	0 (0.0)	21 (0.5)
Substance Use during pregnancy						
Yes	5 (19.2)	147 (3.6)	5 (5.3)	152 (1.3)	1 (2.6)	33 (0.8)
p value	0.002*		0.008*		0.274*	

Characteristics	Indigenous (n=20273)					
	Major City (n=4169)		Regional (n=11920)		Remote (n=4184)	
	Stillbirth (n=26)	Livebirth (n=4143)	Stillbirth (n=95)	Livebirth (n=11825)	Stillbirth (n=39)	Livebirth (n=4145)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Accommodation status						
Public patient	25 (96.2)	3949 (95.3)	93 (97.9)	11613 (98.2)	39 (100.0)	4134 (99.7)
p value	1.000*		0.689*		1.000*	
Assisted Conception						
Yes	0 (0.0)	51 (1.2)	1 (1.1)	33 (0.3)	0 (0.0)	7 (0.2)
p value	1.000*		0.238*		1.000*	
Primigravidity						
Yes	6 (23.1)	1022 (24.7)	24 (25.3)	2816 (23.8)	7 (18.0)	959 (23.1)
p value	0.851		0.741		0.444	
Number of antenatal care visits						
Less than 2	8 (30.8)	174 (4.2)	22 (23.2)	650 (5.5)	17 (43.6)	231 (5.6)
2 – 4	10 (38.5)	700 (16.9)	35 (36.8)	2007 (17.0)	12 (30.8)	641 (15.5)
5 – 7	3 (11.5)	1160 (28.1)	15 (15.8)	3427 (29.0)	5 (12.8)	1218 (29.4)
8 or more	5 (19.2)	2101 (50.8)	21 (22.1)	5731 (48.5)	5 (12.8)	2048 (49.5)
p value	<0.001		<0.001		<0.001	
missing	0 (0.0)	8 (0.2)	2 (2.1)	10 (0.1)	0 (0.0)	7 (0.2)
Gestational age at birth						
<24 weeks	8 (30.8)	5 (0.1)	33 (34.7)	36 (0.3)	15 (38.5)	12 (0.3)
24-27 weeks	2 (7.7)	17 (0.4)	11 (11.6)	67 (0.6)	8 (20.5)	26 (0.6)
28-32 weeks	5 (19.2)	53 (1.3)	10 (10.5)	220 (1.9)	6 (15.4)	78 (1.9)
33-36 weeks	2 (7.7)	298 (7.2)	12 (12.6)	934 (7.9)	5 (12.8)	327 (7.9)
≥37 weeks	9 (34.6)	3768 (91.0)	29 (30.5)	10559 (89.4)	5 (12.8)	3702 (89.3)
p value	<0.001*		<0.000		<0.001*	
missing	0 (0.0)	2 (0.0)	0 (0.0)	8 (0.1)	0 (0.0)	0 (0.0)
Baby's gender						
Male	11 (42.3)	2137 (51.6)	56 (59.6)	6089 (51.5)	26 (66.7)	2105 (50.8)
p value	0.346		0.118		0.048	
missing	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
Small-for-gestational age						
Yes	11 (42.3)	532 (12.9)	36 (37.9)	1899 (16.1)	11 (28.2)	590 (14.2)
p value	<0.001		<0.001		0.013	
missing	0 (0.0)	2 (0.0)	3 (3.2)	11 (0.1)	0 (0.0)	0 (0.0)
Antepartum haemorrhage						
Yes	8 (30.8)	107 (2.6)	24 (25.3)	221 (1.9)	12 (30.8)	84 (2.0)
p value	<0.001		<0.001		<0.001	
Essential hypertension (with or without superimposed pre-eclampsia)						
Yes	0 (0.0)	30 (0.7)	6 (6.3)	109 (0.9)	1 (2.6)	51 (1.2)
p value	1.000*		<0.001		0.387*	
Eclampsia/Pre-eclampsia						
Yes	0 (0.0)	84 (2.0)	4 (4.2)	321 (2.7)	1 (2.6)	169 (4.1)
p value	1.000*		0.332*		1.000*	

Characteristics	Indigenous (n=20273)					
	Major City (n=4169)		Regional (n=11920)		Remote (n=4184)	
	Stillbirth (n=26)	Livebirth (n=4143)	Stillbirth (n=95)	Livebirth (n=11825)	Stillbirth (n=39)	Livebirth (n=4145)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Pregnancy Induced hypertension						
Yes	0 (0.0)	100 (2.4)	1 (1.1)	271 (2.3)	0 (0.0)	117 (2.8)
p value	1.000*		0.727*		0.627*	
Pre-existing diabetes						
Yes	2 (7.7)	37 (0.9)	7 (7.4)	142 (1.2)	3 (7.7)	69 (1.7)
p value	0.024*		<0.001		0.029*	
Gestational diabetes						
Yes	1 (3.9)	201 (4.9)	3 (3.2)	777 (6.6)	0 (0.0)	346 (8.4)
p value	1.000*		0.215*		0.072*	

Percentages may add up to greater than 100% due to rounding ICD10-AM codes: Antepartum haemorrhage (O44.1, O45-46), Essential hypertension (O10.0, O10.2-10.4, O10.9, O11), Pregnancy Induced hypertension (O13), Pre-eclampsia/Eclampsia (O14, O15), Pre-existing diabetes (O24.0, O24.1, O24.3, O24.8), Gestational diabetes (O24.4, O24.9).

In Table 4.7 is presented the distribution of maternal, medical and obstetric factors by birth outcome and geographic location for non-Indigenous women. Maternal age profile for non-Indigenous women was significantly different between those with a stillbirth and those with a livebirth. Among women with a stillbirth, there was a higher proportion of younger women aged 18 years or younger in urban, regional and remote areas; there was also a higher proportion of older women aged 35 years or older in urban and regional areas.

Regardless of geographic location, non-Indigenous women with a stillbirth were more likely to: attend fewer antenatal care visits, not have a domestic partner, have a preterm birth, have a growth restricted infant and antepartum haemorrhage. Among women living in urban areas, non-Indigenous women with a stillbirth were more likely to: smoke, have substance use issues, utilise health services as a public patient, have essential hypertension, pre-eclampsia or eclampsia and pre-existing diabetes. In contrast, non-Indigenous women with a stillbirth living in regional areas were more likely to: smoke, utilise health services as a public patient, utilise assisted conception technology, have essential hypertension, pre-eclampsia or eclampsia and gestational diabetes. Non-Indigenous women with a stillbirth in remote areas were more likely to be primigravid.

Table 4.7: Maternal and pregnancy characteristics by birth outcome and geographic location, non-Indigenous women, Queensland, mid 2005–2011

Characteristics	Non-Indigenous (n=340,714)					
	Major City (n=209,778)		Regional (n=122,590)		Remote (n=8,334)	
	Stillbirth (n=835)	Livebirth (n=208,943)	Stillbirth (n=525)	Livebirth (n=122,065)	Stillbirth (n=31)	Livebirth (n=8303)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Maternal age (years)						
≤18 years	19 (2.3)	2290 (1.1)	20 (3.8)	1985 (1.6)	3 (9.7)	85 (1.0)
19-24 years	177 (21.2)	36689 (17.6)	127 (24.2)	28968 (23.7)	8 (25.1)	1922 (23.2)
25-30 years	257 (30.8)	71128 (34.0)	166 (31.6)	44472 (36.4)	14 (45.2)	3212 (38.7)
31-34 years	190 (22.8)	53482 (25.6)	96 (18.3)	25790 (21.1)	4 (12.9)	1760 (21.2)
≥35 years	192 (23.0)	45354 (21.7)	116 (22.1)	20850 (17.1)	2 (6.5)	1324 (16.0)
p value	<0.001		<0.001		0.008*	
Marital Status						
Partner	680 (81.5)	183808 (88.0)	444 (84.7)	109596 (89.8)	24 (77.4)	7655 (92.2)
No partner	154 (18.5)	25097 (12.0)	80 (15.3)	12461 (10.2)	7 (22.6)	647 (7.8)
p value	<0.001		<0.001		0.002	
missing	1 (0.1)	38 (0.0)	1 (0.2)	8 (0.0)	0 (0.0)	1 (0.0)
Relative socioeconomic disadvantage						
Highest 20% (least disadvantaged)	182 (21.8)	49513 (23.7)	18 (3.5)	5368 (4.4)	1 (3.2)	541 (6.6)
Lowest 20% (most disadvantaged)	98 (11.7)	21390 (10.2)	84 (16.1)	16127 (13.2)	8 (25.8)	1796 (21.8)
p value	0.211		0.106		0.776*	
missing	0 (0.0)	3 (0.0)	3 (0.6)	281 (0.2)	0 (0.0)	64 (0.8)
Any smoking during pregnancy						
Yes	172 (21.3)	29809 (14.4)	154 (30.1)	25069 (20.6)	6 (19.4)	1505 (18.2)
p value	<0.001		<0.001		0.795	
missing	28 (3.4)	1245 (0.6)	14 (2.7)	383 (0.3)	1 (3.2)	20 (0.2)
Substance Use during pregnancy						
Yes	12 (1.4)	1218 (0.6)	3 (0.6)	450 (0.4)	0 (0.0)	20 (0.2)
p value	0.001		0.450*		1.000*	
Accommodation status						
Public patient	634 (76.1)	133001 (63.7)	423 (80.6)	89416 (73.3)	27 (87.1)	6207 (74.8)
p value	<0.001		<0.001		0.146	
missing	2 (0.2)	0 (0.0)	0 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)
Assisted Conception						
Yes	41 (4.9)	9418 (4.5)	23 (4.4)	3216 (2.6)	2 (6.5)	209 (2.5)
p value	0.570		0.012		0.176	
missing	1 (0.1)	3 (0.0)	2 (0.4)	15 (0.0)	1 (3.2)	2 (0.0)
Primigravidity						
Yes	263 (31.5)	64544 (30.9)	137 (26.2)	34683 (28.4)	17 (54.8)	2444 (29.4)

Characteristics	Non-Indigenous (n=340,714)					
	Major City (n=209,778)		Regional (n=122,590)		Remote (n=8,334)	
	Stillbirth (n=835)	Livebirth (n=208,943)	Stillbirth (n=525)	Livebirth (n=122,065)	Stillbirth (n=31)	Livebirth (n=8303)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
p value	0.705		0.250		0.002	
missing	0 (0.0)	1 (0.0)	1 (0.2)	1 (0.0)	0 (0.0)	0 (0.0)
Number of antenatal care visits						
Less than 2	94 (11.3)	1290 (0.6)	48 (9.2)	812 (0.7)	5 (16.1)	40 (0.5)
2 – 4	264 (31.6)	10392 (5.0)	187 (35.8)	6027 (4.9)	8 (25.8)	469 (5.7)
5 – 7	221 (26.5)	38642 (18.5)	136 (26.0)	22540 (18.5)	10 (32.3)	1835 (22.1)
8 or more	247 (29.6)	158528 (75.9)	152 (29.1)	92602 (75.9)	8 (25.8)	5954 (71.8)
p value	<0.001		<0.001		<0.001*	
missing	9 (1.1)	91 (0.0)	2 (0.4)	84 (0.1)	0 (0.0)	5 (0.1)
Gestational age at birth						
<24 weeks	272 (32.7)	163 (0.1)	170 (32.4)	75 (0.1)	9 (29.0)	5 (0.1)
24-27 weeks	113 (13.6)	362 (0.2)	81 (15.4)	275 (0.2)	5 (16.1)	21 (0.3)
28-32 weeks	113 (13.6)	1645 (0.8)	68 (13.0)	1014 (0.8)	4 (12.9)	55 (0.7)
33-36 weeks	120 (14.4)	10386 (5.0)	72 (13.7)	6052 (5.0)	3 (9.7)	370 (4.5)
≥37 weeks	215 (25.8)	196373 (94.0)	134 (25.5)	114644 (93.9)	9 (29.0)	7852 (94.6)
p value	<0.001		<0.001		<0.001	
missing	2 (0.2)	14 (0.0)	0 (0.0)	5 (0.0)	1 (3.2)	0 (0.0)
Baby's gender						
Male	439 (52.6)	107095 (51.3)	263 (50.1)	62865 (51.5)	12 (38.7)	4272 (51.5)
p value	0.426		0.520		0.210	
missing	1 (0.1)	1 (0.0)	0 (0.0)	0 (0.0)	1 (3.2)	0 (0.0)
Small-for-gestational age						
Yes	244 (29.2)	17174 (8.2)	160 (30.5)	10393 (8.5)	6 (19.4)	645 (7.8)
p value	<0.001		<0.001		0.007	
missing	9 (1.1)	27 (0.0)	3 (0.6)	20 (0.0)	3 (9.7)	2 (0.0)
Antepartum haemorrhage						
Yes	194 (23.2)	6025 (2.9)	136 (25.9)	2741 (2.3)	7 (22.6)	181 (2.2)
p value	<0.001		<0.001		<0.001	
Pre-existing hypertension (with or without superimposed pre-eclampsia)						
Yes	18 (2.2)	1293 (0.6)	12 (2.3)	831 (0.7)	1 (3.2)	65 (0.8)
p value	<0.001		<0.001		0.219*	
Eclampsia/Pre-eclampsia						
Yes	45 (5.4)	4085 (2.0)	32 (6.1)	2991 (2.5)	0 (0.0)	282 (3.4)
p value	<0.001		<0.001		0.626	
Pregnancy Induced hypertension						
Yes	17 (2.0)	5778 (2.8)	10 (1.9)	3776 (3.1)	0 (0.0)	343 (4.1)
p value	0.199		0.116		0.638*	
Pre-existing diabetes						

Characteristics	Non-Indigenous (n=340,714)					
	Major City (n=209,778)		Regional (n=122,590)		Remote (n=8,334)	
	Stillbirth (n=835)	Livebirth (n=208,943)	Stillbirth (n=525)	Livebirth (n=122,065)	Stillbirth (n=31)	Livebirth (n=8303)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Yes	15 (1.8)	1003 (0.5)	6 (1.1)	663 (0.5)	0 (0.0)	36 (0.4)
p value	<0.001		0.063		1.000*	
Gestational diabetes						
Yes	42 (5.0)	11234 (5.4)	16 (3.1)	6438 (5.3)	0 (0.0)	463 (5.6)
p value	0.658		0.023		0.416	

Data missing on geographic location for 12 births (1 stillbirth and 11 livebirths). Percentages may add up to greater than 100% due to rounding ^ ICD10-AM codes: . ICD10-AM codes: Antepartum haemorrhage (O44.1, O45-46), Essential hypertension (O10.0, O10.2-10.4, O10.9, O11), Pregnancy Induced hypertension (O13), Pre-eclampsia/Eclampsia (O14, O15), Pre-existing diabetes (O24.0, O24.1, O24.3, O24.8), Gestational diabetes (O24.4, O24.9).

Table 4.8 and 4.9 show adjusted odds ratios for stillbirth associated with antepartum haemorrhage, hypertension, diabetes and small-for-gestational age by gestational age group and Indigenous status for regional (Table 4.8) and remote residence (Table 4.9). No significant association was found between regional residence and stillbirth for all of the conditions examined. However, the results suggest differences in the gestational age specific risk profiles for Indigenous and non-Indigenous women. These differences were particularly evident at 28-32 weeks and 33-36 weeks. At 28-32 weeks, regional residence was associated with 28-43% reduction in risk of stillbirth among Indigenous women and a 1-5% increase in risk among non-Indigenous women. Likewise at 33-36 weeks, regional residence was associated with 261-280% increased risk of stillbirth among Indigenous women compared with a 5-10% increase in risk for non-Indigenous women. However, none of these risk estimates reached statistical significance. Similarly, remote residence was not significantly associated with stillbirth after adjusting for other maternal factors for all the conditions examined. There were also marked differences in the gestational age specific risk profile between Indigenous and non-Indigenous women. For example, at 33-36 weeks, remote residence was associated with 295-330% increase in risk of stillbirth for Indigenous women, while among non-Indigenous women, remote residence was associated with 35-38% decreased risk of stillbirth. However, none of these risk estimates reached statistical significance.

Table 4.8: Gestational age-specific stillbirth risk by Indigenous status, regional areas, Queensland, mid 2005–2011

Conditions	Indigenous (n=20,273 births)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Antepartum haemorrhage^	1.62 (0.66-4.01)	1.26 (0.27-5.92)	0.72 (0.21-2.48)	3.80 (0.73-19.79)	1.38 (0.61-3.15)
Essential hypertension*~	1.58 (0.65-3.85)	1.25 (0.27-5.84)	0.62 (0.19-2.04)	3.71 (0.72-19.19)	1.28 (0.57-2.91)
Pre-Eclampsia/Eclampsia~	1.60 (0.66-3.90)	1.29 (0.28-6.00)	0.71 (0.22-2.32)	3.61 (0.71-18.48)	1.31 (0.58-2.97)
Pre-existing diabetes^~	1.58 (0.65-3.85)	1.25 (0.27-5.84)	0.62 (0.19-2.04)	3.71 (0.72-19.19)	1.28 (0.57-2.91)
Gestational diabetes^~	1.62 (0.66-3.95)	1.28 (0.27-5.97)	0.66 (0.20-2.18)	3.71 (0.72-19.04)	1.31 (0.58-2.97)
Small-for-gestational age	1.58 (0.65-3.85)	1.26 (0.27-5.89)	0.57 (0.17-1.92)	3.79 (0.73-19.84)	1.28 (0.57-2.89)
Conditions	**Non-Indigenous (n=340,714 births)**				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Antepartum haemorrhage^	1.12 (0.91-1.38)	1.30 (0.96-1.76)	1.05 (0.76-1.44)	1.10 (0.81-1.50)	1.09 (0.87-1.37)
Essential hypertension*	1.13 (0.92-1.39)	1.30 (0.96-1.75)	1.03 (0.75-1.41)	1.05 (0.77-1.42)	1.05 (0.84-1.32)
Pre-eclampsia/Eclampsia	1.12 (0.91-1.38)	1.29 (0.96-1.75)	1.02 (0.74-1.40)	1.05 (0.77-1.42)	1.05 (0.83-1.31)
Pre-existing diabetes^	1.13 (0.92-1.39)	1.30 (0.96-1.75)	1.03 (0.75-1.41)	1.05 (0.77-1.42)	1.05 (0.84-1.32)
Gestational diabetes^	1.13 (0.91-1.38)	1.30 (0.96-1.75)	1.02 (0.75-1.41)	1.05 (0.77-1.43)	1.05 (0.84-1.32)
Small-for-gestational age	1.10 (0.89-1.36)	1.28 (0.95-1.74)	1.01 (0.74-1.39)	1.06 (0.78-1.44)	1.05 (0.84-1.32)

All models adjusted for maternal age, smoking status, gravidity, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. [a]Indigenous models include the following interaction terms: smoking*maternal age and marital status*maternal age. [b] Non-Indigenous models include the following interaction term: smoke*FGR10. ^These models additionally adjusted for pre-existing hypertension. *These models additionally adjusted for pre-existing diabetes. ~Exact logistic regression model

Table 4.9: Gestational age-specific stillbirth risk by Indigenous status, remote areas, Queensland, mid 2005–2011

Conditions	Indigenous (n=20,273 births)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Antepartum haemorrhage^	1.83 (0.68-4.95)	2.53 (0.51-12.46)	1.24 (0.30-5.14)	4.01 (0.65-24.83)	0.77 (0.24-2.53)
Essential hypertension*~	2.11 (0.80-5.58)	2.97 (0.61-14.34)	1.34 (0.35-5.03)	3.95 (0.64-24.54)	0.72 (0.22-2.34)
Pre-Eclampsia/Eclampsia~	2.16 (0.52-5.71)	3.07 (0.64-14.84)	1.65 (0.44-6.17)	4.00 (0.66-24.41)	0.75 (0.23-2.43)
Pre-existing diabetes^~	2.11 (0.80-5.58)	2.97 (0.61-14.34)	1.34 (0.35-5.03)	3.95 (0.64-24.54)	0.72 (0.22-2.34)
Gestational diabetes^~	2.19 (0.83-5.79)	3.05 (0.63-14.77)	1.39 (0.37-5.24)	4.04 (0.66-24.75)	0.77 (0.24-2.49)
Small-for-gestational age	2.12 (0.80-5.60)	3.01 (0.63-14.52)	1.37 (0.36-5.14)	4.30 (0.69-26.78)	0.77 (0.24-2.48)
Conditions	**Non-Indigenous (n=340,714 births)**				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Antepartum haemorrhage^	0.65 (0.31-1.34)	1.00 (0.40-2.50)	0.87 (0.32-2.37)	0.65 (0.21-2.06)	1.10 (0.56-2.15)
Essential hypertension*	0.67 (0.33-1.37)	1.04 (0.42-2.56)	0.84 (0.31-2.30)	0.63 (0.20-1.99)	1.07 (0.55-2.08)
Pre-eclampsia/Eclampsia	0.71 (0.35-1.45)	0.98 (0.40-2.42)	0.80 (0.29-2.18)	0.62 (0.20-1.97)	1.04 (0.53-2.03)
Pre-existing diabetes^	0.67 (0.33-1.37)	1.04 (0.42-2.56)	0.84 (0.31-2.30)	0.63 (0.20-1.99)	1.07 (0.55-2.08)
Gestational diabetes^	0.68 (0.33-1.39)	1.03 (0.42-2.55)	0.84 (0.31-2.29)	0.63 (0.20-1.98)	1.06 (0.54-2.08)
Small-for-gestational age	0.73 (0.36-1.50)	0.90 (0.33-2.46)	0.86 (0.32-2.35)	0.65 (0.21-2.06)	1.08 (0.55-2.12)

All models adjusted for maternal age, smoking status, gravidity, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. [a]Indigenous models include the following interaction terms: smoking*maternal age and marital status*maternal age. [b] Non-Indigenous models include the following interaction term: smoke*FGR10. ^These models additionally adjusted for pre-existing hypertension. *These models additionally adjusted for pre-existing diabetes. ~Exact logistic regression model

4.4 Discussion

Main findings

The first objective of this study was to describe the absolute risk of stillbirth by gestational age among Indigenous women and non-Indigenous women. The profile was characterised by low risk during much of the gestational ages; with a dramatic increase in risk around term. This profile of all-cause stillbirth risk was similar to profiles reported in USA and UK populations using a fetus-at-risk methodology [187, 227]. However, the overall magnitude of risk for Indigenous women was about twice that of non-Indigenous women.

The second objective of our study was to examine the gestational age specific risk of stillbirth associated with diabetes, hypertension, small-for-gestational age and antepartum haemorrhage. The prevalence of these conditions in our study was comparable to national estimates [24] and international estimates from other high income countries [32]. There were differences in the profile and magnitude of risk between Indigenous and non-Indigenous women. This study found increased odds of stillbirth associated with pre-existing diabetes, pre-existing hypertension, antepartum haemorrhage and small for gestational age across most gestational age groups for both Indigenous and non-Indigenous women. However, there were mixed results for pre-eclampsia/eclampsia and gestational diabetes. The odds of stillbirth for pre-existing diabetes and small for gestational age were twice as high for Indigenous women as non-Indigenous women.

The third objective of this study was to examine the effect of geographic location on gestational age specific risk of stillbirth associated with the aforementioned conditions of interest. The findings suggest an elevated risk of stillbirth for Indigenous women living in regional and remote areas particularly around 33-36 weeks. There was also a suggestion of increased risk of stillbirth for non-Indigenous women living in regional areas. These findings mirror reports of higher rates of stillbirth among Indigenous women living in regional and remote areas [190, 223]. There is evidence for the need to improve the quality of antenatal care for Indigenous women living in remote areas [231].

Interpretation of findings

Diabetes

Increased risk of stillbirth associated with pre-existing diabetes was found from 33 weeks onwards for both Indigenous and non-Indigenous women. Similar findings of increased risk of stillbirth due to pre-existing diabetes from 32 weeks onwards have been reported elsewhere [35, 232]. A two-fold disparity in the magnitude of stillbirth risk associated with pre-existing diabetes between Indigenous and non-Indigenous women also mirror higher rates of pre-existing diabetes among Indigenous women in this study (1.3% vs 0.5%). Higher rates of pre-existing diabetes among pregnant Indigenous women have also been reported nationally [89]. Furthermore, there was disparity in the population attributable fractions associated with pre-existing diabetes among Indigenous and non-Indigenous women (7.4% vs 1.6%); however, these were similar to those reported for other high income countries (3-5%) [32]. Similarly, this study found increased risk of stillbirth due to gestational diabetes from 28 weeks onwards, in concordance with Hutcheon and colleagues [233]. It has been argued that the 'protective' effect observed in relation to gestational diabetes at earlier gestational ages may be due to routine screening for GDM around 24-28 weeks [233]. There is evidence of higher rates of increase in gestational diabetes among non-Indigenous women, despite currently lower absolute rates of GDM compared with Indigenous women [87].

Current management for pre-existing diabetes includes strict glycaemic control, pre-conceptual folate supplementation, cessation of oral hypoglycaemic agents, diabetes complication review, periodic ultrasound scans for fetal morphology (18-20 weeks), cardiac views (24 weeks), fetal growth (28-30 and 34-36 weeks)[13]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommend screening all women at their first antenatal visit for gestational diabetes or previously undiagnosed pre-existing diabetes [234]; however, Australian and New Zealand guidelines recommend a tiered approach with early screening of women at high risk or with multiple risk factors [9, 235]. Perinatal mortality audits in high income countries have identified poor glycaemic control [236, 237] and inadequate screening among women at risk [238] as suboptimal care factors associated with stillbirth. Conversely, pre-pregnancy counselling has been found to significantly lower the risk of major congenital anomalies associated with diabetes during pregnancy (RR 0.36, 95% CI 0.22-0.59; absolute risk 2.1% versus 6.5%) [9]. Pre-conception care was found to reduce perinatal mortality while optimal vs suboptimal serum

blood glucose control was associated with reduced perinatal mortality (RR 0.40, 95% CI 0.25-0.63) but not stillbirth (RR 0.51 95% CI 0.14-1.88) [239]. Our findings highlight the need for early initiation of monitoring of women with pre-existing diabetes, especially for Indigenous women; and early identification and management of gestational diabetes.

Hypertension

An increased risk of stillbirth associated with pre-existing hypertension was suggested at all gestational ages assessed; and pre-eclampsia/eclampsia was likely to be associated with increased risk of stillbirth (although the numbers were small and did not reach statistical significance). However, increased risk of stillbirth associated with pre-existing hypertension and pregnancy induced hypertension has been reported by others [35]. Our findings in relation to population attributable risk associated with pre-existing hypertension [(1.7% for Indigenous women and 0.2% for non-Indigenous women] was much lower than national estimates (6.9%) and estimates from other high income countries (7-14%) [32]. However, our estimate of 3.5% among non-Indigenous women was similar to findings from other high income countries (about 3%) [32].

The main objectives of antenatal care for women with hypertensive disorders during pregnancy are: blood pressure control, early diagnosis of pre-eclampsia, eclampsia prevention and optimising pregnancy outcomes [94].

Antepartum Haemorrhage

This study found increased risk of stillbirth due to antepartum haemorrhage at all gestational age groups assessed; and the magnitude of risk for Indigenous women was nearly two fold higher than for non-Indigenous women. Despite differences in methodology, similar magnitude of risk has been reported in population based studies from Canada and USA with adjusted odds ratios ranging from 11.40-18.90 for stillbirth associated with placental abruption in births of at least 20 weeks [240, 241]. Our study found population attributable fractions associated with antepartum haemorrhage of 28.5% and 22.4% for Indigenous and non-Indigenous women, respectively. This is comparable to estimates of 15.2% for abruption only in other high income countries [32]. The disparity in risk seen between Indigenous and non-Indigenous women may be a reflection of higher

prevalence of risk factors for placenta praevia and abruption such as maternal smoking (52.7% vs 16.6%), substance use (1.7% vs 0.5%) and small for gestational age (15.2% vs 8.4%). At present, there is limited evidence for the prediction or prevention of abruption; and antepartum haemorrhage usually constitutes a sudden obstetric emergency. The mainstay of management includes: assessment of maternal and fetal condition, prompt resuscitation if required and early delivery if there is fetal distress or the baby is suitably mature [242, 243]. It is estimated that up to 70% of APH cases occur in apparently low risk pregnancies [244].

Small-for-gestational age

Increased risk of stillbirth associated with SGA was found from 24 weeks onwards for both Indigenous and non-Indigenous women; and similar findings have been reported elsewhere [35]. Although not reflected in the stillbirth risk, Indigenous women in this study had higher prevalence of SGA (15.2% vs 8.4%), similar to reports from the Northern Territory (Indigenous 11.9% vs non-Indigenous 5.0%) [245]. The higher prevalence of SGA was also not reflected in the population attributable risk (16.9% for Indigenous women versus 20.0% for non-Indigenous women), which was similar to estimates from other high income countries (23%) [32]. Indigenous women in this study also had higher prevalence of risk factors for SGA as follows: maternal smoking (52.7% vs 16.6%), substance use (1.7% vs 0.5%), pre-existing hypertension (1.0% vs 0.7%), diabetes (7.9% vs 5.8%) and pre-eclampsia/eclampsia (2.9% vs 2.2%). This study found the risk of stillbirth associated with SGA was modified by maternal smoking status, as has been reported by others [246, 247]. The association between SGA and placental dysfunction has been established [248]; however, the interaction with smoking suggests there may be other factors at play in the aetiology of stillbirth among maternal non-smokers.

SGA has been used as a proxy for fetal growth restriction and undetected fetal growth restriction has been identified as a significant potentially modifiable risk factor for stillbirth [247]. There are currently no antenatal interventions to treat fetal growth restriction and the mainstay of management is fetal monitoring to determine the optimal timing for delivery (balancing risks and benefits of adverse fetal outcomes against morbidity and mortality associated with early delivery at a given gestational age) [248]. Management for SGA involves accurate determination of gestational age and serial monitoring of fetal growth (using symphysis-fundal height measurement or ultrasound biometry). However,

controversy exists over the accuracy of symphysis-fundal height measurement especially in obese women [249] and the use of customised growth charts due to lack of high level evidence [250]. A number of interventions have been found to be effective in the prevention of SGA among women at increased risk, including: antiplatelet agents, smoking cessation, progesterone therapy, anti-thrombotic therapy and interventionist care in severe pre-eclampsia [251]. Further studies are needed into preventive strategies for SGA that also include pre-eclampsia and preterm birth [251], as well as investigating the serious adverse effects of antenatal antithrombotic therapies [252].

Equity in access to antenatal care

Overall, this study highlights the importance of optimal maternal health prior to pregnancy as well as early initiation of high quality antenatal care in the context of continued disparity in risk of stillbirth among Indigenous and non-Indigenous women. Equity in access and utilisation antenatal care services is important to addressing disparities in health outcomes for Indigenous women [197]. Indigenous women in our study were more likely to have fewer antenatal care visits, a finding supported by others [24, 200]. Limited availability of culturally appropriate services may affect attendance for antenatal care; for example there were on average 5.5 antenatal care visits within mainstream services versus 10.5 visits within community controlled services setting for Indigenous women [253]. Active efforts to ensure appropriate and responsive care in the clinical environment both at the level of the individual health practitioner and within mainstream health care services are essential to reduce or eliminate social barriers to accessing health care. Embedding cultural competence in continuing organisational quality improvement processes has been shown to enhance health outcomes for Indigenous people [254]. This is especially important for Indigenous women who seek care within mainstream health services. Factors affecting provision of high quality antenatal care to Indigenous women are likely to be different in rural and remote areas because of the challenges of delivering services to small discrete communities in sparsely populated areas; a limited workforce has been identified as such [253].

The Australian government has recognised the importance of maternal and child health to the “Closing the Gap” initiative and has prioritised maternal and child health [255]. It has been shown that an investment in stillbirth prevention provides a three-fold return in terms of maternal, neonatal and child health [256]. While there has been continued support for

community controlled health centres and their Mums and Bubs centres, many health and lifestyle modification programs have been defunded. Declines seen in smoking and under-5 child mortality rates are further evidence for the need to maintain funding for successful lifestyle modification programs and antenatal care services operated by the community controlled health services [255]. More broadly, access to primary care services is critical to reducing health inequity and policies that undermine universal health care pose a significant threat to this goal by presenting further financial barriers that are likely to disproportionately affect the most vulnerable [257].

4.5 Conclusion

In summary, this study highlights the stillbirth risk associated with diabetes, hypertension, antepartum haemorrhage and small for gestational age. It also highlights the disparity in stillbirth risk between Indigenous and non-Indigenous women and the need to prioritise early detection and management of these conditions and to work with women before, during and between pregnancies. Improving access to and utilisation of appropriate and responsive healthcare may help to address disparities in stillbirth risk for Indigenous women.

Chapter 5

Prediction of term antepartum stillbirth risk

5.1 Introduction

In Chapter 3 and 4 it was shown that stillbirth rates at term have not decreased for Indigenous women and stillbirth risk varies with gestational age and increases sharply around term. At present, fetal deaths occurring prior to delivery (antepartum stillbirths) constitute nearly 80% of stillbirths within the Queensland and Australian context [258]. Risk factors for antepartum stillbirth include advanced maternal age, smoking, primiparity, pre-existing hypertension and pre-existing diabetes [259]. There is significantly increased risk of antepartum stillbirth beyond 40 weeks gestation for older (aged 40 years or older) and primiparous women [259]. These deaths may potentially be preventable by elective delivery; however, this is dependent on gestational age [260]. While elective delivery at extremely premature gestation may lead to neonatal death or survival with long-term morbidity or disability [261]; there is also increased risk of morbidity [262] and long term mortality associated with delivery at early term (37-38 weeks) gestation [263]. Therefore, the timing of elective delivery during early term gestation requires careful consideration of the risk of stillbirth with continuation of the pregnancy versus the risk of morbidity and mortality associated with delivery. Therefore, the ability to predict pregnancies at increased risk of stillbirth around term is important to preventing term antepartum stillbirths.

A number of studies have examined the ability to predict stillbirth risk at term using maternal factors alone [230, 264], and could not recommend screening pregnancies based on individual maternal factors alone [264]. Furthermore, a recent systematic review assessing the ability of ultrasound biometry and biomarker testing during the first and second trimester to predict stillbirth found that such testing either singly or in combination was not useful in predicting stillbirth, however, uterine artery pulsativity index and pregnancy associated plasma protein A during the first trimester were useful to predicting stillbirths related to placental dysfunction [265]. At present, only a few studies have been undertaken to predict antepartum stillbirth risk around term within the Australian context. From Chapter 3, we found geographic location was an important risk factor for stillbirth in the Australian context, especially for Indigenous women. We found that Indigenous

women living in regional and remote areas had significantly higher rates of stillbirth than their counterparts living in major cities.

In this study, the aim was to determine whether geographic location of maternal usual residence could improve the ability of a statistical model based on maternal clinical factors to detect women at increased risk of antepartum stillbirth at term. The specific objectives of this study were to: 1) derive and validate a statistical model to predict antepartum stillbirth for pregnancies that reach 37 weeks gestation, based on maternal clinical factors available in a routinely-maintained population-based perinatal database, 2) assess the effect of addition of geographic location to the described model, and 3) determine the screening properties of the models.

Presented in this chapter are findings from this population based study (n=352,515 singleton term births).

5.2 Methods

Study Population

This population based retrospective database study involved all singleton livebirths and stillbirths of at least 37 weeks gestational age born in Queensland between July 2005 and December 2011. This time period was chosen to maximise the available data on maternal characteristics such as smoking status and whether or not a woman had diabetes (pre-existing or gestational) which have been found to be associated with stillbirth [32]. There were 379 102 singleton births registered in Queensland during this period. Of these, 108 births with unknown maternal Indigenous status were excluded as were a further 100 births resulting in intrapartum stillbirth or stillbirths where it was unknown if the timing of death was antepartum or intrapartum (Figure 5.1).

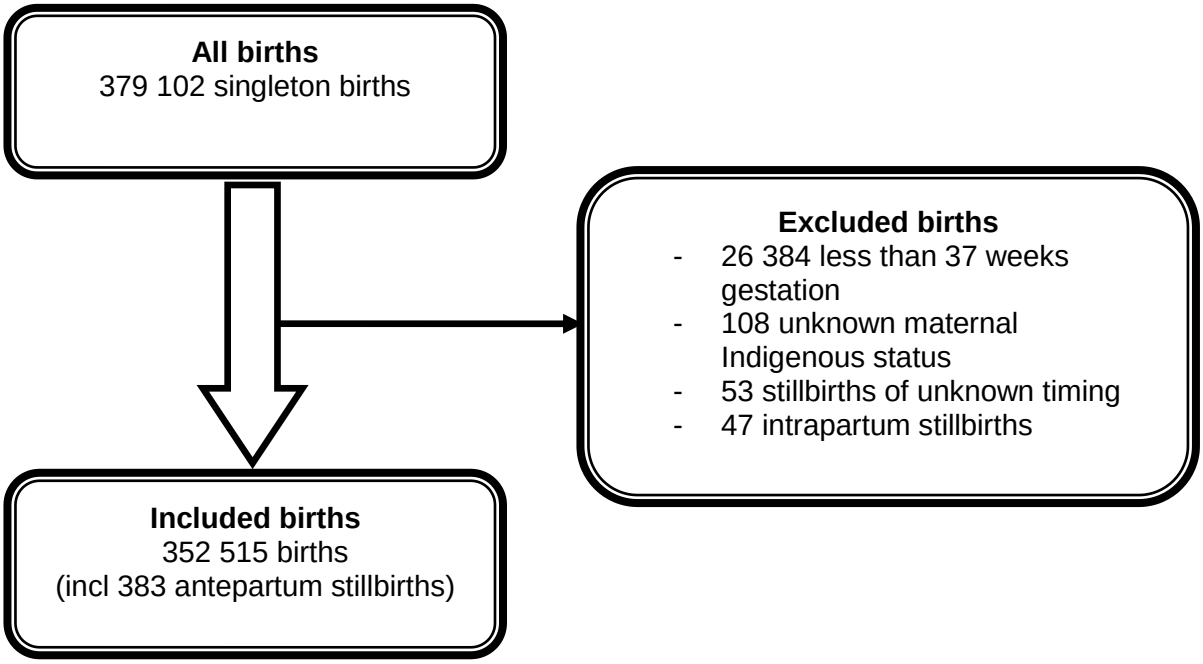


Figure 5.1: Flowchart showing study population and exclusions, Stillbirth Risk Prediction Study, mid 2005-2011

Statistical Analysis

The K fold approach was utilised to derive and validate the stillbirth risk prediction models. The study population was randomly divided into 8 roughly equal groups. Differences in the characteristics of the subgroups were assessed using Chi square or Fisher's exact test,

where appropriate. Within each 'fold', one subgroup was designated the validation cohort and the other seven subgroups combined were designated the derivation cohort. As shown in Figure 5.2, each subgroup was subsequently designated as the validation cohort.

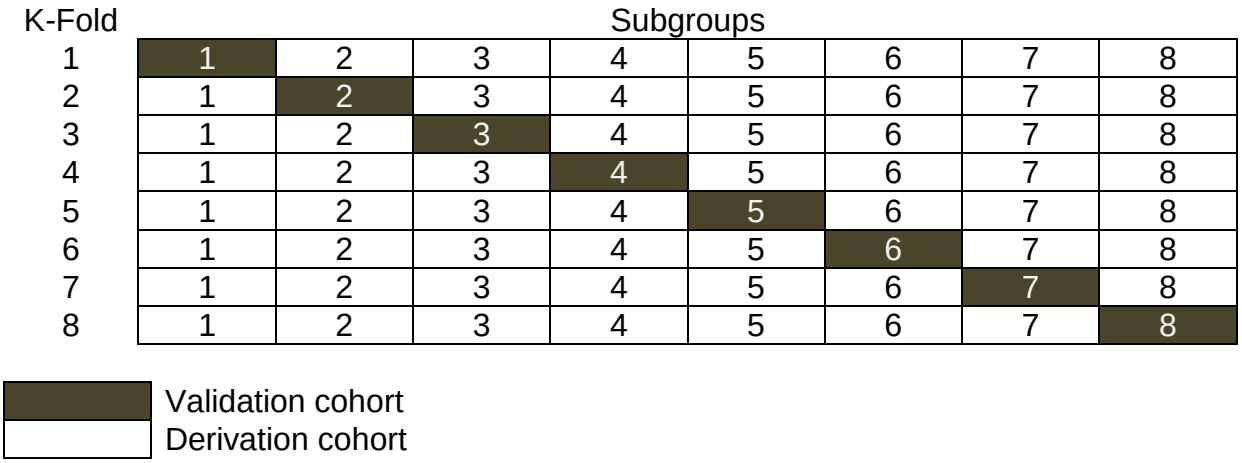


Figure 5.2: Diagram showing derivation and validation cohorts within 8 folds

Selection of variables and fitting the model

Using the derivation cohort, univariate logistic regression was used to assess the relationship between maternal sociodemographic, pregnancy and medical factors and the outcome of antepartum stillbirth. All factors associated with antepartum stillbirth ($p<0.05$) were retained in the multivariate logistic regression model except gestational age. The effect of gestational age on the multivariate model as a categorical and continuous variable was assessed and found to be minimal. Other population based studies did not adjust for gestational age within the strata of ≥37 week births [230, 264]. Furthermore, the variable fetal growth included in the model was derived from birthweight and gestational age. For these reasons, gestational age was not included in the final multivariate model. Factors such as primiparity and socioeconomic status were considered for inclusion in the model because of *a-priori* knowledge of their association with stillbirth [32], however they were not significantly associated with antepartum stillbirth within this population and were ultimately not included in the multivariate model. An exploration of two way interactions between factors was undertaken informed by the literature [32]. Two significant interactions were found for maternal age*smoking status and pre-eclampsia/eclampsia*antepartum haemorrhage. The effects of these interaction terms

collectively and individually on the predictive ability of the multivariate model were assessed and they were ultimately not included in the model as the effect on the model was minimal. The final parsimonious model was then assessed with and without inclusion of geographic location.

To assess the proportion of stillbirths that would be eliminated if each of the factors associated with antepartum stillbirth was eliminated, population attributable risk or fractions (PAR/PAF) were calculated using the adjusted effect estimates. In the literature, the terms population attributable risk (PAR) and fraction (PAF) are used interchangeably.

Assessing performance of the predictive models

Calibration of the model with the validation cohort, that is agreement between predicted and observed probabilities of antepartum stillbirth or livebirth was assessed using the Hosmer-Lemeshow goodness of fit test [266]. The discriminative ability (or the ability of the model to differentiate low from high risk women) was assessed using the area under the receiver operating characteristics (ROC) curve [267]. The sensitivity, specificity, negative predictive and positive predictive values for the models using each of the eight validation cohorts were calculated. In order to obtain meaningful values for these screening characteristics, the cut-offs for the predicted probabilities were set at 0.01 and 0.005. This procedure was repeated for the remaining seven 'folds', so that each subgroup was used once as a validation cohort. The entire process was repeated for the parsimonious model including geographic location.

Validation of the model

This population based study utilised the k fold cross validation methodology to derive and validate the prediction model. Cross validation was used to address the issue of model overfitting which arises when a model performs well during derivation but poorly during later validation [268]. A number of cross validation methods were available, namely the hold-out, k-fold and leave-one-out (LOO) methods. The hold out method involves a single derivation and validation cohort and produces estimates with large variance depending on which data points are included in the respective cohorts [269]. In contrast, the k-fold method involves k trials in which the data is divided into k groups with each group used

once as the validation cohort and k-1 times as the derivation cohort [269]. Variance in the estimate is reduced as k increases. In contrast, the leave-one-out method is an extension of the k-fold method in which k=N, the number of data points in the dataset. One point is left out and derivation and validation is carried out on the remaining points and this is repeated N times. It has been reported that there is greater variance in the estimates of prediction error for the LOO cross validation than for K-fold validation [270]. For this reason, the k-fold methodology was utilised.

5.3 Results

Characteristics of the study population

A total of 352,515 singleton births were included in these analyses; among these were 383 antepartum stillbirths. The antepartum stillbirth rate was 1.1 per 1000 total births (95% CI 1.0-1.2 per 1000 total births). The characteristics of the study population are summarised in Table 5.1. Of 352 515 women, 5595 (1.6%) were aged 18 years or younger while 6658 (1.9%) were 41 years or older. About 5.3% of women self-identified as Aboriginal or Torres Strait Islander. A majority of women (60.1%) lived in major cities while 12.9% of women lived in the most socioeconomically disadvantaged neighbourhoods. About 18.3% of women reported smoking during pregnancy and nearly a third (29.7%) were primiparous. The prevalence of pre-existing diabetes and pre-existing hypertension were 0.4% and 0.6% among the study population, respectively. As shown in Table 1, the distribution of maternal sociodemographic, pregnancy and medical characteristics was similar across the eight subgroups, including marital status although it was associated with a Chi square test result of p=0.021.

Table 5.1: Characteristics of the study population, by subgroups and total, mid 2005-2011

Characteristics	Group 1 (n=44,070)	Group 2 (n=44,065)	Group 3 (n=44,064)	Group 4 (n=44,065)	Group 5 (n=44,064)	Group 6 (n=44,066)	Group 7 (n=44,061)	Group 8 (n=44,060)	Total (n=352,515)	p value
Maternal age (years)										
18 or less	686 (1.6)	648 (1.5)	708 (1.6)	701 (1.6)	746 (1.7)	716 (1.6)	698 (1.6)	692 (1.6)	5,595 (1.6)	
19-24	9,467 (21.5)	9,271 (21.0)	9,228 (20.9)	9,361 (21.2)	9,310 (21.1)	9,367 (21.3)	9,320 (21.2)	9,384 (21.3)	74,708 (21.2)	
25-30	15,341 (34.8)	15,333 (34.8)	15,366 (34.9)	15,283 (34.7)	15,266 (34.7)	15,239 (34.6)	15,301 (34.7)	15,271 (34.7)	122,400 (34.7)	0.931
31-34	10,231 (23.2)	10,316 (23.4)	10,227 (23.2)	10,244 (23.3)	10,295 (23.4)	10,246 (23.3)	10,174 (23.1)	10,297 (23.4)	82,030 (23.3)	
35-40	7,509 (17.0)	7 684 (17.4)	7 625 (17.3)	7 668 (17.4)	7 626 (17.3)	7 651 (17.4)	7 740 (17.6)	7 621 (17.3)	61,124 (17.3)	
40+	836 (1.9)	813 (1.9)	910 (2.1)	808 (1.8)	821 (1.9)	847 (1.9)	828 (1.9)	795 (1.8)	6,658 (1.9)	
Indigenous status										
Indigenous	2,331 (5.3)	2,251 (5.1)	2,365 (5.4)	2,348 (5.3)	2,351 (5.3)	2,341 (5.3)	2,343 (5.3)	2,446 (5.6)	18,776 (5.3)	
Non-Indigenous	41,739 (94.7)	41,814 (94.9)	41,699 (94.6)	41,717 (94.7)	41,713 (94.7)	41,725 (94.7)	41,718 (94.7)	41,614 (94.5)	333,739 (94.7)	0.261
Marital status										
Domestic partner	38 416 (87.2)	38 725 (87.9)	38 500 (87.4)	38 699 (87.8)	38 513 (87.4)	38 531 (87.5)	38 510 (87.4)	38 607 (87.6)	308 501 (87.5)	0.021
No Domestic partner	5 646 (12.8)	5 333 (12.1)	5 552 (12.6)	5 359 (12.2)	5548 (12.6)	5527 (12.5)	5546 (12.6)	5450 (12.4)	43,961 (12.5)	
Relative socioeconomic disadvantage										
Highest 20%	6,956 (15.8)	7,010 (15.9)	6,915 (15.7)	6,967 (15.8)	6,905 (15.7)	6,896 (15.7)	6,986 (15.9)	6,919 (15.7)	55,554 (15.8)	
Middle 60%	31,374 (71.3)	31,303 (71.1)	31,408 (71.4)	31,444 (71.4)	31,361 (71.3)	31,454 (71.5)	31,432 (71.4)	31,416 (71.4)	251,192 (71.3)	0.977
Lowest 20%	5,698 (12.9)	5,710 (13.0)	5,690 (12.9)	5,621 (12.8)	5,752 (13.1)	5,668 (12.9)	5,588 (12.7)	5,672 (12.9)	45,399 (12.9)	
Geographic location										
Major city	26 490 (60.1)	26 438 (60.0)	26 402 (59.9)	26 473 (60.1)	26 375 (59.9)	26 564 (60.3)	26 486 (60.1)	26 501 (60.2)	211 729 (60.1)	
Regional area	16 075 (36.5)	16 166 (36.7)	16 118 (36.6)	16 142 (36.6)	16 163 (36.7)	16 026 (36.4)	16 118 (36.6)	16 083 (36.5)	128 891 (36.6)	0.905
Remote area	1 503 (3.4)	1 458 (3.3)	1 544 (3.5)	1 449 (3.3)	1 526 (3.5)	1 475 (3.4)	1 456 (3.3)	1 476 (3.4)	11 887 (3.4)	
Maternal region of birth										
Africa	746 (1.7)	707 (1.6)	720 (1.6)	720 (1.6)	743 (1.7)	719 (1.6)	772 (1.8)	707 (1.6)	5 834 (1.7)	0.726*
Americas and	483 (1.1)	473 (1.1)	491 (1.1)	494 (1.1)	490 (1.1)	479 (1.1)	467 (1.1)	477 (1.1)	3 854 (1.1)	

Characteristics	Group 1 (n=44,070)	Group 2 (n=44,065)	Group 3 (n=44,064)	Group 4 (n=44,065)	Group 5 (n=44,064)	Group 6 (n=44,066)	Group 7 (n=44,061)	Group 8 (n=44,060)	Total (n=352,515)	p value
Caribbean										
East Asia	841 (1.9)	883 (2.0)	863 (2.0)	866 (2.0)	780 (1.8)	788 (1.8)	854 (1.9)	841 (1.9)	6 716 (1.9)	
Central, South & West Asia	783 (1.8)	787 (1.8)	782 (1.8)	795 (1.8)	775 (1.8)	813 (1.9)	850 (1.9)	794 (1.8)	6 379 (1.8)	
South East Asia	1 173 (2.7)	1 141 (2.6)	1 143 (2.6)	1 233 (2.8)	1 148 (2.6)	1 181 (2.7)	1 176 (2.7)	1 144 (2.6)	9 339 (2.7)	
Europe	1,849 (4.2)	1,947 (4.4)	1,921 (4.4)	1,968 (4.5)	1,901 (4.3)	1,854 (4.2)	1,950 (4.4)	1,840 (4.2)	15,230 (4.3)	
Australia & New Zealand	37,490 (85.1)	37,438 (85.0)	37,441 (85.0)	37,271 (84.6)	37,520 (85.2)	37,523 (85.2)	37,315 (84.7)	37,594 (85.4)	299,592 (85.0)	
Oceania (excl ANZ)	686 (1.6)	668 (1.5)	682 (1.6)	696 (1.6)	680 (1.5)	692 (1.6)	657 (1.5)	638 (1.5)	5,399 (1.5)	
Smoking during pregnancy	7,971 (18.2)	7,972 (18.2)	8,022 (18.3)	8,086 (18.4)	8,071 (18.4)	7,999 (18.2)	8,026 (18.3)	7,903 (18.0)	64,050 (18.3)	0.804
Substance Use during pregnancy	201 (0.5)	240 (0.5)	241 (0.6)	209 (0.5)	224 (0.5)	219 (0.5)	219 (0.5)	245 (0.6)	1,798 (0.5)	0.333
Assisted conception use	1,497 (3.4)	1,500 (3.4)	1,490 (3.4)	1,499 (3.4)	1,643 (3.7)	1,539 (3.5)	1,546 (3.5)	1,537 (3.5)	12,251 (3.5)	0.101
Primiparity	13,203 (30.0)	13,003 (29.5)	13,029 (29.6)	13,089 (29.7)	13,235 (30.0)	13,005 (29.5)	13,029 (29.6)	13,051 (29.6)	104,644 (29.7)	0.525
Hospital accommodation status										
Private	13,420 (30.5)	13,575 (30.8)	13,527 (30.7)	13,453 (30.5)	13,516 (30.7)	13,532 (30.7)	13,497 (30.6)	13,261 (30.1)	107,781 (30.6)	0.412
Public	30,650 (69.6)	30,490 (39.2)	30,537 (69.3)	30,610 (69.5)	30,547 (69.3)	30,534 (69.3)	30,564 (69.4)	30,799 (69.9)	244,731 (69.4)	
Hospital level										
Level 1	3,802 (8.6)	3,858 (8.8)	3,838 (8.7)	3,724 (8.5)	3,899 (8.9)	3,858 (8.8)	3,852 (8.7)	3,814 (8.7)	30,645 (8.7)	
Level 2	29,347 (66.6)	29,350 (66.6)	29,329 (66.6)	29,351 (66.6)	29,294 (66.5)	29,499 (66.9)	29,337 (66.6)	29,133 (66.1)	234,640 (66.6)	0.503
Level 3	10,551 (23.9)	10,515 (23.9)	10,553 (24.0)	10,633 (24.1)	10,498 (23.8)	10,378 (23.6)	10,499 (23.8)	10,745 (24.4)	84,372 (23.9)	
Number of antenatal visits										
Less than 2	352 (0.8)	319 (0.7)	324 (0.7)	303 (0.7)	311 (0.7)	308 (0.7)	309 (0.7)	321 (0.7)	2,547 (0.7)	
2-4	2,169 (4.9)	2,236 (5.1)	2,227 (5.1)	2,221 (5.0)	2,174 (4.9)	2,275 (5.2)	2,240 (5.1)	2,261 (5.1)	17,803 (5.1)	
5-7	8,167 (18.5)	8,054 (18.3)	8,244 (18.7)	8,057 (18.3)	8,121 (18.4)	8,242 (18.7)	8,083 (18.4)	8,299 (18.8)	65,267 (18.5)	0.514
8 or more	33,364 (75.7)	33,434 (75.9)	33,237 (75.5)	33,463 (76.0)	33,433 (75.9)	33,219 (75.4)	33,404 (75.9)	33,162 (75.3)	266,716 (75.7)	
Gestational age at birth										
mean(sd)	39.3 (1.1)	39.3 (1.2)	39.3 (1.2)	39.3 (1.1)	39.3 (1.1)	39.3 (1.1)	39.3 (1.2)	39.3 (1.1)	39.3 (1.1)	0.971^
37 weeks	2,726 (6.2)	2,824 (6.4)	2,835 (6.4)	2,767 (6.3)	2,721 (6.2)	2,803 (6.4)	2,831 (6.4)	2,813 (6.4)	22,320 (6.3)	0.959*

Characteristics	Group 1 (n=44,070)	Group 2 (n=44,065)	Group 3 (n=44,064)	Group 4 (n=44,065)	Group 5 (n=44,064)	Group 6 (n=44,066)	Group 7 (n=44,061)	Group 8 (n=44,060)	Total (n=352,515)	p value
38 weeks	9,183 (20.8)	9,077 (20.6)	9,058 (20.6)	9,090 (20.6)	9,087 (20.6)	8,976 (20.4)	9,063 (20.6)	9,022 (20.5)	72,556 (20.6)	
39 weeks	12,259 (27.8)	12,181 (27.7)	12,227 (27.8)	12,351 (28.0)	12,213 (27.7)	12,283 (27.9)	12,093 (27.5)	12,231 (27.8)	97,838 (27.8)	
40 weeks	13,373 (30.4)	13,414 (30.4)	13,335 (30.3)	13,334 (30.3)	13,427 (30.5)	13,384 (30.4)	13,491 (30.6)	13,388 (30.4)	107,146 (30.4)	
41 weeks	6,202 (14.1)	6,252 (14.2)	6,271 (14.2)	6,205 (14.1)	6,289 (14.3)	6,326 (14.4)	6,285 (14.3)	6,311 (14.3)	50,141 (14.2)	
42 weeks	319 (0.7)	306 (0.7)	327 (0.7)	308 (0.7)	319 (0.7)	286 (0.7)	291 (0.7)	288 (0.7)	2,444 (0.7)	
43 weeks	4 (0.0)	7 (0.0)	3 (0.0)	4 (0.0)	2 (0.0)	3 (0.0)	2 (0.0)	5 (0.0)	30 (0.0)	
Male sex	22,505 (51.1)	22,541 (51.2)	22,812 (51.8)	22,568 (51.2)	22,687 (51.5)	22,644 (51.3)	22,614 (51.3)	22,644 (51.4)	181,015 (51.4)	0.553
Small for gestational age	3,885 (8.8)	3,952 (9.0)	3,872 (8.8)	3,919 (8.9)	3,918 (8.9)	3,909 (8.9)	3,962 (9.0)	3,932 (8.9)	31,349 (8.9)	
Appropriate for gestational age	35,070 (79.6)	35,036 (79.5)	35,053 (79.6)	34,999 (79.4)	35,005 (79.5)	34,884 (79.2)	35,071 (79.6)	34,971 (79.4)	380,089 (79.5)	0.811
Large for gestational age	5,113 (11.6)	5,069 (11.5)	5,132 (11.7)	5,141 (11.7)	5,135 (11.7)	5,267 (12.0)	5,022 (11.4)	5,153 (11.7)	41,032 (11.6)	
Gestational diabetes	2,379 (5.4)	2,374 (5.4)	2,329 (5.3)	2,295 (5.2)	2,343 (5.3)	2,342 (5.3)	2,327 (5.3)	2,382 (5.4)	18,771 (5.3)	0.894
Pre-existing diabetes	186 (0.4)	187 (0.4)	210 (0.5)	177 (0.4)	198 (0.5)	208 (0.5)	179 (0.4)	180 (0.4)	1,525(0.4)	0.503
Pregnancy induced hypertension	1,267 (2.9)	1,324 (3.0)	1,277 (2.9)	1,282 (2.9)	1,321 (3.0)	1,237 (2.8)	1,242 (2.8)	1,243 (2.8)	10,193 (2.9)	0.471
Pre-eclampsia/Eclampsia	682 (1.6)	753 (1.7)	721 (1.6)	719 (1.6)	727 (1.7)	785 (1.8)	777 (1.8)	773 (1.8)	5,937 (1.7)	0.091
Pre-existing hypertension	257 (0.6)	256 (0.6)	271 (0.6)	257 (0.6)	257 (0.6)	249 (0.6)	245 (0.6)	290 (0.7)	2,082 (0.6)	0.605
Antepartum haemorrhage	878 (2.0)	848 (1.9)	903 (2.1)	937 (2.1)	873 (2.0)	880 (2.0)	886 (2.0)	876 (2.0)	7,081 (2.0)	0.609
Antepartum stillbirth	**46 (0.1)**	**42 (0.1)**	**51 (0.1)**	**50 (0.1)**	**51 (0.1)**	**48 (0.1)**	**50 (0.1)**	**45 (0.1)**	**383 (0.1)**	**0.980**

*Fisher's exact test ^ANOVA p value

Derivation of the prediction model

Table 5.2 shows the magnitude of univariate associations between maternal sociodemographic, pregnancy and medical factors and stillbirth as an indication of the univariate associations within the various derivation cohorts. For derivation cohort 1 (that is subgroups 2-8), factors associated with increased risk of stillbirth included: Indigenous race (OR 2.26, 95% CI 1.61-3.17), maternal age [19-24 years (OR 1.50, 95% CI 1.12-2.01) and ≥41 years (OR 2.57, 95% CI 1.44-4.60)], smoking during pregnancy (OR 1.96, 95% CI 1.55-2.47), substance use during pregnancy (OR 2.90, 95% CI 1.20-7.02) and accessing health care as a public patient (OR 1.64, 95% CI 1.26-2.13). Women who had a stillbirth were more likely to have pre-existing diabetes (OR 11.6, 95% CI 6.98-19.2) and pre-existing hypertension (OR 3.05, 95% CI 1.36-6.85)(Table 5.2). Geographic location was not associated with antepartum stillbirth.

Table 5.2: Univariate association between stillbirth and maternal factors for derivation cohort 1 (subgroups 2-8)

Characteristics	Stillbirth (n=337)	Livebirth (n=308 108)	Odds ratio (95% CI)
Maternal age (years)			
18 or less	7 (2.1)	4 902 (1.6)	1.64 (0.76-3.54)
19-24	85 (25.2)	65 156 (21.2)	1.50 (1.12-2.01)
25-30	93 (27.6)	106 966 (34.7)	1.00 (Ref)
31-34	78 (23.2)	71 721 (23.3)	1.25 (0.93-1.69)
35-40	61 (18.1)	53 554 (17.4)	1.31 (0.95-1.81)
41+	13 (3.9)	5 809 (1.9)	2.57 (1.44-4.60)
Indigenous status			
Indigenous	38 (11.3)	16 407 (5.3)	2.26 (1.61-3.17)
Non-Indigenous	299 (88.7)	291 701 (94.7)	1.00 (Ref)
Marital status			
No Partner	56 (16.7)	38 259 (12.4)	1.42 (1.06-1.89)
Partner	279 (83.3)	269 806 (87.6)	1.00 (Ref)
Socioeconomic disadvantage			
Highest 20%	41 (12.2)	48 557 (15.8)	1.00 (Ref)
Middle 60%	249 (73.9)	219 569 (71.3)	1.34 (0.97-1.87)
Lowest 20%	47 (14.0)	39 654 (12.9)	1.40 (0.92-2.13)
Geographic location			
Major city	207 (61.4)	185 032 (60.1)	1.00 (Ref)
Regional area	122 (36.2)	112 694 (36.6)	0.97 (0.77-1.21)
Remote area	8 (2.4)	10 376 (3.4)	0.69 (0.34-1.40)
Maternal Region of birth			
Africa	7 (2.1)	5 081 (1.7)	1.27 (0.60-2.69)
Americas and Caribbean	5 (1.5)	3 366 (1.1)	1.37 (0.57-3.32)
East Asia	4 (1.2)	5 871 (1.9)	0.63 (0.23-1.69)
Central, South & West Asia	8 (2.4)	5 589 (1.8)	1.32 (0.65-2.67)
South East Asia	8 (2.4)	8 158 (2.7)	0.90 (0.45-1.83)
Europe	10 (3.0)	13 371 (4.3)	0.69 (0.37-1.30)

Characteristics	Stillbirth (n=337)	Livebirth (n=308 108)	Odds ratio (95% CI)
Australia & New Zealand	284 (84.8)	261 818 (85.0)	1.00 (Ref)
Oceania (excl ANZ)	9 (2.7)	4 704 (1.5)	1.76 (0.91-3.43)
Smoking during pregnancy			
No	229 (69.6)	250 726 (81.8)	1.00 (Ref)
Yes	100 (30.4)	55 979 (18.3)	1.96 (1.55-2.47)
Substance Use during pregnancy			
No	332 (98.5)	306 516 (99.5)	1.00 (Ref)
Yes	5 (1.5)	1 592 (0.5)	2.90 (1.20-7.02)
Assisted Conception Use			
No	324 (96.7)	297 350 (96.5)	1.00 (Ref)
Yes	11 (3.3)	10 743 (3.5)	0.94 (0.52-1.71)
Primigravidity			
No	235 (69.9)	216 765 (70.4)	1.00 (Ref)
Yes	101 (30.1)	91 340 (29.7)	1.02 (0.81-1.29)
Hospital accommodation status			
Private	71 (21.2)	94 290 (30.6)	1.00 (Ref)
Public	264 (78.8)	213 817 (69.4)	1.64 (1.26-2.13)
Hospital level			
Level 1	24 (7.1)	26 819 (8.7)	0.77 (0.49-1.21)
Level 2	225 (66.8)	205 068 (66.6)	0.94 (0.73-1.21)
Level 3	86 (25.5)	73 735 (23.9)	1.00 (Ref)
Number of antenatal care visits			
Less than 2	14 (4.2)	2 181 (0.7)	7.30 (4.24-12.6)
2-4	36 (10.8)	15 598 (5.1)	2.62 (1.84-3.74)
5-7	79 (23.7)	57 021 (18.5)	1.58 (1.22-2.04)
8 or more	205 (61.4)	233 147 (75.7)	1.00 (Ref)
Gestational age at birth			
mean (sd)	*38.9 (1.4)*	*39.3 (1.1)*	*p<0.001**
37 weeks	66 (19.6)	19 528 (6.3)	1.00 (Ref)
38 weeks	84 (25.0)	63 289 (20.5)	0.39 (0.28-0.54)
39 weeks	67 (19.9)	85 512 (27.8)	0.23 (0.16-0.33)
40 weeks	76 (22.6)	93 697 (30.4)	0.24 (0.17-0.33)
41 weeks	36 (10.7)	43 903 (14.3)	0.24 (0.16-0.36)
42 weeks	6 (1.8)	2 119 (0.7)	0.84 (0.36-1.93)
43 weeks	1 (0.3)	25 (0.0)	11.8 (1.58-88.6)
Baby's sex			
Male	167 (49.6)	158 343 (51.4)	0.93 (0.75-1.15)
Gestational diabetes	24 (7.1)	16 368 (5.3)	1.37 (0.90-2.07)
Pre-existing diabetes	16 (4.8)	1 323 (0.4)	11.6 (6.98-19.2)
Pregnancy Induced hypertension	9 (2.7)	8 917 (2.9)	0.92 (0.47-1.79)
Pre-eclampsia/Eclampsia	9 (2.7)	5 246 (1.7)	1.58 (0.82-3.07)
Pre-existing hypertension	6 (1.8)	1 819 (0.6)	3.05 (1.36-6.85)

*t test

Table 5.3 shows the final parsimonious model predicting antepartum stillbirth risk at term from derivation cohort 1. After adjusting for maternal, pregnancy and medical risk factors, increased risk of stillbirth persisted for: maternal age 41+ years (adjusted OR 2.40, 95% CI 1.31-4.40), less than 8 antenatal care visits [(adjusted OR less than 2 visits 5.20, 95% CI 2.89-9.37), (adjusted OR 2-4 visits 2.25, 95% CI 1.55-3.26) and (adjusted OR 5-7 visits

1.48, 95% CI 1.14-1.94)]. Pre-existing diabetes (adjusted OR 10.9, 95% CI 6.45-18.3) and maternal smoking (adjusted OR 1.49, 95% CI 1.15-1.94).

Table 5.3: Predictors of antepartum stillbirth risk at term for derivation cohort 1 (subgroups 2-8)

Characteristic	Adjusted Odds Ratio	95% CI
Maternal age (Ref: 25-30 years)		
18 or less	1.02	0.44-2.38
19-24	1.23	0.91-1.67
31-34	1.31	0.96-1.78
35-40	1.38	0.99-1.92
41+	2.40	1.31-4.40
Indigenous status (Ref: Non-Indigenous)		
Indigenous	1.37	0.95-1.99
Marital Status (Ref: Domestic partner)		
No Partner	0.99	0.72-1.35
Any smoking during pregnancy (Ref: No)		
Yes	1.49	1.15-1.94
Substance Use during pregnancy (Ref: No)		
Yes	1.48	0.60-3.67
Hospital Accommodation status (Ref: Private)		
Public	1.23	0.92-1.65
Number of antenatal care visits (Ref: 8 or more)		
Less than 2	5.20	2.89-9.37
2-4	2.25	1.55-3.26
5-7	1.48	1.14-1.94
Pre-existing diabetes (Ref: No)		
Yes	10.9	6.45-18.3
Pre-existing hypertension (Ref: No)		
Yes	2.17	0.94-5.00

Predicted probability of stillbirth = $e^x/(1+e^x)$

where X = -7.82 + (0.02 x maternal age ≤18 years, 0.21 x maternal age 19-24 years, 0.27 x maternal age 31-34years, 0.32 x maternal age 35-40 years, 0.87 x maternal age >41 years) + (0.32 x Indigenous ethnicity) + (-0.01 x no partner) + (0.40 x smoker) + (0.39 x substance use) + (0.21 x public patient) + (1.65 x less than 2 antenatal care visits, 0.81 x 2 to 4 antenatal care visits; 0.39 x 5 to 7 antenatal care visits) + (2.39 x pre-existing diabetes) + (0.78 x pre-existing hypertension)

Figure 5.3: Prediction model for risk of antepartum stillbirth at term

The prediction model for antepartum stillbirth risk at term is given in Figure 5.3. The adjusted population attributable fraction for factors with a significant association with term antepartum stillbirth is shown in Table 5.4. The population attributable fractions associated with less than 8 antenatal care visits, maternal smoking and pre-existing diabetes were 15.4%, 8.2% and 3.8%, respectively.

Table 5.4: Population attributable fractions

Characteristic	Adjusted Odds Ratio	P (%)	PAF%
Maternal age			
41 years and older	2.40 (1.31-4.40)	1.9	2.6
Number of antenatal care visits			
Less than 2	5.20 (2.89-9.37)	0.7	2.9
2 to 4	2.25 (1.55-3.26)	5.1	6.0
5 to 7	1.48 (1.14-1.94)	18.5	8.2
Less than 8	1.75 (1.38-2.21)	24.3	15.4
Pre-existing diabetes	10.9 (6.45-18.3)	0.4	3.8
Maternal smoking	1.49 (1.15-1.94)	18.3	8.2

Model validation and screening properties

Presented in Table 5.5 and 5.6 are results of the Hosmer-Lemeshow goodness of fit tests using the derivation and validation cohorts for both models (final model and final model including geographic location). The test p values indicate that the fit of the models to the derivation and validation cohorts was reasonable. There was no material difference in the value of pseudo R^2 averaged over the eight folds between the model with and without geographic location (0.03 versus 0.03).

Table 5.5: Calibration of the final model without geographic location using the derivation and validation cohorts

Fold	Derivation Cohort		Validation Cohort
	p value	Pseudo R^2	p value
1	0.39	0.03	0.57
2	0.77	0.02	0.95
3	0.60	0.03	0.65
4	0.83	0.02	0.57
5	0.59	0.03	0.85
6	0.83	0.02	0.41
7	0.47	0.03	0.93
8	0.52	0.03	0.79

Table 5.6: Calibration of the final model with geographic location using the derivation and validation cohorts

Fold	Derivation Cohort		Validation Cohort
	p value	Pseudo R^2	p value
1	0.38	0.03	0.24
2	0.66	0.03	0.93
3	0.86	0.03	0.32
4	0.43	0.03	0.09
5	0.67	0.03	0.32
6	0.82	0.03	0.47
7	0.58	0.03	0.96
8	0.39	0.03	0.67

Presented in Table 5.7 are the areas under the receiver operating curve (AUROC) for the model with and without geographic location. Similar to the pseudo R^2, there was little difference in the discriminative ability of the models in the validation cohort evidenced by the average values of AUROC (0.63 vs 0.62). The average AUROC for the model without geographic location (0.62) means that there was a 62% probability that a woman with an antepartum stillbirth had a higher predicted probability that a woman with a livebirth for a random pair of women with and without antepartum stillbirth.

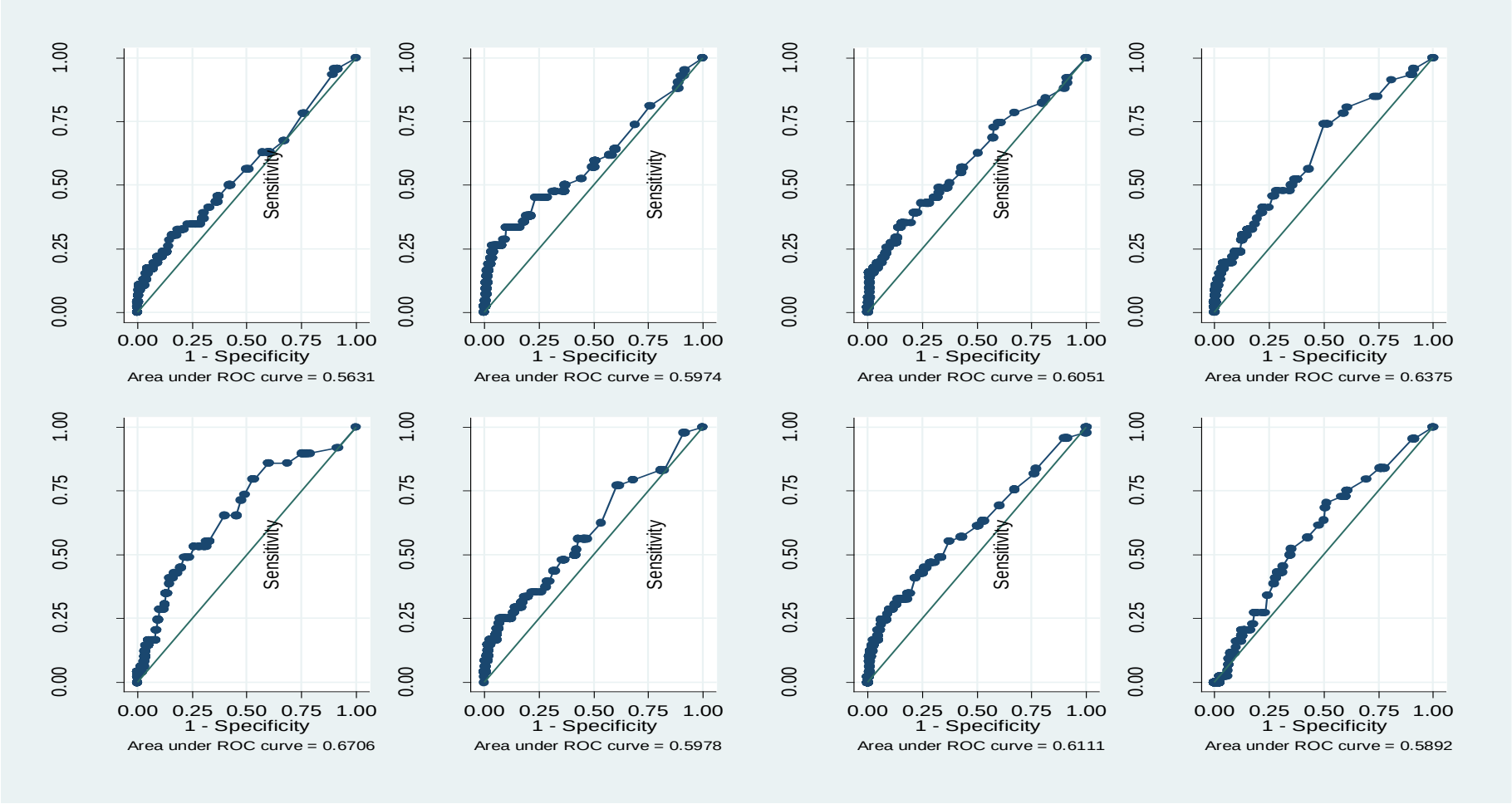
Table 5.7: Area under the curve (AUC) values for the stillbirth risk prediction model using derivation and validation cohorts

Fold	Derivation Cohort			Validation Cohort		
	AUC	95% CI	SE	AUC	95% CI	SE
Final model (without geographic location)						
1	0.63	0.60-0.66	0.02	0.56	0.47-0.65	0.05
2	0.63	0.60-0.66	0.02	0.60	0.50-0.70	0.05
3	0.62	0.59-0.65	0.02	0.67	0.59-0.75	0.04
4	0.62	0.59-0.65	0.02	0.60	0.51-0.68	0.04
5	0.62	0.59-0.66	0.02	0.61	0.52-0.69	0.05
6	0.62	0.59-0.65	0.02	0.64	0.55-0.72	0.04
7	0.62	0.59-0.66	0.02	0.61	0.52-0.70	0.05
8	0.63	0.60-0.66	0.02	0.59	0.51-0.67	0.04
Final model (with geographic location)						
1	0.64	0.61-0.67	0.02	0.56	0.46-0.65	0.05
2	0.63	0.60-0.67	0.02	0.61	0.50-0.71	0.05
3	0.63	0.59-0.66	0.02	0.68	0.60-0.76	0.04
4	0.63	0.59-0.66	0.02	0.61	0.53-0.70	0.04
5	0.63	0.60-0.66	0.02	0.60	0.51-0.69	0.05
6	0.62	0.59-0.66	0.02	0.64	0.56-0.72	0.04
7	0.63	0.60-0.67	0.02	0.60	0.51-0.69	0.05
8	0.64	0.60-0.67	0.02	0.59	0.51-0.67	0.04

AUC = Area under the curve
SE = Standard Error
95% CI = 95% Confidence interval

Presented in Figure 5.4 are the ROC curves using the validation cohorts for the model without geographic location.

Figure 5.4: Receiver Operating Characteristic (ROC) curves for antepartum stillbirth prediction model <u>without geographic location</u> using validation cohorts



Tables 5.8 and 5.9 show the screening characteristics of the prediction model without and with geographic location, respectively. The positive likelihood ratios fell over a wide range of values while most of the negative likelihood ratios failed to reach statistical significance. As with the AUROC values, there was little difference in the values for the screening characteristics between the model with or without geographic location.

Table 5.8: Screening characteristics for the model without geographic location using the validation cohorts at two predicted probability cut-offs.

Fold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive LR (95% CI)	Negative LR (95% CI)
Predicted probability cutoff = 0.01						
1	4.4	99.8	2.4	99.9	23.8 (6.03-93.9)	0.96 (0.90-1.02)
2	2.4	99.8	1.2	99.9	12.4 (1.77-87.1)	0.98 (0.93-1.03)
3	4.1	99.7	1.6	99.9	14.2 (3.61-55.7)	0.96 (0.91-1.02)
4	4.2	99.9	2.9	99.9	27.2 (6.87-108)	0.96 (0.91-1.02)
5	2.0	99.9	1.5	99.9	13.2 (1.87-93.3)	0.98 (0.94-1.02)
6	6.5	99.8	3.4	99.9	33.6 (11.0-102)	0.94 (0.87-1.01)
7	2.0	99.8	1.1	99.9	9.71 (1.38-68.3)	0.98 (0.94-1.02)
8	0.0	99.7	0.0	99.9	-	1.00 (1.00-1.00)
Predicted probability cutoff = 0.005						
1	10.9	99.1	1.2	99.9	11.5 (4.99-26.4)	0.90 (0.81-1.00)
2	11.9	99.1	1.3	99.9	13.5 (5.90-31.0)	0.89 (0.80-0.99)
3	4.1	98.9	0.4	99.9	3.64 (0.93-14.2)	0.97 (0.92-1.03)
4	8.3	99.1	1.0	99.9	9.27 (3.61-23.8)	0.93 (0.85-1.01)
5	15.7	99.1	2.0	99.9	17.9 (9.39-34.0)	0.85 (0.76-0.96)
6	10.9	99.1	1.2	99.9	11.4 (4.98-26.3)	0.90 (0.81-1.00)
7	10.2	99.1	1.2	99.9	10.8 (4.69-25.0)	0.91 (0.83-1.00)
8	0.0	98.9	0.0	99.9	-	1.01 (1.01-1.01)

PPV = positive predictive value
NPV = negative predictive value
LR = likelihood ratio

Table 5.9: Screening characteristics for the model with geographic location using the validation cohorts at two predicted probability cut-offs.

Fold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive LR (95% CI)	Negative LR (95% CI)
Predicted probability cutoff = 0.01						
1	4.4	99.8	2.1	99.9	20.7 (5.25-81.5)	0.96 (0.90-1.02)
2	2.4	99.8	0.9	99.9	9.66 (1.38-67.6)	0.98 (0.93-1.03)
3	4.1	99.7	1.3	99.9	11.7 (2.98-45.8)	0.96 (0.91-1.02)
4	4.2	99.8	2.7	99.9	25.0 (6.32-99.0)	0.96 (0.91-1.02)
5	2.0	99.8	1.4	99.9	11.9 (1.69-84.1)	0.98 (0.95-1.02)
6	6.5	99.8	2.9	99.9	28.0 (9.22-85.1)	0.94 (0.87-1.01)
7	2.0	99.7	0.8	99.9	7.57 (1.08-53.1)	0.98 (0.94-1.02)
8	0.0	99.6	0.0	99.9	-	1.00 (1.00-1.00)
Predicted probability cutoff = 0.005						
1	10.9	99.1	1.3	99.9	12.4 (5.40-28.6)	0.90 (0.81-1.00)
2	11.9	99.1	1.3	99.9	13.8 (6.01-31.5)	0.89 (0.80-0.99)
3	4.1	98.9	0.4	99.9	3.78 (0.97-14.7)	0.97 (0.92-1.03)
4	8.3	99.1	1.1	99.9	9.68 (3.77-24.9)	0.93 (0.85-1.01)
5	15.7	99.2	2.1	99.9	18.5 (9.69-35.2)	0.85 (0.76-0.96)
6	10.9	99.1	1.3	99.9	12.0 (5.22-27.7)	0.90 (0.81-1.00)
7	8.2	99.1	1.0	99.9	9.16 (3.56-23.6)	0.93 (0.85-1.01)
8	0.0	98.9	0.0	99.9	-	1.01 (1.01-1.01)

PPV = positive predictive value
NPV = negative predictive value
LR = likelihood ratio

5.4 Discussion

Main findings

This large population based study aimed to derive and validate a prediction model for antepartum stillbirth at term (≥ 37 weeks) based on maternal, pregnancy and medical factors. A number of factors were found to be independently associated with term antepartum stillbirth including advanced maternal age (41 years and older), fewer than eight antenatal care visits, pre-existing diabetes and maternal smoking.. Despite the strong association between these characteristics and term antepartum stillbirth risk, very little of the stillbirth risk was explained by the variables in the prediction model.

Interpretation of findings

Term antepartum stillbirth is an endpoint of various etiological pathways, and our results suggest that many factors not included in this model influence the risk of stillbirth. These findings are in accordance with studies in USA and UK that report poor ability to predict antepartum stillbirth at term based on maternal risk factors alone [230, 264]. Antepartum stillbirth is a rare outcome and as such a useful diagnostic test should yield high positive likelihood ratios (>10) and low negative likelihood ratios (<0.10) [271]. However, the negative likelihood ratios from our model were greater than 0.10 and many did not reach statistical significance. Nevertheless, our model had a slightly reduced ability to discriminate low from high risk women (average area under the ROC curve 0.61) compared to a UK study which reported area under ROC curve of 0.64 (95% CI 0.60-0.68) for a model with maternal risk factors predicting antepartum stillbirth risk between 37-43 weeks [230]. This may be due to our model adjusting for maternal and pregnancy factors only.

Our study identified a number of maternal medical and pregnancy factors that were independently associated with antepartum stillbirth at term. There was limited published data on population attributable fraction or risk associated with these factors for stillbirths occurring at term; therefore, direct comparisons could not be made.

Antenatal Care

Antenatal care is associated with improved perinatal and maternal outcomes [9]; however it is unclear which specific components are associated with decreased risk of stillbirth [100]. Both WHO and Australian national antenatal care guidelines recommend antenatal care as an opportunity to identify and manage any underlying conditions or obstetric complications so that the woman is as healthy as possible during pregnancy [272]. WHO recommends a minimum of 4 antenatal care visits [272]; while the Australian national antenatal care guidelines recommend a schedule of 10 visits for an initial uncomplicated pregnancy and seven visits for a subsequent uncomplicated pregnancy [273]. Our study found increased odds of stillbirth associated with attending fewer than 8 antenatal care visits; with a corresponding PAF of 15.1%. It was difficult to quantify a measure of inadequate antenatal care as data was unavailable for the gestational age at initiation of antenatal care. However, it can be proposed that delayed initiation of antenatal care represents limited opportunity to access information and interventions to optimise maternal and fetal health during pregnancy. This study suggested higher risk with fewer antenatal care visits, a finding reported by others [274]. PARs of up to 8% have been reported for receiving no antenatal care [32]. Reports on institution-based audits of perinatal mortality have found the presence of preventable factors leading to mortality in 25-44% of cases [275-277]. Inadequate management of suspected fetal growth restriction, hypertension and decreased fetal movements have been identified as suboptimal care factors associated with term antepartum stillbirth [278].

Maternal Smoking

Maternal smoking has been identified as an important modifiable risk factor for stillbirth as well as other adverse pregnancy outcomes. Smoking is associated with stillbirth in a dose-dependent fashion [59]. It has been suggested that smoking increases the risk of stillbirth through the mechanism of tobacco-induced placental pathology and fetal growth restriction [279, 280]. Our study found a population attributable fraction of 8.2%; similar to reports for Australia (6.2%) and other high income countries (3.9-7.1%) [32]. It has been estimated that for Indigenous Australian women, the population attributable fraction may be as high as 20%, reflecting the higher maternal smoking rates [32]. There is evidence to support stillbirth risk reduction with smoking cessation during pregnancy [62, 63], as well

as high level evidence for the effectiveness of smoking cessation interventions for pregnant women. However, smoking cessation rates have been consistently lower for Indigenous compared with non-Indigenous women [24]. Recent smoke-free legislation has been shown to reduce the risk of preterm birth [67], while incentives-based interventions show promise in increasing smoking cessation rates during and post pregnancy [205].

Pre-existing diabetes

The association between pre-existing diabetes and stillbirth has been established. Our study found associated population attributable fraction of 4.3% for term antepartum stillbirths, which is somewhat similar to estimates of 3-5% from a number of high income countries for stillbirths of >22 weeks or >500g birthweight [32]. It is proposed that fetal demise in diabetes-related stillbirths is as a result of hyperglycaemia leading to fetal anaerobic metabolism with hypoxia and acidosis [88]. There is controversy around the screening and management of women with diabetes during pregnancy. The International Association of Diabetes and Pregnancy Study Group recommend screening all women at their first antenatal visit for gestational diabetes or previously undiagnosed pre-existing diabetes [234], a similar approach is recommended in New Zealand [281] while a tiered approach with early screening of women at high risk or with multiple risk factors is recommended in Australia [9]. Antenatal care for women with pre-existing diabetes focuses on glycaemic control and also includes folate supplementation, ceasing oral hypoglycaemic agents in favour of insulin and screening for diabetic complications [234]. Currently, there is limited evidence on the long term maternal and infant outcomes of oral hypoglycaemic agent use during pregnancy [206, 234]. Areas for future research include large scale randomised trials to assess: the effect of diet in combination with lifestyle advice compared with pharmacotherapy on the development of gestational diabetes and maternal and fetal outcomes, the effect of early diagnosis and treatment on maternal and fetal outcomes, as well as the effect of diet and lifestyle advice compared with pharmacotherapy for the prevention of type II diabetes among women with a history of gestational diabetes [281]

Maternal age

A significant association was found between advanced maternal age (41 years and older) and term antepartum stillbirth, with a corresponding population attributable fraction of 2.3%. In comparison, PAR% of 6-8% was reported across five high income countries including Australia for maternal age of ≥35 years [32]. Our lower value may be explained by the smaller proportion of women aged ≥ 41 years compared with those aged ≥35 years for a similar effect size. These findings of increased risk of term antepartum stillbirth with advanced maternal age after adjusting for maternal medical conditions are corroborated by others [35, 264, 282, 283]. Although not examined in our results, increased risk of stillbirth with advanced maternal age was found to be higher among primiparous compared with multiparous women [284]. It has been proposed that maternal age may affect the ability of the vascular system to respond to the increased requirements of pregnancy [35], however the exact aetiology of stillbirth in relation to advanced maternal age is unknown [264]. However, it is important to advice women on the associations between advanced maternal age and the risk of stillbirth, especially with the increasing rates of delayed childbearing [32].

Identifying women at increased risk

A number of studies have explored prediction models for identifying pregnancies at increased risk of antepartum stillbirth. Maternal serum plasma protein A (PAPP-A) and uterine artery pulsativity index have been shown to be useful in the first and second trimester, respectively, in predicting abruption, pre-eclampsia and SGA related stillbirth [265]. However, biophysical and biochemical tests, either singly or in combination had low ability to predict stillbirth as a whole [265].

Antepartum stillbirth is commonly preceded by decreased fetal movements (DFM) [285]. It has been established that DFM is an indicator of adaptation to chronic placental insufficiency [286]. Maternal perception of decreased fetal movements is used as a means of monitoring fetal wellbeing [287]. However, many women delay reporting DFM and there is wide variation in management of DFM by health care providers. Currently, two large step wedge cluster randomised trials are underway in the UK and Australia. The UK study (AFFIRM) is evaluating a package of care including increasing awareness and reporting of DFM, identification of placental insufficiency and timely delivery [288]. The Australian study

(My Baby's Movements) is using mobile phone technology to increase maternal awareness of DFM along with a clinician education program to increase compliance with the DFM clinical practice guidelines [289]. Both studies will assess the effect on stillbirth rates.

Unexplained antepartum stillbirth at term is a rare but devastating pregnancy outcome. This highlights the need for further research into the underlying aetiological mechanisms. Supine sleep position resulting in inferior vena cava compression has been proposed as an additional stressor in an already vulnerable fetus [290]. Similarly, genetic predisposition and acute placental dysfunction may be possible aetiologic factors. However, research is made difficult by relatively small numbers and may be aided by the use of composite outcomes.

5.5 Conclusion

The predictive ability of the statistical model based on maternal risk factors was poor. The addition of geographic location made no material difference to the results. This study highlights the need for further research into the aetiology of antepartum stillbirth at term.

Chapter 6

Stillbirth Classification Agreement Study

6.1 Introduction

Accurate cause of death information is essential to guide stillbirth prevention interventions as well as counselling women and families for management of future pregnancies. The Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ PDC) system was developed for use alongside the Clinical Practice Guidelines for Perinatal Mortality to ensure systematic and high quality approach to stillbirth investigation and classification [124]. However, uptake of the guidelines by healthcare providers has been poor [158]. Furthermore, it has been suggested that there may be differences in the application of the perinatal death classification system across states and territories [23].

Across Australia, each state and territory has processes for multidisciplinary review of perinatal deaths and these vary with population size, available resources and legislative arrangements [160]. Reviews may be carried out within hospitals (usually large tertiary centres) or centrally; each with their relative merits. In NSW, an electronic system is being trialled, allowing clinical staff with access to the full medical record to more accurately assign cause of death through a series of cascading questions in a decision tree [160]. To address the issue of access to comprehensive data for perinatal mortality audit and reporting, the PSANZ Perinatal Mortality Group and the Australia and New Zealand Stillbirth Alliance (ANZSA) developed the National Perinatal Death Clinical Audit Tool (NPDCAT) which is currently being pilot tested [291]. Accurate and consistent classification of stillbirth across Australian states and territories is important for: assessing trends in stillbirth causes, evaluating effectiveness of interventions to prevent stillbirth and for comparisons across states and territories.

A population based study in New South Wales assessing agreement between hospital committee and expert panel review of stillbirths classification found low level of agreement and attributed this to lack of familiarity with the perinatal mortality guidelines [131]. Since that study was conducted, an education program was developed and rolled out to hospitals across Australia to train healthcare providers in the use of the guidelines and classification system [159].

This study aims to assess consistency in application of the PSANZ-PDC in a cohort of stillbirths investigated according to the perinatal mortality audit guidelines in an environment where healthcare providers have been trained in the use of the guidelines. It is anticipated that this study will identify areas for quality improvement and possibly inform future updates to the perinatal mortality audit guidelines.

Presented in this chapter are findings from an agreement study involving 217 stillbirth cases from 12 hospitals across Australia.

6.2 Methods

Study Design and Population

This prospective cohort study was nested in a larger multi-centre prospective cohort study. The larger study titled "*Investigating the cause of stillbirth: a prospective cohort study examining use and effectiveness of a comprehensive investigation protocol (short title: Stillbirth Investigation study)*" aimed to: 1) identify causes of stillbirth in a cohort of stillbirths investigated according to the PSANZ guidelines, 2) utilise expert panel review to determine yield from stillbirth investigations, and 3) undertake cost effectiveness analysis comparing a comprehensive versus selective approach to stillbirth investigation.

The nested study involved comparison of hospital and expert panel review of a cohort of stillbirths investigated according to the Perinatal Mortality Guidelines and classified according to PSANZ Perinatal Death Classification system. This methodology was employed to assess application of the PSANZ PDC guidelines in an environment where clinicians undertaking classification were familiar with and regularly utilised the classification system.

The study population included all stillbirths of at least 20 weeks gestation or 400g birthweight occurring at the participating hospitals. The details of ethics approvals for this study are outlined in Appendix A. Participating hospitals included all level 2 and level 3 hospitals across Australia where the PSANZ guidelines on audit of perinatal mortality had been implemented and lead clinicians in stillbirth investigation and audit received training on the use of the guidelines. All eligible study participants were identified at the participating hospitals as part of routine procedures. Data was collected for 226 eligible stillbirth cases. Of these, stillbirth classification data was missing for 2 and 7 cases from the expert panel and hospital reviews, respectively.

Sample Size

The sample size calculation for this study was based on determining the level of agreement between the hospital review and the independent expert panel review with regards to stillbirth classification using the PSANZ perinatal death classification system. A sample size of 385 stillbirths would give precision of around ± 0.1 around the estimated kappa statistic. This was based on an expected kappa of 0.60 and a 'proportion positive'

by each reviewing group ranging from 0.5 to 0.8, with an alpha of 0.05. A conservative estimate of kappa was used, based on data from international studies (kappa of 0.55 to 0.67) [157] and an Australian study (0.64) using the PSANZ-PDC [131]. However, due to delays with obtaining ethics and governance approvals and relatively slow rates of case submission, a total of 217 stillbirth cases were available for classification by both groups. A sample size of 217 would give precision of around ± 0.10 to 0.12 around the estimated kappa of 0.60, with an alpha of 0.05 and a proportion positive by each group ranging from 0.5 to 0.8.

Study Procedures

Hospital committee review

Hospital review and classification of cause of stillbirth was carried out according to the PSANZ perinatal mortality investigation protocol as part of routine procedures at the participating hospitals. This included taking a full history, undertaking specific diagnostic tests, and review and classification of death through a multidisciplinary perinatal mortality audit committee. Data on hospital review of stillbirth cases was collected in the online study database as part of the *Stillbirth Investigations Study.* The data collected in the study database was based on the National Perinatal Death Clinical Audit Tool (NPDCAT) and the PSANZ stillbirth investigation checklist [124]. All stillbirths fulfilling the inclusion criteria over the study period at the participating hospitals were identified as part of routine procedures within each hospital and included in the study. Prior to the commencement of the study, training in the use of the PSANZ perinatal mortality guidelines was implemented. Following the completion of investigations, the NPDCAT and PSANZ stillbirth investigation checklist were completed by the clinician for review by the hospital committee. This information was entered into the online study database. Following review and assignment of clinical classification of stillbirth by the hospital committee, the entry for each participant was completed and submitted to the study team through the online study database.

Expert panel review

A multidisciplinary expert panel consisting of obstetrics, maternal fetal medicine, neonatology, perinatal pathology and perinatal epidemiology disciplines was convened to review the stillbirth cases. A number of the panel members were involved in the development of the PSANZ perinatal classification system and all were actively involved in perinatal mortality reviews at hospital and state levels. Cases were assigned to panel members according to discipline based on case summary information and panel members were excluded from reviewing cases from their organisations. Each case was assigned a lead reviewer. The lead reviewer was responsible for reviewing and classifying the case prior to the panel meetings. At the panel meetings, the lead reviewer presented the facts of the case for discussion and any differences in opinion regarding classification were discussed and resolved. The panel was blinded to the hospital classification of cause of stillbirth. Cases were reviewed using both electronic and hardcopy reports from the online study database.

Data Management

Following submission of a stillbirth case by the participating hospital using the online study database, an extract was taken. Part of the expert panel review included verifying that data was not missing or inappropriately entered for key fields. In addition, the lead reviewer for a case checked that reports were included for investigations reported as performed. For cases with missing or interim reports, the submitting hospital was contacted for additional details or reports and the case was held over for review by the expert panel until the missing information was uploaded to the study database. For a small number of cases, interim classification was undertaken by both hospital and expert panel where there were lengthy waits for final pathology reports but the findings were unlikely to change the probable cause of death. A paper-based data collection form was used to capture data from the expert panel review. The data collection form was completed by the lead reviewer prior to and during the panel review meetings. Classification data from the expert panel review was input into a standalone database along with the corresponding participant study number. The complete dataset for analysis was obtained by taking an extract from the online study database and linking it to expert panel review data in the stand-alone database using the unique participant study number.

Statistical Analysis

Data on demographic, pregnancy, birth outcomes and stillbirth investigation were obtained from the online study database. Maternal demographic data included: age, body mass index, marital status, occupation, ethnicity and level of English comprehension. Pregnancy data included pre-existing medical conditions, fertility treatment, any smoking during pregnancy, any alcohol or drug use during pregnancy and suspected fetal growth restriction. Pregnancy outcomes included: baby's birthweight, sex, gestational age at birth, type of stillbirth and termination of pregnancy. Data on stillbirth investigations included: whether or not parents were offered autopsy, parental consent for autopsy and placental histopathology.

Characteristics of the study population and investigations performed were summarised using frequency and percentages for categorical variables and mean (standard deviation) or median (interquartile range) as appropriate for continuous variables. The main outcome measure was primary classification of cause of stillbirth using the PSANZ-PDC system. Inter-observer agreement between hospital and expert panel classification was assessed by calculating overall Cohen's kappa with 95% confidence intervals across the eleven (11) PSANZ PDC categories. Agreement within each PSANZ PDC category and within gestational age groups (20-27, 28-36, and ≥37 weeks) were also calculated. Values for kappa were interpreted using guidelines proposed by Landis and Koch [292] as follows:

Poor	below 0.0
Slight	0.00-0.20
Fair	0.21-0.40
Moderate	0.41-0.60
Substantial	0.61-0.80
Almost perfect	0.81-1.00
Perfect	1.00

All statistical analysis was performed using Stata 13.1 (StataCorp LP 2013, Texas, USA).

6.3 Results

Study population characteristics

During the period 2013-2015, hospital and expert panel classification of stillbirth was collated for 217 stillbirths across 12 (two level II and ten level III) hospitals across six Australian states and territories. The characteristics of the study cohort are shown in Table 1. The mean maternal age was 30.7 years; and 181 women (83.4 %) lived with a domestic partner. A large proportion of women in this cohort (69.6 %) identified as Māori or Pacific Islander and 83.4% of women understood English very well. Ninety six women (44.2%) had a pre-existing medical condition and forty two women (19.4%) reported smoking during pregnancy (Table 6.1).

The mean birthweight was 1360 grams and the median gestational age was 25 weeks. More than two thirds of stillbirths occurred during the antepartum period and 24.9% of stillbirths were terminations of pregnancy (Table 6.2).

Table 6.1: Maternal characteristics of the study cohort

Characteristics	n(%)
Maternal age*	30.7 (6.4) 95% CI 29.8-31.6
Maternal body mass index (kg/m^2)*	25.8 (5.5) 95% CI 25.0-26.7
Marital status	
Partner	181 (83.4)
No Partner	26 (12.0)
Unknown	10 (4.6)
Maternal occupation	
Unemployed/pension	28 (12.9)
Student	11 (5.1)
Home maker	42 (19.4)
Manual/farm/trade	2 (0.9)
Service/Retail	42 (19.4)
Clerical/Management	21 (9.7)
Professional	29 (13.4)
Unknown	42 (19.4)
Ethnicity	
Australian Aboriginal and/or Torres Strait Islander	22 (10.1)
Māori/Pacific Islander	151 (69.6)
Caucasian	14 (6.5)
Mediterranean	4 (1.8)
Indian/Pakistani/Bangladeshi/Sri Lankan	5 (2.3)
Cambodian/Lao/ Viet/ Thai	5 (2.3)
Chinese/Korean/ Hong Kong	4 (1.8)
Japanese	6 (2.8)
Middle East/North African	2 (0.9)
African	1 (0.5)
Unknown	3 (1.4)
Maternal English level	
Very well	181 (83.4)
Well	17 (7.8)
Not well	11 (5.1)
Not at all	6 (2.8)
Unknown	2 (0.9)
Pre-existing medical conditions	
Yes	96 (44.2)
No	116 (53.5)
unknown	5 (2.3)
Fertility treatment	
Yes	33 (15.2)
No	181 (83.4)
unknown	3 (1.4)
Maternal smoking	
Yes	42 (19.4)
No	161 (72.2)
unknown	14 (6.5)
Alcohol use	
Yes	8 (3.7)

Characteristics	n(%)
No	175 (80.6)
Unknown	34 (15.7)
Suspected fetal growth restriction	
No	160 (73.7)
Yes, confirmed by scan	30 (13.8)
Yes, but normal growth on scans	3 (1.4)
Yes, no scan performed	4 (1.8)
Unknown	20 (9.2)

*mean (standard deviation), 95% CI

Table 6.2: Birth outcomes for the study cohort

Characteristics	n(%)
Baby's birthweight (grams)*	1360 (1450), 95% CI 1166-1554
Gestational age at birth (weeks)^	25 (22-35)
Type of stillbirth	
Antepartum	152 (70.1)
Intrapartum	51 (23.5)
Unknown	14 (6.4)
Termination of pregnancy	
Yes	54 (24.9)
No	163 (75.1)
Baby's sex	
Male	129 (59.5)
Female	85 (39.2)
Undeterminate	3 (1.4)

*mean(standard deviation); 95% CI ^median(interquartile range)

Table 6.3 presents selected post mortem investigations conducted. Of the 200 parents offered the option of an autopsy, 40.0% consented to a full autopsy and 10.0% consented to a limited autopsy. Placental histopathology tests were performed in 91.2% of stillbirth cases. Among the 217 stillbirth cases, 56 (25.8%) were classified as 'unexplained' by either hospital or expert review. Autopsy rates were 57.1% and 42.2% among unexplained and explained cases, respectively among parents offered the option of autopsy. Placental histopathology was performed among 94.6% and 90.1% of unexplained and explained stillbirth cases, respectively.

Table 6.3: Post mortem investigations by explained or unexplained status

Investigations	Total n=217	"Unexplained" n=56	"Explained" n=161
Parents offered option of autopsy			
Yes	200 (92.2)	56 (100.0)	144 (89.4)
No	5 (2.3)	0 (0.0)	5 (3.1)
Unknown	7 (3.2)	0 (0.0)	7 (4.3)
missing	5 (2.3)	0 (0.0)	5 (3.1)
Parents consented to autopsy (n=200)			
No	99 (49.5)	24 (42.9)	75 (52.1)
Yes, full autopsy	80 (40.0)	27 (48.2)	53 (36.8)
Yes, limited autopsy	20 (10.0)	5 (8.9)	15 (10.4)
Unknown	1 (0.5)	0 (0.0)	1 (0.7)
Magnetic Resonance Imaging			
Yes	15 (6.9)	2 (3.6)	13 (8.1)
No	198 (91.2)	53 (94.6)	145 (90.1)
Unknown	1 (0.5)	1 (1.8)	0 (0.0)
missing	3 (1.4)	0 (0.0)	3 (1.9)
Placental histopathology			
Yes	198 (91.2)	53 (94.6)	145 (90.1)
No	10 (4.6)	3 (5.4)	7 (4.3)
Unknown	3 (1.4)	0 (0.0)	3 (1.9)
missing	6 (2.8)	0 (0.0)	6 (3.7)
Chromosomal analysis			
Yes	90 (41.5)	26 (46.4)	64 (39.8)
No	80 (36.9)	21 (37.5)	67 (41.6)
Unknown	20 (9.2)	6 (10.7)	14 (8.7)
missing	27 (12.4)	3 (5.4)	16 (7.4)

Table 6.4 shows classification of the 217 stillbirth cases according to PSANZ PDC by hospital review (rows) and expert panel review (columns). Among hospital classifications, the leading categories of stillbirth were: congenital abnormality (26.7%), unexplained antepartum fetal death (19.4%) and spontaneous preterm births (12.0%). Among reviews by the expert panel, the leading categories were: congenital abnormality (26.7%), unexplained antepartum fetal death (20.7%) and spontaneous preterm birth (14.7%) (Table 6.4). There were no stillbirths in this cohort coded under PSANZ PDC category 11 "No obstetric antecedent".

Table 6.4: Cross-tabulation of classification by PSANZ-PDC by hospital and expert panel

		Expert										
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Total**
Hospital	**1**	56	1	0	0	0	0	0	0	0	1	**58**
	2	1	6	0	0	0	0	0	0	2	2	**11**
	3	0	0	11	0	0	1	0	0	0	1	**13**
	4	0	0	1	5	0	1	0	1	3	2	**13**
	5	0	1	1	1	5	0	0	0	0	1	**9**
	6	0	0	0	1	0	18	0	1	2	2	**24**
	7	0	0	0	0	0	0	1	0	0	0	**1**
	8	0	1	2	0	0	0	1	11	0	5	**20**
	9	0	0	0	1	0	0	0	0	25	0	**26**
	10	1	1	0	0	3	2	0	4	0	31	**42**
	Total	**58**	**10**	**15**	**8**	**8**	**22**	**2**	**17**	**32**	**45**	**217**

κ = 0.737 (0.638-0.759), agreement = 77.9%, expected agreement = 15.8%

PSANZ PDC categories: 1) Congenital abnormality, 2) Perinatal Infection, 3) Hypertension, 4) Antepartum haemorrhage, 5) Maternal conditions, 6) Specific perinatal conditions, 7) Hypoxic peripartum deaths, 8) Fetal growth restriction, 9) Spontaneous preterm birth, and 10) Unexplained antepartum death.

There was substantial agreement overall between hospital and expert panel classifications (κ = 0.737, 95% CI 0.638-0.759). However, agreement by PSANZ-PDC categories varied as shown in Table 6.5. The categories with the highest levels of agreement were: congenital abnormality (κ = 0.953), spontaneous preterm birth (κ =0.841), hypertension (κ = 0.771) and specific perinatal conditions (κ = 0.757). The categories with the lowest levels of agreement were: antepartum haemorrhage (κ = 0.451), perinatal infection (κ = 0.550), fetal growth restriction (κ = 0.557) and maternal conditions (κ = 0.572).

Table 6.5: Kappa values for PSANZ PDC categories

PSANZ PDC Category	Kappa	95% Confidence Interval	Interpretation
1 Congenital abnormality	0.953	0.907-0.999	Almost perfect
2 Perinatal Infection	0.550	0.288-0.812	Moderate
3 Hypertension	0.771	0.594-0.948	Substantial
4 Antepartum haemorrhage	0.451	0.181-0.722	Moderate
5 Maternal Conditions	0.572	0.286-0.857	Moderate
6 Specific perinatal conditions	0.757	0.613-0.901	Substantial
7 Hypoxic peripartum deaths	0.665	0.047-1.000	Substantial
8 Fetal Growth Restriction	0.557	0.357-0.757	Moderate
9 Spontaneous preterm birth	0.841	0.734-0.948	Almost perfect
10 Unexplained antepartum death	0.641	0.512-0.770	Substantial

Presented in Tables 6.6 and 6.7 are the investigations performed for the concordantly and discordantly classified stillbirths.

Table 6.6: Investigations performed among concordantly classified stillbirths

PSANZ PDC Category	Autopsy	MRI	Placental histopathology	Chromosomal analysis
Congenital abnormality (n=56)	21 (37.5)	8 (14.3)	48 (85.7)	25 (44.6)
Perinatal Infection (n=6)	4 (66.7)	0 (0.0)	6 (100.0)	3 (50.0)
Hypertension (n=11)	4 (36.4)	0 (0.0)	9 (81.8)	5 (45.5)
Antepartum haemorrhage (n=5)	2 (40.0)	0 (0.0)	5 (100.0)	2 (40.0)
Maternal Conditions (n=5)	3 (60.0)	0 (0.0)	5 (100.0)	4 (80.0)
Specific perinatal conditions (n=18)	5 (27.8)	3 (16.7)	17 (94.4)	8 (44.4)
Hypoxic peripartum deaths (n=1)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)
Fetal Growth Restriction (n=11)	9 (81.8)	0 (0.0)	11 (100.0)	6 (54.5)
Spontaneous preterm birth (n=25)	8 (32.0)	0 (0.0)	23 (92.0)	5 (20.0)
Unexplained antepartum death (n=31)	18 (58.1)	2 (6.5)	28 (90.3)	17 (54.8)

Table 6.7: Investigations performed among discordantly classified stillbirths

PSANZ PDC Category	Autopsy	MRI	Placental histopathology	Chromosomal analysis
Congenital abnormality (n=4)	3 (75.0)	1 (25.0)	3 (75.0)	2 (50.0)
Perinatal Infection (n=9)	6 (66.7)	1 (11.1)	8 (88.9)	5 (55.6)
Hypertension (n=6)	3 (50.0)	0 (0.0)	5 (83.3)	1 (16.7)
Antepartum haemorrhage (n=11)	7 (63.6)	1 (9.1)	11 (100.0)	3 (27.3)
Maternal Conditions (n=7)	4 (57.1)	0 (0.0)	7 (100.0)	2 (28.6)
Specific perinatal conditions (n=10)	6 (60.0)	0 (0.0)	8 (80.0)	2 (20.0)
Hypoxic peripartum deaths (n=1)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)
Fetal Growth Restriction (n=15)	5 (33.3)	0 (0.0)	15 (100.0)	4 (26.7)
Spontaneous preterm birth (n=8)	3 (37.5)	1 (12.5)	7 (87.5)	2 (25.0)
Unexplained antepartum death (n=25)	14 (56.0)	0 (0.0)	25 (100.0)	9 (36.0)

Agreement between hospital and expert panel classification by gestational age

20-27 weeks

Table 6.8 shows classification by hospital and expert panel for stillbirth occurring between 20 and 27 weeks. There was substantial agreement for classifications in this gestational age group (κ = 0.784).

Table 6.8: Cross-tabulation of classification by PSANZ-PDC by hospital and expert panel, stillbirths 20-27 weeks

Hospital	Expert 1	2	3	4	5	6	8	9	10	Total
1	36	1	0	0	0	0	0	0	1	**38**
2	1	3	0	0	0	0	0	1	0	**5**
3	0	0	8	0	0	1	0	0	0	**9**
4	0	0	0	5	0	0	1	3	1	**10**
5	0	1	1	1	2	0	0	0	1	**6**
6	0	0	0	0	0	10	0	2	0	**12**
8	0	0	1	0	0	0	7	0	3	**11**
9	0	0	0	1	0	0	0	25	0	**26**
10	0	0	0	0	0	1	0	0	6	**7**
Total	**37**	**5**	**10**	**7**	**2**	**12**	**8**	**31**	**12**	**124**

κ = 0.784 (0.721-0.820), agreement = 82.3%, expected agreement = 17.8%

PSANZ PDC categories: 1) Congenital abnormality, 2) Perinatal Infection, 3) Hypertension, 4) Antepartum haemorrhage, 5) Maternal conditions, 6) Specific perinatal conditions, 8) Fetal growth restriction, 9) Spontaneous preterm birth, and 10) Unexplained antepartum death.

The PSANZ category specific agreement is shown in Table 6.9. Agreement was highest for congenital abnormality (κ = 0.943) and lower values were found for maternal conditions (κ = 0.488) and antepartum haemorrhage (κ = 0.559).

Table 6.9: Kappa values for PSANZ PDC categories (20-27 weeks)

PSANZ PDC Category	Kappa	95% Confidence Interval	Interpretation
1 Congenital abnormality	0.943	0.879-1.000	Almost perfect
2 Perinatal Infection	0.583	0.213-0.953	Moderate
3 Hypertension	0.829	0.640-1.000	Almost perfect
4 Antepartum haemorrhage	0.559	0.268-0.850	Moderate
5 Maternal Conditions	0.488	0.063-0.912	Moderate
6 Specific perinatal conditions	0.815	0.640-0.991	Almost perfect
8 Fetal Growth Restriction	0.716	0.480-0.951	Substantial
9 Spontaneous preterm birth	0.841	0.727-0.954	Almost perfect
10 Unexplained antepartum death	0.603	0.338-0.868	Moderate

28-36 weeks

Overall agreement for classification of stillbirth occurring between 28 and 36 weeks is shown in Table 6.10. There was substantial agreement (κ = 0.624) for review of stillbirths within this gestational age group.

Table 6.10: Cross-tabulation of classification by PSANZ PDC by hospital and expert panel, stillbirths 28-36 weeks

		Expert									
		1	**2**	**3**	**4**	**5**	**6**	**8**	**9**	**10**	**Total**
Hospital	**1**	15	0	0	0	0	0	0	0	0	**15**
	2	0	1	0	0	0	0	0	1	1	**3**
	3	0	0	2	0	0	0	0	0	1	**3**
	4	0	0	1	0	0	1	0	0	0	**2**
	5	0	0	0	0	2	0	0	0	0	**2**
	6	0	0	0	1	0	3	1	0	1	**6**
	8	0	0	1	0	0	0	3	0	0	**4**
	10	1	0	0	0	0	1	4	0	9	**15**
	Total	**16**	**1**	**4**	**1**	**2**	**5**	**8**	**1**	**12**	**50**

κ = 0.624 (0.560-0.776), agreement = 70.0%, expected agreement = 20.1%

PSANZ PDC categories: 1) Congenital abnormality, 2) Perinatal Infection, 3) Hypertension, 4) Antepartum haemorrhage, 5) Maternal conditions, 6) Specific perinatal conditions, 8) Fetal growth restriction, 9) Spontaneous preterm birth, and 10) Unexplained antepartum death.

Almost perfect agreement was found for congenital abnormalities (κ = 0.953) and perfect agreement was found for maternal conditions (based on 2 cases). Conversely, lower levels of agreement were found for antepartum haemorrhage (κ = -0.027 based on zero agreement between hospital and expert panel reviews), fetal growth restriction (κ = 0.440), perinatal infection (κ = 0.485, based on 1 case) (Table 6.11).

Table 6.11: Kappa values for PSANZ PDC categories (28-36 weeks)

PSANZ PDC Category	Kappa	95% Confidence Interval	Interpretation
1 Congenital abnormality	0.953	0.863-1.000	Almost perfect
2 Perinatal Infection	0.485	-0.115-1.000	Moderate
3 Hypertension	0.540	0.080-0.999	Moderate
4 Antepartum haemorrhage	-0.027	-0.084-0.030	Poor
5 Maternal Conditions	1.000	1.000-1.000	Perfect
6 Specific perinatal conditions	0.490	0.105-0.874	Moderate
8 Fetal Growth Restriction	0.440	0.077-0.804	Moderate
9 Spontaneous preterm birth	-	-	-
10 Unexplained antepartum death	0.545	0.286-0.805	Moderate

37+ weeks

For term stillbirths, there was substantial agreement between hospital and expert panel reviews (Table 6.12). There was perfect agreement for the category of congenital abnormality and hypertension (based on 1 case). While lower levels of agreement were found for fetal growth restriction (κ = 0.306) and maternal conditions (κ = 0.376). However, caution should be exercised when interpreting these results as the cell sizes were small and the corresponding confidence intervals around the estimates of κ are wide (Table 6.13).

Table 6.12: Crosstabulation of classification by PSANZ-PDC by hospital and expert panel, stillbirths of 37 or more weeks

		Expert								
		1	**2**	**3**	**5**	**6**	**7**	**8**	**10**	**Total**
Hospital	**1**	5	0	0	0	0	0	0	0	**5**
	2	0	2	0	0	0	0	0	1	**3**
	3	0	0	1	0	0	0	0	0	**1**
	4	0	0	0	0	0	0	0	1	**1**
	5	0	0	0	1	0	0	0	0	**1**
	6	0	0	0	0	5	0	0	1	**6**
	7	0	0	0	0	0	1	0	0	**1**
	8	0	1	0	0	0	1	1	2	**5**
	10	0	1	0	3	0	0	0	15	**19**
	Total	**5**	**4**	**1**	**4**	**5**	**2**	**1**	**20**	**42**

κ = 0.646 (0.537-0.821), agreement = 73.8%, expected agreement = 26.0%

PSANZ PDC categories: 1) Congenital abnormality, 2) Perinatal Infection, 3) Hypertension, 4) Antepartum haemorrhage, 5) Maternal conditions, 6) Specific perinatal conditions, 7) Hypoxic peripartum deaths, 8) Fetal growth restriction and 10) Unexplained antepartum death.

Table 6.13: Kappa values for PSANZ PDC categories (≥37 weeks)

PSANZ PDC Category	Kappa	95% Confidence Interval	Interpretation
1 Congenital abnormality	1.000	1.000-1.000	Perfect
2 Perinatal Infection	0.533	0.069-0.997	Moderate
3 Hypertension	1.000	1.000-1.000	Perfect
4 Antepartum haemorrhage	-	-	-
5 Maternal Conditions	0.376	-0.155-0.908	Fair
6 Specific perinatal conditions	0.896	0.694-1.000	Almost perfect
7 Hypoxic peripartum death	0.656	0.030-1.000	Substantial
8 Fetal Growth Restriction	0.306	-0.160-0.772	Fair
10 Unexplained antepartum death	0.569	0.321-0.818	Moderate

Agreement between hospital and expert panel classification

Excluding congenital abnormalities

There were 157 stillbirth cases not classified as due to congenital abnormality by either the hospital or expert panel reviews. Of these, 15 (9.6%) were terminations of pregnancy. There were similar leading categories of PSANZ PDC as classified by the hospital committees [unexplained antepartum fetal death (26.1%), spontaneous preterm birth (16.6%) and specific perinatal conditions (15.3%)] and the expert panel [unexplained antepartum fetal death (28.0%), spontaneous preterm birth (20.4%) and specific perinatal conditions (14.0%)] (Table 6.14). There was substantial agreement overall within this subgroup (κ = 0.666, 95% CI 0.538-0.740. Among stillbirths less than 37 weeks, there was substantial agreement (κ = 0.672, 95% CI 0.608-0.808) and moderate agreement among stillbirths of 37 weeks or older (κ = 0.565, 95% CI 0.406-0.649).

Table 6.14: Cross-tabulation of classification by PSANZ PDC by hospital and expert panel, excluding congenital abnormalities

		Expert									
		2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Total**
Hospital	**2**	6	0	0	0	0	0	0	2	2	**10**
	3	0	11	0	0	1	0	0	0	1	**13**
	4	0	1	5	0	1	0	1	3	2	**13**
	5	1	1	1	5	0	0	0	0	1	**9**
	6	0	0	1	0	18	0	1	2	2	**24**
	7	0	0	0	0	0	1	0	0	0	**1**
	8	1	2	0	0	0	1	11	0	5	**20**
	9	0	0	1	0	0	0	0	25	0	**26**
	10	1	0	0	3	2	0	4	0	31	**41**
	Total	**9**	**15**	**8**	**8**	**22**	**2**	**17**	**32**	**44**	**157**

κ = 0.666 (0.538-0.740), agreement = 72.0%, expected agreement = 15.5%

PSANZ PDC categories: 2) Perinatal Infection, 3) Hypertension, 4) Antepartum haemorrhage, 5) Maternal conditions, 6) Specific perinatal conditions, 7) Hypoxic peripartum deaths, 8) Fetal growth restriction, 9) Spontaneous preterm birth, and 10) Unexplained antepartum death.

The values of kappa within categories of PSANZ PDC varied as shown in Table 6.15. The highest levels of kappa were found for: spontaneous preterm birth (κ = 0.831), hypertension (κ = 0.765) and specific perinatal conditions (κ = 0.745). The lowest levels of kappa were found for: antepartum haemorrhage (κ = 0.441), fetal growth restriction (κ = 0.541) and maternal conditions (κ = 0.565).

Table 6.15: Kappa values for PSANZ PDC categories (excluding congenital abnormalities)

PSANZ PDC Category	Kappa	95% Confidence Interval	Interpretation
2 Perinatal Infection	0.608	0.342-0.874	Moderate
3 Hypertension	0.765	0.584-0.946	Substantial
4 Antepartum haemorrhage	0.441	0.168-0.714	Moderate
5 Maternal Conditions	0.565	0.276-0.854	Moderate
6 Specific perinatal conditions	0.745	0.595-0.895	Substantial
7 Hypoxic peripartum death	0.664	0.045-1.000	Substantial
8 Fetal Growth Restriction	0.541	0.336-0.746	Moderate
9 Spontaneous preterm birth	0.831	0.719-0.944	Almost perfect
10 Unexplained antepartum death	0.629	0.492-0.767	Substantial

Excluding terminations of pregnancy

Of the 217 stillbirth cases, 54 were terminations of pregnancy. The majority of these terminations (72.2%) were classified as congenital abnormality by either expert or hospital review. There were 163 stillbirths after excluding all terminations of pregnancy. The leading categories according to PSANZ PDC as assigned by the hospital reviews were: unexplained antepartum stillbirth (25.8%), spontaneous preterm birth (14.1%) and specific perinatal conditions (12.9%). Similarly for reviews by the expert panel, the leading categories were: unexplained antepartum stillbirth (27.6%), spontaneous preterm birth (16.0%), and 12.3% each for congenital abnormality and specific perinatal conditions (Table 6.16). There was substantial agreement between hospital and expert panel reviews for this subgroup ($\kappa = 0.691$, 95% CI 0.641-0.725). There was substantial agreement for stillbirths less than 37 weeks ($\kappa = 0.694$, 95% CI 0.613-0.738) and those of 37 weeks or older ($\kappa = 0.634$, 95% CI 0.349-0.706).

Table 6.16: Cross-tabulation of classification by PSANZ PDC by hospital and expert panel, excluding terminations of pregnancy

Hospital	Expert 1	2	3	4	5	6	7	8	9	10	Total
1	18	0	0	0	0	0	0	0	0	1	**19**
2	1	6	0	0	0	0	0	0	2	2	**11**
3	0	0	8	0	0	1	0	0	0	1	**10**
4	0	0	1	4	0	1	0	1	1	2	**10**
5	0	0	1	1	5	0	0	0	0	1	**8**
6	0	0	0	1	0	16	0	1	1	2	**21**
7	0	0	0	0	0	0	1	0	0	0	**1**
8	0	1	2	0	0	0	1	9	0	5	**18**
9	0	0	0	1	0	0	0	0	22	0	**23**
10	1	1	0	0	3	2	0	4	0	31	**42**
Total	**20**	**8**	**12**	**7**	**8**	**20**	**2**	**15**	**26**	**45**	**163**

κ = 0.691 (0.641-0.725), agreement = 73.6%, expected agreement = 14.7%

PSANZ PDC categories: 1) Congenital abnormality, 2) Perinatal infection, 3) Hypertension, 4) Antepartum haemorrhage, 5) Maternal conditions, 6) Specific perinatal conditions, 7) Hypoxic peripartum deaths, 8) Fetal growth restriction, 9) Spontaneous preterm birth, and 10) Unexplained antepartum death.

Table 6.17: Kappa values for PSANZ PDC categories, excluding terminations of pregnancy

PSANZ PDC Category	Kappa	95% Confidence Interval	Interpretation
1 Congenital abnormality	0.913	0.815-1.000	Almost perfect
2 Perinatal Infection	0.609	0.345-0.873	Moderate
3 Hypertension	0.708	0.486-0.929	Substantial
4 Antepartum haemorrhage	0.442	0.140-0.745	Moderate
5 Maternal Conditions	0.606	0.317-0.894	Moderate
6 Specific perinatal conditions	0.749	0.593-0.905	Substantial
7 Hypoxic peripartum death	0.664	0.045-1.000	Substantial
8 Fetal Growth Restriction	0.495	0.274-0.715	Moderate
9 Spontaneous preterm birth	0.880	0.777-0.983	Almost perfect
10 Unexplained antepartum death	0.608	0.470-0.747	Moderate

Variation in agreement across the categories of PSANZ PDC are shown in Table 6.17. Almost perfect agreement was found for the categories of congenital abnormality (κ = 0.913) and spontaneous preterm birth (κ = 0.880); while lower levels of agreement were found for antepartum haemorrhage (κ = 0.442) and fetal growth restriction (κ = 0.495).

6.4 Discussion

Main findings

The aim of this study was to assess consistency in the application of the Perinatal Society of Australia and New Zealand perinatal death classification (PSANZ PDC) between hospital and expert panel review of a cohort of stillbirths investigated according to the Clinical Practice Guidelines for Perinatal Mortality Audit. A substantial level of agreement was found overall (κ = 0.737), however, there were variations in agreement within categories of the PSANZ PDC. Compared with the other PSANZ PDC categories, congenital abnormalities had the highest level of agreement, followed by spontaneous preterm birth and hypertension (even after excluding congenital abnormalities and terminations of pregnancy). Conversely, the lowest levels of agreement were found consistently for antepartum haemorrhage and fetal growth restriction.

Our findings of substantial agreement (κ = 0.737) were slightly higher than those reported for a large population based study in New South Wales published in 2008 (κ = 0.638) [131]. The higher level of overall agreement found in our study may be due to refinement of the PSANZ PDC descriptions within the perinatal mortality audit guidelines in the 2009 edition as well as increased familiarity with the classification system with the national roll out of the IMPROVE and other similar education programs [159]. In contrast the level of agreement in our study was lower than the agreement reported previously in validation studies for the PSANZ PDC [83% agreement for stillbirths using PSANZ PDC with three classifiers (κ ranging from 0.83 to 0.95)] [64].

Despite differences in the method of calculation of PSANZ PDC category-specific agreement, our study and that of Gordon and colleagues found relatively high levels of agreement for congenital abnormalities [κ = 0.953 versus 95.0% agreement], spontaneous preterm birth (κ = 0.841 versus 76.1% agreement) and specific perinatal conditions (κ = 0.757 versus 77.6% agreement). Similarly, lower levels of agreement were found for perinatal infection (κ = 0.550 versus 56.5% agreement) and maternal conditions (κ = 0.572 versus 44.7% agreement). However, there were marked differences in findings relating to antepartum haemorrhage (κ = 0.451 versus 90.1% agreement) and hypertension (κ = 0.771 versus 49.0% agreement) [131]. The reasons for these differences in relation to antepartum haemorrhage and hypertension are not immediately obvious and do not relate to changes to the PSANZ PDC made since the first edition. However, it should be noted

that our sample size was significantly smaller and may be subject to wider variation in estimates of agreement.

Interpretation of findings

Determining the cause of stillbirth is important for identifying focal areas for improvement in care provision and further reducing stillbirth rates. However, identifying the cause of death is often difficult because of complex pathophysiological processes and their interactions within the mother, baby and placenta [293]. The Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ PDC) system uses largely clinical categories with few categories for placental pathology and aims to identify the antecedent cause of death. The variation in agreement observed may derive largely from the complexity of the stillbirth case, whereby identifying a possible cause of death in the presence of many associated possible conditions.

Congenital abnormality

We found almost perfect agreement in the classification of stillbirths attributed to congenital abnormality. This may be explained by the hierarchical nature of the PSANZ PDC system [124] whereby the presence of a congenital abnormality supersedes any other associated causes as the main cause of death. Hierarchical classification systems tend to preferentially prioritise categories nearer to the top of the list. This has been demonstrated in a study by Ego and colleagues where modification of the hierarchy of the ReCoDe system resulted in a reduction in the proportion of stillbirths attributed to fetal growth restriction the reduction from 38% to 14% [294]. It can be argued that the relatively high proportion of stillbirths classified as due to congenital abnormality using the PSANZ PDC system may be as a result of congenital abnormality being at the top of the list. It was interesting to note that disagreement in classification for this category included perinatal infection and unexplained antepartum fetal death. It was also interesting to note that the autopsy rates among concordantly classified stillbirth was lower than among discordantly classified stillbirths (37.5% versus 75.0%), however there were only 4 discordantly classified stillbirths. There were similar rates of placental histopathology, chromosomal analysis and MRI between the groups of stillbirths. The category of

unexplained antepartum fetal death mainly contained deaths that could not be definitively classified elsewhere.

Perinatal Infection

In comparison to the other PSANZ PDC categories, agreement levels for perinatal infection were low. This may be a reflection of the difficulty in determining whether infection was the cause of stillbirth, particularly where autopsy and histologic examinations suggest infection as well as other aetiologic factors [295]. Determination of infection depends on histological evidence of infection in the fetus or cord or clinical evidence of infection in the mother and evidence of infection in the mother or placenta [124]. However, evidence of infection does not necessarily prove causation [295, 296] and conversely, stillbirth due to infection may not initially appear to be related to the infection [296]. Infection may be due to a wide range of bacterial, viral or protozoal agents and routine histologic examination of the placenta and fetal autopsy may miss some infectious organisms [295]. In our study we found disagreement in classification of perinatal infection mainly included congenital abnormality, unexplained antepartum fetal death and spontaneous preterm birth. The finding regarding spontaneous preterm birth is understandable given the association between perinatal infection and preterm birth [297].

Spontaneous preterm birth

We found high levels of agreement for this category. These findings may be explained by clear definitions within the classification system based on gestational age, duration of labour or rupture of membranes and findings from microscopic and macroscopic examination of the placenta [124]. However, there was some disagreement in classification with the categories of antepartum haemorrhage (abruption and other antepartum haemorrhage), specific perinatal conditions and perinatal infection. It is particularly challenging to determine the sequence of events involving bleeding with preterm birth or antepartum haemorrhage and further instructions within the perinatal mortality audit guidelines may assist in reducing ambiguity when assigning classification categories.

Antepartum haemorrhage

In ranking levels of agreement across the PSANZ PDC categories, antepartum haemorrhage consistently ranked lowest compared with the other categories. These findings may be explained by clinical scenarios wherein there are other associated probable causes or classification categories such as hypertension or spontaneous preterm birth; which make it difficult to unravel which condition initiated the chain of events resulting in the stillbirth. Where there was discordant classification within this category, the alternate classifications were: spontaneous preterm birth, specific perinatal conditions (twin-twin transfusion and fetomaternal haemorrhage), hypertension (pre-eclampsia) and maternal conditions (accidental maternal injury), unexplained antepartum fetal death and fetal growth restriction. The hierarchical nature of the classification system may have played a role in some of the discordant classifications. It was interesting to note that autopsy rates were higher among the discordantly classified stillbirths in this category (63.6% vs 40.0%).

Fetal growth restriction

Agreement was relatively low for fetal growth restriction compared with other PSANZ PDC categories. This may relate to difficulty in classifying cases with borderline biometric measurements, especially where there is maceration or where there is insufficient supporting evidence despite suspicion of growth restriction. Classification is based on antenatal ultrasound evidence of growth restriction, or brain:liver ratio from autopsy examination and histopathological examination of the placenta [124]. Where there is maceration and an absence of prior ultrasound evidence of growth restriction and an autopsy was not performed or the brain:liver ratio is less than 4:1, the PSANZ Perinatal Mortality Audit guidelines recommend classification as unexplained antepartum fetal death [124]. This hypothesis was supported by the large number of cases involved in disagreement between classification as fetal growth restriction and unexplained antepartum fetal death found in this cohort. Interestingly, the autopsy rate among concordantly classified stillbirths was significantly higher than among the discordantly classified stillbirths (81.8% vs 33.3%), this may reflect the importance of information from autopsy to assist in classification of stillbirth to the category of fetal growth restriction.

Hypertension

There was relatively high level of agreement for hypertension compared with other categories within this cohort. This may be explained by the well-defined diagnostic criteria for hypertensive disorders and information can be easily ascertained from maternal history. Furthermore, the well-established association between maternal hypertensive disorders and placental dysfunction can be observed in disagreement in the classification of stillbirth cases as due to hypertension (abruption) or fetal growth restriction or maternal conditions. The study findings imply that some of the ambiguity in determining cause of death may be due to incomplete information from investigations not performed, as suggested by findings for fetal growth restriction. This information may assist by ruling in or ruling out possible causes of death. The study also highlights difficulty with unravelling the sequence of events that lead to a stillbirth, particularly for strongly inter-related aetiologies.

Stillbirth Investigations

The PSANZ Clinical Practice Guideline for Perinatal Mortality recommends a comprehensive suite of investigations for stillbirth while acknowledging the limited evidence for many of the tests. However, placental histopathology, perinatal autopsy and cytogenetic analysis have been identified as important investigations for determining cause of stillbirth [298, 299]; as well as changing cause of death classification [126]. Although the overall autopsy rate in this study cohort was about 46%, well below the recommended 75% [129], the rate of placental histopathology was 91%. Placental histopathology has been shown to be particularly useful in determining cause of death, perhaps more so than perinatal autopsy. Chromosomal analysis was undertaken in 42% of cases.

The rate of magnetic resonance imaging (MRI) in this cohort of stillbirths was 6.9%. Post mortem MRI has been proposed as a non-invasive alternative to autopsy, especially where parents decline conventional autopsy examination [300]. The main advantages of MRI include its non-invasive nature and its accuracy in detecting cerebral, cardiac and renal abnormalities [301]. While there is a lack of tissue sampling [300]; MRI can be used to estimate organ weight and volume [302, 303]. There is some evidence that post-mortem MRI combined with blood tests and other non-invasive ancillary testing may provide similar information to conventional autopsy examination in a proportion of perinatal deaths [301].

The proportion of unexplained stillbirths was 20.7% and 22.8% among hospital and expert panel reviews, respectively. These values were lower than those reported for the state of Queensland for 2004 to 2008 (29.9%) [4]; and significantly lower than the proportion of unexplained antepartum fetal death classified by the expert panel in NSW during 2002-2004 (41.5%). This may reflect the slightly higher autopsy rates among our study cohort (47.8% vs 30.7% for Queensland during 2004-2008 vs 37.5% for NSW during 2002-2004) [4, 131] as well as the higher rates of placental histopathology in our cohort compared with the NSW cohort (92.4% vs 84.7%) [131]. In addition, the lower limit of gestational age for the reviews in NSW was 22 weeks compared with 20 weeks for our cohort, this may have impacted on the proportion of unexplained antepartum fetal deaths, as it has been reported that this proportion increases with gestational age (Chapter 3).

In our study cohort, it was interesting that there were higher rates of placental histopathology, autopsy and chromosomal analysis among unexplained stillbirths compared with 'explained' stillbirths. These findings suggest that for these cases, perhaps these investigations provided information to rule out a possible cause of death but not definitively point to a cause of death.

Strengths and Limitations

A substantial number of participating hospitals did not provide data for the study. It is possible that this may have introduced bias whereby hospitals more likely to participate were also more likely to comply with the perinatal mortality audit guidelines. A possible outcome of this might be more optimistic estimates of agreement between hospital and expert panel review.

Another related issue was regarding representativeness of the stillbirth cohort. There was limited national data available on maternal and pregnancy characteristics of stillbirth. Comparison with population data from Queensland showed this study cohort to be similar across a number of characteristics including gestational age at birth, maternal smoking, type of stillbirth, maternal age and sex distribution; although it should be noted that the Queensland data was for singleton stillbirths. Furthermore, there was a significant proportion of women of Maori or Pacific Islander background within this cohort. Further research is needed to determine if this finding was as a result of bias or if this group of women were truly over-represented among women with a stillbirth.

All attempts were made to ensure the expert panel had access to the same information as the hospital committees; however, it is possible that hospital committees had more detailed information from maternal history to inform their classifications.

6.5 Conclusion

This study found substantial agreement between hospital and expert panel classifications of stillbirth, however, there is need for additional training and guidance in assigning classification for the categories of antepartum haemorrhage and fetal growth restriction, in particular. These findings can inform the education program for the PSANZ perinatal mortality audit guidelines and the perinatal death classification system.

Chapter 7

Parental Consent to Stillbirth Autopsy Study

7.1 Introduction

Stillbirth is a devastating pregnancy outcome for women and families. In 2012, one in 139 pregnancies reaching 20 weeks ended in stillbirth in Queensland [24]. In recent times, there has been little reduction in stillbirth rates in many high income countries [13] and Australian reports suggest national rates may be increasing [23, 174]. Accurate determination of cause of death is critical to effective prevention; and current lack of knowledge about the underlying causes of stillbirth is a barrier to progress with further reducing national rates. A large proportion of stillbirths are unexplained and in Queensland nearly 60% of stillbirths occurring around term (37 weeks or older) are unexplained (Chapter 3). The disparity in stillbirth rates and risk observed between Indigenous and non-Indigenous women also extends to unexplained stillbirths which are higher among Indigenous women (3.2 vs 2.0/1000, RR 1.61, 95% CI 1.37-1.90 [223].

Autopsy is the gold standard for determining cause of death following a stillbirth [125]. International guides recommend that all parents should be offered the option of an autopsy following a stillbirth [28] but perinatal autopsy rates are declining [127, 304]. The stillbirth autopsy rate in Queensland is around 37% [223]. Since thorough post mortem investigation reveals a cause of death in a substantial number of stillbirths of unknown clinical cause it has been argued that many stillbirths are unexplored rather than unexplained [305]. The reasons for this decline in autopsy rates are varied; however, parental consent is a major factor [132]. The process of counselling and consent is difficult for both clinicians and parents. It is an intrusive process for parents and requires understanding of detailed consent procedures in a state of acute grief. Studies show that clinicians often feel ill-equipped to initiate such discussions with parents [126]. At present, approaches to communication and consent procedures are not evidence-based and therefore must rely on the ad hoc knowledge and experience of staff [306]. It is unclear how healthcare professionals can support parents in this difficult decision. Gaining an understanding of the factors associated with autopsy consent is important to improving the

quality of data on causes of stillbirth and to the wellbeing of bereaved parents including the management of subsequent pregnancies.

Presented in this chapter are findings from a mixed methods investigation aiming to gain an understanding of parents' views and experiences of the autopsy consent process to inform clinical practice. The analysis presented uses three data sources (two quantitative, one qualitative) from two separate studies. These are:

- Population based analysis of predictors of autopsy using perinatal data from the Queensland Perinatal Data Collection (quantitative)
- Information and communication about autopsy following stillbirth: meeting the needs of parents (*Stillbirth Autopsy Consent Study* – mixed methods)
- Investigating the cause of stillbirth: a prospective cohort study examining use and effectiveness of a comprehensive investigation protocol (*Stillbirth Investigations Study* - quantitative)

The qualitative component of the study is informed by quantitative analyses to identify sociodemographic, pregnancy and medical factors which are associated with whether or not autopsy is performed following a stillbirth. To our knowledge, no recent studies have assessed predictors of stillbirth autopsy. The qualitative component aims to explore and understand parents' experiences of the autopsy consent process within the dimensions of factors identified as predictors of parental consent for autopsy.

Findings from the qualitative and quantitative components of this study were presented at the Perinatal Society of Australia and New Zealand (PSANZ) conference in April 2015 (Appendix G2 and G1) and a manuscript based on the quantitative component of the study has been submitted for publication.

7.2 Methods

Theoretic Framework and Research Design

This study focuses primarily on the qualitative component of a study nested in the *Stillbirth Autopsy Consent Study (SACS)*. The overall aim of *SACS* was to improve communication regarding perinatal autopsy to increase autopsy rates and enhance bereaved parents' long term mental and reproductive health. The primary objectives were:

- determine factors that predict consent, regret and decisional conflict with regards to perinatal autopsy,
- determine parental views and experiences with communication about post mortem investigations and autopsy consenting process, and
- determine effect of parents' decisions regarding autopsy on longer term psychosocial outcomes such as grief.

The above described *SACS* was in turn linked to the *Stillbirth Investigations Study* discussed in Chapter 6. The online database used in the Chapter 6 study was used to collect sociodemographic, medical and pregnancy data for women involved in both studies.

The nested mixed methods study involved a quantitative population-based analysis of predictors of autopsy to inform recruitment of participants for in-depth qualitative interviews exploring the views and experiences of parent going through the autopsy consent process. A pragmatic approach was taken in relation to the study design and methodology; this meant that the research question was central and any data collection and analysis methods that provided insight were utilised [307]. The mixed methods study design was particularly appropriate because of the complex nature of the study topic, and the ability to explore and integrate lines of enquiry that require qualitative and quantitative methods. A number of issues relating to the mixed methods study design were considered, namely: which aspects would be emphasised (**priority**), how the study would be implemented (**implementation)** and how the qualitative and quantitative components would be connected (**integration**) [307]. Priority was given to the qualitative components of the study as these were involved in addressing the main study objective. The qualitative line of enquiry was also a natural progression to exploration of the quantitative findings. Implementation of the study was carried out sequentially:

- Phase 1 was a population based retrospective analysis aiming to determine which maternal demographic, pregnancy and medical factors were associated with consent to an autopsy following stillbirth; and
- Phase 2 consisted of in-depth telephone interviews with parents to gain an understanding of parents' experience of autopsy consent processes following a stillbirth.

It was intended that integration of the qualitative and quantitative components occurred at the beginning of the qualitative phase with purposive sampling of participants based on findings from the quantitative analysis and integration of the components during the interpretation and discussion of findings. However, in practice purposive sampling was not possible as a result of prolonged ethics and governance processes and significant barriers to recruitment at the hospital level. Figure 7.1 shows the intended sequence of study implementation.

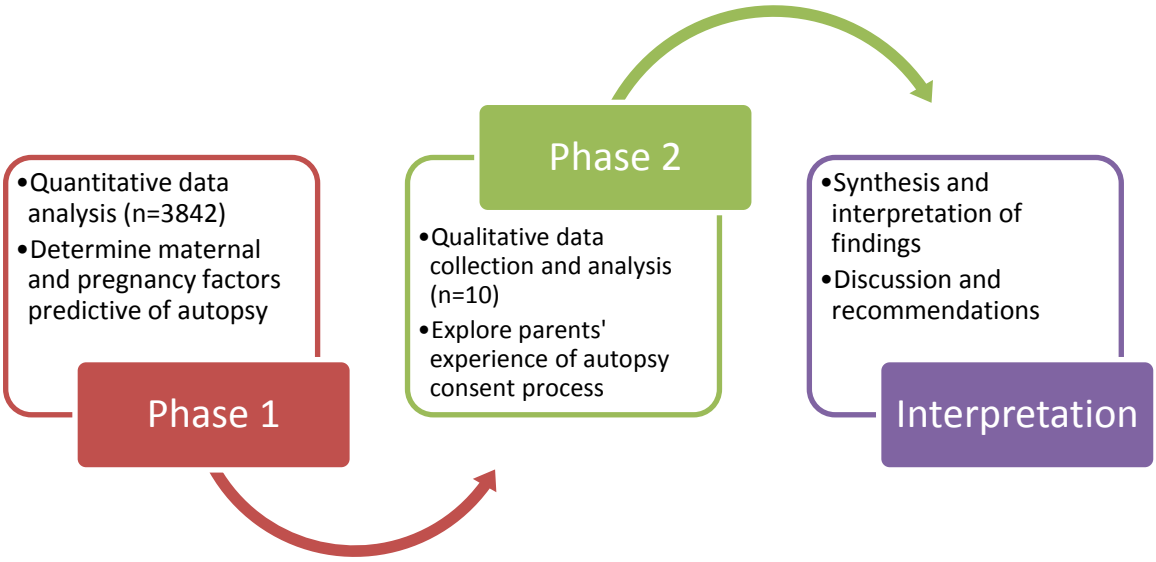


Figure 7.1: Relationship between the study phases, Parental Consent to Stillbirth Autopsy Study

Phase 1 Quantitative Methods: Study Population and Data source

This study involved all women with a singleton stillbirth of at least 20 weeks gestation or 400grams birthweight in Queensland between July 2000 and December 2011. Excluded from analyses were stillbirths as a result of termination of pregnancy for maternal

psychosocial reasons and stillbirths with unknown maternal Indigenous status (Figure 7.2). Terminations for maternal psychosocial reasons were excluded because it was hypothesised that factors affecting decisions for autopsy may apply differently within this group. Indigenous women have higher rates of stillbirth and are a subgroup of interest within this thesis, and for these reasons women with missing data on Indigenous status were excluded from analysis. The timeframe for births was chosen because mid 2000 was the earliest period with complete data on whether or not an autopsy was performed.

Data for this study was obtained from the Queensland Perinatal Data Collection (QPDC). Maternal demographic data included age, Indigenous status, region of birth, marital status, socioeconomic status and geographic location. Pregnancy and medical data included parity, hospital accommodation, smoking, substance use, assisted conception use, diabetes (pre-existing and gestational), hypertensive disorders (pre-existing, pregnancy induced and pre-eclampsia/eclampsia) and antepartum haemorrhage. Birth outcome data included congenital abnormality, small for gestational age (defined as birthweight less than 10th Australian population percentile by gender and plurality), gestational age at birth, diagnosis of unexplained stillbirth on the death certificate, and type of stillbirth (antepartum, intrapartum and unknown if antepartum or intrapartum). Data management was undertaken as outlined in section 2.2.

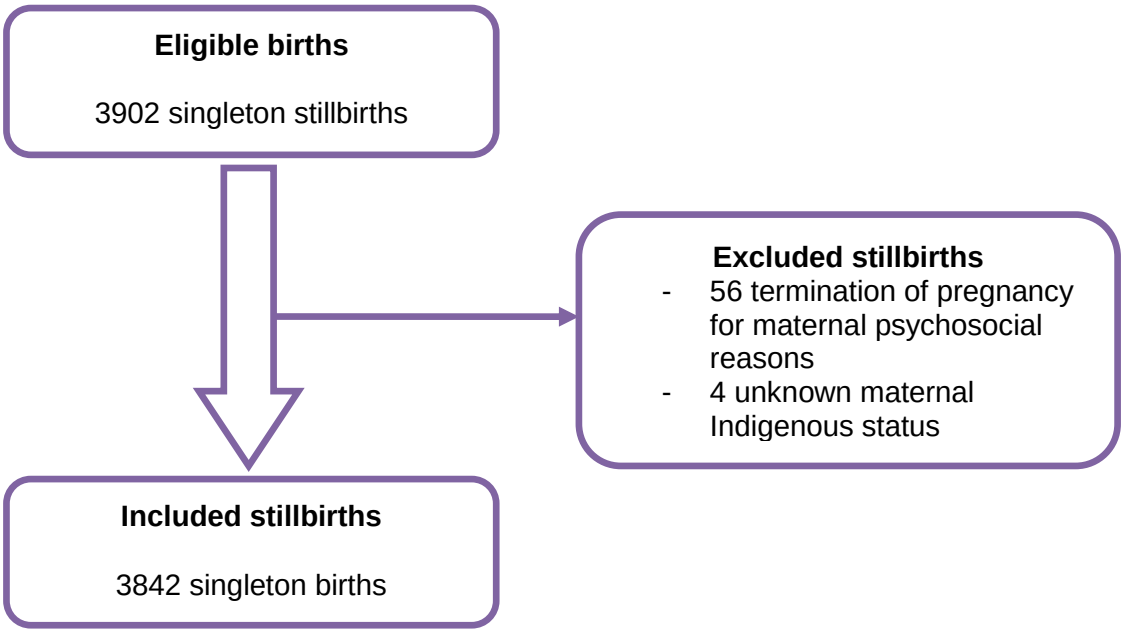


Figure 7.2: Flowchart showing study population and exclusions, Parental Consent to Stillbirth Autopsy Study

Statistical analysis

The primary outcome measure was autopsy following stillbirth (either full or partial). This measure was used as a proxy to indicate parental consent for autopsy. Triennial perinatal autopsy rate per 100 singleton stillbirths were calculated overall and by subgroups. Differences in characteristics between women who consented to an autopsy for their baby and those who did not were assessed using Chi square test. Univariate association between maternal characteristics and autopsy was explored using logistic regression. In addition, interactions were explored between closely related predictor variables. Statistically significant interactions were found between gestational age group and whether or not a stillbirth was unexplained on the death certificate, as well as between gestational age group and whether or not there was a congenital abnormality. The odds ratios for the interaction terms were as follows:

Gestational age group AND Unexplained fetal death	
20-23 weeks AND unexplained fetal death	1.92 (1.31-2.81)
24-27 weeks AND unexplained fetal death	1.88 (1.18-3.01)
28-36 weeks AND unexplained fetal death	1.58 (1.08-2.33)
Relative to: ≥ 37 weeks AND explained fetal death	
Gestational age group AND congenital abnormality	
20-23 weeks AND congenital abnormality	0.44 (0.28-0.70)
24-27 weeks AND congenital abnormality	0.37 (0.21-0.66)
28-36 weeks AND congenital abnormality	0.35 (0.21-0.58)
Relative to: ≥ 37 weeks AND no congenital abnormality	

Multivariate analysis was undertaken including all predictors that were significantly associated with autopsy in univariate analyses and analysis was stratified by gestational age (<24, 24-27, 28-36 and ≥37 weeks). These groups were chosen to reflect commencement of active management (24 weeks), for international comparison (28 weeks) and to differentiate preterm and term stillbirths (37 weeks). Statistical analysis was performed using Stata/SE for Windows 13.1 (StataCorp LP 2013, College Station, TX, USA).

Phase 2 Qualitative Methods: Study Population/Participants

This qualitative study was nested in a larger prospective mixed methods study (*SACS*) involving 5 Queensland hospitals. All women (and their partners) who experienced stillbirth (a baby born without signs of life of at least 20 weeks gestation or 400g

birthweight) at a participating hospital during a defined 6-month recruitment period were eligible to participate in *SACS*. As the purpose of the study was to gain understanding of the range of needs and experiences of parents faced with decisions about autopsy following stillbirth, a wide cross section of participants were included. *SACS* was expected to recruit approximately 60 women (and 30 partners) during a 6 month period.

For the qualitative study involving in-depth interviews, a subset of 10 participants from *SACS* were to be selected based on key relevant dimensions (ie demographic and pregnancy factors) found to be associated with consent for autopsy. The only group specifically excluded from this study design were people with a cognitive impairment, an intellectual disability or a mental illness, due to the excessive burden likely to be imposed by participation. Women deemed by their attending clinician to be unsuitable to approach for any reason relating to their personal or social circumstances were also excluded from the study. Parents whose first language was not English were excluded as accessing interpreter services for the telephone interview was outside the scope of the study.

As noted previously, significant delays in obtaining ethics and governance authorisations delayed commencement of the study (see Appendix A for details of ethics approvals); as well as staffing resource issues at the participating hospitals resulted in slower recruitment rates than anticipated. Despite extending the recruitment period, a total of six parents instead of ten were recruited to the study.

Recruitment and Consent for study

Potentially eligible women and their partners were identified and with the approval of the treating doctor were advised of the study. Full oral and written information about the study (Appendix C) was given to women and their partners prior to hospital discharge, where possible and appropriate, and informed written consent was obtained from those parents who wished to participate. Where it was not possible or appropriate to discuss the study with parents at or prior to discharge, the information sheet and consent form was included in their take-home pack. Parents wishing to take part in the study could return the completed consent form by mail or at their 6-8 week hospital follow up visit. Only parents who gave consent to the SACS study were eligible to participate in the in-depth interviews.

Procedures

Six parents were interviewed via telephone at a time period 4-6 months after stillbirth as stipulated by the study protocol. Partners were given the option of being interviewed together with the mother or separately. Parents were contacted by the study interviewer to arrange a suitable time and verify telephone contact details. Semi structured interviews with broad, open ended questions were used to elicit responses from parents regarding their experiences of the autopsy consenting process. The broad nature of the questions allowed further exploration of topics raised by parents. The interview schedule is presented in Appendix D. The interviews ranged from 20 to 40 minutes.

Data Management

All women in the study were assigned a unique study ID which was included on all components of the data collection to enable data linkage. The in-depth qualitative interviews were digitally recorded (with the consent of the participants) and transcribed in full into a text file that was stored on a password-protected computer. A professional transcription service was used to guarantee accuracy and confidentiality. All hard copies of the interview transcripts were rendered non-identifiable and stored securely in a locked filing cabinet accessible only to authorised members of the research team.

Data Analysis

Analysis involved a detailed reading of the transcript by two study team members to generate initial categories and codes and identify patterns contained in the data. The use of at least two team members during this process provided analytic triangulation which helped to reduce researcher bias and address issues of internal reliability. The data from the transcripts was then grouped and classified according to initial codes. The transcripts were reviewed and coded independently, conceptual consistency of the themes was checked by the two coders and any differences resolved via discussion. Themes were developed and defined using an iterative process in order to capture a meaningful and rigorous account of the data relevant to the research questions. Data management and analysis was done manually.

7.3 Results

Phase 1 Quantitative Results

During the study period, a total of 3,842 women with a singleton stillbirth were included in the analysis. Of these women, 1356 (35.3%) had an autopsy for their baby following stillbirth. Further, the autopsy rate over the study period was 25.1% and 36.3%, respectively among Indigenous and non-Indigenous women. There was a non-statistically significant trend towards a 1% per annum increase in overall autopsy rates (OR 1.01, 95% CI 0.99-1.03; p_{trend}=0.205) over the study period. Likewise there was no statistically significant trend in autopsy rates among Indigenous (p_{trend}=0.363) and non-Indigenous women (p_{trend}=0.335). Assessing autopsy rates by gestational age groups, a significant increase of 9% per annum over the study period was found for stillbirths occurring at 24-27 weeks (OR 1.09, 95% CI 103-1.15; p_{trend}=0.004). No significant trends were found for other gestational age groups. Triennial autopsy rates for the whole population and by gestational age group are presented in Figures 7.3 and 7.4, respectively.

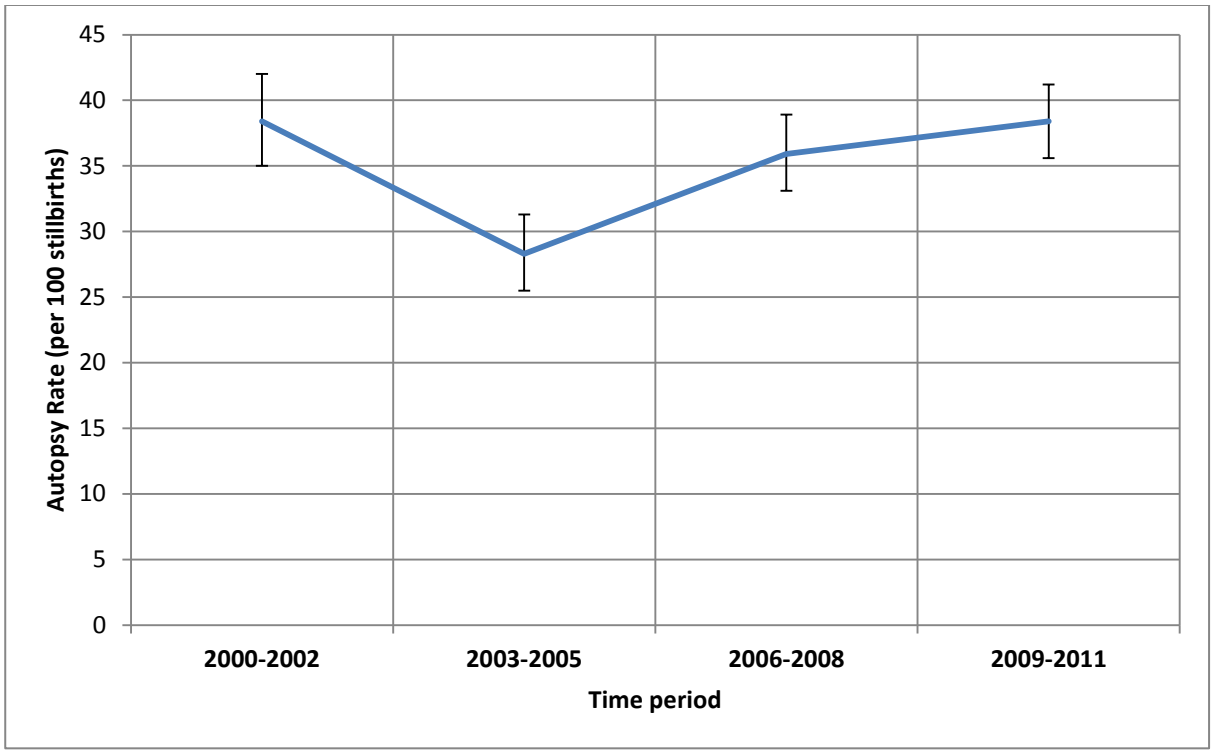


Figure 7.3: Triennial autopsy rates (per 100 singleton stillbirths), Queensland, mid 2000-2011

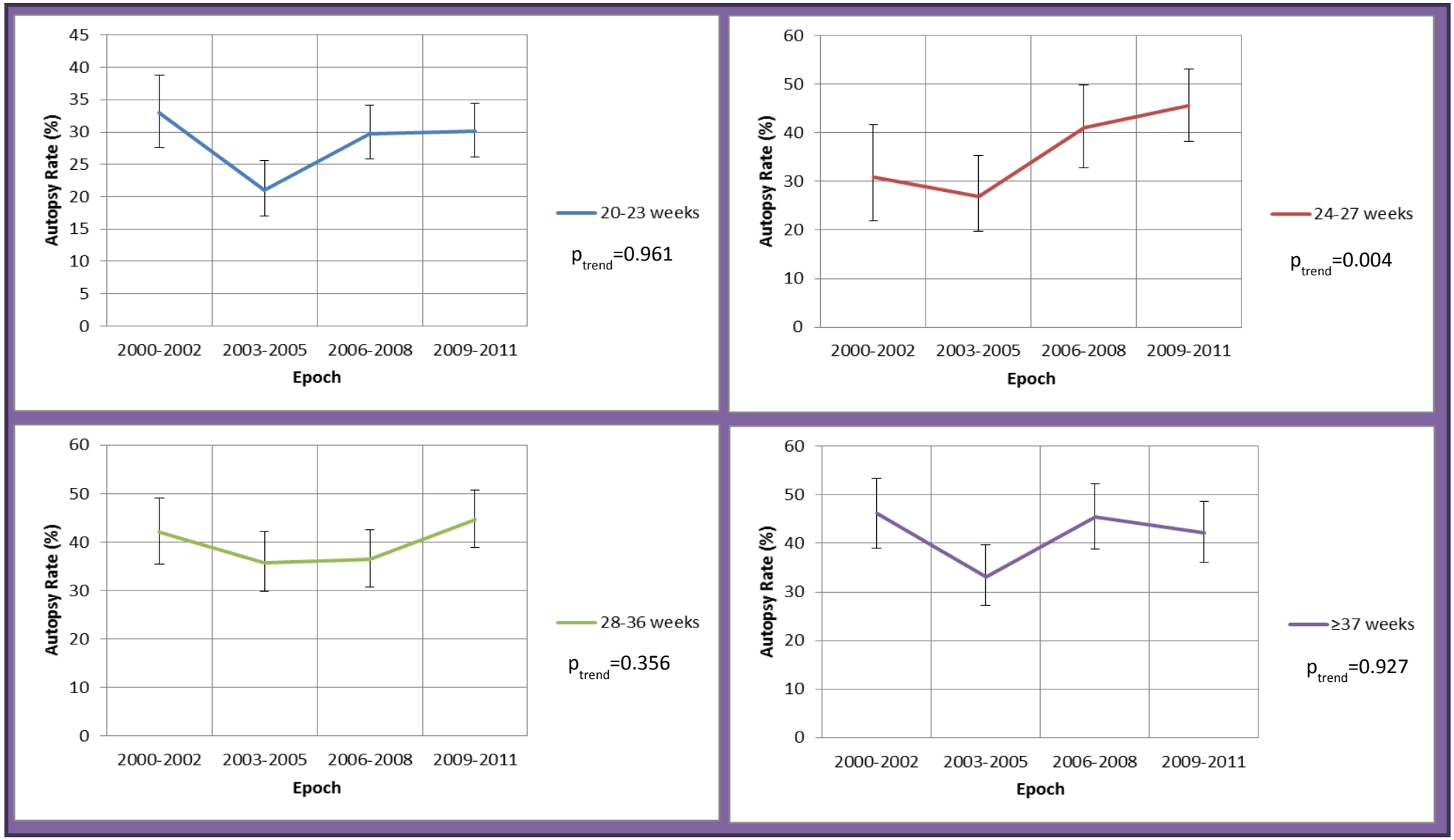


Figure 7.4: Triennial autopsy rates by gestational age group, Queensland, mid 2000-2011

The characteristics of the cohort of women and babies by autopsy status are given in Table 7.1. Where an autopsy was performed for a stillborn baby, mothers were more likely to be primiparous (OR 1.47, 95% CI 1.28-1.70), aged 19-24 years (OR 1.24, 95% CI 1.04-1.48), have been born in Europe (OR 1.43, 95% CI 1.02-2.01), have gestational diabetes (OR 1.47, 95% CI 1.03-2.09), pregnancy-induced hypertension (OR 1.61, 95% CI 1.01-2.57), have a baby with a congenital abnormality (OR 1.30, 95% CI 1.13-1.50) or have a small-for-gestational age baby (OR 1.28, 95% CI 1.11-1.48). Conversely, where an autopsy was performed for a stillborn baby, mothers were less likely to be Indigenous (OR 0.59, 95% CI 0.46-0.76), socioeconomically disadvantaged (OR 0.73, 95% CI 0.58-0.93), aged 35 years or older (OR 0.81, 95% CI 0.67-0.98), live in a regional area (OR 0.84, 95% CI 0.73-0.96), have been born in the Oceania region (OR 0.54, 95% CI 0.33-0.90), have antepartum haemorrhage (OR 0.70, 95% CI 0.58-0.83), have a very preterm baby (20-23 weeks) (OR 0.56, 95% CI 0.47-0.67), have an initially unexplained stillbirth (OR 0.83, 95% CI 0.72-0.95) or an intrapartum stillbirth (OR 0.55, 95% CI 0.46-0.66)(Table 7.2).

Table 7.1: Maternal and pregnancy characteristics by autopsy status for 3,842 women with a singleton stillbirth, Queensland, mid 2000-2011

Characteristics	Autopsy (n=1 356)	No Autopsy (n=2 486)	p value
Maternal age			
≤18 years	39 (2.9)	71 (2.9)	
19-24 years	368 (27.1)	558 (22.5)	
25-30 years	422 (31.1)	794 (31.9)	0.001
31-34 years	279 (20.6)	489 (19.7)	
35+ years	248 (18.3)	574 (23.1)	
Smoking status*			
Non smoker	631 (46.5)	1 029 (41.4)	
Smoker	204 (15.0)	375 (15.1)	0.234
missing	521 (38.4)	1082 (43.5)	
Indigenous status			
Indigenous	89 (6.6)	265 (10.7)	<0.001
Non Indigenous	1 267 (93.4)	2 221 (89.3)	
Maternal region of birth			
Africa	21 (1.5)	27 (1.1)	
Americas and Caribbean	13 (1.0)	20 (0.8)	
Eastern Asia	16 (1.2)	40 (1.6)	0.057
Central, South and West Asia	22 (1.6)	36 (1.4)	
South East Asia	33 (2.4)	63 (2.5)	
Europe	63 (4.6)	81 (3.3)	

Characteristics	Autopsy (n=1 356)	No Autopsy (n=2 486)	p value
Australia and New Zealand	1 164 (85.8)	2 145 (86.3)	
Oceania	20 (1.5)	68 (2.7)	
missing	4 (0.3)	6 (0.2)	
Socioeconomic status			
Highest ranked 20%	174 (12.8)	270 (10.9)	
Middle ranked 60%	926 (68.3)	1 679 (67.5)	0.038
Lowest ranked 20%	251 (18.5)	531 (21.4)	
missing	5 (0.4)	6 (0.2)	
Substance Use			
Yes	28 (2.1)	38 (1.5)	0.221
No	1 328 (97.9)	2 448 (98.5)	
Primiparity			
Yes	473 (34.9)	662 (26.6)	
No	883 (65.1)	1 822 (73.3)	<0.001
missing	-	2 (0.1)	
Assisted Conception			
Yes	51 (3.8)	96 (3.9)	
No	1 301 (95.9)	2 385 (95.9)	0.881
missing	4 (0.3)	5 (0.2)	
Hospital accommodation status			
Public	1 113 (82.1)	2 020 (81.3)	
Private	241 (17.8)	461 (18.5)	0.549
missing	2 (0.1)	5 (0.2)	
Any pregnancy complications			
Yes	1 336 (98.5)	2 445 (98.4)	
No	20 (1.5)	40 (1.6)	0.748
missing	-	1 (0.0)	
Antepartum haemorrhage			
Yes	201 (14.8)	497 (20.0)	<0.001
Pre-existing diabetes			
Yes	35 (2.6)	52 (2.1)	0.330
Gestational diabetes			
Yes	56 (4.1)	71 (2.9)	0.035
Any diabetes			
Yes	91 (6.7)	123 (5.0)	0.023
Pre-existing hypertension			
Yes	28 (2.1)	52 (2.1)	0.956
Pregnancy-induced hypertension			
Yes	34 (2.5)	39 (1.6)	0.042
Pre-eclampsia/Eclampsia			
Yes	58 (4.3)	82 (3.3)	0.122
Any hypertension			
Yes	120 (8.9)	171 (6.9)	0.027
Preterm birth			
Yes	1 004 (74.0)	1 988 (80.0)	
No	348 (25.1)	490 (19.7)	<0.001
missing	4 (0.3)	8 (0.3)	
Gestational age group			

Characteristics	Autopsy (n=1 356)	No Autopsy (n=2 486)	p value
20-23 weeks	441 (32.5)	1 106 (44.5)	
24-27 weeks	186 (13.7)	311 (12.5)	
28-36 weeks	377 (27.8)	571 (23.0)	<0.001
≥ 37 weeks	348 (25.7)	490 (19.7)	
missing	4 (0.3)	8 (0.3)	
Gender			
Male	721 (53.2)	1 284 (51.6)	
Female	612 (45.1)	1 171 (47.1)	0.283
Undetermined	23 (1.7)	29 (1.2)	
missing	-	2 (0.1)	
Small for gestational age			
Yes	460 (33.9)	716 (28.8)	
No	859 (63.3)	1 718 (69.1)	0.001
missing	37 (2.7)	52 (2.1)	
Congenital abnormality			
Yes	483 (35.6)	741 (29.8)	
No	871 (64.2)	1 742 (70.1)	<0.001
missing	2 (0.1)	3 (0.1)	
Unexplained stillbirth**			
Yes	523 (38.6)	1 071 (43.1)	0.007
No	833 (61.4)	1 415 (56.9)	
Type of stillbirth			
Antepartum	1 024 (75.5)	1 574 (63.3)	
Intrapartum	179 (13.2)	501 (20.2)	<0.001
Unknown	153 (11.3)	411 (16.5)	
Geographic location			
Major city	803 (59.2)	1 358 (54.6)	
Regional	501 (36.9)	1 009 (40.6)	0.015
Remote	51 (3.8)	119 (4.8)	
missing	1 (0.1)	-	
Epoch			
2000-2002	282 (20.8)	452 (18.2)	
2003-2005	260 (19.2)	659 (26.5)	<0.001
2006-2008	378 (27.9)	674 (27.1)	
2009-2011	436 (32.2)	701 (28.2)	

Percentages may add up to greater than 100% due to rounding.
Missing values omitted from Chi square and Fisher's exact tests.
*Data on maternal smoking collected from mid 2005 onwards.
** Initially unexplained on death certificate (ICD10AM code: P95) before investigations performed

Table 7.2: Univariate association between maternal and pregnancy factors and stillbirth autopsy, mid 2000-2011 (n=3 842)

Characteristics	Odds Ratio (95% Confidence Interval)
Maternal Age (Ref: 25-30 years)	
≤18 years	1.03 (0.69-1.55)
19-24 years	1.24 (1.04-1.48)
31-34 years	1.07 (0.89-1.30)
35+ years	0.81 (0.67-0.98)
Smoking status (Ref: Non-smoker)	
Smoker	0.89 (0.73-1.08)
Indigenous status (Ref: Non Indigenous)	
Indigenous	0.59 (0.46-0.76)
Maternal Region of birth (Ref: Australia and New Zealand)	
Africa	1.43 (0.81-2.55)
Americas and Caribbean	1.20 (0.59-2.42)
East Asia	0.74 (0.41-1.32)
Central, South and West Asia	1.13 (0.66-1.92)
South East Asia	0.97 (0.63-1.48)
Europe	1.43 (1.02-2.01)
Oceania	0.54 (0.33-0.90)
Socioeconomic status (Ref: Highest ranked 20%)	
Middle ranked 60%	0.86 (0.70-1.05)
Lowest ranked 20%	0.73 (0.58-0.93)
Substance Use (Ref: No)	
Yes	1.36 (0.83-2.22)
Primiparity (Ref: No)	
Yes	1.47 (1.28-1.70)
Assisted Conception (Ref: No)	
Yes	0.97 (0.69-1.38)
Hospital accommodation status (Ref: Private)	
Public	1.05 (0.89-1.25)
Pregnancy complications (Ref: No)	
Yes	1.09 (0.63-1.88)
Antepartum haemorrhage (Ref: No)	
Yes	0.70 (0.58-0.83)
Pre-existing diabetes (Ref: No)	
Yes	1.24 (0.80-1.91)
Gestational diabetes (Ref: No)	
Yes	1.47 (1.03-2.09)
Any diabetes (Ref: No)	
Yes	1.38 (1.05-1.83)
Pre-existing hypertension (Ref: No)	
Yes	0.99 (0.62-1.57)
Pregnancy-induced hypertension (Ref: No)	
Yes	1.61 (1.01-2.57)
Pre-eclampsia/Eclampsia (Ref: No)	
Yes	1.31 (0.93-1.85)
Any hypertension (Ref: No)	

Characteristics	Odds Ratio (95% Confidence Interval)
Yes	1.31 (1.03-1.68)
Preterm birth (Ref: ≥37 weeks)	
20-23 weeks	0.56 (0.47-0.67)
24-27 weeks	0.84 (0.67-1.06)
28-36 weeks	0.93 (0.77-1.12)
Gender (Ref: Female)	
Male	1.07 (0.94-1.23)
Undetermined	1.52 (0.87-2.65)
Small for gestational age (Ref: No)	
Yes	1.28 (1.11-1.48)
Congenital abnormality (Ref: No)	
Yes	1.30 (1.13-1.50)
Unexplained stillbirth (Ref: No)	
Yes	0.83 (0.72-0.95)
Type of stillbirth (Ref: Antepartum)	
Intrapartum	0.55 (0.46-0.66)
Unknown	0.57 (0.47-0.70)
Geographic location (Ref: Major City)	
Regional	0.84 (0.73-0.96)
Remote	0.72 (0.52-1.02)
Epoch (Ref: 2000-2002)	
2003-2005	0.63 (0.51-0.78)
2006-2008	0.90 (0.74-1.09)
2009-2011	1.00 (0.82-1.21)

Initially unexplained on death certificate (ICD10AM code: P95) before investigations performed

Multivariate association between maternal/pregnancy characteristics and autopsy status

Less than 24 weeks

In the less than 24 week gestation group, women with a small-for-gestational age baby (aOR 1.49, 95% CI 1.15-1.95) or a baby with a congenital abnormality (aOR 1.62, 95% CI 1.22-2.16) were more likely to have an autopsy performed for their stillborn baby. Maternal age of 35 years or older (aOR 0.70, 95% CI 0.49-0.99), Indigenous status (aOR 0.53, 95% CI 0.32-0.90), socioeconomic disadvantage (aOR 0.57, 95% CI 0.36-0.89), intrapartum stillbirth (aOR 0.64, 95% CI 0.47-0.87) and stillbirths where it was unknown if they were antepartum or intrapartum (aOR 0.60, 95% CI 0.43-0.82) were associated with decreased odds of having an autopsy performed (Table 7.3).

Table 7.3: Maternal and pregnancy factors associated with autopsy, less than 24 weeks, mid 2000-2011 (n=1 547)

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
Maternal Age (Ref: 25-30 years)	
≤18 years	1.23 (0.55-2.76)
19-24 years	1.25 (0.91-1.73)
31-34 years	0.92 (0.66-1.29)
35+ years	0.70 (0.49-0.99)
Australian Indigenous status (Ref: Non Indigenous)	
Indigenous	0.53 (0.32-0.90)
Maternal region of birth (Ref: Australia and New Zealand)	
Africa	1.40 (0.50-4.00)
Americas and Caribbean	0.60 (0.16-2.24)
East Asia	1.03 (0.43-2.47)
Central, South and West Asia	1.65 (0.69-3.95)
South East Asia	0.73 (0.30-1.80)
Europe	1.60 (0.89-2.89)
Oceania (excl Australia and New Zealand)	0.80 (0.26-2.49)
Socioeconomic status (Ref: Highest ranked 20%)	
Middle ranked 60%	0.70 (0.49-1.00)
Lowest ranked 20%	0.57 (0.36-0.89)
Primiparity (Ref: No)	
Yes	1.15 (0.88-1.52)
Antepartum haemorrhage (Ref: No)	
Yes	1.26 (0.90-1.76)
Pregnancy-induced hypertension (Ref: No)	
Yes	0.80 (0.08-7.69)
Gestational diabetes (Ref: No)	
Yes	2.33 (0.73-7.44)
Small for gestational age (Ref: No)	
Yes	1.49 (1.15-1.95)
Unexplained fetal death (Ref: No)	
Yes	0.86 (0.62-1.21)
Congenital abnormality (Ref: No)	
Yes	1.62 (1.22-2.16)
Type of stillbirth (Ref: Antepartum)	
Intrapartum	0.64 (0.47-0.87)
Unknown	0.60 (0.43-0.82)
Remoteness (Ref: Major City)	
Regional	0.97 (0.75-1.26)
Remote	1.82 (0.97-3.40)
Epoch (Ref: 2000-2002)	
2003-2005	0.57 (0.39-0.83)
2006-2008	0.85 (0.60-1.20)
2009-2011	0.80 (0.57-1.14)

Initially unexplained on death certificate (ICD10AM code: P95) Gestational age missing for 12 births

24 – 27 weeks

Among those with a stillbirth in the 24-27 week gestational age group, women with a small-for-gestational age baby were more likely to have an autopsy performed for their stillborn baby (aOR 1.56, 95% CI 1.02-2.38). Conversely, autopsy was less likely to be performed for a stillborn baby among women who had antepartum haemorrhage (aOR 0.53, 95% CI 0.31-0.89), an intrapartum stillbirth (aOR 0.38, 95% CI 0.18-0.81) or where it was unknown if the stillbirth was antepartum or intrapartum (aOR 0.23, 95% CI 0.08-0.65) (Table 7.4).

Table 7.4: Maternal and pregnancy factors associated with autopsy, 24-27 weeks, mid 2000-2011 (n=497)

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
Maternal Age (Ref: 25-30 years)	
≤18 years	0.54 (0.15-1.96)
19-24 years	1.50 (0.83-2.70)
31-34 years	1.17 (0.66-2.07)
35+ years	0.67 (0.37-1.21)
Australian Indigenous status (Ref: Non Indigenous)	
Indigenous	0.44 (0.18-1.12)
Maternal region of birth (Ref: Australia and New Zealand)	
Africa	0.24 (0.04-1.38)
Americas and Caribbean	0.37 (0.03-4.66)
East Asia	0.25 (0.03-2.36)
Central, South and West Asia	0.43 (0.07-2.51)
South East Asia	0.26 (0.06-1.03)
Europe	0.96 (0.38-2.45)
Oceania (excl Australia and New Zealand)	0.80 (0.19-3.31)
Socioeconomic status (Ref: Highest ranked 20%)	
Middle ranked 60%	0.80 (0.41-1.55)
Lowest ranked 20%	0.59 (0.27-1.29)
Primiparity (Ref: No)	
Yes	1.15 (0.71-1.84)
Antepartum haemorrhage (Ref: No)	
Yes	0.53 (0.31-0.89)
Pregnancy-induced hypertension (Ref: No)	
Yes	2.43 (0.69-8.50)
Gestational diabetes (Ref: No)	
Yes	1.31 (0.39-4.37)
Small for gestational age (Ref: No)	
Yes	1.56 (1.02-2.38)
Unexplained fetal death (Ref: No)	

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
Yes	0.73 (0.46-1.16)
Congenital abnormality (Ref: No)	
Yes	1.02 (0.61-1.71)
Type of stillbirth (Ref: Antepartum)	
Intrapartum	0.38 (0.18-0.81)
Unknown	0.23 (0.08-0.65)
Remoteness (Ref: Major City)	
Regional	0.70 (0.45-1.09)
Remote	0.61 (0.20-1.83)
Epoch (Ref: 2000-2002)	
2003-2005	0.69 (0.35-1.35)
2006-2008	1.35 (0.70-2.59)
2009-2011	1.68 (0.90-3.13)

Initially unexplained on death certificate (ICD10AM code: P95). Gestational age missing for 12 births

28-36 weeks

Women aged 19-24 years (aOR 1.46, 95% CI 1.01-2.11) and primiparous women (aOR 1.45, 95% CI 1.06-1.98) were more likely to have an autopsy performed for their stillborn baby when stillbirth occurred at 28-36 weeks gestation. In contrast, women who had an antepartum haemorrhage (aOR 0.68, 95% CI 0.48-0.95), an intrapartum stillbirth (aOR 0.35, 95% CI 0.17-0.74) or an initially unexplained stillbirth (aOR 0.64, 95% CI 0.47-0.87) were less likely to have an autopsy performed for their stillborn baby (Table 7.5).

Table 7.5: Maternal and pregnancy factors associated with autopsy, 28-36 weeks, mid 2000-2011 (n= 948)

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
Maternal Age (Ref: 25-30 years)	
≤18 years	0.92 (0.43-1.95)
19-24 years	1.46 (1.01-2.11)
31-34 years	1.05 (0.71-1.57)
35+ years	0.82 (0.55-1.23)
Australian Indigenous status (Ref: Non Indigenous)	
Indigenous	0.87 (0.50-1.52)
Maternal region of birth (Ref: Australia and New Zealand)	
Africa	1.58 (0.46-5.42)
Americas and Caribbean	2.52 (0.53-11.9)

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
East Asia	0.59 (0.18-1.96)
Central, South and West Asia	1.53 (0.55-4.23)
South East Asia	1.20 (0.55-2.64)
Europe	1.35 (0.66-2.75)
Oceania (excl Australia and New Zealand)	0.37 (0.14-1.02)
Socioeconomic status (Ref: Highest ranked 20%)	
Middle ranked 60%	1.22 (0.77-1.95)
Lowest ranked 20%	1.28 (0.74-2.21)
Primiparity (Ref: No)	
Yes	1.45 (1.06-1.98)
Antepartum haemorrhage (Ref: No)	
Yes	0.68 (0.48-0.95)
Pregnancy-induced hypertension (Ref: No)	
Yes	2.00 (0.86-4.65)
Gestational diabetes (Ref: No)	
Yes	0.83 (0.43-1.58)
Small for gestational age (Ref: No)	
Yes	0.84 (0.63-1.13)
Unexplained fetal death (Ref: No)	
Yes	0.64 (0.47-0.87)
Congenital abnormality (Ref: No)	
Yes	1.15 (0.81-1.63)
Type of stillbirth (Ref: Antepartum)	
Intrapartum	0.35 (0.17-0.74)
Unknown	0.60 (0.31-1.16)
Remoteness (Ref: Major City)	
Regional	0.88 (0.65-1.19)
Remote	0.95 (0.44-2.02)
Epoch (Ref: 2000-2002)	
2003-2005	0.78 (0.52-1.17)
2006-2008	0.88 (0.59-1.32)
2009-2011	1.22 (0.82-1.83)

Initially unexplained on death certificate (ICD10AM code: P95) Gestational age missing for 12 births

37 weeks and older

Among those women who had term stillbirths, primiparity (aOR 1.70, 95% CI 1.22-2.39) and the presence of congenital abnormality (aOR 2.84, 95% CI 1.81-4.46) were associated with increased odds of having an autopsy performed. In contrast, Indigenous status (aOR 0.53, 95% CI 0.29-0.96), antepartum haemorrhage (aOR 0.59, 95% CI 0.36-0.97), remote residence (aOR 0.30, 95% CI 0.11-0.83) and

initially unexplained stillbirth (aOR 0.51, 95% CI 0.37-0.71) were associated with decreased odds of having an autopsy performed for a stillborn baby (Table 7.6).

Table 7.6: Maternal and pregnancy factors associated with autopsy, ≥37 weeks, mid 2000-2011 (n=838)

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
Maternal Age (Ref: 25-30 years)	
≤18 years	0.82 (0.23-2.88)
19-24 years	1.16 (0.77-1.76)
31-34 years	1.23 (0.80-1.90)
35+ years	0.93 (0.60-1.44)
Australian Indigenous status (Ref: Non Indigenous)	
Indigenous	0.53 (0.29-0.96)
Maternal region of birth (Ref: Australia and New Zealand)	
Africa	2.67 (0.58-12.3)
Americas and Caribbean	1.47 (0.32-6.80)
East Asia	1.37 (0.26-7.31)
Central, South and West Asia	0.20 (0.04-1.03)
South East Asia	1.29 (0.52-3.18)
Europe	1.68 (0.71-4.00)
Oceania (excl Australia and New Zealand)	0.40 (0.15-1.09)
Socioeconomic status (Ref: Highest ranked 20%)	
Middle ranked 60%	1.01 (0.61-1.68)
Lowest ranked 20%	0.84 (0.46-1.52)
Primiparity (Ref: No)	
Yes	1.70 (1.22-2.39)
Antepartum haemorrhage (Ref: No)	
Yes	0.59 (0.36-0.97)
Pregnancy-induced hypertension (Ref: No)	
Yes	0.80 (0.36-1.81)
Gestational diabetes (Ref: No)	
Yes	1.58 (0.84-2.98)
Small for gestational age (Ref: No)	
Yes	1.15 (0.82-1.62)
Unexplained fetal death (Ref: No)	
Yes	0.51 (0.37-0.71)
Congenital abnormality (Ref: No)	
Yes	2.84 (1.81-4.46)
Type of stillbirth (Ref: Antepartum)	
Intrapartum	1.03 (0.61-1.74)
Unknown	0.81 (0.47-1.39)
Remoteness (Ref: Major City)	
Regional	0.89 (0.64-1.23)
Remote	0.30 (0.11-0.83)
Epoch (Ref: 2000-2002)	

Characteristics	Adjusted Odds Ratios (95% Confidence Interval)
2003-2005	0.60 (0.38-0.93)
2006-2008	1.06 (0.68-1.66)
2009-2011	0.95 (0.61-1.47)

Initially unexplained on death certificate (ICD10AM code: P95) Gestational age missing for 12 births

Phase 2 Qualitative Results

The results presented in the previous section show the maternal characteristics associated with consent for or decline of autopsy but not the lived experience of parents faced with the decision of whether or not to consent to autopsy for their stillborn baby. In-depth qualitative interviews sought to include parents' voices and perspectives on the autopsy consent process. The interviews yielded rich data that illuminated the complexity of factors affecting parents' decision making.

Interviews were conducted with six parents (5 mothers and 1 father) of six babies during the study period. The characteristics of the study participants are shown in Table 7.7. Two of the stillbirths occurred during labour (intrapartum) and one of these was a termination of pregnancy. Autopsy was performed for four babies. Although the small number of study participants precludes meaningful comparison across key characteristics, a range of experiences and views about the autopsy consent process were captured helping to bring to life and explain some of the associations found in the quantitative analysis.

Direct quotations from parents are presented in italics with unique identifiers (A-F) to differentiate respondents and are used to illustrate the themes and subthemes.

Table 7.7: Characteristics of the participants in the in-depth interviews

	Participant A	Participant B	Participant C	Participant D	Participant E	Participant F	
Parent Characteristics							
Parent	Mother	Father	Mother	Mother	Mother	Mother	
Parent age	30-39	30-39	30-39	20-29	≥40	20-29	
Residence	Major city	Major city	Major city	Major city	Major city	Remote	
Indigenous status	Non Indigenous	Non Indigenous	Non Indigenous	Non Indigenous	Non Indigenous	Non Indigenous	
Maternal region of birth	Australia and New Zealand	-	Americas and Caribbean	Australia and New Zealand	Australia and New Zealand	Australia and New Zealand	
Marital status	married	married	married	de facto	married	de facto	
Ethnicity/Race	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	
Education	Tertiary	Secondary	Tertiary	Tertiary	Tertiary	Technical college	
Religion	No religion	No religion	No religion	Buddhist	No religion	No religion	
Primiparity	Yes	Yes	No	No	Yes	Yes	
Baby's Characteristics							
Baby	A		C	D	E	F	G
Type of stillbirth	Antepartum		Intrapartum	Intrapartum (Termination)	Antepartum	Antepartum	Antepartum
Gestational age	42 weeks		23 weeks	21 weeks	30 weeks	23 weeks	28 weeks
Autopsy	Yes		No	Yes	No	Yes	Yes
Hospital Characteristics							
Hospital	A		A	B	A	B	
Hospital level	Level 3 referral		Level 3 referral	Level 3 referral	Level 3 referral	Level 3 referral	

The distressing nature of the circumstances in which the decision making process around autopsy occurs and the need for parents to find answers were overarching themes. There were a range of approaches to decision making; it is notable that three parents stated that the decision itself was "easy" as they knew this was the way to find answers and contribute to knowledge. Some parents had strong opinions either way while other parents struggled with a decision (Table 7.8).

Table 7.8: Quotes from respondents showing the spectrum of approaches to decision making regarding consent to autopsy

"Probably because they weren't 100% sure what was actually wrong, for us it's quite vital. So it wasn't too hard of a decision for me" (Participant F, mother, consented to autopsy)
"For me it wasn't a hard decision. It was quite an easy decision because I wanted to know what had gone on. We had no idea." (Participant B, father, consented to autopsy)
"I'm a nurse so I know the importance of evidence-based research … I guess it wasn't that big a decision compared to the other decisions we were having to make … if there was any way that we could find out what caused it or prevent any future pregnancies from ending like that, then we were going to take any available option to do that. So it wasn't a significant decision on the scale of decisions that we had to make". (Participant D, mother, consented to autopsy)
"For me, it was much harder, you know, someone says autopsy and just the thought of them cutting up my little baby. That was awful and I really didn't like the thought of that at all, [but] I wanted to know the

cause of death. So I said yes just … to discover why, really. That was more important to me than them not interfering with his body". (Participant A, mother, consented to autopsy)
"I felt like the autopsy wouldn't answer the question for me about why the membranes broke and the other part to my decision I think was that if those results were going to be used in a study, I would have been more likely to decide to have an autopsy". (Participant C, mother, declined consent to autopsy)
"When we were told that she didn't have a heart beat I think immediately I had already thought no autopsy at all. Like because I didn't even know what the reasoning was why she had died but I honestly didn't think that I could handle seeing, you know, feeling that they were cutting her up" (Participant E, mother, declined consent to autopsy)

Four additional themes emerged relating to the context surrounding the decision making process and motivating factors for parents in relation to decisions regarding stillbirth autopsy. These themes were: 1) *a precious and time limited moment*, 2) taking care of the body, 3) the need for an explanation, and 4) a station along the bereavement journey.

A Precious and Time-limited moment

The context within which parents were making decisions was described as *"quite a precious and time-limited moment"*. The notion of limited time featured prominently in comments from parents: the time they had with their baby was limited and the time they had to make numerous decisions that involved interactions with numerous staff was limited. The decision about autopsy was characterised by competing priorities for both parents and health care staff; including care of the mother, providing parents with

information and support, and providing space and time for parents and families to spend with the baby. As one mother articulated:

> *"There was quite a lot of things that they had to talk to us about in that period of time and it is quite a precious and time-limited moment in your life because from when the baby is born, their body is changing and so as the hours go by, you can see the baby change and you also know that you're going to have to say goodbye. So on the one hand it's good to have information but on the other hand you really don't want to spend a long time being caught up with all of this other stuff and I think that's a really hard balance possibly for the staff to make because there's lots of different people – I mean, I know that they were trying to give us time but on the other hand there's a lot of different people coming in and out of the room and then they had to look after me as well as ask us about various things"* (Participant C, mother, declined consent for autopsy)

The amount of time available before having to address a decision about autopsy was also important. Two of the mothers had intrapartum stillbirths but in both cases they were aware that the baby would be unlikely to survive the birth.

> *"We seemed to have what felt like a long time so I felt like that somehow made things easier. It made us calmer just after birth and it wasn't so much a shock … I don't know if relaxed is the right word but yeah, [we were] not in a really terrible state of shock. I could imagine for families where everything happens much more quickly."* (Participant C, mother, declined consent for autopsy)

Time also meant parents were more likely to receive the information and support they needed and, ideally, the opportunity to develop a relationship with one or more care providers. During this time, parents appreciated fore-warning of the discussion as well as having just one staff member go through the details of the information around stillbirth investigation. Continuity and rapport were important to parents. Parents reported preferring if the staff member discussing with them regarding autopsy consent had built rapport with them before initiating the discussion.

> *"I had a bit of a relationship with the lady who organised the autopsy … it went fairly well and they gave you enough time, like I spoke to my partner*

and that sort of thing about it. So they do give you time to talk about it"
(Participant F, mother, consented to autopsy)

Parents also appreciated receiving both written and verbal information as a number of parents interviewed described being overwhelmed by the situation and the amount of information being presented.

"At that particular time you can't think straight so there's not a lot of information you can take in and retain through those pamphlets, where[as] someone sitting down and making sure that you understand it"
(Participant F, mother, consented to autopsy)

"The Registrar that was talking to us about the autopsy was someone that we had met – maybe not before I went into labour but we'd certainly talked to her a number of times and trusted her … I guess we liked her and she was very considerate towards us and what we needed at different times before the birth but also after the birth" (Participant C, mother, did not consent to autopsy)

Taking care of the body

Regardless of the decision parents ultimately made about autopsy, or of the degree of difficulty they experienced in making that decision, all expressed heartfelt concerns relating to the importance of taking care of their baby's body. Parents comments related specifically to the autopsy procedure, for example, "cutting up", concerns about the retention of body parts or tissue, "keeping the baby whole" and treating the baby with respect. Despite the death of the baby prior to birth, there was recognition of parents as parents; as protectors of their baby. To this end, healthcare providers facilitated opportunities for parents to establish bonds with their infant through holding and memory creation activities such as taking photographs and inviting other family members to meet the baby; which may assist with grieving. This was an acknowledgement of the uniqueness and preciousness of the limited amount of time parents had with their baby following birth.

Given the role of parents as caregivers and protectors of their baby, being asked for consent to autopsy appears to be the antithesis of parenting. As one parent expressed:

> *"I didn't want to be separated from my baby. If I could have kept him with me, I would have done that and keeping him whole would have been really important, not having bits of his brain taken that wouldn't be returned. I really didn't like that notion at all. That didn't sit well. I mean, the whole thing of autopsy is pretty terrible – you don't ever want to imagine someone you love having that procedure performed on their body".* (Participant D, mother, consented for autopsy)

However, being asked for consent to autopsy was for parents another opportunity to demonstrate their role as protector and caregiver to their baby and to exercise some control in a situation where they felt somewhat powerless.

> *"I can't change the circumstances that she is gone but I still have control over how I want her to be treated in her death"* (Participant E, mother, declined consent for autopsy)

In deciding for or against consent to an autopsy for their baby, parents described weighing up a number of competing factors. The first of these was taking care of the body and not having it "cut". This was particularly important to parents, as one mother expressed:

> *"I still imagine it would be a very difficult decision just because of the physicality of what you imagine an autopsy to be, that you have this beautiful little baby and then to think that they would be cut or changed in a way – it would be difficult. I think that was one thing very important for us, that we took care of his body and I imagine that would be very similar for many parents, that you really feel like you want to take care of the body even though the baby is not alive."* (Participant C, mother, declined consent for autopsy)

Parents who chose to have an autopsy examination of their baby described weighing up the need for an explanation and the physical reality of the autopsy examination against the need to protect the integrity of the baby's body.

> *"I wanted to know the cause of death and I knew that that [autopsy] would help in finding out what happened. So I said yes… That was more important to me than them not interfering with his body. I'm very grateful that we did actually because …he died of an infection and they wouldn't*

have known that had they not done an autopsy." (Participant A, mother, consented to autopsy)

Also related to maintaining the integrity of the baby's body was the subtheme of tissue retention. This caused further distress to parents especially when they were unprepared for it. As one mother expressed:

> *"We weren't told at that point that he wasn't whole, that he wasn't all in there. So then we had the funeral assuming that it was all there, didn't even think that it wasn't and he was cremated. We got his ashes and then we came back eight weeks later and met with [bereavement midwives], the obstetrician and went over the results and it was then that they said,* "Okay, so you know when we said that we can retain parts of him, we've actually kept his brain. We've finished testing on it. What do you want to do with it now?" *and I was like,* "What do you mean? Where is it? What are the options?" *That was a bit of a shock for me,… kind of traumatic… that he wasn't all where I thought he was. We had to kind of repeat the process, like they go,* "Okay, do you want to take the brain? You can bury it, you can get it cremated or we send it off with all of the other, you know, baby bits" *and then they cremate it somewhere else and scatter the ashes. So yeah, that brought all that up again and I thought the funeral and the cremation was all done".* (Participant A, mother, consented to autopsy)

Another aspect of taking care of the baby's body was treating the body with respect. This was evidenced by the distress caused when this was not done.

> *"We went back the day after and they [babies] were brought into the room from the morgue still encased in plastic bags and everything. I think it was an orderly who brought the babies in and I think it was probably just either lack of training or lack of understanding that there was someone actually in that room because I don't think he even knew there was anyone in there"* (Participant F, mother, consented to autopsy)

The need for an explanation

The need for an explanation was an important factor for parents regardless of whether they ultimately decided for or against an autopsy examination. Parents who chose not to have an autopsy described having to come to terms with not having an explanation for what happened to their baby.

> *"I think that's probably one of the things that over time that you have to learn to accept in a way, that there isn't always an explanation for things"* (Participant C, mother, declined consent for autopsy)

Likewise, among parents who chose to have an autopsy, some described concern that they would be left wondering if the results were inconclusive. In contrast, having a clinical cause of death did not necessarily answer parents' questions about what happened to their baby; parents were seeking answers to what initiated the chain of events that lead to their baby's death and that might still be unknown.

A subtheme within the need for an explanation was the value of an autopsy to find the cause of death. This varied with clinical scenario and parents relied heavily on the professional opinion of their health care provider regarding the value of an autopsy examination. The following quote highlights the importance of messages conveyed either implicitly or explicitly by health care providers.

> *"The obstetricians and so on felt like it wouldn't – I guess my impression was that they felt like it wouldn't be able to explain why the membranes ruptured… So I felt like the autopsy wouldn't really give information that would help answer our questions and maybe the test that I was more keen to have was this – some testing of the umbilical cord I think and the placenta, to look at that and that would then tell you about infection and so on. That was more the kind of – I guess that was what they were suggesting, that maybe the membranes ruptured because of an infection or something".* (Participant C, mother, declined consent for autopsy)

Parents considered how the information from their child's autopsy would be of benefit to them personally and to others when making their decision for or against autopsy.

> *"We certainly weren't ever feeling like, "*Oh no, that's out of the question." *The decision-making was more around not seeing any real benefit either to us or to anyone else from going through that and that it's not the kind of thing that you think,* "Oh, we may as well just do it anyway" *because it's so invasive."* (Participant C, mother, declined consent for autopsy)

Some parents described consenting for autopsy as "*making a sacrifice for science*" and there was an expectation of reciprocal responsibility from healthcare providers particularly when the benefit to others was an important factor in their decision making.

Numerous factors influenced parents' decision making; their professional background was one such factor. In the scenario of a poor prognosis during the antenatal period, parents described seeking health information in relation to their baby's diagnosis via online resources.

The need for an explanation of what happened to the baby was important to parents as a means of dealing with feelings of guilt; as mothers did blame themselves and their bodies.

> *"Was it good to know or not to know, being that listeria is something that's transmitted through food. I always carry that guilt that I ate something that was the [cause of the] demise and I was so careful. I kind of always walk past something and think gosh was it that that caused it?"* (Participant E, mother, declined consent for autopsy)

However, for some parents an explanation was helpful in alleviation feelings of guilt.

> *"I'm very grateful that we did actually because it wasn't that he was overdue or that my placenta had shut down. He died of an infection and they wouldn't have known that had they not done an autopsy. So then I would have been left with all the questioning, the guilt, the uncertainty, the "there's something wrong with me…" So to actually get – it was a freak thing, completely undetectable and [midwife] says it's one in a billion chance that that can happen, so very relieved we made that decision"* (Participant A, mother, consented to autopsy)

An explanation was also important for parents planning a future pregnancy, as shown in the following quote and as highlighted in the next section.

"*I don't want to have another pregnancy until I know those results … in case there's something we could do to prevent it happening [again].*"
(Participant D, mother, consented to autopsy)

A station along the bereavement journey

A major theme was recognition that the autopsy consent process was not an endpoint in itself but rather a station along the bereavement journey. This theme and the preceeding themes are represented visually in Figure 7.5. For parents, it was one decision among many decisions to be made – and the decision made also had significant ramifications for parents. Ramifications included when and how they received autopsy results, whether the autopsy findings would be conclusive or inconclusive, and other possible unforseen outcomes from the autopsy process.

Parents who consented to an autopsy described putting their lives on hold while waiting for autopsy results. Some parents interviewed had lengthy and frustrating waits for autopsy results in excess of 6 and 12 months and suggested fast tracking of autopsy results for very young children.

"I think it would help me to move on to get those results and put it to rest in my mind, that it wasn't me that did something wrong or it wasn't something that was likely to happen again with another pregnancy" (Participant D, mother, consented to autopsy)

"We received one result for one of the babies, we weren't told that the other results weren't there so that was a bit of a shock but you'd think they'd both come together but you only got one so like we've then got to go and ask again for the results of the other child" (Participant F, mother, consented to autopsy)

Of great importance to these parents was also the manner in which autopsy results were communicated to them. As one parent expressed:

"I don't want a call at work or when I'm out telling me the results of my son's autopsy. How are they going to approach that? Am I going to get a doctor's appointment to talk about it sensitively? There hasn't really been discussion in that way. I'd be pretty pissed off if I did get a call when I was

out and about to tell me those results because that would be an insensitive manner to do it but nor can I imagine them booking an appointment just to discuss that." (Participant D, mother, consented to autopsy)

These parents have suggested ideally an appointment with their treating obstetrician with the opportunity to discuss autopsy results, allay fears and consider management options for the next pregnancy would be an appropriate manner to convey autopsy results.

"I think when I received them [results] I was sitting there with a doctor, she went through it and explained it to me and that would be a lot better than receiving it say in the mail or something like that where you might read through it and a lot of the wording you won't understand" (Participant F, mother, consented to autopsy)

Parents also commented on the limited availability of follow up support and care after leaving hospital. This was particularly so for parents living in remote areas.

"When I was there [hospital], they give you all the pamphlets and the information or everything and it really is once you've left the hospital that there is absolutely no follow up care, there's no offering of a counsellor, there was no counselling while I was in hospital even after the first child. Once you leave hospital, there is no aftercare … being in such an isolated area, having that contact or someone making contact or referral to a service out where you are but that doesn't exist unfortunately"
(Participant F, mother, consented to autopsy)

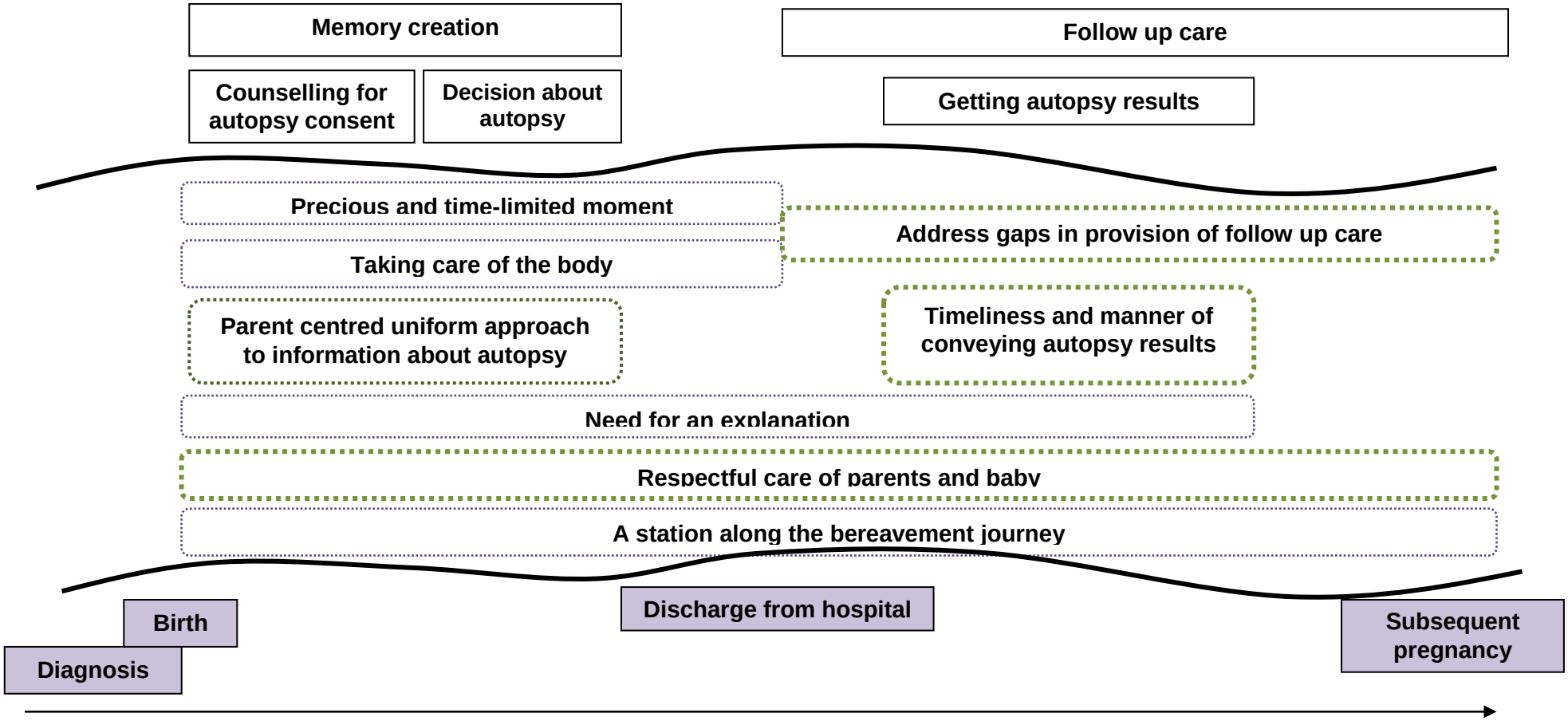


Figure 7.5: Journey map showing the interaction points between parents and health care providers in relation to the autopsy consent process.

The solid purple-shaded boxes (below the winding path) indicate key events relating to the autopsy consent process. The solid boxes (above the winding path) indicate processes triggered by the key events. The dashed purple boxes (within the winding path) indicate the key themes from interviews with parents while the dashed green boxes indicate the key implications for clinical practice.

7.4 Discussion

Main findings

The objectives of this study were: to identify sociodemographic, pregnancy and medical factors which are associated with whether or not autopsy was performed following stillbirth and to gain an understanding of parents' experiences of the autopsy consent process. This study found various sociodemographic, pregnancy and maternal factors were associated with autopsy after stillbirth and the associations varied with gestational age. To our knowledge no recent studies have examined associations between stillbirth autopsy and maternal factors in a quantitative manner using population data. This study also found that decision making around stillbirth autopsy for parents is influenced by various contextual and psychological factors. Four main themes relating to the context and motivation surrounding parents' decision making were uncovered, namely: 1) a precious and time-limited moment, 2) taking care of the body, 3) the need for an explanation, and 4) a station along the bereavement journey.

Interpretation of findings

Perinatal autopsy has been shown to change diagnosis of cause of death or add important information in 22-76% of cases [308]. However the quality of autopsy varies [309]; and improved quality of autopsy as well as reporting and interpretation was found when performed by a perinatal pathologist [310, 311]. Furthermore, it is unclear which clinical scenario results in the highest yield of information for autopsy following stillbirth. It has been reported that autopsy together with placental examinations could contribute to decreasing the rate of unexplained stillbirths [312].

It was a paradoxical finding that stillbirths occurring at 28 weeks or more that were unexplained at the time of completing the death certificate were less likely to have an autopsy. The reason for this was not immediately clear. We were unable to determine which investigations besides stillbirth autopsy were subsequently conducted. However, among stillbirths which were unexplained on the death certificate, the leading categories after subsequent investigation and classification according to PSANZ PDC were: unexplained antepartum fetal death (55.8%), spontaneous preterm (11.7%), antepartum haemorrhage (9.0%) and fetal growth restriction (5.5%). Classification to the latter three

categories were less likely to rely on autopsy findings [124]. Furthermore, these findings may reflect barriers to autopsy consent that have been observed in surveys of health care professionals' view and practices, these include gaps in knowledge and training and an underestimation of the value of autopsy [126]. More broadly, an attitude of fatalism or "these things happen" is prevalent in relation to stillbirth [5] and combined with the message from some healthcare providers that the autopsy may not reveal an explanation for the cause of death may deter parents who are faced with this difficult decision.

Indigenous women were less likely to have an autopsy, particularly for stillbirths occurring at 20-23 weeks and at term. These findings are particularly important as Indigenous women have higher rates and risk of stillbirth [4, 223], as well as higher rates of unexplained stillbirth [223]. There is very limited research into the views and experiences of Indigenous parents and families following stillbirth. Further research is needed into the underlying factors affecting decision making in relation to autopsy consent for Indigenous parents and families.

The presence of antepartum haemorrhage was associated with decreased odds of consenting to autopsy for stillbirths occurring at 24 weeks gestation or older. This may reflect the ability of clinicians to discern cause of death from comprehensive maternal clinical history and evaluation in such instances [124, 313]; and that post mortem examination may not necessarily provide much additional information.

We found intrapartum stillbirth was associated with decreased odds of autopsy particularly for stillbirths occurring at less than 37 weeks. These findings are supported by a qualitative study by Meaney and colleagues which showed that parents were more likely to have an autopsy for antepartum stillbirth than intrapartum stillbirth [314]. These findings may reflect the importance of having time to separate the autopsy decision from the immediate shock of the baby's death. Further analysis of these preterm intrapartum stillbirths showed that the leading categories of stillbirth based on the PSANZ PDC were: congenital abnormality (44.3%), spontaneous preterm (34%) and antepartum haemorrhage (8.0%). Apart from congenital abnormality, classification to the latter two categories depend on information from clinical history and placental histopathology [124].

The concentration of specialist pathology services within larger urban centres requiring transportation of babies to these centres for investigation may explain the decreased likelihood of consent for autopsy for women living in remote areas. Socioeconomic disadvantage was associated with decreased likelihood of consent to autopsy for stillbirths occurring at 20-23 weeks gestation. The driving factors for these findings are not clear, however, it is unlikely to be wholly financial. Within the public health system, the financial cost to the parents and families associated with the autopsy itself or transfer of the baby to another facility is minimal [124, 128].

The presence of congenital abnormality was associated with increased odds of consenting to autopsy, particularly in stillbirths occurring around 20-23 weeks gestation and at term (≥37 weeks). This finding may reflect the value of autopsy to determine the cause of death in stillbirths where the suspected cause of death is congenital abnormality [7, 132]. We found increased odds of autopsy associated with small-for-gestational age (SGA) for stillbirths occurring at less than 28 weeks. SGA is a proxy measure for fetal growth restriction which is an important risk factor for stillbirth [247]. It is determined from biometric measurements at autopsy or antenatal ultrasound evidence of growth restriction after excluding infection and congenital abnormality which are associated with SGA [124]. Information from autopsy may assist in management of subsequent pregnancies as there is evidence of increased risk of SGA recurrence [315].

This study found primiparity was associated with increased odds of consenting to autopsy where stillbirth occurred at 28 weeks gestation or older. This may reflect parents' concerns or need for reassurance about achieving a successful pregnancy outcome. Autopsy results may assist in determining cause of death and inform management of future pregnancies. Contrasting results for maternal age and gestational age group were found. Women aged 19-24 years were more likely to consent to autopsy for stillbirths occurring at 28-36 weeks; while women aged 35 years and older were less likely to consent to autopsy for stillbirths occurring at less than 24 weeks gestation. The latter findings may reflect early fetal deaths with a known or suspected probable cause of death.

What parents are saying following a stillbirth

The qualitative study sought to explore the lived experiences of parents to gain an understanding of the autopsy consent process. Despite only 6 interviews, the qualitative findings revealed a continuum of approaches to autopsy decision-making – from the three parents whose decision was relatively "easy" because for them autopsy had clear benefits including answers for themselves, subsequent pregnancies, and broader science. At the other end of the spectrum was the mother who, from the outset, was resolute in her decision not to proceed with autopsy to protect her baby from further harm. For two other mothers making a decision about autopsy was less clear cut and followed much consideration of potential benefits, harms and reservation. In one case, the need for an explanation (possibly also influenced by the views of her husband) was an overriding consideration. In the second case, the parents declined autopsy for their baby after concluding that information gained would be of little use to themselves or broader scientific knowledge.

Acknowledging and understanding the different ways parents may approach the decision-making process is essential to providing a care environment that addresses parents' concerns and supports them in making an informed decision.

Regardless of the decision made, all parents acknowledged a number of salient factors that influence the decision making process. Our study found that parents took on the role of carer and protector for their infant and consequently respect for the infant's body was an important consideration in the decision-making process. Along a similar vein, Meaney and colleagues reported that parents who declined autopsy did so to protect their baby from further harm [314].

We found for some parents in our study, the need for an explanation was a more overriding consideration in their decision for autopsy. The importance for parents of having an explanation for what happened to their baby was a finding supported by various studies [123, 126, 134, 314]. In our study cohort, some mothers found the cause of death helpful in allaying their feelings of guilt, similar to findings reported by Meaney and colleagues [314]. Having information on the cause of death was also useful to parents for future pregnancies [134].

An overarching theme from the qualitative analysis was the need for recognition of the significance and uniqueness of the death of a baby before birth. This had implications for

the various interactions between health care providers and parents during the counselling process for autopsy consent.

Implications for clinical practice

Implications for clinical practice are drawn from the study findings relating to interviews with parents. Many of the implications for clinical practice are supported by the PSANZ Clinical Practice Guideline for Perinatal Mortality [124].

Counselling for autopsy

Our study showed that parents relied heavily on the opinion of healthcare providers regarding the value of an autopsy and other investigations to provide information to determine the cause of death. Studies have shown that the attitude of health care providers towards autopsy can influence whether parents are approached regarding autopsy and their parent's ultimate decision regarding consent to autopsy [135, 316]. Health care providers should provide objective and realistic estimation of the usefulness of autopsy and other post mortem investigations to determine cause of death. Health care providers should balance guidance with parental autonomy and ensure that their own values and opinions do not unduly influence parents [317]. In the provision of information, both verbal and parent-focussed printed materials are recommended [126, 317]. The re-iteration of information could help to address parents questions and concerns about the autopsy process, what will happen to the baby's body as well as the how the autopsy results will be conveyed.

Conveying autopsy results

The timeliness and manner of conveying autopsy results was an important aspect of the process for parents. Horey and colleagues propose that autopsy results be conveyed to parents in a formal session (ie a designated appointment) in a manner that matches the gravity of the situation [318]. This recommendation was also confirmed within our study population and demonstrates an appreciation for the importance of the loss of the baby for parents. Our finding that some parents had lengthy wait periods for autopsy results have

been confirmed in studies elsewhere [126, 317]. It was suggested that tests for very young children could be fast tracked; or at least healthcare providers could provide some estimate of the length of the waiting period with periodic communication to provide some indication of progress with results. It was important to parents that their case was not forgotten and periodic communication was a suggested means to address this.

Follow up care

Parents who were planning for a subsequent pregnancy reported high levels of anxiety about the recurrence of stillbirth [319]. Parents indicated that they needed additional support during the management of the subsequent pregnancy. A recent qualitative meta analysis found parents' need for support did not end immediately and highlighted the importance of follow up care [123]. This study also found that there was a gap in the provision of emotional support for parents following discharge from hospital, particularly for parents living in remote areas. It is unclear who is best situated and equipped to provide such services.

Study Limitations and strengths

This large population study (quantitative component) is to our knowledge the first study exploring quantitatively the association between autopsy and maternal factors within an Australian context. In this study, whether or not autopsy was performed was used as a proxy measure to indicate parental consent for autopsy, as consent is required for autopsy. However, there may be instances where consent was given but autopsy was not performed although we suspect this would have occurred in a very small number of cases with minimal effect on the study findings. Furthermore, data was unavailable on the proportion of parents who were approached for consent for autopsy. Another limitation of the quantitative component was that it was not possible to evaluate the comprehensiveness of stillbirth investigations as data was unavailable on the other tests or investigations performed. Moreover, a limitation of the qualitative component of this mixed methods study was the small number of interviews which did provide valuable insights, however, further qualitative interviews with a wider range of participants were needed.

7.5 Conclusion

This study confirms that sociodemographic and pregnancy factors are associated with parental consent for autopsy post stillbirth. Of concern was the decreased likelihood of consent for autopsy where the stillbirth was initially unexplained on the death certificate. It highlights the importance of ensuring that parents are provided with appropriate counselling and information regarding autopsy to ensure they make a fully informed decision. There is a need for further studies to explore the factors that drive decision-making for parents, particularly among subgroups identified as being less likely to consent to autopsy, and how these factors can be addressed in order to potentially increase autopsy consent rates.

The in-depth interviews highlight the factors that motivate parents in their decision making as well the context within which decisions are made. The findings add important insights into the autopsy consent process for parents within a contemporary Australian setting. The findings of this study have direct implications for improving clinical practice including providing appropriate information to parents; and the timeliness and manner in which autopsy results are delivered to parents.

Chapter 8

Synthesis of studies and findings

This chapter presents a summary of the findings and limitations of the studies described in Chapters 3, 4, 5, 6 and 7. Furthermore, the implications for public health policy are considered as well as directions for future research.

8.1 Overview of the findings

The primary aims of this Thesis were to better describe the epidemiology of stillbirth in an Australian context specifically among Aboriginal and Torres Strait Islander (Indigenous) and non-Indigenous women; and contribute to improving the quality of data through appropriate investigation of stillbirths. The main objectives addressed were to:

1. Examine trends in stillbirth by clinical classification of cause of death, Indigenous status and gestational age, to identify focal areas for preventive efforts (Chapter 3)
2. Assess gestational age specific risk of stillbirth associated with four important contributors (diabetes, hypertension, antepartum haemorrhage and small-for-gestational age) to higher stillbirth rates among Indigenous women in order to identify periods of increased risk (Chapter 4)
3. Develop and validate a statistical model to predict the risk of antepartum stillbirth at term (≥37 weeks) using maternal and pregnancy factors as a potential decision-making aid for clinicians and women (Chapter 5)
4. Assess consistency in application of the Perinatal Society of Australia and New Zealand Perinatal Death Classification system between hospital committees and an independent expert panel, to identify areas for quality improvement (Chapter 6)
5. Determine maternal and pregnancy factors associated with parental consent to autopsy following stillbirth and explore parents' views and experiences of the autopsy consent process to inform clinical practice (Chapter 7)

The population based *Stillbirth trends analysis* (n=881,211 births) presented in Chapter 3 assessed trends in stillbirth rates by geographic location, gestational age and clinical classification of cause of stillbirth to determine whether the gap in stillbirth rates between

Indigenous and non-Indigenous women was closing. Although stillbirth rates among Indigenous women were consistently higher than non-Indigenous, the gap had narrowed over the period 1995 to 2011. Indigenous women living in regional and remote areas experienced greater reductions in stillbirth rates than their urban counterparts. There was little narrowing of the gap at term gestational ages (37 weeks and older). The categories that contributed to higher overall stillbirth rates among Indigenous women included: perinatal infection, preterm birth, hypertension, antepartum haemorrhage, maternal conditions (mainly diabetes), fetal growth restriction and unexplained antepartum fetal death. Many of these categories are potentially amenable to intervention in the pre-pregnancy and antenatal periods using strategies addressing risk factors for adverse pregnancy outcomes.

The population based *Gestational age specific stillbirth risk analysis* (n=360,987 births) presented in Chapter 4 advanced the line of enquiry from Chapter 3 and examined gestational age-specific risk of stillbirth associated with four conditions [diabetes, hypertension, antepartum haemorrhage and small-for-gestational age (SGA) (a proxy for fetal growth restriction)] highlighted in the previous study as important contributors to increased stillbirth rates among Indigenous women. After stratification by Indigenous status and controlling for sociodemographic, pregnancy and medical factors, increased risk of stillbirth associated with SGA and antepartum haemorrhage was found at all gestational ages assessed. Diabetes was associated with increased risk of stillbirth during late preterm and term gestational ages and results were mixed for hypertensive disorders. Indigenous women had around twice the magnitude of stillbirth risk for pre-existing diabetes and SGA compared with non-Indigenous women. This study highlighted the disparity in stillbirth risk and the need to prioritise early detection and management of these conditions.

Expanding on the findings from Chapter 3 and 4 regarding the sharp increase in risk at term and the lack of decrease in term stillbirth rates among Indigenous women, Chapter 5 described a study that aimed to derive and validate a statistical model based on maternal clinical factors to predict the risk of antepartum stillbirth at term. Despite strong association between maternal clinical factors and antepartum stillbirth risk, very little of the stillbirth risk was explained by the clinical factors in the model. The study findings are

supported by other reports of poor ability to predict stillbirth risk at term based on maternal clinical factors alone [230, 264] suggesting that factors which are predictive of antepartum stillbirth at term remain unknown at present.

In Chapter 6, the focus of the Thesis was in exploring the quality of data on clinical causes of stillbirth. The study aimed to assess consistency in application of the PSANZ perinatal death classification system between hospital committee and expert panel review of 217 stillbirth cases in order to identify areas for quality improvement. A substantial level of agreement was found overall; with high level of agreement for the categories of congenital abnormalities, spontaneous preterm and hypertension. There were lower levels of agreement for the categories of antepartum haemorrhage and fetal growth restriction suggesting that improvements could be made to the category descriptions within the perinatal mortality audit guidelines as well as modules within the education program focussed on these categories.

Chapter 7 continued the focus on data quality and the possibility of improving stillbirth autopsy rates. The study presented in Chapter 7 was a mixed methods study that aimed to gain an understanding of parents' views and experiences of the autopsy consent process in order to inform clinical practice. The quantitative component sought to identify maternal and pregnancy characteristics associated with parental consent or non-consent for autopsy following stillbirth; while the qualitative component explored parents lived experiences of the autopsy consent process. A number of overarching themes emerged from the in-depth interviews regarding the context and motivation around decision making for parents: 1) *a precious and time-limited moment*, 2) taking care of the body, 3) the need for an explanation, and 4) autopsy consent as a station along the bereavement journey. Timeliness and the manner in which autopsy results were communicated to parents was an important issue for parents who chose to have an autopsy.

8.2 Limitations of the studies and directions for future research

Limitations of routinely collected data

There were a number of limitations relating to the use of routinely collected data in the population based analyses presented in Chapters 3, 4, 5 and 7. The population based studies utilised routinely collected data from the Queensland Perinatal Data Collection (QPDC). Data was unavailable for factors such as education level, coffee consumption, paternal age, previous small-for-gestational age and previous preterm birth; which have been identified by others as associated with increased risk of stillbirth [32]. Furthermore, ascertainment of factors such as previous stillbirth, alcohol use and previous caesarean section varied during the data collection period or was unreliable.

Data for body mass index and gestational age at initiation of antenatal care were not routinely collected until July 2007 and July 2009, respectively. As a result, the direct effect of overweight/obesity and early initiation of antenatal care could not be assessed over the duration of the study period. However, in the analyses presented there was adjustment for maternal conditions associated with overweight and obesity such as diabetes and hypertension; likewise analyses including number of antenatal care visits were adjusted for gestational age. Indices quantifying adequacy of antenatal care (which are derived from the number of antenatal care visits and gestational age at initiation of antenatal care) have been shown to introduce subtle biases depending on the method of calculation used [320].

The analyses presented in Chapters 3, 4 and 5 showed pre-existing diabetes to be a major risk factor for stillbirth within the Australian context. However, data obtained from the QPDC was not sufficiently detailed to determine the type of pre-existing diabetes (whether Type I or Type II). Further study could assess whether there was a differential in stillbirth risk between Type I and Type II diabetes.

The QPDC is unique in its combination of population registry information with clinical cause of death assigned by a multidisciplinary committee at state level. However, data collection systems were not equipped to capture detailed coding on terminations other than for maternal psychosocial reasons. In Chapter 3, it would have been useful to examine trends in terminations for congenital abnormalities or for other medical conditions.

Ethnicity is a complex construct which is difficult to measure and it is difficult to obtain detailed and nuanced data on ethnicity from routinely collected data. At present

Indigenous status and country of birth are the only ethnicity-related variables mandatorily collected across maternity centres [3]. While the level of accuracy of country of birth data in administrative data collections such as hospital admissions is generally high [321], it has been suggested that country of birth is not a reliable measure of ethnicity as women identify differently across and within country of birth groups [322].

Potential underestimation of the proportion of Indigenous women was a possibility if women did not identify as Aboriginal and/or Torres Strait Islander during clinical interview. Data was not available on the Indigenous status of the father or baby and so our studies were unable to identify Indigenous infants born to non-Indigenous mothers. However, Queensland birth registration data indicates that 30% of babies registered as Indigenous had an Indigenous father and a non-Indigenous mother and analyses of these data showed that maternal Indigenous status was a more significant predictor of adverse perinatal outcomes than the Indigenous status of the infant [323]. A limitation of the population based investigations in this Thesis was that rates and risk of stillbirth for Torres Strait Islander women and Aboriginal women were not examined separately as it has been suggested that perinatal outcome profiles are different between the two groups of women [324, 325].

A substantial focus within this Thesis was on Aboriginal and Torres Strait Islander (Indigenous women) as a subgroup of the Australian population with higher rates and risk of stillbirth. However, reports suggest that overseas born women may have slightly higher stillbirth rates than Australian born women [3]; particularly women from the Indian subcontinent [25]. At present there is limited information about pregnancy outcomes for women of migrant or refugee backgrounds [273]. This presents an opportunity for further study. In these groups, it would be important to consider the effects of length of stay in Australia, English language skills and acculturation.

Term antepartum stillbirth risk prediction

It was concluded from Chapter 5 that at present maternal factors explain only a small proportion of the risk of antepartum stillbirth risk at term; taken together with reports that up to 60% of stillbirths at term are unexplained [131], this is an area for further research.

The aetiology of stillbirth is varied, however, placental dysfunction has been suggested an important pathway [326] in the development of pre-eclampsia/eclampsia, fetal growth restriction and placental abruption [252]. Further research into the aetiology of placental dysfunction resulting in fetal death at later gestational ages could be useful in addressing the large proportion of term stillbirths with unknown cause of death.

Stillbirth Classification Agreement Study

This study was nested in the larger *Stillbirth Investigation study* which was to include all level 2 and level 3 hospitals with trained clinicians utilising the Perinatal Mortality Audit guidelines. However, data had been received from a fraction of the participating hospitals. It is possible that there may have been "healthy volunteer" bias, whereby hospitals more likely to participate are also more likely to follow the guidelines. This may result in overly optimistic estimates of agreement between hospital and expert panel reviews. It was difficult to estimate the extent of this bias as the data collection period was ongoing at the time of writing this Thesis.

Parental Consent to Stillbirth Autopsy Study

The quantitative component of the *Parental Consent to Stillbirth Autopsy Study* identified maternal and pregnancy characteristics associated with whether or not stillbirth autopsy was performed. Whether or not autopsy was performed was used as a proxy measure of parental consent for autopsy, as consent was required for autopsy. However, there may have been instances where consent was given but autopsy was not performed although we suspect this would have occurred in a very small number of cases with minimal effect on the study findings. Furthermore, it was unknown what proportion of parents was approached for consent for stillbirth autopsy. Further study is needed into underlying factors that influence parent's decisions, particularly for parents who decline autopsy.

8.3 Public health implications

The public health implications of the key findings of the studies have been reported in each of the respective chapters. These implications fall into two broad categories, namely those relating to provision of primary health care and antenatal care and secondly those relating

to improving the quality of data available to inform stillbirth prevention strategies. Many of the implications for antenatal care provision are addressed in the national antenatal care guidelines [273]. A number of the implications for improving the quality of data for stillbirth prevention can be addressed in future updates to the PSANZ Clinical Practice Guideline for Perinatal Mortality [124] and the IMPROVE education program [159]. These implications are summarised as follows:

Figure 8.1: Public health implications of key study findings

Public Health Implications

Primary care services

- Improving equity in access to primary care services
- Education of primary care providers about assessing women's risk of adverse pregnancy outcomes
- Management of pre-existing medical conditions such as diabetes and hypertension before, during and between pregnancies
- Follow up care for women following a stillbirth

Antenatal care

- Improving access to and utilisation of antenatal care through:
  - Appropriate and responsive care
  - Embedding cultural competence into mainstream services at the level of individual healthcare providers and at the organisational level
- Provision of high quality antenatal care including:
  - Culturally appropriate service delivery models
  - Screening for risk factors of stillbirth and other adverse pregnancy outcomes
  - Diabetes management
  - Smoking cessation
  - Specialist assessment and support for substance-dependent pregnant women
  - STI screening and treatment
  - Folic acid supplementation
  - Fetal growth monitoring

Improving the quality of data for stillbirth prevention

- Updates to PSANZ Clinical Practice Guideline for Perinatal Mortality and its associated IMPROVE education program
  - Clear descriptions and case study examples for the categories of *Antepartum Haemorrhage* and *Fetal Growth Restriction*
  - Information for parents about autopsy (brochure)
    Tailoring information about autopsy to the needs of parents
  - Information for the health professional seeking consent (brochure)
    Communication of autopsy results to parents in a sensitive and respectful manner

- Improving autopsy rates
  - Further research into underlying factors driving decision making for parents who decline autopsy
  - Interventions to reduce wait times for stillbirth autopsy results

8.4 Conclusions

The primary aim of this Thesis was to improve the quality of data on stillbirths to inform interventions for prevention. The research studies within this Thesis confirmed that although there was an overall decreasing trend in stillbirth rates among Indigenous women, there was disparity in stillbirth risk between Indigenous and non-Indigenous women due to potentially preventable conditions. The findings of the population based studies highlighted the importance of early detection and management of pre-existing conditions prior to, during and between pregnancies. However, it was also found that factors predictive of antepartum stillbirth at term remain largely unknown at present.

In relation to the quality of data on causes and contributing factors for stillbirth, the research study found consistent application of the perinatal death classification system overall, however, there was scope to improve consistency in the classification to the categories of antepartum haemorrhage and fetal growth restriction. Moreover, the studies identified maternal and pregnancy characteristics associated with whether or not stillbirth autopsy was performed; furthermore various factors affected parents' decision making in relation to stillbirth autopsy. The findings from in-depth interviews with parents had implications for clinical practice including the manner in which autopsy results are communicated.

A number of areas for future research were identified to address study limitations reported in this Thesis. The study findings have the potential to inform interventions to optimise women's health prior to, during and between pregnancies; as well as inform guidelines on perinatal mortality audit and the care of bereaved parents.

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Appendix A: Details of ethics and governance approvals for the various studies

Study	Site	Ethics Committee		Site specific assessment / Governance approval	
		Committee	**Ref and date**	**Committee**	**Ref and date**
Stillbirth trends analysis (Chapter 3) Gestational age specific stillbirth risk analysis (Chapter 4) Term antepartum stillbirth risk prediction (Chapter 5) Predictors of autopsy following stillbirth (Chapter 7)	University of Queensland	UQ Human Research Ethics Committee	II180313	Not required	n/a
	Queensland	Queensland Health Central Office HREC	HREC/05/QHC/009 Original approval 16 May 2005 Amendment 1: Amendment 2 & 3: 15 Oct 2012 Amendment 4: 5 June 2013 Amendment 5: 1 July 2014 ***Study transferred to Mater Health Services HREC following shut down of this HREC***	Not required	n/a
	Queensland	Mater Health Services HREC	HREC/15/MHS/36/AM07	Not required	n/a
	Queensland	Queensland Health *(Public Health Act 2005)*	RD000796 – 30 June 2008 RD004654 - 25 Feb 2013 RD004800 - 22 Aug 2013 RD005423 – 22 Dec 2014	Not required	n/a
	All states and territories	Australian Institute of Health and Welfare HREC	EC2009/3/34 Original approval: 11 Aug 2009 Amendment 1: 9 Dec 2011 Amendment 2: 13 Dec 2012 Amendment 3: 11 Nov 2013 Amendment 4: 2 Sep 2014	Not required	n/a
Stillbirth Classification Agreement Study (Chapter 6)	University of Queensland	UQ Human Research Ethics Committee	2014000454 3 April 2014	Not required	n/a
	Canberra Hospital	ACT Government Health HREC	ETH.10.12.220 28 November 2012	Not required	n/a
	Royal Prince Alfred Hospital	Northern Sydney Local Health District HREC	1212-411M 13 January 2013 27 May 2013 (Amendment)	Sydney Local Health District	SSA/13/RPAH/257 6 Mar 2014
	Royal North Shore Hospital	Northern Sydney Local Health District HREC	1212-411M 13 January 2013	Northern Sydney Local Health District	1303-083M 21 Jan 2014

Study	Site	Ethics Committee		Site specific assessment / Governance approval	
		Committee	**Ref and date**	**Committee**	**Ref and date**
			27 May 2013 (Amendment)	HREC	
	Royal Hospital for Women Sydney	Northern Sydney Local Health District HREC	1212-411M 13 January 2013 27 May 2013 (Amendment)	South Eastern Sydney Local Health District	13/G/065 22 Mar 2013
	John Hunter Hospital	Northern Sydney Local Health District HREC	1212-411M 13 January 2013 27 May 2013 (Amendment)	Hunter New England Local Health District	SSA/13/HNE/131 9 May 2013
	Liverpool Hospital	Northern Sydney Local Health District HREC	1212-411M 13 January 2013 27 May 2013 (Amendment)	South Western Sydney Local Health District HREC	SSA/13/LPOOL/344 12 Dec 2013
	Nepean Hospital	Northern Sydney Local Health District HREC	1212-411M 13 January 2013 27 May 2013 (Amendment)	Nepean Blue Mountain Local Health District	SSA/13/NEPEAN/70 19 May 2014
	Royal Darwin Hospital	NT Dept of Health and Menzies School of Health Research HREC	HREC-2012-1876 11 October 2012	Support from Director of Medical Services at Royal Darwin Hospital	23 Oct 2012
Stillbirth Classification Agreement Study (Chapter 6)	Mater Mother's Hospital Mater Research Institute - UQ	Mater Health Services HREC Royal Brisbane and Women's Hospital HREC	1745M 20 December 2011 HREC/12/QRBW/284 20 December 2012	Mater Health Services HREC	1745M 14 Apr 2014 1 Apr 2015 (Amendment)
	Royal Brisbane and Women's Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004663 12 Mar 2013 14 Oct 2014 (extension)	Metro North Health Service	HREC/12/QRBW/284 27 Sep 2013
	Townsville Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004663 12 Mar 2013	Townsville Hospital and Health Service	SSA/13/QTHS/68 12 Jul 2013 17 Nov 2014 (extension)
	Ipswich Hospital	Royal Brisbane and	HREC/12/QRBW/284	West Moreton	SSA/13/QWMS/5

Study	Site	Ethics Committee		Site specific assessment / Governance approval	
		Committee	**Ref and date**	**Committee**	**Ref and date**
Stillbirth Classification Agreement Study (Chapter 6)		Women's Hospital HREC	20 December 2012 RD004663 12 Mar 2013	Hospital and Health Service	21 Mar 2014
	Toowoomba Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004663 12 Mar 2013	Darling Downs Hospital and Health Service	SSA/13/QTDD/58 9 Aug 2013
	Gold Coast Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004663 12 Mar 2013	Gold Coast Hospital Research, Ethics and Governance Unit	SSA/14/QGC/109 2 Dec 2014
	Cairns Base Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004729 19 Jun 2013	Cairns and Hinterland Hospital and Health Service	SSA/14/QCH/49 16 Mar 2015
	Logan Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004729 19 Jun 2013	Metro South Hospital and Health Service	SSA/13/QPAH/220 21 Aug 2014
	Nambour General Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/284 20 December 2012 RD004729 19 Jun 2013	Sunshine Coast Hospital and Health Service	SSA/13/QNB/61 24 Oct 2013
	South Australian sites	Aboriginal Health Research Ethics Committee	04-12-480 5 November 2012	Not Required	n/a
	Women and Children's Hospital	Women and Children's Hospital Network HREC	HREC/12/WCHN/69 5th December 2012	Women and Children's Hospital Research Secretariat	SSA/13/WCHN/125 16 Aug 2013
	Lyell McEwin Hospital	Women and Children's Hospital Network HREC	HREC/12/WCHN/69 5th December 2012	SA Health Human Research Governance Office	SSA/13/TQEHLMH/246 4 Nov 2013

Study	Site	Ethics Committee		Site specific assessment / Governance approval	
		Committee	**Ref and date**	**Committee**	**Ref and date**
Stillbirth Classification Agreement Study (Chapter 6)	Flinders Medical Centre	Women and Children's Hospital Network HREC	HREC/12/WCHN/69 5th December 2012	pending	pending
	SA Pathology	Women and Children's Hospital Network HREC	HREC/12/WCHN/69 5th December 2012	Central Adelaide Local Health Network	SSA/14/RAH/10 21 Jan 2014
	Royal Hobart Hospital	HREC Tasmania Network	H0012864 30 November 2012	Southern Tasmania Area Health Service	approved by Chief Medical Officer 5 Aug 2013
	Launceston General Hospital	HREC Tasmania Network	H0012864 30 November 2012	pending	pending
	Sunshine Hospital	Melbourne Health HREC	2012.269 21 November 2012	pending	pending
	Mercy Hospital for Women	Mercy Health Human Research Ethics Committee	R13/07 13 February (expedited); 11 June 2013	Not required	n/a
	Royal Women's Hospital	Royal Women's Hospital HREC	Quality Assurance 1 May 2013	Not Required	n/a
	Western Australian sites	Western Australia Aboriginal Health Ethics Committee	447 14 November 2012	Not Required	n/a
	King Edward Memorial Hospital	WNHS	Quality Activity 4362 20 August 2012	Not Required	n/a
	Mater Mothers' Hospital Mater Research Institute - UQ	Mater Health Services HREC	1910M 22 Aug 2012 HREC/14/MHS/62/AM02 (1910M) (Lead HREC transfer to RBWH)	Mater Health Services HREC	1910M (RG) 10 Apr 2014
	Royal Brisbane and Women's Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/239 19 Nov 2012 HREC/14/MHS/62	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/239 27 Mar 2014 05 May 2014

Study	Site	Ethics Committee		Site specific assessment / Governance approval	
		Committee	Ref and date	Committee	Ref and date
Stillbirth Autopsy Study (Chapter 7) Qualitative component			6 Jan 2015 (new lead HREC)		
	Ipswich Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/239 19 Nov 2012	West Moreton Hospital and Health Service	SS/14/QWMS/21 30 Jan 2015
	Toowoomba Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/239 19 Nov 2012	pending	pending
	Townsville Hospital	Royal Brisbane and Women's Hospital HREC	HREC/12/QRBW/239 19 Nov 2012	pending	pending
	University of Queensland	UQ Behavioural and Social Sciences Ethical Review Committee	2012001397 14 Dec 2012 20 Nov 2014	Not Required	n/a

Appendix B

Presented in this appendix are results relating to Chapter 4.

Appendix B1: Significant interaction terms by Indigenous status

Interaction terms	Indigenous Hazard Ratio (95% CI)	Non-Indigenous Hazard Ratio (95% CI)
Smoking AND Small-for-gestational age		
Smoking AND small-for-gestational age	0.61 (0.30-1.23)	**0.59 (0.45-0.77)**
Relative to: No smoking AND No SGA		
Smoking AND Maternal age		
Smoking AND 18 or younger	0.31 (0.08-1.26)	0.92 (0.47-1.80)
Smoking AND 19-24 years	1.15 (0.51-2.63)	0.74 (0.54-1.03)
Smoking AND 31-34 years	0.49 (0.14-1.70)	0.89 (0.61-1.31)
Smoking AND 35+ years	**0.32 (0.10-0.97)**	1.05 (0.73-1.51)
Relative to: No smoking AND 25-30 years		
Marital status AND Maternal age		
No partner AND 18 years or younger	**0.20 (0.05-0.77)**	0.76 (0.37-1.54)
No partner AND 19-24 years	0.58 (0.28-1.24)	0.71 (0.49-1.02)
No partner AND 31-34 years	0.67 (0.18-2.43)	0.88 (0.54-1.44)
No partner AND 35+ years	**0.08 (0.01-0.68)**	0.97 (0.62-1.52)
Relative to: Domestic partner AND 25-30 years		
Accommodation AND Socioeconomic status		
Public status AND Middle ranked 60%	**	0.81 (0.59-1.13)
Public status AND Lowest ranked 20%	0.95 (0.35-2.64)	1.27 (0.63-2.55)
Relative to: Private status AND Highest ranked 20%		
Geographic location AND Socioeconomic status		
Regional area AND Middle ranked 60%	1.13 (0.11-11.7)	1.12 (0.68-1.85)
Regional area AND Lowest ranked 20%	0.83 (0.08-9.17)	1.22 (0.69-2.15)
Remote area AND Middle ranked 60%	**	1.68 (0.22-12.58)
Remote area AND Lowest ranked 20%	**	1.85 (0.23-14.98)
Relative to: Major cities AND Highest ranked 20%		
Socioeconomic status AND Maternal age		
Middle ranked 60% AND 18 or less	0.09 (0.00-1.93)	1.41 (0.33-6.04)
Middle ranked 60%AND 19-24 years	**	0.83 (0.52-1.33)
Middle ranked 60% AND 31-34 years	0.30 (0.02-5.52)	1.00 (0.67-1.49)
Middle ranked 60% AND 35+ years	0.81 (0.05-13.9)	1.40 (0.92-2.11)
Lowest ranked 20% AND 18 or less	0.26 (0.01-4.93)	1.05 (0.22-5.06)
Lowest ranked 20% AND 19-24 years	**	0.65 (0.36-1.15)
Lowest ranked 20% AND 31-34 years	0.62 (0.03-11.42)	0.84 (0.47-1.49)
Lowest ranked 20% AND 35+ years	0.48 (0.03-9.23)	1.55 (0.89-2.68)
Relative to: Highest ranked 20% AND 25-30 years		

Bold estimates indicate significant interaction terms ** unreliable estimates

Appendix B2: Univariate assessment of proportionality for conditions of interest

Conditions	Indigenous	Non-Indigenous
	p value	p value
Antepartum haemorrhage	0.301	0.953
Essential hypertension	0.709	**0.042**
Pre-eclampsia/Eclampsia	0.199	**0.030**
Pre-existing diabetes	**0.001**	**<0.001**
Gestational diabetes	0.168	**<0.001**
Small for gestational age	0.494	**0.045**

Bold estimates indicate violation of proportionality

Appendix B3: Univariate association between maternal and pregnancy factors and stillbirth by Indigenous status, Queensland, mid 2005-2011

Characteristics	Indigenous	Non-Indigenous
	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)
Maternal age (Ref: 25-30 years)		
18 or younger	0.81 (0.41-1.60)	2.58 (1.88-3.54)
19-24 years	0.90 (0.62-1.30)	1.23 (1.07-1.43)
31-34 years	0.70 (0.38-1.26)	0.99 (0.85-1.15)
35 or older	1.32 (0.79-2.21)	1.29 (1.11-1.49)
Geographic Location (Ref: Major city)		
Regional area	1.30 (0.84-2.00)	1.07 (0.96-1.20)
Remote area	1.52 (0.93-2.50)	0.90 (0.63-1.30)
Marital status (Ref: Domestic partner)		
No domestic partner	1.04 (0.75-1.44)	1.63 (1.41-1.87)
Relative socioeconomic disadvantage (Ref: Highest 20%)		
Middle 60%	1.10 (0.41-3.00)	1.12 (0.97-1.31)
Lowest 20%	1.12 (0.41-3.08)	1.33 (1.09-1.62)
Any smoking during pregnancy (Ref: No)		
Yes	1.48 (1.07-2.06)	1.64 (1.45-1.86)
Substance Use during pregnancy (Ref: No)		
Yes	4.80 (2.60-8.86)	2.33 (1.40-3.87)
Hospital accommodation status (Ref: Private)		
Public	1.08 (0.35-3.39)	1.63 (1.43-1.85)
Assisted Conception (Ref: No)		
Yes	1.45 (0.21-10.6)	1.34 (1.05-1.72)
Primiparity (Ref: No)		
Yes	0.92 (0.64-1.33)	0.96 (0.86-1.08)
Number of antenatal care visits (Ref: 8 or more visits)		
Less than 2	16.4 (10.4-25.8)	46.9 (38.8-56.7)
2 – 4	5.94 (3.83-9.20)	18.3 (16.1-21.0)
5 – 7	1.34 (0.78-2.29)	3.81 (3.31-4.39)
Baby's gender (Ref: Female)		
Male	1.33 (0.97-1.82)	1.01 (0.91-1.12)

Appendix B4: Univariate association between conditions of interest and stillbirth, by Indigenous status

Characteristics	Indigenous	Non-Indigenous
	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)
Pre-existing diabetes	8.03 (4.44-14.5)	3.63 (2.36-5.59)
Gestational diabetes	0.41 (0.15-1.10)	0.84 (0.64-1.09)
Pre-existing hypertension	5.58 (2.61-11.9)	3.84 (2.69-5.48)
Pre-eclampsia/Eclampsia	1.31 (0.54-3.20)	3.09 (2.45-3.89)
Antepartum Haemorrhage	22.7 (16.0-32.3)	13.7 (12.1-15.5)
Small-for-gestational age	3.33 (2.41-4.61)	4.62 (4.12-5.19)

Appendix B5: Adjusted hazard ratios for stillbirth by medical condition and Indigenous status, Queensland, mid 2005–2011

Conditions	Indigenous[a]		Non-Indigenous[b]	
	Adjusted HR (95% CI)	p value	Adjusted HR (95% CI)	p value
Antepartum haemorrhage^	18.7 (12.9-27.3)	<0.001	11.6 (10.2-13.2)	<0.001
Essential hypertension~	2.82 (1.11-7.19)	0.030	3.67 (2.54-5.31)	<0.001
Pre-eclampsia/Eclampsia	1.35 (0.55-3.34)	0.514	2.67 (2.11-3.39)	<0.001
Pre-existing diabetes^	7.28 (3.70-14.3)	<0.001	4.20 (2.70-6.56)	<0.001
Gestational diabetes^	0.43 (0.14-1.37)	0.154	1.22 (0.93-1.60)	0.145
Small-for-gestational age	2.34 (1.65-3.30)	<0.001	-	-
Non-smoker	-	-	4.61 (4.00-5.30)	<0.001
Smoker	-	-	2.68 (2.14-3.37)	<0.001

All models adjusted for maternal age, smoking status, parity, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. For Indigenous women, smoking status, number of antenatal care visits and prevalence of pre-existing diabetes mellitus varied with gestational age. For non-Indigenous women, most variables in the models varied with gestational age.

[a]Indigenous models include the following interaction terms: smoking*maternal age and marital status*maternal age.

[b] Non-Indigenous models include the following interaction term: smoke*FGR10. ^These models additionally adjusted for pre-existing hypertension.

^ These models additionally adjusted for pre-existing hypertension. ~ These models additionally adjusted for pre-existing diabetes.

Appendix B6: Stillbirth risk for conditions of interest by geographic location, Indigenous women, Queensland, mid 2005-2011

Conditions	Indigenous					
	Major City		Regional		Remote	
	Prev (%)	aHR (95% CI)	Prev (%)	aHR (95% CI)	Prev (%)	aHR (95% CI)
Antepartum haemorrhage^	2.76	1.00	2.06	1.58 (0.97-2.57)	2.29	1.69 (0.97-2.95)
Essential hypertension*	0.72	1.00	0.96	1.47 (0.90-2.38)	1.24	1.83 (1.06-3.18)
Pre-eclampsia/Eclampsia	2.01	1.00	2.73	1.49 (0.92-2.41)	4.06	1.88 (1.08-3.25)
Pre-existing diabetes^	0.94	1.00	1.25	1.47 (0.90-2.38)	1.72	1.83 (1.06-3.18)
Gestational diabetes^	4.85	1.00	6.54	1.49 (0.92-2.42)	8.27	1.88 (1.08-3.27)
Small-for-gestational age	13.03	1.00	16.25	1.40 (0.87-2.27)	14.36	1.82 (1.05-3.15)

Models adjusted for maternal age, smoking status, parity, remoteness, substance use, gender, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. ^ These models additionally adjusted for pre-existing hypertension. * These models additionally adjusted for pre-existing diabetes.

Appendix B7: Stillbirth risk for conditions of interest by geographic location, non-Indigenous women, Queensland, mid 2005-2011

Conditions	Non - Indigenous					
	Major City		Regional		Remote	
	Prev (%)	aHR (95% CI)	Prev (%)	aHR (95% CI)	Prev (%)	aHR (95% CI)
Antepartum haemorrhage^	2.96	1.00	2.35	1.14 (1.01-1.28)	2.26	0.87 (0.60-1.27)
Essential hypertension*	0.62	1.00	0.69	1.11 (0.99-1.25)	0.79	0.88 (0.60-1.29)
Pre-eclampsia/Eclampsia	1.97	1.00	2.47	1.11 (0.99-1.25)	3.38	0.86 (0.59-1.26)
Pre-existing diabetes^	0.49	1.00	0.55	1.11 (0.99-1.25)	0.43	0.88 (0.60-1.29)
Gestational diabetes^	5.38	1.00	5.26	1.11 (0.99-1.25)	5.56	0.87 (0.60-1.28)
Small-for-gestational age	8.30	1.00	8.61	1.10 (0.99-1.25)	7.82	0.89 (0.61-1.30)

Models adjusted for maternal age, smoking status, parity, remoteness, substance use, gender, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits. ^ These models additionally adjusted for pre-existing hypertension. * These models additionally adjusted for pre-existing diabetes.

Appendix C: Parent Information Sheet - Parental Consent to Stillbirth Autopsy Study

PARENT INFORMATION SHEET

Information and communication about autopsy following stillbirth: Meeting the needs of parents

A Pilot Research Project

Project Team Contacts:

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Thank you for thinking about taking part in this study about autopsy consent. We understand that this is a very difficult time for you and your family as you grieve the loss of your baby. The information you provide may help us to help other families in the future. This sheet explains important details about the project and is for you to keep.

What is the purpose of this project?

This study is being conducted by The University of Queensland and Mater Medical Research Institute. It is supported by Stillbirth and Neonatal Death Support Group (Sands), the Perinatal Society of Australia and New Zealand (PSANZ), and the Australian and New Zealand Stillbirth Alliance (ANZSA), with funding from the Stillbirth Foundation Australia (SFA). The purpose of the study is to learn more about parents' decisions about autopsy (often referred to as perinatal autopsy) and whether parents are satisfied with the information given to them about autopsy. The lessons we learn from this pilot study will give us useful information that will help to improve care for parents at this difficult time. It will also help us develop a high quality nationwide survey. The nationwide survey will help:

- develop appropriate information for parents
- develop appropriate training for staff
- increase parent satisfaction with the decision making process.

This study and the planned national study will also explore how decisions about perinatal autopsy might be associated with parents' grief.

In order to achieve our best results we need to hear from parents who have been asked to decide about an autopsy for their baby. Even if you don't think you have much to say, we would still very

much like to hear from you. We would like to hear from mothers and fathers. This information sheet describes the types of things we would like to learn from you.

What information will be collected and why?

We need some background information about you and how you felt about your pregnancy. This will assist in identifying the specific needs of parents as a result of pregnancy experiences. We also want to know about your experience and views of:

- How the idea of an autopsy was first introduced and discussed
- How you made your decision about whether to have an autopsy
- Receiving the autopsy results if you had one performed
- How you feel about your decision now.

We would also like to know the ways in which your decision about whether or not to consent to an autopsy examination might have affected you. In particular we want to understand its impact on the levels of grief in the months after the death of your baby.

Finally, as this is a pilot project we would like your views on the questionnaire. For example, is it appropriate and user friendly for parents?

How is the project being done?

Six hospitals are taking part in the study. We will collect information and feedback from parents whose baby was stillborn at any of those hospitals.

If you do choose to take part in the project you will be asked to complete a questionnaire. It will take about 30 minutes to complete. You will also be asked if you might be willing for one of the research team members to contact you again at a later time to learn more about your experience.

The first questionnaire is at about 6-8 weeks after your baby died. You may choose to do this with the bereavement midwife at a return hospital visit, or it can be posted to you to complete and mail back in your own time.

If we don't receive your questionnaire within a couple of weeks, your midwife or another member of the research team will contact you by telephone or mail to see if you still want to be part of the study.

For those parents who have agreed, we may contact you again about two months later to ask if you would be willing to tell us more about your experience. This would involve a telephone interview with a trained interviewer at a time that suits you.

What does the project hope to gain?

The goal of this project is to improve parents' satisfaction with the process, information and decision-making around autopsy examination consent. There is unlikely to be any direct benefit to you but we know from other research that many grieving parents want to give feedback. Many people value doing so as they hope it will make a difference for others.

Are there any costs in taking part?

There are no costs to you or your family to take part in the project.

Will parents receive feedback about the project?

The results from this pilot study and the national study will be published and widely disseminated. If you are interested in the final results of this study and want a summary report to be sent to you, please let us know by marking this on the consent form.

Are there any risks?

We are aware that the death of a baby is one of the most difficult times to endure. Our hope is that this study will not cause any additional distress to parents who take part. We are aware that some parents may be upset by recounting events around the time that their baby died. If this occurs and you need to talk to someone, please use the contact details on page one for the project team who can be contacted during office hours. In addition the Stillbirth and Neonatal Death Support (Sands) association and the Sudden Infant Death Syndrome (SIDS) organisation SIDS and KIDS provide bereavement support and/or counselling services to any family affected by the sudden or unexpected death of their baby. Their contact details are:

SANDS: 13 000 SANDS (13 000 72637)

SIDS and KIDS: 1800 628 648

If any information that we collect indicates that you may be experiencing a form of grief that raises concern for your wellbeing or safety, you will be contacted by a bereavement research midwife. The midwife will recommend that you consult your GP or seek other appropriate care and support.

Is participation in the study voluntary?

You are free to decide whether or not to take part in the study. If you choose to not be involved in the project you will not be disadvantaged in any way. All staff will provide you with the same care and support whatever you decide.

Do you have any questions?

The project team are available to answer any questions you may have about the project. Please do not hesitate to contact the project team. Contact details are on the first page of this information sheet.

This project has been approved by the Mater Health Services Human Research Ethics Committee. If you have any complaints or concerns about the way the project is being conducted, you may contact the Research Ethics Coordinator at the coordinating centre on (07) 3163 1585. The Research Ethics Coordinator may decide to contact the Patient Representative or Hospital Ethicist at your local hospital if necessary.

What if I do not want to be in the project?

You are free to decide whether to participate or not. If you agree to take part you are also free to change your mind at any time, and **you do not have to give a reason**. We will respect the decision as the right one for you. If you wish to tell us why you have declined or want to withdraw during the project we would be grateful but it is not necessary. This type of information helps us to be more sensitive to grieving parents approached to be involved in projects in the future. Declining the project or withdrawing from the project will not affect the care and support you will be given during this time.

This study is supported by the Stillbirth Foundation Australia

Appendix D: Interview Schedule - Parental Consent to Stillbirth Autopsy Study

Qualitative Telephone Interviews

Information and communication about autopsy following stillbirth: Meeting the needs of parents

Draft interview schedule

1. Introduction and preamble [standard script to be used by interviewers]
2. Request for permission to record interview (and reminder that the participant can stop the interview at any time)
3. Preliminary question

How have things been for you since your baby died? (Ask if it's okay to call the baby by his/her name during the interview)

4. As you know, we want to find out how we might be able to improve care for parents, especially in relation to autopsy. That was probably one of the very difficult decisions you had to make … looking back now, can you tell me what it was like making that decision?
5. What were some of the things that worried or concerned you most?
6. Can you think of anything – or anyone – that stands out as being particularly helpful?
7. Anything that stands out as being particularly unhelpful?
8. Looking back, can you think of any ways in which things might have been made a little easier for you? Are there things that you wish had been done differently? Is there anything you might want to say to other parents faced with the death of their baby and the decision about autopsy?
9. Is there anything at all you would like to add?
10. Thank you for your time and willingness to be involved in this study.

Reminder about available sources of support -- SANDS: 13 000 SANDS (13 000 72637); SIDS and KIDS: 1800 628 648

Appendix E: Paper 1 - Final version of submitted manuscript (Published online 3 Sep 2014)

Title Page

The disparity gap in Indigenous stillbirth in Queensland (Running title)

Full title of the paper

Stillbirth rates among Indigenous and non-Indigenous women in Queensland, Australia: Is the gap closing?

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Objective: To determine whether the disparity gap is closing between stillbirth rates for Indigenous and non-Indigenous women and to identify focal areas for future prevention efforts according to gestational age and geographic location

Design: Population based retrospective cohort study

Setting: Queensland, Australia

Population: All singleton births of at least 20 weeks gestation or at least 400g birthweight

Methods: Routinely collected data on births were obtained for the period 1995 to 2011. Indigenous and non-Indigenous stillbirth rates and percent reduction in the gap were compared over time and by geographic location and gestational age.

Main Outcome Measures: All-cause and cause-specific stillbirth rates (per 1000 ongoing pregnancies)

Results: Over the study period there was a 57.3% reduction in the disparity gap. While marked reductions in the gap were shown for women in regional (57.0%) and remote (56.1%) locations, these women remain at increased risk compared to those in urban regions. There was no reduction for term stillbirths. Major conditions contributing to the disparity were maternal conditions (diabetes) (RR 3.78, 95% CI 2.59-5.51), perinatal infection (RR 3.70, 95%CI 2.54-5.39), spontaneous preterm (RR 3.08, 95% CI 2.51-3.77), hypertension (RR 2.2, 95% CI 1.45-3.39), fetal growth restriction (RR 1.78, 95% CI 1.17-2.71) and antepartum haemorrhage (RR 1.58, 95% CI 1.13-2.22).

Conclusions: The gap in stillbirth rates between Indigenous and non-Indigenous women is closing, but Indigenous women continue to be at increased risk due to a number of potentially preventable conditions. There is little change in the gap at term gestational ages.

Keywords

Stillbirth; urban; fetal death; trends; cause of death; Aboriginal and Torres Strait Islander; Indigenous

Introduction

Stillbirth is devastating to families and remains a challenging problem globally, with an estimated 3 million deaths occurring during the third trimester of pregnancy each year[1]. Applying the standard lower gestational age definition used in many high income countries, the numbers of stillbirths are likely to be at least double this estimate[2]. Despite significant reductions in stillbirth rates in high income countries over the past 50 years, reduction has slowed in recent times[3]. National reports from Canada[4] and Australia[5, 6] indicate that stillbirth rates may be increasing. In comparison, neonatal death rates in many of these countries have continued to decline. In Australia[5] and USA[7], neonatal death rates declined at a faster pace than stillbirths. Between 1990 and 2000, the fetal and neonatal death rates in USA declined by an average of 1.3% and 2.4% per year, respectively[7]. Likewise in Australia during the same period, fetal and neonatal death rates declined by an annual average rate of 1.0% and 4.5%, respectively[5, 8]. In Queensland during this period, fetal death rates increased by 0.14% per year while neonatal death rates decreased by 2.5% per year[9].

The need to address existing disparities across different population groups was recently highlighted as a priority in high income countries [10]. In Australia and other high income countries, marked disparity in stillbirth rates between Indigenous and non-Indigenous populations are evident[6, 11 6, 11, 12]. A number of factors including physical and social environment, maternal behaviour, access to and quality of health care have been suggested as contributing to this disparity[3, 13]. Geographic location (regional or remote residence) has been identified as an important risk factor for stillbirth in the Australian context[14, 15].

The study of temporal trends in rates and underlying cause of death is important to gaining an understanding of the scope for further reductions in stillbirth rates and to direct further clinical and research efforts[16, 17]. The objective of this study was to assess the differences in stillbirth rates over time among Australian Aboriginal and Torres Strait Islander (Indigenous) and non-Indigenous women based on their geographic location and gestational age to determine whether the gap was closing. Additionally, this study aimed to assess cause-specific stillbirth rates to determine where the greatest disparities lie in order to identify focal areas for preventive efforts.

Methods

Maternal demographic and pregnancy outcome data were obtained from the Queensland Perinatal Data Collection (QPDC) for singleton births occurring over the period 1995 to 2011. It is a requirement that all births of at least 20 weeks regardless of birthweight, and births of at least 400g birthweight regardless of gestational age are registered in the QPDC. During 1995 to 2011, 881,654 singleton births were registered in Queensland. Of these, a total of 443 births were excluded from the analysis for the following reasons: 148 terminations of pregnancy for maternal psychosocial reasons; 270 births with unknown maternal Indigenous status; 25 births occurred at less than 20 weeks gestation and were also less than 400g birthweight.

Indigenous status was defined as whether or not the woman identified as Aboriginal and/or Torres Strait Islander. Geographic location was based on postcodes of maternal usual place of residence according to the Australian Standard Geographical Classification (ASGC) Remoteness structure[18], and was categorised as: urban (major cities), regional (inner and outer) and remote (remote and very remote).

Causes of death were classified according to the Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ-PDC)[19]. The classification of cause of death available from the QPDC dataset was assigned by a multidisciplinary perinatal mortality review committee as part of routine procedure. The overall autopsy rate during the study period was 37.6% (25.4% among Indigenous women and 38.9% among non-Indigenous women). Autopsy rates among Indigenous women were 28.7%, 27.4% and 18.6% among urban, regional and remote residents; while rates among their non-Indigenous counterparts were 40.0%, 36.9% and 42.7%, respectively. Over the study period, there were four predecessors to the current PSANZ-PDC in use. These classification systems were mapped to the current PSANZ-PDC[19] with minimal adjustment of subcategories to fit with the current system. A full description of the system with instructions for use is available[19]. A brief description of the intent of the PSANZ-PDC categories is provided in Table S1.

Outcome Measures

The primary outcome measures were stillbirth rate per 1000 ongoing pregnancies and cause-specific stillbirth rate per 1000 ongoing pregnancies by Indigenous status, geographic location and gestational age grouping. The gestational age groups used were "<24 weeks", "24-27 weeks", "28-

36 weeks" and "≥37 weeks". These groups were chosen to reflect the commencement of active clinical management (≥24 weeks), for international comparison (≥28 weeks) and to distinguish between preterm and term births (≥37 weeks).

Gestational age specific-stillbirth rate was calculated by dividing the number of stillbirths occurring within a specified gestational age window by the number of ongoing pregnancies at the start of the gestational age window[20]. Cause and gestational age specific stillbirth rate was calculated using the number of stillbirths occurring within a specified gestational age window that were attributed to a specified cause as the numerator; and the number of ongoing pregnancies at the start of the gestational age window as the denominator.

Statistical Analyses

Descriptive statistics were used to characterise the population on a range of maternal sociodemographic and pregnancy attributes. All variables measured on a continuous scale were classified into categories and Chi square and Fisher's exact tests were used to assess differences in proportions between groups. Percentage differences in stillbirth rates were assessed in 2-3 year groupings and over the whole study period. Non-parametric test of trend was used to assess changes in stillbirth rates over the study period. Relative risk and 95% confidence intervals were estimated for cause specific stillbirth rates for Indigenous women compared with non-Indigenous women by geographic location and gestational age grouping. Relative risk and 95% confidence intervals for having an autopsy performed following a stillbirth were also estimated for Indigenous women compared with non-Indigenous women. Data analysis was undertaken using Stata 11.2 (StataCorp LP 2009, Texas, USA).

Results

A total of 881,211 births (including 5425 stillbirths) were included in these analyses. Of these, 49,450 births (5.6%) were to Indigenous women and 831,761 births (94.4%) were to non-Indigenous women. The characteristics of the cohort are summarised in Table 1. During the study period, there were increases in the proportion of women birthing at 35 years or older among

Indigenous (5.5% to 10.1%, $p_{trend}<0.001$) and non-Indigenous women (12.9% to 20.4%, $p_{trend}<0.001$).

Temporal trends in stillbirth rates by Indigenous status and geographic location

Over the period 1995 to 2011, the stillbirth rate for all women birthing in Queensland was steady around 6.2/1000 ongoing pregnancies. Trends in stillbirth rates by Indigenous status and geographic location are shown in Figure 1. Indigenous stillbirth rates decreased 31.9% from 13.3 to 9.1/1000 ongoing pregnancies ($p_{trend}=0.014$); while stillbirth rates among non-Indigenous women was steady around 5.9/1000 ongoing pregnancies. The difference in overall stillbirth rates between Indigenous and non-Indigenous women reduced by 57.3% from 7.5 to 3.2/1000 ongoing pregnancies over this period (Figure 1).

Stillbirth rates among Indigenous women decreased by 10.2%, 29.2% and 49.9% for women living in urban, regional and remote areas, respectively. In contrast, stillbirth rates among non-Indigenous women increased by 0.9% and 11.4% for women living in urban and regional areas and decreased by 39.2% among non-Indigenous women living in remote areas (Figure 1). The difference in stillbirth rates between Indigenous and non-Indigenous women decreased by 25.7%, 57.0% and 56.1% for urban, regional and remote areas, respectively.

Temporal trends in stillbirth rates by Indigenous status and gestational age

Stillbirth rates were higher among Indigenous women for all gestational age groups assessed (Figure 2). Among Indigenous women, stillbirth rates decreased by 9.5%, 29.3%, 69.1% and 7.1% for births at <24 weeks, 24-27 weeks, 28-36 weeks and ≥37 weeks, respectively. Among non-Indigenous women, there was a 36.3% increase in stillbirth rates at <24 weeks and decreases in the remaining groups of 9.0%, 12.4% and 21.7%, respectively (Figure 2). The difference in stillbirth rates reduced between Indigenous and non-Indigenous women birthing at all gestational age groups except ≥37 weeks, where the difference increased by 18.0%. Between 2001 and 2011, the gap was steady around 1.2/1000 ongoing pregnancies (Figure 2).

Temporal trends in cause-specific stillbirth rates by Indigenous status

Among Indigenous women, decreasing rates of stillbirth due to perinatal infection (p_{trend}<0.001) and conversely, increasing rates of stillbirth due to fetal growth restriction (p_{trend}=0.040) were shown over the study period. (Table S2). Among non-Indigenous women, significant increases in the rates of stillbirth due to congenital abnormality (p_{trend}<0.001) and spontaneous preterm birth (p_{trend}=0.013) were shown concurrent with decreases in the rates of stillbirth due to hypertension (p_{trend}<0.001), antepartum haemorrhage (p_{trend}<0.001), perinatal infection (p_{trend}=0.029), maternal conditions (p_{trend}=0.044) and unexplained antepartum fetal death (p_{trend}=0.011) (Table S3). The increases in rates of congenital abnormality among non-Indigenous women may be due to higher proportions of older mothers among this population. Presented in Table S4 are trends in cause-specific relative risk for Indigenous women relative to non-Indigenous women.

Comparison of cause-specific stillbirth rates

The overall stillbirth rate for the 17 year study period among Indigenous women was higher than for non-Indigenous women (RR 1.81, 95%CI 1.66-1.98)(Table 2). The major PSANZ-PDC categories contributing to the disparity were: maternal conditions, perinatal infection, no obstetric antecedent, spontaneous preterm, hypertension, fetal growth restriction, unexplained antepartum fetal death and antepartum haemorrhage (Table 2).

Overall, Indigenous women had a nearly four-fold increased risk of stillbirth due to maternal conditions (RR 3.78, 95%CI 2.59-5.51) and perinatal infection (RR 3.70, 95% CI 2.54-5.39). Pre-existing and gestational diabetes constituted a large component (42.2%) of maternal conditions; and Indigenous women had over a six-fold increased risk of stillbirth due to diabetes (RR 6.42, 95% 3.89-10.62). Perinatal infections were comprised of bacterial infections (53.0%), viral and other (fungal and protozoal) infections. While numbers were small, there was a significantly increased risk of stillbirth due to syphilis infection among Indigenous women (Table 2).

More than half (56.0% Indigenous and 56.3% non-Indigenous) of all stillbirths assigned to the category of spontaneous preterm had evidence of chorioamnionitis on placental histopathology and a further 7.6% (6.7% Indigenous and 7.8% non-Indigenous) had clinical chorioamnionitis (i.e. without placental confirmation). Indigenous women had a three-fold increased risk of stillbirth due to spontaneous preterm birth (RR 3.08, 95% CI 2.51-3.77).

The majority of stillbirths (65.5%) attributed to hypertension were due to pre-eclampsia with or without superimposed chronic hypertension. The risk of stillbirth due to hypertension was significantly higher for Indigenous compared to non-Indigenous women (RR 2.22, 95% CI 1.45-3.39). Indigenous women had an increased risk of stillbirth due to fetal growth restriction (RR 1.78, 95% CI 1.17-2.71) and antepartum haemorrhage (RR 1.58, 95% CI 1.13-2.22). Placental abruption accounted for 86.0% of all stillbirths attributed to antepartum haemorrhage.

The risk of unexplained antepartum fetal death was higher for Indigenous women (RR 1.61, 95% CI 1.37-1.90), further, there were 69 stillbirths classified as having no obstetric antecedent identified and births to Indigenous women were over-represented within this category (RR 3.19, 95% CI 1.67-6.08).

No increased risk of stillbirth was evident for the main categories of congenital abnormality, hypoxic peripartum death or stillbirth due to specific perinatal conditions (including antenatal cord complication and feto-maternal haemorrhage) among Indigenous women compared with non-Indigenous women (Table 2). However, within subgroups an increased risk of stillbirth due to central nervous system (CNS) abnormality (RR 1.84, 95% CI 1.27-2.66) and uterine abnormalities (including cervical incompetence) (RR 2.59, 95% CI 1.10-6.11) was observed.

Cause-specific stillbirth rates by geographic location

In urban areas, Indigenous women had increased risk of stillbirth due to perinatal infection and spontaneous preterm; while Indigenous women living in remote areas had increased risk of stillbirth due to central nervous system abnormality (RR 3.38, 95% CI 1.31-8.72), maternal

conditions, spontaneous preterm birth and unexplained antepartum fetal death. Indigenous women living in regional areas had increased risk of stillbirth due to perinatal infection [particularly syphilis and non GBS bacterial infection], hypertension including gestational hypertension and pre-eclampsia with or without chronic hypertension (RR 2.26, 95% CI 1.14-4.48), maternal conditions including diabetes (RR 6.38, 95% CI 3.12-13.05), fetal growth restriction, spontaneous preterm and unexplained antepartum fetal death (Table 3, subcategory data not shown).

Cause-specific stillbirth rates by gestational age

No change was shown in all-cause stillbirth risk for Indigenous women as gestational age increased. However, Indigenous women had increased risk of stillbirth due to perinatal infection and spontaneous preterm at all gestational ages assessed (Table 4).

Discussion

Main Findings

We found that although Indigenous stillbirth rates were consistently higher than non-Indigenous rates, the gap had narrowed. These findings mirror national reports of declining Australian Indigenous stillbirth rates over the period 1991-2004[21] and US reports among American Indian and Alaskan Native women (7.5 to 6.2/1000 births between 1990 and 2005)[22]. Our study found that Indigenous women living in regional and remote areas experienced greater reductions in stillbirth rates than their urban counterparts.

There was little narrowing of the stillbirth rate gap at gestational ages of 37 weeks or more largely due to preventable conditions of diabetes, infection and fetal growth restriction. These findings highlight the opportunity for further reductions in term stillbirths among the Indigenous population.

Overall, we found an increased risk of stillbirth due to maternal conditions, perinatal infection, spontaneous preterm birth, hypertension, fetal growth restriction, antepartum haemorrhage and

unexplained antepartum fetal death among Indigenous women compared with non-Indigenous women. Most of these categories of stillbirth are potentially amenable to interventions in the pre-pregnancy and antenatal periods[3]. Similar findings were reported among Inuit and First Nation women in Canada, where excess stillbirths compared with non-Aboriginal women were attributed to fetal growth restriction, placental disorders and congenital anomalies among Inuit women and diabetes and hypertension among First Nation women[11]. In New Zealand, Māori women had increased risk for all PSANZ-PDC categories compared with New Zealand European women except hypoxic peripartum death and specific perinatal conditions, although the differences were not statistically significant[23].

Strengths and Limitations

Consistent allocation of cause of death to a large population based vital registry by a multidisciplinary expert panel using clinical practice guidelines is a major strength of this study.

One limitation is the possible underestimation of the proportion of Indigenous women which could be the case if Indigenous women did not identify themselves at clinical interview. This may have resulted in an underestimation of the disparity gap in stillbirth rates between Indigenous and non-Indigenous women. Secondly, stillbirth rates for Torres Strait Islander women and Aboriginal women were not examined separately as reports suggest that perinatal outcome profiles are different between the two groups[24, 25]. Thirdly, trends in terminations of pregnancy for reasons other than maternal psychosocial reasons could not be assessed, as they were not routinely collected in the QPDC. Therefore, disparity in cause-specific stillbirth rates may be underestimated if there are lower rates of terminations among Indigenous women. Lastly, the autopsy rate from our study was low and data were unavailable on the rates of other stillbirth investigations undertaken, including placental pathology investigation an important investigation for determining cause of death[3]. Therefore, misclassification of cause of death as a result of suboptimal investigations cannot be ruled out. Furthermore, it is possible that increased rates of unexplained antepartum fetal death and stillbirths with no obstetric antecedent observed among Indigenous women may reflect differing autopsy rates.

Interpretation of findings

Antenatal Care

Differentials in the rates of attendance and early initiation of antenatal care have been reported between Indigenous and non-Indigenous women[6]. In addition, significant variation in the quality of antenatal care received by Indigenous women has been reported including low rates of morphology ultrasound and screening for gestational diabetes and infection[26]. Service delivery models incorporating community-based or controlled services, respect for Indigenous people and culture, continuity of care, integrated spectrum of services, and consideration of logistic issues have been shown to be successful in improving maternal and child health outcomes for women in Indigenous communities[27].

Maternal smoking

Smoking during pregnancy is an important modifiable risk factor for Indigenous women requiring urgent attention through effective policy and guidelines for smoking cessation interventions tailored and targeted to Indigenous women. Smoking rates among Indigenous women in our study (53.0%) were over 3 times that of non-Indigenous women; similar to national rates (50.0% versus 11.7% in 2011)[6] . The population attributable risk for stillbirth has been estimated at 6.2%[2]. Furthermore, smoking quit rates during pregnancy among Indigenous women are lower than for non-Indigenous women[6]. While there is evidence to show that psychosocial interventions can increase smoking cessation rates in late pregnancy and decrease rates of preterm birth and low birthweight[28] overall, little research has focussed on interventions specific to Indigenous women. The role of nicotine replacement therapy in pregnancy is unclear, but may hold some promise[29].

Diabetes

There was a six-fold increased risk of stillbirth due to diabetes among Indigenous mothers. These findings are consistent with national reports that Indigenous women have disproportionally higher rates of pre-existing and gestational diabetes in pregnancy than non-Indigenous women[30]. At present there is little evidence for or against pre-conception care for women with pre-existing diabetes[31], although lower rates of congenital abnormalities have been reported among women with Type 1 diabetes receiving pre-conception care compared to those who did not[32]. Likewise,

lifestyle modifications in combination with insulin were found to improve birth outcomes for women with mild gestational diabetes[33]. However, interventions to prevent or manage diabetes have not had the same magnitude of impact within the Indigenous population and not enough clinical focus on women at risk or women with diabetes has been given as a possible explanation for this[27].

Congenital abnormalities

Our study suggested an increased risk of stillbirth due to CNS abnormalities among Indigenous women, especially those living in remote areas. These findings are supported by national reports of higher rates of neural tube defects (NTDs), the most common CNS abnormalities, among Indigenous women and women living in remote areas[34]. The association between folate and reduced risk of NTDs has been well established. Lifestyle factors such as low fruit and vegetable intake, smoking and high levels of alcohol consumption have been associated with folate deficiency[35]. Peri-conceptual folic acid supplementation, smoking cessation and avoidance of alcohol consumption during pregnancy are recommended as part of antenatal care practices[36].

Perinatal Infection

The results indicate a disproportionately high burden of stillbirth due to perinatal infection among Indigenous women. This finding is somewhat consistent with several studies that found high rates of sexually transmitted infections (STIs) among Indigenous women of reproductive age living in rural communities[37, 38] and pregnant Indigenous women living in urban areas[39]. Early diagnosis and treatment of syphilis has been shown to be associated with similar risk of stillbirth as the general uninfected population[40]. A number of programs which demonstrated sustained reductions in rates of STIs in Aboriginal and Torres Strait Islander communities have highlighted the need for STI screening to be incorporated into antenatal care protocols for Indigenous women[27].

Preterm birth

Spontaneous preterm labour and birth is linked with socioeconomic disadvantage, infection, chronic diseases (diabetes and hypertension), genetic influence; however many are idiopathic [41]. We found higher rates of preterm birth overall and higher risk of stillbirth following idiopathic spontaneous onset of preterm labour among Indigenous compared with non-Indigenous women. Evidence for strategies to reduce preterm birth is limited and a better understanding of the mechanisms and causes of preterm to enable focused intervention studies is required[41, 42] .

Conclusion

The gap in stillbirth rates between Indigenous and non-Indigenous women is narrowing, but Indigenous women continue to be at increased risk of stillbirth due to a number of potentially preventable causes. There has been little reduction in the gap between Indigenous and non-Indigenous women in relation to term stillbirth rates and this presents an area of focus for further preventive efforts. At term, Indigenous women had increased risk of stillbirth due to maternal conditions (mainly diabetes), perinatal infection, fetal growth restriction and unexplained antepartum fetal death. High quality antenatal care at all levels using culturally appropriate service delivery models which incorporate diabetes management, smoking cessation, STI screening and treatment, folic acid and fetal growth monitoring hold some promise of helping to improve pregnancy outcomes for Indigenous women.

Acknowledgements

We wish to thank Yvette Roe for critically reading the manuscript. Ibinabo Ibiebele is a recipient of the National Health and Medical Research Council Postgraduate Public Health scholarship and the University of Queensland Research Scholarship.

Disclosure of interests

None

Contribution to authorship

II undertook data management and analysis and wrote the manuscript. VF, MC and FB were responsible for the concept of the study, gave technical assistance with data analysis and interpretation of results and helped write the manuscript. MH and SV gave technical assistance with interpretation of results. All authors reviewed and approved the final version of this manuscript before submission.

Details of Ethics Approval

Non-identifiable routinely collected data from the QPDC was utilised for this study. Ethics approval was obtained from the Queensland Health Central Office (Ref: HREC/05/QHC/009) and University of Queensland School of Population Health Human Research Ethics Committees (Ref: II180313).

Funding

None

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Table 1: Comparison of sociodemographic characteristics of Indigenous versus non-Indigenous mothers and babies, Queensland, 1995-2011

Characteristics	Indigenous n(%)	Non-Indigenous n(%)
All births	**49 450 (5.6)**	**831 761 (94.4)**
Maternal age (years)		
≤ 20	12 888 (26.1)	66 171 (8.0)
21-34	32 577 (65.9)	623 301 (74.9)
≥ 35	3 985 (8.1)	142 289 (17.1)
Primiparous		
Yes	11 624 (23.5)	250 877 (30.2)
Baby sex^		
Male	25 548 (51.7)	428 092 (51.5)
Gestational age at birth (weeks)		
<24 weeks	355 (0.7)	2 646 (0.3)
24-27 weeks	386 (0.8)	2 701 (0.3)
28-36 weeks	4 913 (9.9)	48 605 (5.8)
37-41 weeks	43 044 (87.1)	767 101 (92.2)
42+ weeks	723 (1.5)	10 654 (1.3)
Birthweight		
Less than 10th centile~	7 995 (16.2)	76 024 (9.1)
Index of relative socioeconomic disadvantage*		
Highest 20%	1 110 (2.3)	110 013 (13.3)
Middle 60%	28 727 (58.4)	585 074 (70.6)
Lowest 20%	19 340 (39.3)	133 460 (16.1)
Accommodation status		
Private	1 127 (2.3)	255 685 (30.7)
Public	48 322 (97.7)	576 056 (69.3)
Smoker^^		
Yes	11 140 (53.0)	59 680 (16.8)
Substance Use		
Yes	785 (1.6)	4 514 (0.5)
Pregnancy complications**		
Yes	19 903 (61.6)	344 075 (63.4)
Remoteness		
Urban	10 281 (20.8)	503 085 (60.5)
Regional	28 820 (58.3)	306 402 (36.8)
Remote	10 347 (20.9)	22 255 (2.7)
Stillbirth		
Yes	527 (1.1)	4 898 (0.6)

^Data was missing for 4 births and sex was indeterminate for 108 births (97 non-Indigenous and 11 Indigenous). ~Australian population birthweight centile. *Index of relative socioeconomic disadvantage was based on postcode of maternal place of residence. ^^Data on smoking was collected from July 2005, smoking status was unknown for 504 307 births (28 404 Indigenous and 475 903 non-Indigenous births). **pregnancy complication data consistently collected from July 2001

Figure 1: Stillbirth rates by Indigenous status and geographic location, singleton births, Queensland, 1995-2011

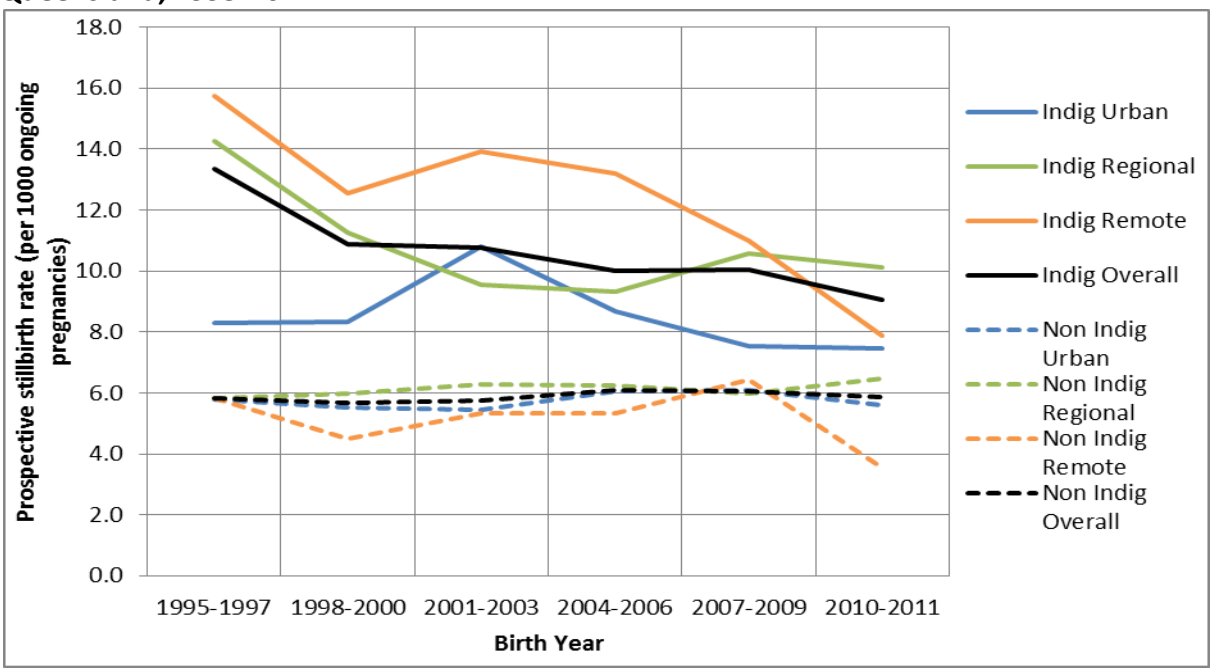

Figure 2: Stillbirth rates by Indigenous status and gestational age grouping, singleton births, Queensland, 1995-2011

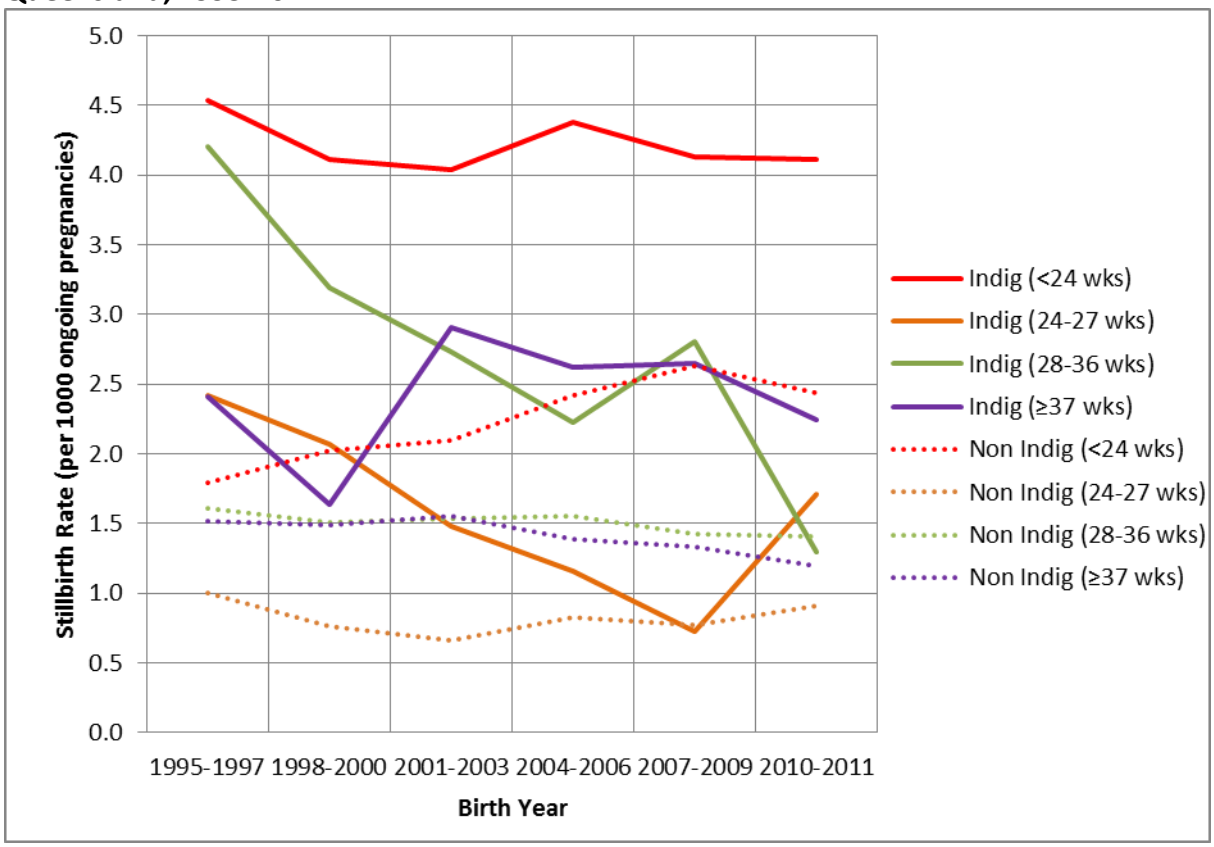

Table 2: Comparison of cause specific stillbirth rates by Indigenous status, singleton births, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Indigenous (n=49,450)		Non-Indigenous (n=831,761)		Total (n=881,211)		
	n	rate	n	rate	n	Rate	RR
All cause*	**527**	**10.7**	**4898**	**5.9**	**5425**	**6.2**	**1.81 (1.66-1.98)**
Congenital Abnormality	**75**	**1.5**	**1138**	**1.4**	**1213**	**1.4**	**1.11 (0.88-1.40)**
Central nervous system	31	0.6	284	0.3	315	0.4	1.84 (1.27-2.66)
Cardiovascular system	5	0.1	122	0.1	127	0.1	0.69 (0.28-1.69)
Chromosomal	13	0.3	352	0.4	365	0.4	0.62 (0.36-1.08)
Multiple	13	0.3	161	0.2	174	0.2	1.36 (0.77-2.39)
Other	13	0.3	219	0.3	232	0.3	1.00 (0.57-1.75)
Perinatal Infection	**33**	**0.7**	**150**	**0.2**	**183**	**0.2**	**3.70 (2.54-5.39)**
GBS	3	0.1	30	0.0	33	0.0	1.68 (0.51-5.51)
Syphilis	15	0.3	1	0.0	16	0.0	252 (33-1910)
Other bacterial	7	0.1	41	0.0	48	0.1	2.87 (1.29-6.40)
Viral	1	0.0	43	0.1	44	0.0	0.39 (0.05-2.84)
Fungal/Protozoal/other	7	0.1	35	0.0	42	0.0	3.36 (1.49-7.57)
Hypertension	**24**	**0.5**	**182**	**0.2**	**206**	**0.2**	**2.22 (1.45-3.39)**
Pre-existing	9	0.2	53	0.1	62	0.1	2.86 (1.41-5.79)
Pregnancy induced/Pre-eclampsia	14	0.3	127	0.2	141	0.2	1.85 (1.07-3.22)
Unspecified	1	0.0	2	0.0	3	0.0	8.41 (0.76-92.7)
Antepartum Haemorrhage	**37**	**0.7**	**393**	**0.5**	**430**	**0.5**	**1.58 (1.13-2.22)**
Abruption	31	0.6	339	0.4	370	0.4	1.54 (1.06-2.22)
Other	6	0.1	54	0.1	60	0.1	1.87 (0.80-4.34)
Maternal conditions	**33**	**0.7**	**147**	**0.2**	**180**	**0.2**	**3.78 (2.59-5.51)**
Diabetes	21	0.4	55	0.1	76	0.1	6.42 (3.88-10.62)
Autoimmune (lupus)	3	0.1	7	0.0	10	0.0	7.21 (1.86-27.9)
Other	9	0.2	85	0.1	94	0.1	1.78 (0.90-3.54)
Specific Perinatal conditions	**16**	**0.3**	**261**	**0.3**	**277**	**0.3**	**1.03 (0.62-1.71)**
Fetomaternal haemorrhage	4	0.1	49	0.1	53	0.1	1.37 (0.50-3.80)
Antenatal cord complication	3	0.1	83	0.1	86	0.1	0.61 (0.19-1.92)
Uterine abnormalities	6	0.1	39	0.0	45	0.1	2.59 (1.10-6.11)
Other	3	0.1	90	0.1	93	0.1	0.56 (0.18-1.77)
Hypoxic peripartum death	**6**	**0.1**	**103**	**0.1**	**109**	**0.1**	**0.98 (0.43-2.23)**
With intrapartum complications	2	0.0	49	0.1	51	0.1	0.69 (0.17-2.82)
No/Unspecified intrapartum complications	4	0.1	54	0.1	58	0.1	1.25 (0.45-3.44)
Fetal growth restriction	**24**	**0.5**	**227**	**0.3**	**251**	**0.3**	**1.78 (1.17-2.71)**
Reduced vascular perfusion	13	0.3	128	0.2	141	0.2	1.71 (0.97-3.02)
Other	11	0.2	99	0.1	110	0.1	1.87 (1.00-3.48)
Spontaneous preterm	**110**	**2.2**	**601**	**0.7**	**711**	**0.8**	**3.08 (2.51-3.77)**
Unexplained antepartum fetal death	**157**	**3.2**	**1638**	**2.0**	**1795**	**2.0**	**1.61 (1.37-1.90)**
No obstetric antecedent	**11**	**0.2**	**58**	**0.1**	**69**	**0.1**	**3.19 (1.67-6.08)**

* Clinical classification data missing for 1 stillbirth (Indigenous). "Other" category consists of combinations of subcategories.

Table 3: Relative risk of stillbirth for Indigenous versus non-Indigenous women by geographic location, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Relative Risk Indigenous versus Non Indigenous			
	Urban	**Regional**	**Remote**	**Total**
Congenital abnormality	1.02 (0.60-1.73)	1.06 (0.78-1.45)	1.11 (0.63-1.95)	1.11 (0.88-1.40)
Perinatal Infection	3.09 (1.35-7.05)	3.67 (2.18-6.19)	-	3.70 (2.54-5.39)
Hypertension	0.81 (0.20-3.27)	3.17 (1.85-5.45)	2.69 (0.72-10.01)	2.22 (1.45-3.39)
Antepartum haemorrhage	1.75 (0.82-3.71)	1.31 (0.85-2.03)	1.37 (0.53-3.52)	1.58 (1.13-2.22)
Maternal conditions	2.15 (0.79-5.85)	4.38 (2.63-7.28)	3.44 (1.13-10.52)	3.78 (2.59-5.51)
Specific perinatal conditions	0.63 (0.16-2.53)	0.87 (0.42-1.78)	1.84 (0.62-5.48)	1.03 (0.62-1.71)
Hypoxic peripartum death	0.78 (0.11-5.60)	1.22 (0.43-3.42)	0.43 (0.05-3.68)	0.98 (0.43-2.23)
Fetal growth restriction	1.31 (0.49-3.55)	2.70 (1.61-4.52)	0.61 (0.13-2.96)	1.78 (1.17-2.71)
Spontaneous preterm	2.45 (1.54-3.88)	2.99 (2.24-3.99)	6.26 (3.16-12.41)	3.08 (2.51-3.77)
Unexplained antepartum fetal death	1.39 (0.95-2.03)	1.50 (1.20-1.86)	2.64 (1.64-4.23)	1.61 (1.37-1.90)
No obstetric antecedent	1.69 (0.23-12.39)	2.28 (0.94-5.50)	8.60 (0.96-76.96)	3.19 (1.67-6.08)
All cause	**1.47 (1.18-1.81)**	**1.76 (1.56-1.98)**	**2.37 (1.84-3.04)**	**1.81 (1.66-1.98)**
Autopsy rate (Indigenous, Non-Indigenous)	28.7%, 40.0%	27.4%, 36.9%	18.6%, 42.7%	25.5%, 38.9%
Relative Risk (95% CI)	0.72 (0.51-1.00)	0.74 (0.61-0.90)	0.44 (0.29-0.66)	0.65 (0.56-0.76)

Table 4: Causes specific relative risk of stillbirth, Indigenous versus non-Indigenous mothers by gestational age grouping, Queensland, 1995-2011

PSANZ Perinatal Death Classification Category	Relative Risk (95% CI) Indigenous versus Non Indigenous				
	< 24 weeks	**24 - 27 weeks**	**28 – 36 weeks**	**≥ 37 weeks**	**Total**
Congenital abnormality	1.03 (0.77-1.38)	0.99 (0.46-2.13)	1.63 (1.00-2.64)	0.85 (0.27-2.69)	1.11 (0.88-1.40)
Perinatal Infection	**2.63 (1.35-5.12)**	**4.22 (1.85-9.67)**	**6.79 (3.26-14.14)**	**3.23 (1.35-7.71)**	**3.70 (2.54-5.40)**
Hypertension	**2.99 (1.41-6.35)**	**2.41 (1.09-5.33)**	1.67 (0.77-3.64)	1.05 (0.14-7.85)	**2.22 (1.45-3.40)**
Antepartum haemorrhage	**2.24 (1.33-3.78)**	1.88 (0.81-4.36)	0.88 (0.43-1.79)	1.64 (0.71-3.79)	**1.58 (1.13-2.22)**
Maternal conditions	**5.89 (2.49-13.93)**	1.69 (0.52-5.54)	**2.83 (1.40-5.73)**	**5.79 (3.17-10.57)**	**3.78 (2.59-5.51)**
Specific perinatal conditions	1.55 (0.71-3.36)	-	2.06 (0.99-4.29)	0.21 (0.03-1.54)	1.03 (0.62-1.71)
Hypoxic peripartum death	-	-	1.13 (0.15-8.57)	1.08 (0.44-2.67)	0.98 (0.43-2.23)
Fetal growth restriction	-	1.69 (0.60-4.72)	**2.12 (1.13-3.97)**	**2.86 (1.41-5.77)**	**1.78 (1.17-2.71)**
Spontaneous preterm	**3.01 (2.40-3.79)**	**3.26 (1.94-5.49)**	**3.40 (1.41-8.16)**	**-**	**3.08 (2.51-3.77)**
Unexplained antepartum fetal death	1.53 (0.98-2.39)	**1.81 (1.19-2.76)**	**1.63 (1.23-2.16)**	**1.67 (1.28-2.17)**	**1.61 (1.37-1.90)**
No obstetric antecedent	**4.39 (1.79-10.78)**	**-**	**6.17 (1.97-19.39)**	1.11 (0.15-8.37)	**3.19 (1.68-6.08)**
All cause	**1.87 (1.62-2.16)**	**1.87 (1.47-2.37)**	**1.83 (1.53-2.18)**	**1.71 (1.40-2.09)**	**1.81 (1.65-1.98)**
Autopsy rates (Indigenous, Non-Indigenous)	19.71%, 31.07%	22.67%, 42.71%	31.34%, 43.09%	30.19%, 45.05%	25.48%, 38.87%
Relative Risk (95% CI)	**0.63 (0.48-0.84)**	**0.53 (0.35-0.81)**	**0.73 (0.56-0.94)**	**0.67 (0.50-0.90)**	**0.66 (0.56-0.76)**

Appendix F: Paper 2 – Final version of submitted manuscript (Published online 15 July 2016)

Gestational age specific stillbirth risk among Indigenous and non-Indigenous women in Queensland, Australia: a population based study

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Abstract

Background

In Australia, significant disparity persists in stillbirth rates between Aboriginal and Torres Strait Islander (Indigenous Australian) and non-Indigenous women. Diabetes, hypertension, antepartum haemorrhage and small-for-gestational age (SGA) have been identified as important contributors to higher rates among Indigenous women. The objective of this study was to examine gestational age specific risk of stillbirth associated with these conditions among Indigenous and non-Indigenous women.

Methods

Retrospective population-based study of all singleton births of at least 20 weeks gestation or at least 400 grams birthweight in Queensland between July 2005 and December 2011 using data from the Queensland Perinatal Data Collection, which is a routinely-maintained database that collects data on all births in Queensland. Multivariate logistic regression was used to calculate adjusted odds ratios (aOR) and 95% confidence intervals, adjusting for maternal demographic and pregnancy factors.

Results

Of 360987 births analysed, 20273 (5.6%) were to Indigenous women and 340714 (94.4%) were to non-Indigenous women. Stillbirth rates were 7.9 (95% CI 6.8-9.2) and 4.1 (95% CI 3.9-4.3) per 1000 births, respectively. For both Indigenous and non-Indigenous women across most gestational age groups, antepartum haemorrhage, SGA, pre-existing diabetes and pre-existing hypertension were associated with increased risk of stillbirth. There were mixed results for pre-eclampsia and eclampsia and a consistently raised risk of stillbirth was not seen for gestational diabetes.

Conclusion

This study highlights gestational age specific stillbirth risk for Indigenous and non-Indigenous women; and disparity in risk at term gestations. Improving access to and utilisation of appropriate and responsive healthcare may help to address disparities in stillbirth risk for Indigenous women.

Keywords:

Aboriginal and Torres Strait Islander Australians, Indigenous, fetal death, stillbirth, risk, diabetes, hypertension, antepartum haemorrhage, small for gestational age

Background

Stillbirth rates in Australia have failed to improve over the past two decades. Marked disparity in stillbirth rates persist between Aboriginal and Torres Strait Islander (Indigenous Australian) and non-Indigenous women [1-3]. In 2012, national stillbirth rates among Indigenous women were one and a half times higher (10.8 vs 7.1/1000) than among non-Indigenous women [2]. Moreover, this disparity persists in the rate of term stillbirths (RR 1.71, 95% CI 1.40-2.09) with little change over time [1].

Diabetes, hypertension, antepartum haemorrhage and small-for-gestational age are important contributors to the higher stillbirth rates observed among Indigenous women [1]. In Queensland, pre-existing and gestational diabetes affected approximately 0.6% and 6.7% of pregnancies [2]; while Australian national estimates are 0.6% and 4.7%, respectively [4]. There is evidence of increasing prevalence of pre-existing and gestational diabetes within Queensland[2, 5]; with consistently higher rates of diabetes for Indigenous women compared with non-Indigenous women [4]. However, larger increases in the prevalence of gestational diabetes have been reported for non-Indigenous women [6]. Hypertensive disorders of pregnancy (including pre-existing and pregnancy-induced hypertension) affects around 0.6% and 4.4% of pregnancies in Queensland [2]. Antepartum haemorrhage (including placenta praevia and abruption) is associated with up to 20% of very preterm births [7] and affects 2.4% of pregnancies in Queensland [2]. Indigenous women have higher rates of small-for-gestational age births than non-Indigenous women [8].

Given the contribution of these conditions to stillbirth rates and the disproportionate burden among disadvantaged groups, determining the specific periods of increased risk of stillbirth associated with these conditions is important for clinical management and potential further reductions in stillbirth rates. The objective of this study was to examine the gestational age-specific risk of stillbirth associated with antepartum haemorrhage, hypertension, diabetes and small-for-gestational age among Indigenous and non-Indigenous women in Queensland to determine if there are differential effects of risk factors.

Methods

We conducted a population-based study utilising data from the Queensland Perinatal Data Collection (QPDC) for the period July 2005 to December 2011. The QPDC is an administrative database which holds data on all births occurring in Queensland. It is a requirement that all births in Queensland are registered in the QPDC for administrative purposes [9].

Demographic factors assessed included maternal Indigenous status, age, marital status, socioeconomic status and geographic location. Indigenous status was based on maternal self-identification as Aboriginal or Torres Strait Islander or not. Relative socioeconomic disadvantage (based on residential postcode) was defined as residing in the lowest ranked 20% of neighbourhoods. Geographic location (based on residential postcode) was classified as major city, regional or remote. Pregnancy factors assessed included smoking status, substance use, hospital accommodation status, assisted conception use, primiparity, number of antenatal care visits, gestational age at birth, baby's sex and small-for-gestational age (SGA). SGA was defined as birthweight less than the 10th Australian population percentile by gestational age, plurality and sex [10].

Medical conditions of interest included: antepartum haemorrhage, essential hypertension, pre-eclampsia/eclampsia, gestational and pre-existing diabetes. Unfortunately, we were unable to assess the effect of overweight/obesity over the study duration. Midwives, who are directly involved in the clinical care of the individual mothers, provide the data to the QPDC. Data audits completed in other Australian states show that false positives and false negatives are generally <5% for diabetes, hypertensive disorders and antepartum haemorrhage [11]. Stillbirth was defined as fetal death of at least 20 weeks gestation or 400g birthweight. Stillbirths as a result of terminations of pregnancy for maternal psychosocial reasons, births of unknown maternal Indigenous status or gestational age, births less than 20 weeks and less than 400g birthweight, and births with a congenital anomaly were excluded.

Statistical Analysis

The all-cause conditional probability of stillbirth occurring at each gestational age interval was calculated using the number of stillbirths occurring within each gestational age interval as the numerator and the number of ongoing pregnancies minus half the number of births occurring within the gestational age interval as the denominator [12].

Risk ratios were used to quantify the unadjusted risk of stillbirth relative to livebirth associated with the conditions of interest (diabetes, hypertension, antepartum haemorrhage and small-for-gestational age). The adjusted stillbirth risk for each of the conditions of interest was assessed in four gestational age intervals of four weeks and an interval of 37 weeks or more using multivariate logistic regression. Regression models were adjusted for the previously listed demographic and pregnancy factors. The denominator was adjusted to reflect the population-at-risk (i.e. the number of ongoing pregnancies at the start of the gestational age interval of interest). Analysis was stratified by maternal Indigenous status, as we hypothesised that differences would be observed in stillbirth risk between Indigenous and non-Indigenous women, furthermore, both groups of women differed significantly on a number of demographic and pregnancy factors. Similar patterns in stillbirth risk were found across strata of antepartum/intrapartum and unknown stillbirth, therefore, to maintain sample size results are presented for all stillbirths combined. Secondary analysis was undertaken on the whole population (Indigenous and non-Indigenous women combined) to assess stillbirth risk among Indigenous women relative to non-Indigenous women. Statistical analyses were performed using Stata/SE for Windows 13.1 (StataCorp LP, College Station, TX, USA 2013). Ethics approval was obtained from the Queensland Health Central Office (Ref: HREC/05/QHC/009), University of Queensland School of Public Health (Ref: II180313) and Mater Health Services (Ref: HREC/15/MHS/36/AM07) Human Research Ethics Committees.

Results

The characteristics of the study population are summarised in Table 1. A total of 360,987 births were included in the analyses. Of these, 20,273 (5.6%) births were to Indigenous women and 340,714 (94.4%) were to non-Indigenous women. The stillbirth rates were 7.9 (95% CI 6.8-9.2) and 4.1 (95% CI 3.9-4.3) per 1000 births, respectively; giving a risk ratio of 1.9 (95% CI 1.6-2.3). For Indigenous and non-Indigenous women, there were higher rates of smoking, substance use, preterm birth and fewer than 8 antenatal care visits among women with a stillbirth compared to women with a live birth (Supplementary Table 1). Among non-Indigenous women, there were

higher rates of socioeconomic disadvantage (risk ratio 1.18, 95% CI 1.03-1.35) for women with a stillbirth (Supplementary Table 1).

Table 2 shows birth outcomes for the study population. For Indigenous and non-Indigenous women, there were higher rates of pre-existing diabetes, pre-existing hypertension, antepartum haemorrhage and SGA among women with a stillbirth compared to women with a live birth (Table 2). However, there were significant differences in the prevalence of the conditions of interest between Indigenous and non-Indigenous women, respectively as follows: pre-existing diabetes (1.3% vs 0.5%, p<0.001), gestational diabetes (6.6% vs 5.3%, p<0.001), pre-existing hypertension (1.0% vs 0.7%, p<0.001), pre-eclampsia/eclampsia (2.9% vs 2.2%, p<0.001), antepartum haemorrhage (2.3% vs 2.7%, p<0.001) and small-for-gestational age (15.2% vs 8.4%, p<0.001).

The all-cause stillbirth risk profile for Indigenous and non-Indigenous women was characterised by lower rates of stillbirth at gestational ages before 38 weeks (0.2 to 0.6/1000 and 0.1 to 0.3/1000 ongoing pregnancies for Indigenous and non-Indigenous women, respectively). A marked increase in risk was then observed from 39 weeks onwards, with a two-fold or higher risk for Indigenous women compared with non-Indigenous women (Figure 1).

Overall, women with a stillbirth were more likely to have: pre-existing diabetes (2.1% vs 0.5%, risk ratio 3.92, 95% CI 2.79-5.51), pre-existing hypertension (2.5% vs 0.7%, risk ratio 3.70, 95% CI 2.70-5.08), pre-eclampsia/eclampsia (5.3% vs 2.2%, risk ratio 2.39, 95% CI 1.94-2.96), antepartum haemorrhage (24.6% vs 2.6%, risk ratio 9.43, 95% CI 8.62-10.3) and a small for gestational age infant (30.5% vs 8.7%, risk ratio 3.47, 95% CI 3.21-3.75), while women with gestational diabetes (4.0% vs 5.4%, risk ratio 0.74, 95% CI 0.58-0.94) or pregnancy-induced hypertension (1.8% vs 2.9%, risk ratio 0.62, 95% CI 0.43-0.90) were less likely to have a stillbirth.

Gestational age-specific odds of stillbirth are presented by condition for Indigenous and non-Indigenous women separately in Table 3; and for the whole population in Supplementary Table 2. Supplementary Table 3 shows the odds of stillbirth by condition of interest for Indigenous women relative to non-Indigenous women.

Diabetes

There were significantly increased odds of stillbirth associated with pre-existing diabetes from 33 weeks onwards for both groups of women. Among Indigenous women, the odds of stillbirth at 33-36 and 37+ weeks were aOR 19.0 (95% CI 5.3-68) and aOR 15.4 (95% CI 4.8-49), respectively. Among non-Indigenous women, the adjusted odds ratios for the equivalent gestational ages were 7.7 (95% CI 3.4-17.6) and 6.8 (95% CI 3.5-13.2) (Table 3). There was a suggestion of increased odds of stillbirth associated with gestational diabetes from 33 weeks onwards among non-Indigenous women. There were decreased odds of stillbirth associated with diabetes at gestational ages less than 28 weeks for Indigenous women, but increased odds at term (Supplementary Table 3).

Hypertension

There was a suggestion of increased odds of stillbirth associated with pre-existing hypertension at all gestational ages assessed. Pre-eclampsia/eclampsia was likely to be associated with increased

odds of stillbirth for both groups of women, although numbers were too small in some instances to reach conventional statistical significance of 0.05. As with diabetes, there were decreased odds of stillbirth associated with hypertensive disorders at gestational ages less than 28 weeks for Indigenous women, and increased odds at term (Supplementary Table 3).

Antepartum haemorrhage

Antepartum haemorrhage was strongly associated with stillbirth for most gestational age groups and for both Indigenous and non-Indigenous women. Among non-Indigenous women, odds of stillbirth for antepartum haemorrhage was higher at 33-36 weeks (aOR 17.9, 95% CI 13.1-24.4) compared to odds at less than 28 weeks or at term (Table 3). Compared to non-Indigenous women, there were decreased odds of stillbirth at 24-27 weeks (aOR 0.56, 95% CI 0.33-0.96) but increased odds of stillbirth at 37+ weeks (aOR 1.53, 95% CI 1.07-2.21)(Supplementary Table 3).

Small-for-gestational age (SGA)

There were significantly increased odds of stillbirth associated with SGA from 24 weeks gestation onwards for Indigenous women; and at all gestational age groups for non-Indigenous women (Table 3). Indigenous women had decreased odds of stillbirth associated with SGA at gestational ages less than 28 weeks compared with non-Indigenous women, but there was no difference in stillbirth risk at 28 weeks or older (Supplementary Table 3).

Discussion

Main findings

This study found increased odds of stillbirth associated with pre-existing diabetes, pre-existing hypertension, antepartum haemorrhage and SGA across most gestational age groups for both Indigenous and non-Indigenous women after adjusting for potential confounders. There were mixed results for pre-eclampsia/eclampsia and gestational diabetes. At less than 27 weeks, there were decreased odds of stillbirth associated with diabetes, pre-existing hypertension and SGA for Indigenous compared with non-Indigenous women. Conversely, the odds of stillbirth for diabetes, hypertension and antepartum haemorrhage were 1 ½ times higher at term for Indigenous women as non-Indigenous women. The protective effect observed at lower gestational ages may be due to detection bias or differing causes of stillbirth; higher rates of spontaneous preterm birth have been reported for Indigenous women [13]. Likewise, the increased odds of stillbirth may reflect the impact of lower levels of antenatal care such as decreased detection of SGA and suboptimal diabetes management. Few studies have assessed gestational age-specific stillbirth risk using the population-at-risk approach within this study population [14]. The profile of all-cause stillbirth risk for both groups of women was similar to profiles reported in populations in USA [15]. However, the overall magnitude of risk for Indigenous women was about twice that of non-Indigenous women.

We acknowledge that the study was underpowered to detect interactions between Indigenous status and stillbirth risk factors which may have indicated differential effects of risk factors within the two groups of women.

Diabetes

We found increased odds of stillbirth associated with pre-existing diabetes from 33 weeks onwards for both groups of women. Similar findings of increased risk of stillbirth due to pre-existing diabetes from 32 weeks onwards have been reported elsewhere [16, 17]. The one and a half fold disparity in the magnitude of stillbirth risk between Indigenous and non-Indigenous women at term mirrors higher rates of pre-existing diabetes among Indigenous women in our study (1.3% versus 0.5%). Similarly, our finding of increased odds of stillbirth due to gestational diabetes from 28 weeks onwards among non-Indigenous women concurs with Hutcheon and colleagues [18]. While the prevalence of gestational diabetes have been reported to be higher among Indigenous women, the rate of increase of gestational diabetes over time was found to be greater among non-Indigenous women [4].

Current management for pre-existing diabetes includes strict glycaemic control, pre-conceptual folate supplementation, cessation of oral hypoglycaemic agents, diabetes complication review, periodic ultrasound scans for fetal morphology (18-20 weeks), cardiac views (24 weeks), fetal growth (28-30 and 34-36 weeks)[19]. The International Association of Diabetes and Pregnancy Study Group recommend screening all women at their first antenatal visit for gestational diabetes or previously undiagnosed pre-existing diabetes [20]; however, a tiered approach with early screening of women at high risk or with multiple risk factors is recommended in Australia [21]. Perinatal mortality audits in high income countries have identified poor glycaemic control [22, 23] and inadequate screening among women at risk [24] as contributing to stillbirth. Conversely, pre-pregnancy counselling has been found to significantly lower the risk of major congenital anomalies associated with diabetes during pregnancy (RR 0.36, 95% CI 0.22-0.59; absolute risk 2.1% versus 6.5%) [21]. Pre-conception care was found to reduce perinatal mortality while optimal vs suboptimal serum blood glucose control was associated with reduced perinatal mortality (RR 0.40, 95% CI 0.25-0.63) but not stillbirth (RR 0.51 95% CI 0.14-1.88)[25]. Our findings highlight the need for early initiation of monitoring of women with pre-existing diabetes, especially for Indigenous women; and early identification and management of gestational diabetes.

Antepartum haemorrhage

We found increased risk of stillbirth associated with antepartum haemorrhage at all gestational age groups assessed; and the magnitude of risk for Indigenous women was 1 ½ times higher than for non-Indigenous women at term. Despite differences in methodology, similar magnitude of risk has been reported in population based studies from Canada and USA with adjusted odds ratios ranging from 11.40-18.90 for stillbirth associated with placental abruption in births of at least 20 weeks [26, 27]. The disparity in risk seen between Indigenous and non-Indigenous women may be a reflection of higher prevalence of risk factors for placenta praevia and abruption such as maternal smoking (52.7% vs 16.6%), substance use (1.7% vs 0.5%) and small for gestational age

(15.2% vs 8.4%). At present, there is limited evidence for the prediction or prevention of abruption; and antepartum haemorrhage usually constitutes a sudden obstetric emergency. The mainstay of management for antepartum haemorrhage includes: assessment of maternal and fetal condition, prompt resuscitation if required and early delivery if there is fetal distress or the baby is suitably mature [28, 29]. It is estimated that up to 70% of antepartum haemorrhage cases occur in apparently low risk pregnancies [30].

Small-for-gestational age (SGA)

We found increased odds of stillbirth associated with SGA from 24 weeks onwards for both Indigenous and non-Indigenous women; and similar findings have been reported elsewhere [16]. Although not reflected in the stillbirth odds, there was a higher prevalence of SGA among Indigenous women in this study (15.2% vs 8.4%), similar to reports from the Northern Territory (Indigenous 11.9% vs non-Indigenous 5.0%) [31].

SGA has been used as a proxy for fetal growth restriction and undetected fetal growth restriction has been identified as a significant potentially modifiable risk factor for stillbirth [32]. There are currently no antenatal interventions to treat fetal growth restriction and the mainstay of management is fetal monitoring to determine the optimal timing for delivery (balancing risks and benefits of adverse fetal outcomes against morbidity and mortality associated with early delivery at a given gestational age) [33]. Management for SGA involves accurate determination of gestational age and serial monitoring of fetal growth (using symphysis-fundal height measurement or ultrasound biometry). However, controversy exists over the accuracy of symphysis-fundal height measurement especially in obese women [34] and the use of customised growth charts due to lack of high level evidence [35]. A number of interventions have been found to be effective in the prevention of SGA among women at increased risk, including: antiplatelet agents, smoking cessation, progesterone therapy, anti-thrombotic therapy and interventionist care in severe pre-eclampsia [36]. Further studies are needed into preventive strategies for SGA that also include pre-eclampsia and preterm birth [36], as well as investigating the serious adverse effects of antenatal antithrombotic therapies [37].

<u>Equity in access to antenatal care</u>

Overall, this study highlights the importance of optimal maternal health prior to pregnancy as well as early initiation of high quality antenatal care in the context of continued disparity in risk of stillbirth among Indigenous and non-Indigenous women. Equity in access to antenatal care services and their utilisation is important to addressing disparities in health outcomes for all women, particularly Indigenous women [38]. Indigenous women in our study were more likely to have fewer antenatal care visits, a finding supported by others [2, 13]. Limited availability of culturally appropriate services may affect attendance for antenatal care; for example there were on average 5.5 antenatal care visits within mainstream services versus 10.5 visits within community controlled service settings for Indigenous women [39]. Active efforts to ensure appropriate and responsive care in the clinical environment both at the level of the individual health practitioner and within mainstream health care services are essential to reduce or eliminate social barriers to accessing health care. Embedding cultural competence in continuing organisational quality improvement processes has been shown to enhance health outcomes for

Indigenous people [40]. This is especially important for Indigenous women who seek care within mainstream health services.

The Australian government has recognised the importance of maternal and child health to the "Closing the Gap" initiative and has prioritised maternal and child health [41]. It has been shown that an investment in stillbirth prevention provides a three-fold return in terms of maternal, neonatal and child health [42]. While there has been continued support for Aboriginal and Torres Strait Islander community controlled health centres and their Mums and Bubs centres, many health and lifestyle modification programs have been defunded. Declines seen in smoking and under-5 child mortality rates are further evidence for the need to maintain funding for successful lifestyle modification programs and antenatal care services operated by the community controlled health services [41]. More broadly, access to primary care services is critical to reducing health inequity and policies that undermine universal health care pose a significant threat to this goal by presenting further financial barriers that are likely to disproportionately affect the most vulnerable [43].

Conclusions

This study highlights the gestational age specific stillbirth risk associated with diabetes, hypertension, antepartum haemorrhage and small for gestational age. It also highlights the disparity in stillbirth risk between Indigenous and non-Indigenous women at term and the need to prioritise early detection and management of these conditions and to work with women before, during and between pregnancies. Improving access to and utilisation of appropriate and responsive healthcare may help to address disparities in stillbirth risk for Indigenous women. Larger population-based studies are needed to re-evaluate whether there are differences in the effect of risk factors on stillbirth risk among Indigenous and non-Indigenous women.

Declarations

List of Abbreviations

Small for gestational age (SGA)

Adjusted odds ratio (aOR)

Queensland Perinatal Data Collection (QPDC)

Ethics approval

Ethics approval was obtained from the Queensland Health Central Office (Ref: HREC/05/QHC/009), University of Queensland School of Public Health (Ref: II180313) and Mater Health Services (Ref: HREC/15/MHS/36/AM07) Human Research Ethics Committees.

Consent for publication

Not applicable

Availability of data and materials

The data on which the conclusions of this manuscript rely are owned by the Queensland Government Department of Health. Approvals granted for the use of these data to not permit sharing of the data.

Competing Interests

The authors declare that they have no competing interests.

Funding

Not applicable

Author's Contributions

II contributed to concept of the study, undertook data analysis and wrote the manuscript. VF, MC and FB were responsible for the concept of the study, gave technical assistance with data analysis and interpretation of results and helped write the manuscript. SV, PM, YR and GS gave technical assistance with interpretation of results. GS gave technical assistance with data analysis and interpretation of results. All authors reviewed and approved the final version of this manuscript before submission.

Acknowledgements

Ibinabo Ibiebele is a recipient of the National Health and Medical Research Council Postgraduate Public Health scholarship and the University of Queensland Research Scholarship.

Authors' Information

Not applicable

Endnotes

Not applicable

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Figure 1: Gestational age specific risk of stillbirth by Indigenous status

Numerator = the number of stillbirths occurring at each week of gestational age.
Denominator = the number of ongoing pregnancies at each gestational age week minus half the number of births occurring within the gestational age week

Table 1: Maternal and pregnancy characteristics by livebirth or stillbirth and Indigenous status

Characteristics	Indigenous (n=20 273)	Non-Indigenous (n=340 714)
Maternal age (years)		
≤18 years	1 454 (7.2)	4 402 (1.3)
19-24 years	8 765 (43.2)	67 896 (19.9)
25-30 years	5 693 (28.1)	119 253 (35.0)
31-34 years	2 427 (12.0)	81 322 (23.9)
≥35 years	1 934 (9.5)	67 841 (19.9)
Geographic Location		
Major City	4 169 (20.6)	209 778 (61.6)
Regional area	11 920 (58.8)	122 590 (36.0)
Remote area	4 184 (20.6)	8 334 (2.5)
Marital Status		
Domestic partner	13 033 (64.3)	302 212 (88.7)
No domestic partner	7 232 (35.7)	38 452 (11.3)
Relative socioeconomic disadvantage		
Lowest 20%	7 422 (36.7)	39 503 (11.6)
Any smoking during pregnancy		
Yes	10 692 (53.1)	56 720 (16.7)
Substance Use during pregnancy		
Yes	343 (1.7)	1 705 (0.5)
Hospital accommodation status		
Public	19 853 (97.9)	229 717 (67.4)
Assisted Conception		
Yes	92 (0.5)	12 909 (3.8)
Primiparity		
Yes	4 834 (23.8)	102 091 (30.0)
Number of antenatal care visits		
Less than 2	1 102 (5.4)	2 291 (0.7)
2 – 4	3 405 (16.8)	17 349 (5.1)
5 – 7	5 828 (28.8)	63 386 (18.6)
8 or more	9 911 (49.0)	257 496 (75.6)

Table 2: Maternal medical and pregnancy conditions by livebirth or stillbirth and Indigenous status

Characteristics	Indigenous (n=20273)			Non-Indigenous (n=340714)		
	Stillbirth (n=160)	Livebirth (n=20113)	Risk Ratio (95% CI)	Stillbirth (n=1392)	Livebirth (n=339322)	Risk Ratio (95% CI)
Preterm birth	56 (35.0)	53 (0.3)	132 (94.3-187)	451 (32.4)	243 (0.1)	453 (391-525)
Pre-existing diabetes	12 (7.5)	248 (1.2)	6.08 (3.48-10.6)	21 (1.5)	1 702 (0.5)	3.01 (1.96-4.61)
Gestational diabetes	^	1 324 (6.6)	0.38 (0.14-1.00)	58 (4.2)	18 135 (5.3)	0.78 (0.61-1.00)
Pre-existing hypertension	7 (4.4)	190 (0.9)	4.63 (2.21-9.69)	31 (2.2)	2 189 (0.7)	3.45 (2.43-4.90)
Pre-eclampsia/Eclampsia	^	574 (2.9)	1.10 (0.46-2.60)	77 (5.5)	7 359 (2.2)	2.55 (2.05-3.17)
Pregnancy induced hypertension	^	488 (2.4)	0.26 (0.04-1.82)	27 (1.9)	9 897 (2.9)	0.67 (0.46-0.97)
Antepartum haemorrhage	44 (27.5)	412 (2.0)	13.4 (10.3-17.6)	337 (24.2)	8 948 (2.6)	9.18 (8.35-10.1)
Small-for-gestational age	58 (36.3)	3 021 (15.0)	2.46 (2.00-3.02)	410 (29.5)	28 214 (8.3)	3.58 (3.30-3.89)

^Numbers and percentages not displayed for cells with 5 or less observations to protect participant privacy.

ICD10-AM codes: Antepartum haemorrhage (O44.1, O45-O46), Pre-existing hypertension (O10.0, O10.2-10.4, O10.9, O11), Pregnancy Induced hypertension (O13), Pre-eclampsia/Eclampsia (O14, O15), Pre-existing diabetes (O24.0, O24.1, O24.3, O24.8), Gestational diabetes (O24.4, O24.9).

Small-for-gestational age = birthweight less than the 10^{th} Australian population percentile by gestational age, plurality and sex

Table 3: Gestational age-specific risk of stillbirth by medical condition and Indigenous status

Conditions	Indigenous (n=20,273 births)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	**24-27 weeks**	**28-32 weeks**	**33-36 weeks**	**37-42+ weeks**
Pre-existing diabetes[a,c]	1.42 (0.17-11.6)	3.15 (0.31-31.7)	7.81 (1.28-47.8)	19.0 (5.30-68.4)	15.4 (4.79-49.2)
Gestational diabetes[a,c]	-	-	-	0.68 (0.09-5.32)	0.93 (0.22-4.01)
Pre-existing hypertension [b,c]	2.27 (0.27-18.8)	5.62 (0.55-57.7)	13.2 (2.07-84.5)	1.35 (0.14-12.8)	1.49 (0.15-14.8)
Pre-Eclampsia/Eclampsia [c]	0.70 (0.09-5.14)	1.59 (0.21-12.2)	-	1.92 (0.24-15.2)	3.32 (0.79-14.0)
Antepartum haemorrhage[a]	18.1 (9.91-33.1)	14.2 (5.14-39.4)	31.2 (11.9-81.6)	2.53 (0.31-20.3)	17.1 (7.28-40.0)
Small-for-gestational age	1.30 (0.67-2.52)	3.32 (1.31-8.44)	7.04 (2.70-18.4)	3.05 (1.16-8.02)	2.10 (1.08-4.08)
Conditions	**Non-Indigenous (n=340,714 births)**				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	**24-27 weeks**	**28-32 weeks**	**33-36 weeks**	**37-42+ weeks**
Pre-existing diabetes[a]	0.90 (0.21-3.94)	3.23 (0.98-10.7)	1.33 (0.18-9.64)	7.68 (3.36-17.6)	6.77 (3.47-13.2)
Gestational diabetes[a]	0.47 (0.21-1.06)	0.76 (0.31-1.87)	1.25 (0.61-2.56)	1.94 (1.14-3.32)	1.29 (0.84-1.97)
Pre-existing hypertension [b]	7.27 (4.18-12.6)	6.59 (2.99-14.6)	3.35 (1.05-10.7)	2.54 (0.80-8.11)	1.29 (0.41-4.04)
Pre-eclampsia/Eclampsia	0.99 (0.51-1.94)	6.40 (4.14-9.91)	5.55 (3.43-8.99)	2.00 (0.94-4.26)	2.77 (1.65-4.66)
Antepartum haemorrhage[a]	9.03 (7.21-11.3)	7.99 (5.67-11.3)	12.8 (9.25-17.9)	17.9 (13.1-24.4)	7.95 (5.85-10.8)
Small-for-gestational age	3.73 (3.00-4.64)	6.43 (4.78-8.67)	3.85 (2.77-5.33)	3.49 (2.50-4.87)	3.72 (2.91-4.74)

Regression models adjusted for maternal age, smoking status, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits.

[a]Models additionally adjusted for pre-existing hypertension.

[b] These models additionally adjusted for pre-existing diabetes.

[c] Exact logistic regression model

Supplementary Table 1: Maternal and pregnancy characteristics by livebirth or stillbirth and Indigenous status

Characteristics	Indigenous (n=20273)			Non-Indigenous (n=340714)		
	Stillbirth (n=160)	Livebirth (n=20113)	Risk Ratio (95% CI)	Stillbirth (n=1392)	Livebirth (n=339322)	Risk Ratio (95% CI)
Maternal age (years)						
≤18 years	10 (6.3)	1 444 (7.2)	0.87 (0.48-1.59)	42 (3.0)	4 360 (1.3)	2.35 (1.74-3.17)
19-24 years	67 (41.9)	8 698 (43.3)	0.97 (0.81-1.16)	313 (22.5)	67 583 (19.9)	1.13 (1.02-1.24)
25-30 years	48 (30.0)	5 645 (28.1)	1.07 (0.84-1.36)	437 (31.4)	118 816 (35.0)	0.90 (0.83-0.97)
31-34 years	14 (8.8)	2 413 (12.0)	0.73 (0.44-1.20)	290 (20.8)	81 032 (23.9)	0.87 (0.79-0.97)
≥35 years	21 (13.1)	1 913 (9.5)	1.38 (0.92-2.06)	310 (22.3)	67 531 (19.9)	1.12 (1.01-1.23)
Geographic Location						
Major City	26 (16.3)	4 143 (20.6)	0.79 (0.55-1.12)	835 (60.0)	208 943 (61.6)	0.97 (0.93-1.02)
Regional area	95 (59.4)	11 825 (58.8)	1.01 (0.89-1.15)	525 (37.7)	122 065 (36.0)	1.05 (0.98-1.12)
Remote area	39 (24.4)	4 145 (20.6)	1.18 (0.90-1.56)	31 (2.2)	8 303 (2.5)	0.91 (0.64-1.29)
Marital Status						
Domestic partner	102 (63.8)	12 931 (64.3)	0.99 (0.88-1.11)	1 148 (82.5)	301 064 (88.7)	0.93 (0.91-0.95)
No domestic partner	58 (36.3)	7 174 (35.7)	1.02 (0.83-1.25)	241 (17.3)	38 211 (11.3)	1.54 (1.37-1.73)
Relative socioeconomic disadvantage						
Lowest 20%	59 (36.9)	7 363 (36.6)	1.01 (0.82-1.23)	190 (13.6)	39 313 (11.6)	1.18 (1.03-1.35)
Any smoking during pregnancy						
Yes	95 (59.4)	10 597 (52.7)	1.17 (1.03-1.33)	332 (23.9)	56 388 (16.6)	1.47 (1.34-1.62)
Substance Use during pregnancy						
Yes	11 (6.9)	332 (1.7)	4.17 (2.33-7.44)	15 (1.1)	1 690 (0.5)	2.16 (1.31-3.59)
Hospital accommodation status						
Public	157 (98.1)	19 696 (97.9)	1.00 (0.98-1.02)	1 084 (77.9)	228 633 (67.4)	1.16 (1.13-1.19)
Assisted Conception						
Yes	^	91 (0.5)	1.38 (0.19-9.85)	66 (4.7)	12 843 (3.8)	1.26 (0.99-1.59)
Primiparity						
Yes	37 (23.1)	4 797 (23.9)	0.97 (0.73-1.29)	418 (30.0)	101 673 (30.0)	1.00 (0.93-1.09)
Number of antenatal care visits						
Less than 2	47 (29.4)	1 055 (5.2)	5.66 (4.43-7.25)	147 (10.6)	2 144 (0.6)	16.8 (14.4-19.7)
2 – 4	57 (35.6)	3 348 (16.6)	2.16 (1.75-2.67)	459 (33.0)	16 890 (5.0)	6.68 (6.19-7.21)
5 – 7	23 (14.4)	5 805 (28.9)	0.50 (0.35-0.74)	367 (26.4)	63 019 (18.6)	1.43 (1.31-1.56)

Characteristics	Indigenous (n=20273)			Non-Indigenous (n=340714)		
	Stillbirth (n=160)	Livebirth (n=20113)	Risk Ratio (95% CI)	Stillbirth (n=1392)	Livebirth (n=339322)	Risk Ratio (95% CI)
8 or more	31 (19.4)	9 880 (49.1)	0.40 (0.29-0.55)	407 (29.2)	257 089 (75.8)	0.39 (0.36-0.42)

^Numbers and percentages not displayed for cells with 5 observations or less

Supplementary Table 2: Gestational age-specific risk of stillbirth associated with diabetes, hypertension, antepartum haemorrhage and SGA, combined Indigenous and non-Indigenous women, Queensland, mid 2005-2011

Conditions	All births (n=360 987)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Pre-existing diabetes[a]	1.02 (0.31-3.37)	3.34 (1.17-9.57)	3.00 (0.92-9.78)	7.28 (3.35-15.8)	8.26 (4.70-14.5)
Gestational diabetes[a]	0.41 (0.18-0.91)	0.68 (0.28-1.67)	1.12 (0.55-2.28)	1.80 (1.07-3.02)	1.24 (0.82-1.87)
Pre-existing hypertension [b]	6.30 (3.70-10.7)	6.29 (2.97-13.3)	4.39 (1.75-11.0)	2.76 (1.00-7.64)	1.36 (0.50-3.70)
Pre-Eclampsia/Eclampsia	0.92 (0.49-1.73)	5.50 (3.57-8.46)	4.47 (2.76-7.26)	2.10 (1.03-4.27)	2.63 (1.61-4.30)
Antepartum haemorrhage[a]	9.68 (7.85-12.0)	8.49 (6.14-11.7)	13.8 (10.1-18.6)	16.4 (12.1-22.2)	8.44 (6.32-11.3)
Small-for-gestational age	3.26 (2.64-4.02)	5.95 (4.47-7.93)	3.98 (2.93-5.40)	3.51 (2.56-4.81)	3.35 (2.66-4.22)

Regression models adjusted for maternal age, smoking status, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits.

[a]Models additionally adjusted for pre-existing hypertension.

[b] These models additionally adjusted for pre-existing diabetes.

Supplementary Table 3: Effect of Indigenous status on gestational age specific stillbirth risk (Indigenous relative to non-Indigenous)

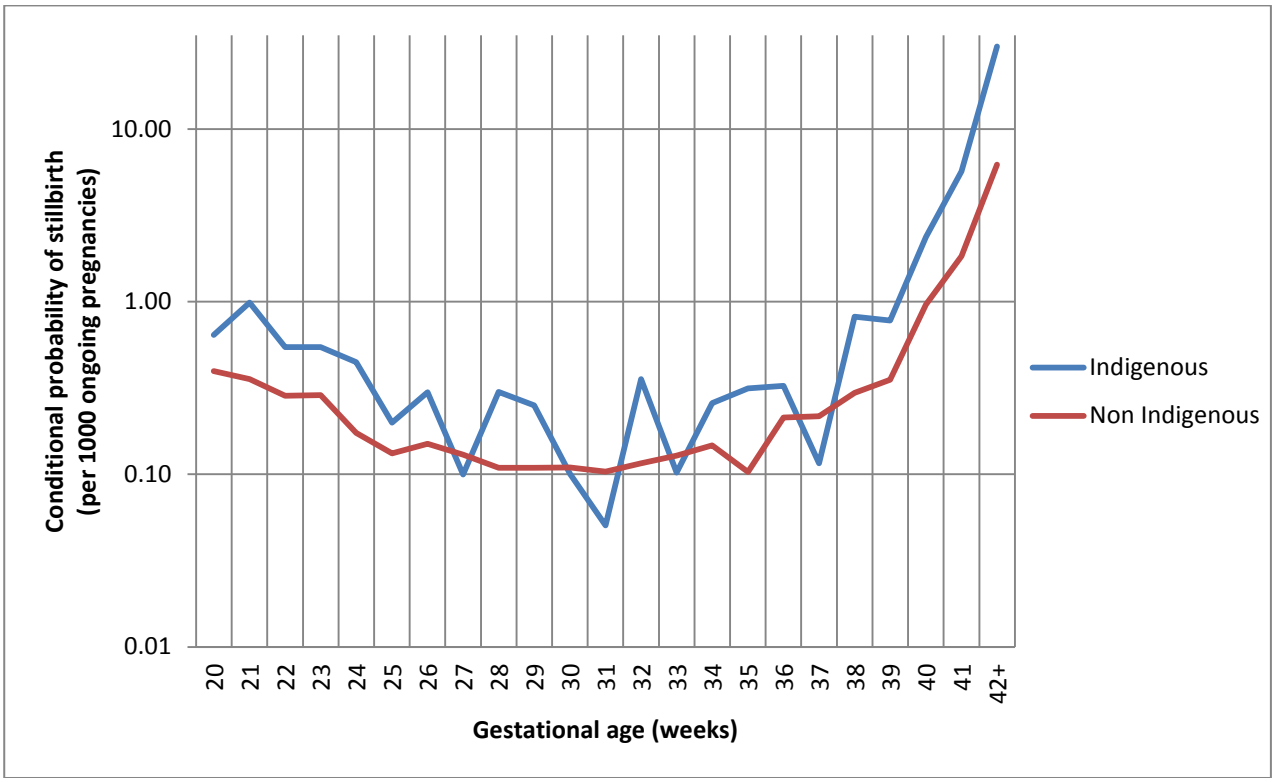
Conditions	All births (n=360 987)				
	Adjusted Odds Ratios (95% Confidence Intervals)				
	20-23 weeks	24-27 weeks	28-32 weeks	33-36 weeks	37-42+ weeks
Pre-existing diabetes[a]	**0.71 (0.51-0.98)**	**0.51 (0.30-0.86)**	0.66 (0.39-1.11)	0.86 (0.51-1.46)	**1.45 (1.01-2.09)**
Gestational diabetes[a]	**0.71 (0.51-0.99)**	**0.53 (0.31-0.89)**	0.67 (0.40-1.12)	0.89 (0.52-1.51)	**1.49 (1.04-2.15)**
Pre-existing hypertension [b]	**0.71 (0.51-0.98)**	**0.51 (0.30-0.86)**	0.66 (0.39-1.11)	0.86 (0.51-1.46)	**1.45 (1.01-2.09)**
Pre-Eclampsia/Eclampsia	0.72 (0.52-1.00)	**0.53 (0.31-0.89)**	0.67 (0.40-1.12)	0.90 (0.53-1.53)	**1.50 (1.04-2.15)**
Antepartum haemorrhage[a]	0.77 (0.55-1.08)	**0.56 (0.33-0.96)**	0.73 (0.43-1.23)	0.99 (0.58-1.69)	**1.53 (1.07-2.21)**
Small-for-gestational age	**0.68 (0.49-0.95)**	**0.49 (0.29-0.83)**	0.58 (0.34-0.99)	0.85 (0.50-1.45)	1.42 (0.98-2.04)

Regression models adjusted for maternal age, smoking status, remoteness, substance use, gender, parity, hospital accommodation status, assisted conception use, socioeconomic status, marital status, number of antenatal care visits.

[a]Models additionally adjusted for pre-existing hypertension.

[b] These models additionally adjusted for pre-existing diabetes.

Figure 1: Gestational age specific risk of stillbirth by Indigenous status



Numerator = the number of stillbirths occurring at each week of gestational age.
Denominator = the number of ongoing pregnancies at each gestational age week minus half the number of births occurring within the gestational age week

Appendix G Conference Abstracts

Appendix G1: Predictors of autopsy following stillbirth

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Background: The stillbirth rate in Australia has not improved for over two decades. Accurate determination of causes of these deaths are critical to effective prevention. In Queensland, nearly 60% of stillbirths at term are "unexplained" with unexplained stillbirth more common for Indigenous women (3.2 vs 2.0/1000). However with low autopsy rates, many stillbirths are "unexplored" rather than " unexplained". This study aims to determine factors associated with autopsy following stillbirth.

Method: Routinely collected population-based data on all singleton stillbirths of at least 400g birthweight or 20 weeks gestation in Queensland between July 2000 and December 2011 were examined. Adjusted odds ratios (aOR, 95%CI) were calculated. Analysis was stratified by gestational age group (<24, 24-27, 28-36 and ≥37 weeks).

Results: Of 3842 women included in these analyses, 1356 (35.3%) consented to autopsy. Factors associated with increased odds of autopsy consent differed across the gestational age groups as follows: fetal growth restriction (aOR ranged from 1.53-1.55, for gestational ages <28 week), primiparity (aOR 1.46-1.60, ≥28 weeks) and maternal age (19-24 years)(aOR 1.45, 28-36 weeks). Factors associated with decreased odds were: intrapartum stillbirth (aOR 0.36-0.65, <37 weeks), antepartum haemorrhage (aOR 0.52-0.67, ≥24 weeks), Indigenous status (aOR 0.50-0.52, 20-23 and ≥37 weeks), initially unexplained stillbirth (aOR 0.42-0.62, ≥28 weeks) and remote residence (aOR 0.27, ≥37 weeks).

Conclusions: Sociodemographic and pregnancy factors are associated with whether or not autopsy is performed following stillbirth. Of concern are associations between no autopsy examination with Indigenous status, and with an initial diagnosis of unexplained stillbirth. Culturally appropriate information and consultation for Indigenous women after stillbirth is warranted.

Citation:
Ibiebele I, Boyle F, Horey D, Wilson P, Coory M, Flenady V**.** Predictors of autopsy following stillbirth. *Perinatal Society of Australia and New Zealand 19th Annual Conference: Discoveries – Improving Perinatal Care*, Melbourne, April 19-22 2015. Journal of Paediatrics and Child Health, 2015. **51 (Suppl. 1)**: p. 28.

Appendix G2: Autopsy consent process: what parents are saying following a stillbirth

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Background: Stillbirth is a devastating pregnancy outcome. There has been little reduction in stillbirth rates in recent times. Autopsy is the gold standard investigation for determining cause of death but rates are declining and parental consent is a major factor. It is unclear how healthcare professionals can support parents in this difficult decision. This study aims to provide a detailed understanding of parents' views and experiences in relation to autopsy following stillbirth.

Method: This qualitative study is nested in a larger prospective study involving 5 Queensland hospitals. Parents complete a questionnaire 6-8 weeks following stillbirth; and semi-structured telephone interviews with a purposive sample of 10 participants 2-3 months later aiming to explore their decision-making process in greater depth. Thematic analysis of interview transcripts is used to identify patterns in the data.

Results: Preliminary analysis confirms the distressing nature of decision-making during the autopsy consent process and highlights three emerging themes : the need for an explanation (importance, value of autopsy, managing feelings of guilt, planning for the future), respecting/honouring the baby (taking care of the baby), and altruism (value of information to others). An important sub-theme within respect for the baby was tissue retention which can invoke further distress especially when parents are unprepared for this.

Conclusions: These preliminary results support findings from other studies into reasons parents decline consent for autopsy and add further important insights into the autopsy consent process for parents in the contemporary Australian setting. The findings have direct implications for improving clinical practice including providing appropriate information to parents.

Citation:
Ibiebele I, Flenady V, Horey D, Wilson P, Coory M, Boyle F. Autopsy consent process: what parents are saying following a stillbirth. *Perinatal Society of Australia and New Zealand 19th Annual Conference: Discoveries – Improving Perinatal Care*, Melbourne, April 19-22 2015. Journal of Paediatrics and Child Health, 2015. **51 (Suppl. 1)**: p. 28.

Appendix G3: Gestational age specific risk of stillbirth among Indigenous and non-Indigenous women in Queensland

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Background: In Australia, significant disparity persists in stillbirth rates between Aboriginal and Torres Strait Islander (Indigenous) and non-Indigenous women. Diabetes, hypertension, fetal growth restriction and antepartum haemorrhage have been identified as important contributors to higher rates among Indigenous women. The objective of this study was to examine gestational age specific risk of stillbirth associated with these conditions among Indigenous and non-Indigenous women.

Methods: Population-based retrospective study involving all singleton livebirths and stillbirth of at least 400g birthweight or 20 weeks gestation in Queensland between July 2005 and December 2011. Stillbirth risk was assessed in five gestational age intervals (<24, 24-27, 28-32, 33-36 and ≥37 weeks). Analysis was stratified by maternal Indigenous status.

Results: Of 360988 births analysed, 20273 (5.6%) were to Indigenous women and 340714 (94.4%) were to non-Indigenous women. Stillbirth rates were 7.9 and 4.1 per 1000 births, respectively. Increased risk of stillbirth associated with fetal growth restriction and antepartum haemorrhage was found throughout the gestational age groups. Diabetes was associated with increased stillbirth risk at later gestational ages. There were differences in the profile and magnitude of stillbirth risk between Indigenous and non-Indigenous women respectively as follows: pre-existing diabetes (adjusted odds ratios ranged from 16.45-18.75 versus 3.32-8.10); antepartum haemorrhage (adjusted odds ratios ranged from 15.40-38.05 versus 7.90-17.86).

Conclusion: This study highlights disparities in stillbirth risk between Indigenous and non-Indigenous women and the need to prioritise prevention and management of diabetes, hypertension, fetal growth restriction and antepartum haemorrhage.

Citation:
Ibiebele I, Flenady V, Coory M, Boyle F, Vlack S, Middleton P, Roe Y, Smith G. Gestational age specific risk of stillbirth among Indigenous and non-Indigenous women in Queensland. *Perinatal Society of Australia and New Zealand 19th Annual Conference: Discoveries – Improving Perinatal Care*, Melbourne, April 19-22 2015. Journal of Paediatrics and Child Health, 2015. **51 (Suppl. 1)**: p. 126.

Appendix G4: Temporal trends and causes of stillbirth among Indigenous and non-Indigenous women in Australia by gestational age: Is the gap closing?

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Background: Progress with reduction in stillbirth rates has slowed in recent times in many high income countries and Australian national reports suggest rates may be increasing. The *Lancet Stillbirth series* highlighted the need to address disparity across population subgroups as a means of further reducing rates in these countries. It has been established that Indigenous women in Australia have higher rates of stillbirth than non-Indigenous women. Examination of temporal trends in rates and underlying cause of death is important to gaining an understanding of the scope for further reductions and to direct further clinical and research efforts.

Objectives: To assess whether the disparity gap is closing in stillbirth rates between Indigenous and non-Indigenous women; and to assess cause-specific stillbirth rates to determine where the greatest disparities lie in order to identify focal areas for future prevention efforts.

Methods: Data on singleton livebirths and stillbirths of at least 400g birthweight and/or 20 weeks gestation in Queensland, Australia (a region of approximately 50,00 births each year) between 1995 and 2011 were obtained. Prospective stillbirth rates (i.e., stillbirths per 1000 ongoing pregnancies) by gestational age (≥24, ≥28 and ≥37 weeks) were calculated for Indigenous and non-Indigenous women. Cause-specific prospective stillbirth rates using the Perinatal Society of Australia and New Zealand Perinatal Death Classification (PSANZ-PDC), relative risk and 95% confidence intervals were also calculated for Indigenous women relative to non-Indigenous women by gestational age.

Results: Over the study period, prospective stillbirth rates for Indigenous women decreased from 13.3 to 9.1/1000 while rates remained steady at 5.9/1000 for non-Indigenous women. There was a 57.3% reduction in the disparity gap between Indigenous and non-Indigenous women. These reductions were more pronounced for women birthing at ≥24 weeks (66.9%) and ≥28 weeks (76.6%), while at term (≥37 weeks), there was an 18.0% increase in the disparity gap. Between 2001 and 2011, the disparity gap at term was steady around 1.2/1000 ongoing pregnancies. Major conditions contributing to the disparity in stillbirth rates at term were: maternal conditions (diabetes), perinatal infection, fetal growth restriction and unexplained antepartum fetal death. Higher rates of undetermined causes may have been driven by lower autopsy rates.

Conclusion: The gap in stillbirth rates between Indigenous and non-Indigenous women is closing; however, Indigenous women continue to be at increased risk of stillbirth due to a number of potentially preventable conditions. High quality antenatal care at all levels using culturally appropriate service delivery models which incorporate diabetes management, smoking cessation, STI screening and treatment, folic acid and fetal growth

monitoring hold some promise of helping to improve pregnancy outcomes for Indigenous women.

Presented at:
ISA/ISPID International Conference on Stillbirth, SIDS and Baby Survival, Amsterdam, September 18-21 2014
Australian Society for Medical Research Postgraduate Student Conference, Brisbane, May 28 2014

Appendix G5: Closing the gap: stillbirth among Indigenous and non-Indigenous women in Queensland by gestation and geographic location, 1995-2011

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Background: Progress with reduction in stillbirth rates has slowed in recent times in many high income countries prompting the need to address disparity across population subgroups. Australian Indigenous women have higher rates of stillbirth than non-Indigenous women and geographic location has been identified as an important risk factor. The objective of this study was to examine differences in prospective stillbirth rates between Indigenous and non-Indigenous women according to gestational age group and geographic location.

Method: Data on singleton livebirths and stillbirths of at least 400g birthweight and/or 20 weeks gestation in Queensland between 1995 and 2011 were obtained. Prospective stillbirth rates (i.e., stillbirths per 1000 ongoing-pregnancies) by gestational age (≥24, ≥28 and ≥37 weeks) and geographic location (urban, regional and remote) were calculated for Indigenous and non-Indigenous women.

Results: Over the study period, prospective stillbirth rates for Indigenous women decreased from 13.3 to 9.1/1000 while rates remained steady at 5.9/1000 for non-Indigenous women. Rates varied significantly for Indigenous women by geographic location (urban 8.5/1000 versus regional 10.8/1000 versus remote 12.5/1000 ongoing pregnancies, p=0.019). The difference in rates between Indigenous and non-Indigenous women decreased by 57.3% overall. These reductions were more pronounced for women living in regional (57.0%) and remote areas (56.1%) than urban (25.7%) areas. Likewise reductions were observed for rates at ≥24 and ≥28 weeks' gestation.

Conclusions: The gap in stillbirth rates between Indigenous and non-Indigenous women is reducing; however, substantial inequities remain especially for Indigenous mothers who live in regional and remote areas.

Citation

Ibiebele I, Flenady V, Coory M, Boyle F, Humphrey M**.** Closing the gap: stillbirth among Indigenous and non-Indigenous women in Queensland by gestation and geographic location, 1995-2011. *Perinatal Society of Australia and New Zealand 18th Annual Congress: Networking – The Final Frontier,* Perth, April 6-9 2014. Journal of Paediatrics and Child Health, 2014. **50 (Suppl. 1)**: p. 14

Appendix G6: Causes of stillbirth in Queensland among Indigenous and non-Indigenous women by gestation and geographic location, 1995-2011

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Background: Reductions in stillbirth rates in many high income countries have slowed or stalled prompting the need to address disparity across population subgroups. In Australia, Indigenous women have higher rates of stillbirth and other adverse pregnancy outcomes compared with non-Indigenous women. Geographic location has also been identified as an important risk factor in the Australian context. The objective of this study was to determine disparity in cause-specific prospective stillbirth rates in order to identify focal areas for preventive efforts.

Method: Data on singleton livebirths and stillbirths of at least 400g birthweight and/or 20 weeks gestation in Queensland between 1995 and 2011 were obtained. Cause-specific prospective stillbirth rates using PSANZ Perinatal Death Classification, relative risk and 95% confidence intervals were calculated for Indigenous women relative to non-Indigenous women by gestational age (≥24, ≥28 and ≥37 weeks) and geographic location (urban, regional and remote).

Results: The all-cause risk of stillbirth was 81% higher for Indigenous women compared with non-Indigenous women and varied by geographic location [urban (RR 1.47, 95%CI 1.18-1.81); regional (RR 1.76, 95%CI 1.56-1.98) and remote (RR 2.37, 95%CI 1.84-3.04)]. Overall, Indigenous women had increased risk of stillbirth categorised as: maternal conditions (mainly diabetes), perinatal infection, spontaneous preterm birth, hypertension, fetal growth restriction, antepartum haemorrhage and unexplained antepartum fetal death. The risk of stillbirth due to fetal growth restriction and maternal conditions increased with gestational age.

Conclusions: Indigenous women remain at increased risk of stillbirth due to a number of potentially preventable causes. These findings identify focal areas for preventative strategies such as improving the quality of care for Indigenous women throughout the reproductive lifespan.

Citation
Ibiebele I, Flenady V, Coory M, Boyle F, Humphrey M**.** Causes of stillbirth in Queensland among Indigenous and non-Indigenous women by gestation and geographic location, 1995-2011. *Perinatal Society of Australia and New Zealand 18th Annual Congress: Networking – The Final Frontier,* Perth, April 6-9 2014. Journal of Paediatrics and Child Health, 2014. **50 (Suppl. 1)**: p. 15