ADVERSE OUTCOMES ASSOCIATED WITH TIMING OF ANTENATAL CARE INITIATION: A RETROSPECTIVE COHORT STUDY OF PREGNANCIES IN CAPE TOWN, SOUTH AFRICA

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Preamble

1 Plagiarism Declaration

This work has not been previously submitted in whole, or in part, for any degree. It is my own work. Each significant contribution to, and quotation, in this dissertation from the work, or works, of other people has been acknowledged, and has been cited and referenced.

Signature:_____ Date:_____

2 Abstract

The medical community tends to advocate for early initiation of antenatal care (ANC) for the prevention of adverse birth outcomes. Despite this suggestion, the population impact of early ANC remains unclear.

To this end, we have undertaken a retrospective cohort study of pregnant women using public perinatal services in Cape Town, South Africa. The study includes all women (n=35,473) from the CRADLE database who gave birth between 01 January 2007 and 31 December 2009 and had a booking examination between 01 April 2006 and 31 March 2009. Using descriptive statistics, as well as linear and logistic regression, we examined how gestation at the booking examination, analysed continuously, in trimesters and in six categories, affects birth outcomes: stillbirths, low birth weight, low 1-min APGAR scores, and caesarean sections. Our results adjust for maternal age, parity, education, race, and smoking status.

Increased gestation at booking did not significantly affect the odds of stillbirths in any of the three sub-analyses. Increased gestation at booking (continuous) had a significant, harmful effect on the odds of having a low birth weight infant (OR 1.01; 95% CI: 1.00-1.02), while being protective for caesarean sections (OR 0.99; 95% CI: 0.98-1.00) and low 1-min APGARs (OR 0.99; 95% CI: 0.98-0.99). Women booking in the third trimester had 20% less risk of having a caesarean section (OR 0.80; 95% CI: 0.65-0.97). Specifically, booking between 30 and 35 weeks reduced a woman's odds of having a caesarean section by 24% (OR 0.76; 95% CI: 0.59-0.97) compared to women booking between 6 and 11 weeks.

There is some evidence to suggest that for every week increase in gestation at booking an infant may be at increased risk for having low birth weight. Most of the results suggest that future studies should investigate the timing of initiation of ANC, but in conjunction with the content of ANC visits, in order to provide sound recommendations for ANC during pregnancy.

3 Acknowledgements

First and foremost, I would like to thank my thesis supervisor, Prof. Landon Myer, for guiding me to this particular research project and funding my research. His ongoing moral support, supervision, critiques, and detailed feedback throughout the process of writing my protocol, conducting my analysis, and writing this opus have been greatly appreciated. More importantly, I would like to thank him for the numerous teaching moments in all of our meetings. Apart from getting me through my dissertation, his inspirational lessons have made me a more critical and aware epidemiologist.

Additionally, I would like to thank Dr. Greg Petro, Chief Specialist and Head of Obstetrics and Gynaecology for City of Cape Town-Metro West, for access to and use of CRADLE data for my thesis. He was instrumental in helping me to interpret the meanings of the data and determine which were usable in this analysis. Along these lines, I would also like to thank Jacques De Villiers in the Division of Health Informatics at Groote Schuur Hospital for his ongoing technical support with the database.

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Part A: Protocol

1 Introduction

1.1 Background

Antenatal care (ANC) during pregnancy, particularly the booking visit (first visit) provides expectant mothers with education and information about pregnancies, facilitates the identification of health problems, allows doctors to review past obstetric complications and perform screening tests to promote healthy deliveries and birth outcomes (1). In South Africa from the late 1990s to 2001 roughly 94% of pregnant women had at least one ANC visit in each pregnancy (2). Such high rates are not surprising considering that ANC services are free in South Africa. Despite this, many women delay the timing of their first visits until late in the pregnancy (3). The determinants of gestation at booking and the resulting pregnancy outcomes have not been fully explored in the context of South Africa. Further exploration of these health-seeking behaviours will elucidate the extent of the problem—if any—and provide a way forward for health professionals and policy makers with regard to provision of ANC.

1.2 Literature Review

The late 80s and early 90s saw an increase in literature on the benefits of ANC and maternal and infant health outcomes in southern Africa (4-6). This literature compared the outcomes of 'unbooked mothers' to those who had access to ANC. More recent literature from all over the world also continues to investigate this issue. Generally speaking, those mothers who have access to and utilize ANC, give birth to infants that have healthy birth weights (7, 8) and higher APGAR scores (9). This is probably due to the effect ANC has on improving the overall health of the fetus and thus increasing the gestational age of the neonate at delivery as well as its foetal growth rate (10). Furthermore, when a pregnant woman attends ANC, she is usually less likely to have a caesarean section (9) and a pregnancy that results in neonatal death (11).

The determinants of utilizing ANC have also been documented widely. Women who are under financial constraints (12), live far away from health facilities (7), and are multiparous (8), tend to use ANC less often than their counterparts. While these determinants might be common knowledge in medical practice, the relationship between number of ANC visits and safe deliveries and healthy infants is still being explored today. Even less is known about the effects of delays in seeking ANC, including birth outcomes.

1.2.1 Number of ANC visits

In most developed countries, the standard schedule of ANC visits requires mothers who have low-risk pregnancies to come in every six weeks until 24 weeks, then every two weeks until 38 weeks, and weekly after that if she is primigravida (13). However, this ANC schedule can be quite demanding of mothers and clinics in resource-constrained settings. Therefore, the World Health Organization (WHO) recommends that mothers in developing countries have at minimum of four ANC visits in order to have a safe delivery and healthy infant outcomes (2). A recent meta-analysis comparing the number of ANC visits in high-income countries to middle and low-income countries found that in low-income countries a reduced visit schedule, similar to the one propounded by the WHO, was associated with greater perinatal mortality (14). Similar findings were also reproduced in a study carried out in England (15). The same study found that as the number of ANC visits per pregnancy increased, so did the average birth weights of infants (15). In mothers who had more than 14 visits per pregnancy there was a greater likelihood that they would have a caesarean section, possibly due to increased pregnancy complications (15). Furthermore, a reduced ANC visit schedule has also been shown to increase the number of infants born prematurely, to result in lower average birth weights, and to produce lower APGAR scores (16). Contrary to these findings, Carroli et al (2001) found that, in developing countries, ANC schedules reduced to two or three visits did not lead to a significant increase in adverse outcomes. For all of these studies, it is unclear at which point in her pregnancy a woman attended her first ANC visit. Timing, and delay in ANC, could shed light on the conflicting evidence for outcomes associated with reduced visit schedules.

1.2.2 Timing of ANC

Ideally, a pregnant woman's first ANC visit—also known as the booking visit—should be between eight and twelve weeks of gestation (1). However, in sub-Saharan Africa, most women only present for ANC in the second and third trimester (2). A study of early, late and non-ANC attendees in Jamaica found that being a teenager, unmarried, having an unplanned pregnancy, using drugs, and being from impoverished communities, were predictors of non-attendance. Multiparous, single women with previously uneventful pregnancies were often late-attendees of ANC, while older, married, more highly educated women tended to have early ANC visits (17). Similar findings were also presented in a study of 'unbooked mothers' in England who had never had an ANC visit before delivering. In addition, these women tended to be recent, non-English speaking immigrants, who had a hard time navigating the healthcare system in England (18).

Few studies have looked at the degree to which delay in the booking visit affects delivery and birth outcomes. In the previously-mentioned study of unbooked mothers in England, it was found that without any ANC, those mothers were more likely to give birth to a preterm, low birth weight baby, as well as suffer from post-partum hemorrhage (18). In another study, conducted in Brazil, comparing groups of infants with and without birth defects, it was found that delay in ANC (measured in weeks) did not have any effect on the birth weight of an infant (10). However, it did increase the likelihood of a pre-term birth in the group without birth defects (10). A study of Finnish mothers and their pregnancies showed that women who attended ANC late (after 16 weeks) had more caesarean sections and labour inductions, as well as infants who tended to be preterm, have lower birth weights and 1-minute APGAR scores, compared to average attendees (8-11 weeks) (19). These studies provide a start, but more research still needs to be done on how much delay in seeking ANC is acceptable if a woman is to produce a healthy infant, specifically in a setting such as South Africa.

1.3 Research Justification

This research will be used to inform healthcare decision makers about the adverse outcomes and risks associated with delay in ANC. It has the potential to aid in interventions that attempt to change health-seeking behaviours for pregnant women.

1.4 Research Question

What is the relationship between the gestational age at which a woman first seeks antenatal care and adverse birth and delivery outcomes[1]?

1.5 Objectives

This study will aim to identify a relationship between the gestation age of a foetus when a woman first seeks ANC and birth and delivery outcomes:

- Stillbirths
- Low birth weights

[1] The manuscript only addresses stillbirths. However, the larger research project looked at several different birth outcomes including caesarean sections, low birth weight, and low 1-min APGAR scores. Tables for these analyses can be found in Appendix C.

- Low 1-min APGAR scores
- Caesarean sections

The study will also investigate the relationship between the gestation age at the booking appointment and other risk factors for adverse outcomes:

- Parity
- Education level
- Race
- Maternal age
- Smoking status

2 Methods

2.1 Study Design

A statistical analysis will be conducted for a retrospective cohort of women who gave birth between 01 January 2007 and 31 December 2009. This analysis will be carried out on the CRADLE Database, which houses the data for the Peninsula Maternal and Neonatal Service (PMNS), a local, public and community-based perinatal service for Cape Town residents.

2.2 Population

The study population will consist of women of all ages who had their booking appointment and deliveries within the PMNS system. Because the data was not necessarily collected and captured by trained researchers with the intent of analyzing it, the integrity of the entire database cannot be guaranteed. Therefore, the analysis will be conducted on individuals who met a set of inclusion and exclusion criteria decided upon because of the higher degree of completeness and presumed accuracy.

2.2.1 Inclusion Criteria

Women may be included in this analysis if they:

- Gave birth between 01 January 2007 and 31 December 2009
- Had their booking examination between 01 April 2006 and 31 March 2009
- Had their booking examination at Hanover Park Community Health Clinic, Mitchell's Plain Medical Centre, False Bay Hospital, and Retreat MOU
- Delivered their infant at either False Bay Hospital, Gugulethu Day Hospital, Hanover Park Community Health Clinic, Retreat MOU, Mowbray Active Birth Unit, Somerset Hospital, Mitchell's Plain Medical Centre, or Groote Schuur Hospital

2.2.2 Exclusion Criteria

Women will be excluded from the analysis if they do not meet the above inclusion criteria or:

- The pregnancy resulted in multiple births
- Data on the timing of their booking visit and delivery date were missing
- The calculated gestation week of the first ANC visit was missing, <6 weeks, or >42 weeks

2.3 Sampling

2.3.1 Sample Size

The sample will contain all of the remaining individuals in the database that meet the afore-mentioned inclusion and exclusion criteria.

2.4 Data Collection

Data for this study were collected from 41 different primary, secondary, and tertiary health facilities in PMNS system in the Western Cape.

2.4.1 Data Management

The data for the facilities were not all collected or captured in a standardized and uniform manner. In some cases, nurses and physicians were the ones to enter the data into the database; in others data capturers, whose sole purpose was to enter the data obtained from patient folders, were hired. As a consequence of the unsystematic data collection, some variables for each pregnancy and delivery were incomplete or inaccurate. Furthermore, there was no standardized training for the data entry and no consistent double-checking for the data entered.

All data was backed up and stored in a central database located at Groote Schuur Hospital using Oracle software.

2.4.2 Instruments

The CRADLE database was the only instrument used for this analysis. However, it goes without saying that data for each of the variables were collected using a combination of various instruments or resources such as the collection of patient histories as well as patient exams, tests and procedures. As in the previous section, the instruments used were not uniform and the people recording and performing the measurement were not trained in a standardized manner.

2.5 Quality Control

As previously mentioned, there was little control over the measurement, collection, and management of the data, so validity cannot be determined. However, in preliminary data exploration, years and facilities were chosen for use in this analysis by comparing actual deliveries recorded in hospital registries to the CRADLE data, by facility and year. The results of this exploration aided in narrowing down what facilities and delivery years were to be used in the analysis.

3 Data Analysis

3.1 Variables

Three outcome variables measuring the infant's health will be included in the analysis.

- Low birth weight: defined in terms of presence or absence of low birth weight (<2.5kg).
- Stillbirth: defined as the presence or absence of this condition.

- Low 1-min APGAR score: defined in terms of presence or absence of a low 1-minute score (<7)

One outcome variable looking at a medical intervention will be included in the analysis.

- Caesarean section: defined as the presence or absence of this procedure, regardless of whether it was an elective or emergency procedure.

The exposure of interest is the *gestation at booking*. This will be defined as the number of gestation weeks at the first ANC visit. It will be calculated using information in the database on the expected delivery date (EDD) at the first booking examination. When the gestation cannot be calculated using an EDD based on an ultrasound, the EDD based on abdominal palpation will be used. When EDDs from those methods are missing or implausible, it will be based on the last menstrual period (LMP). This variable will also be categorised into trimesters and 6 categories (6-11 weeks, 12-17 weeks, 18-23 weeks, 24-29 weeks, 30-35 weeks, 36-42 weeks) in order to gain more highly detailed information about when gestation at booking starts to cause adverse outcomes.

Nine potential confounders and explanatory variables that will be included in the analysis are:

- Maternal age: defined as a continuous variable measured in years.
- Preterm: defined as presence or absence of being preterm (<37 gestation weeks)
- Smoking status of mother: defined as yes or no, regardless of the amount the mother smokes.
- Race: will be used as a proxy for socio-economic status and defined as black, white, coloured, Asian, or other.
- Parity: defined as nulliparous or primi/multiparous
- Education level: defined as the highest level of education the mother had. Choices are either: none or primary, secondary or tertiary, or missing.
- Booking facility: defined as the facility where the first ANC visit took place.
- Booking year: defined as the year the mother had her first ANC visit.
- Delivery facility: defined as the facility where the birth took place.

3.2 Analysis

All data analysis will be conducted with Stata statistical software, version 11.0 (Stata-Corp Inc., College Station, Texas, USA). Summary statistics and frequency distributions will be calculated for all the variables by the booking facility, as

well as the different forms of gestation at booking (e.g. continuous, trimesters, 6-categories). Incidence for each adverse outcome will also be calculated.

Separate logistic regression models will be built for each binary adverse outcome (i.e. *Caesarean Section, Low Birth Weight, Apgar score, and Stillbirths*). All models will include the exposure of interest, *Gestation at Booking*, and then be successively refitted with the other explanatory variables (*Maternal Age, Smoking Status of Mother, Race, Education level, Parity)* that have a significance level of 0.05. Adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI) will be estimated using these methods. The results will be stratified by *Booking Facility*, *Booking Year*, and *Delivery Facility*.

There will not be any exploration or analysis of interactions between *Gestation at Booking* and the other explanatory variables. The literature on this topic does not provide any reason to expect interaction between any of them.

4 Ethical Considerations

4.1 Ethics Approval

Ethics approval will be obtained from the UCT Human Ethics Committee. No informed consent is needed from the individuals who are in the database because this study is considered low-risk and relevant ethics committees have already given approval to my supervisor, Prof. Landon Myer, to audit this large database of routinely collected data.

4.2 Potential risks to participants

This study could potentially emotionally or socially harm individuals in the database if anyone were to link the information from their exposures and outcomes to their identifying information. To prevent this possibility, all personal identifiers like names, South African ID numbers, phone numbers, and addresses were deleted from the dataset. Unique database IDs were used to represent individuals in this study in order to preserve anonymity.

Furthermore, the data for this study has already been collected, and therefore no further time will be required of participants to have interviews or clinical examinations.

Finally, I understand that the use of "Race" as a variable in data analysis is quite controversial in South Africa, given the country's history. It will be used exclusively as a proxy variable for socio-economic status (SES) since SES is probably a confounding variable in my analysis and there are no other complete and accurately recorded variables in the database that could be used as an equivalent proxy. Should "Race" be found to be a significant risk factor, it will be interpreted in light of the health advantages/disadvantages available to those populations.

4.3 Potential benefits to participants

There will be no immediate benefits for individuals that are included in the study because there will be no contact whatsoever with participants. However, long-term benefits of this study come in the form of the production of health knowledge that will ultimately aid in the improvement of ANC services in Cape Town. The results of this study will illuminate weaknesses in the current health care system, and suggest ways to optimize the timing and provision of ANC services in resource-constrained settings.

4.4 Conflicts of Interest

This study will not involve any foreseeable conflicts of interest. The only source of funding for this study came in the form of a departmental bursary from the Centre for Infectious Diseases & Epidemiology Research (CIDER), which has taken an impartial stand on the results of this study. Furthermore, the funder will not hinder or censor the communication of the research results.

5 Time Plan

The analysis of data will commence in April 2011 and the dissemination of results will take place from November 2011 to January 2012. Table 1 provides a detailed timeline of the dissertation activities.

6 Budget

This study will require a very small budget since personnel and supply costs are minimal. Table 2 provides a detailed

breakdown of the costs.

7 Strengths and Limitations

7.1 Strengths

This study will have a very large sample size and is therefore likely to produce statistically significant results with narrow confidence intervals. It is also composed of diverse individuals from all over Cape Town and is not likely to be internally homogenous, thus improving generalizability. Furthermore, the database itself contained a mine of useful information that will be useful in exploring the relationship between several different outcomes and explanatory variables.

7.2 Limitations

Because the measurement, capture, and management of data were not done in a consistent, standardized, or supervised manner, there is likely to be a fair amount of random measurement error in the sample. It is also impossible to estimate the nature and extent of biases that might be occurring within the data, since information about how the data was collected for each variable was not provided with the dataset.

Furthermore, this study would have been improved if the database contained the dates and number of all the ANC visits. As shown in section 1.2.1, the number of ANC visits is also a large determinant of delivery and infant outcomes. Exploring the relationship between the number of ANC visits and the timing of the booking visit would have greatly enhanced the utility of the study results.

8 Reporting of Results

Results of this study will be summarized and formulated in a report that will be disseminated to relevant municipal, provincial and national government departments (e.g. National Department of Health, City of Cape Town Community Health Department) and made available to healthcare facilities in the city as well as other interested researchers in the field. Additionally, an abstract will be submitted for the 2011 PHASA conference as well as other relevant international

conferences. Finally, the results will be written up as a publishable paper for a peer-reviewed obstetrics and gynaecology journal.

Table 1:Timeline of dissertation activities

Activities	Months												
	Nov 2010	Dec 2010	Jan 2011	Feb 2011	Mar 2011	Apr 2011	May 2011	Jun 2011	Jul 2011	Aug 2011	Sep 2011	Oct 2011	Nov 2011
Pre-exploration of data													
Write protocol													
Submit protocol to ethics													
Conduct analysis													
Summarize findings into tables and reports													
Write dissertation													
Finalize paper for publication write reports													

Table 2:Budget of dissertation expenses

Researcher @15 hours/week, R80/hour, 35 weeks	R42, 000
Stata Statistical Software	R800
Printing 2 copies of dissertation @R0.35/page, 100 pages/copy	R80
Total	**R43, 080**

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Part B: Literature Review

1 Introduction

This literature focuses on the use of antenatal care (ANC) by pregnant women and aims to give a brief overview of the benefits and goals of urging mothers to use ANC. Additionally, it will provide a brief sketch of the determinants of its use, as well as what might result if inadequate ANC is sought by mothers. The literature tends to focus on how the number of ANC visits and the timing, or delay, of ANC may affect delivery and birth outcomes. However, literature that is more recent is starting to focus, not on the number of visits or timing of ANC, but rather, a combination of the two in addition to the content of the care. Where possible, this literature review provides evidence from other Lower-Middle Income Country (LMIC) contexts. However, there is a paucity of literature on how ANC timing affects birth outcomes in LMIC. Therefore, this review also provides the justification for my analysis of timing of ANC in Cape Town.

2 Purpose of ANC

The first ANC visit—or, the booking visit—is thought to be an important event in the pregnancy of a woman. During this visit, the doctor typically takes the woman's medical and obstetric history, performs a physical examination, assesses the needs of the mother in terms of future pregnancy interventions and expertise required, and gives advice on diet (1). Subsequent and regular ANC visits usually help to determine whether a woman is at risk for adverse birth outcomes and attempt to foster an intimate relationship between the woman and health care providers (2).

The late 80s and early 90s saw an increase in literature on the benefits of ANC and maternal and infant health outcomes in southern Africa (3-5). This literature compared the outcomes of 'unbooked mothers' with those who had access to ANC. More recent literature from all over the world continues to investigate this issue. Generally, those mothers who have access to and utilize ANC give birth to infants that have healthy birth weights (6, 7) and higher APGAR scores (8). This is probably due to the effect ANC has on improving the overall health of the infant and thus increasing the gestational age of the neonate at delivery as well as its foetal growth rate (9). Furthermore, when a pregnant women attends ANC, she is usually less likely to have a preterm birth (10) and a birth resulting in a neonatal death (7, 11).

Additionally, in contexts where mothers often deliver at home, studies have shown that ANC might prevent delivery complications by creating awareness of the need for delivery care (12). A study in Zimbabwe found that ANC has the

potential to prevent post partum haemorrhage and cephalopelvic disproportion if doctors use a simple algorithm consisting of maternal height, parity, and obstetric history factors to detect risk of delivery complications (13). Lack of any ANC has also been linked to increased risk of having a caesarean section (8).

3 Determinants of ANC use

The determinants of utilizing ANC have also been documented widely. Socio-demographic characteristics, such as low socio-economic status (14, 15) and being multiparous (8, 16-18) are predictive of women using ANC less often. Women in Kenya have been shown to be more likely to utilize ANC if they are married (18). Support from their husbands and a health system that favours married women may provide the much-needed encouragement to take advantage of the services (18). A mother's and her husband's education level are also positively associated with using ANC (16, 19, 20). Another significant determinant in Africa that is presented in the literature is maternal age. Younger women, and particularly teenagers, tend to have inadequate use of ANC and more non-facility births without skilled delivery attendants (21).

A study of rural women in China also found that women who were young, had a low income, and had more than one child, were less likely to have 'adequate' care (22). However, these effects disappeared when they adjusted for sufficiency of content of care, which took into account whether or not a woman obtained advice on nutrition and problems during pregnancy, as well as if she had routine tests, like blood pressure, ultrasounds, and blood tests. This suggests that some of the other studies may have over or underestimated the effects of socio-demographic characteristics on use of ANC.

Factors related to maternal attitudes towards and knowledge about pregnancy have also been shown to be correlated with using ANC. In a study of postpartum women in Brazil, it was shown that both an unplanned pregnancy and dissatisfaction with pregnancy made a woman less likely to use ANC services (23). Along these lines, a meta analysis of qualitative data in developing countries suggests that initiating ANC is largely dependent on acceptance of the pregnancy, upon recognition, and if the mother perceives the benefits of ANC (24). Additionally, a qualitative study about mothers in South Africa, proposes that some mothers might not seek ANC because they do not have a sufficient understanding of complications that can result during pregnancy and therefore do not deem it useful (25).

Accessibility to ANC is also a key determinant of its use. Typically, women in urban areas use ANC more than women in rural areas (26, 27). Also, women who live further away from health facilities use ANC less often (14, 16). In South Africa, it has been noted that the expense of taxi fares to get to a clinic often hinders the use of services (25).

Different characteristics of health services have also been predictive of whether or not a woman continues to access ANC. It is often largely dependent on perceived quality of care by staff, and a whether a relationship develops based respect, no judgment and cultural sensitivity (24, 28). Moreover, women in Turkey are more likely to use ANC if they have health insurance coverage (29, 30).

4 Impact of number of ANC visits on birth outcomes

In most developed countries, the standard schedule of ANC visits requires mothers who have low-risk pregnancies to come in for a visit every six weeks until 24 weeks, then every two weeks until 38 weeks, and weekly after that if she is primigravida (31). This ANC schedule can be quite demanding of mothers in certain contexts and clinics in resource-constrained settings. Therefore, the WHO recommends that mothers in developing countries have a minimum of four ANC visits for safe delivery and healthy infant outcomes (32). A study by Maghadi *et al.*(2000) determined predictors of increasing number of ANC visits among Kenyan women (33). Low household socio-economic status, being unmarried, starting childbearing before the age of 20, having a birth interval of less than two years between births, having an unwanted or mistimed pregnancy, wanting a large family of seven or more children, and increased distance to the nearest health facility, make a woman more likely to have fewer total ANC visits (33). Interestingly, smoking has been associated with fewer ANC visits among women in Finland (34).

A recent meta-analysis comparing the number of ANC visits in high-income countries to middle and low-income countries found that in low-income countries a reduced visit schedule —similar to the one propounded by the WHO— was associated with greater perinatal mortality (35). Similar findings were also reproduced by a study carried out in England (36). The study found that as the number of ANC visits per pregnancy increased, so did the average birth weights of infants (36). In mothers who had more than 14 visits per pregnancy, there was a greater likelihood that they would have a caesarean section, possibly due to increased pregnancy complications (36). Furthermore, a reduced ANC

visit schedule has also been shown to be associated with more infants born prematurely, lower average birth weights, and lower APGAR scores (37).

Contrary to these findings, Carroli *et al*. found that in developing countries, ANC schedules reduced to two or three visits did not lead to a significant increase in adverse outcomes (38). Corroborating this, a randomized controlled trial (RCT) in Zimbabwe compared the standard model of visits to an intervention consisting of a reduced schedule of five planned visits with goal-oriented routines (21). They found that there was no difference in hypertensive disorders between the two treatment groups, and the intervention actually reduced the number of emergency referrals during labour (21). The same study also observed a reduction in home births in the intervention group, from which participants were counselled about place of delivery at one of the visits (21). Four other earlier RCTs also support the notion that a reduced visit schedule is equivalent in terms of outcomes compared to the standard model of 12 visits (39-42). However, there is evidence that a reduced schedule may result in more adverse psychosocial effects (41), possibly due to a mother's concerns with the new schedule and a negative attitude to the change (42). For all of these studies, it is unclear at which point in her pregnancy a woman attended her first ANC visit. Timing and delay in ANC could shed light on the conflicting evidence for outcomes associated with reduced visit schedules.

5 Effects of the timing of ANC initiation on birth outcomes

Ideally, a pregnant woman's first ANC visit—also known as the booking visit—should be between eight and 12 weeks of gestation (43). However, in sub-Saharan Africa, most women only present for ANC in the second and third trimester (32). Determinants of ANC use, generally, were described in an earlier section. Going further, some studies have looked specifically at the determinants of timing. In a study of 'unbooked mothers' in England who had never had an ANC visit before delivering, the authors found that women tended to be recent, non-English-speaking immigrants who had a hard time navigating the healthcare system in England (44). Correspondingly, a Belgian study found that not originally being from Europe and not having a regular obstetrician were related to late initiation (after 12 weeks) (45). In the U.S., having an unwanted pregnancy has also been shown to be associated with late (after 13 weeks) or no prenatal care (46).

Determinants of timing of initiation of ANC have also been looked at in a few LMICs. A study of early (1st trimester),

late (3rd trimester) and non-ANC attendees in Jamaica found that being a teenager, unmarried, using drugs, and being from impoverished communities were predictors of non-attendance (47). Multiparous, single women with previous uneventful pregnancies were often late-attendees of ANC and older, married, more highly-educated women had early ANC visits (47). In Kenya, women belonging to high socio-economic groups, in paid employment, and using modern contraception methods, tended to book earlier in their pregnancies, while women who had higher order births and desired a large family booked late in their pregnancies (33). Interestingly, the same study also noted that the presence of a Community Health Worker was associated with women starting ANC early in the pregnancy (33).

Few studies have looked at the degree to which delay in the booking visit affects delivery and birth outcomes. In the previously mentioned study of unbooked mothers in England, it was found that without any ANC, those mothers were more likely to give birth to a preterm, low birth weight baby, as well as to suffer from post-partum haemorrhage (44). A study of Finnish mothers and their pregnancies showed that women who attended ANC late (after 16 weeks) had more caesarean sections and labour inductions, as well as infants who tended to be preterm, have lower birth weights and lower 1-minute APGAR scores, compared to average attendees (8-11 weeks) (48). Another study in the U.S. found that women who initiate ANC after month seven of gestation have infants with increased risk of congenital malformations (49). The authors of that study hypothesize that women with late or no ANC are also less likely to take prenatal supplements that are instrumental in preventing structural malformations (49).

In conflict with those results are some studies that found no effect of timing of first ANC visit on birth outcomes (50-52). A study conducted in Brazil, comparing groups of infants with and without birth defects, found that delay in ANC (measured in weeks) did not have any effect on the birth weight of an infant (9). However, it did increase the likelihood of a preterm birth in pregnancies without birth defects (9). In accord with this, Hueston *et* al. demonstrate that African-American mothers in the U.S who booked their first ANC visit in the second) or third trimesters, had no increased risk of low birth weight infants (50). In fact, booking in the third trimester was protective. They suggest that women who make it to the third trimester of pregnancy have most likely made it past the point where a low birth weight is likely to occur (50). The few studies that are available on timing of the booking visit are far from conclusive and therefore, there is need for more research on describing outcomes associated with late booking, particularly in LMICs.

6 Areas for Future Research

Several studies have firmly established the determinants of ANC utilization. Typically, mothers belonging to the underserved, marginalized populations and those with larger families are less likely to seek ANC, and when they do, they book late and use it infrequently. Fortunately, many studies, including some high-quality RCTs have demonstrated that a reduced number of ANC visits is not likely to produce more adverse pregnancy and delivery outcomes than the standard visit schedule. These studies provide a start, but more research still needs to be done on how much delay in seeking ANC is acceptable in order to produce a healthy infant, specifically in a setting like South Africa.

An alternative way of looking at the question about how timing of ANC affects birth outcomes, is to examine the risk of 'time-lag'—delay of ANC after recognition of the pregnancy by the mother—on birth outcomes. A study conducted in the U.S. did just that and found that time-lag was not associated with adverse outcomes like preterm births, low birth weight, ICU admission, or infant mortality (53). However, in this study early recognition was associated with a longer time-lag (53). This suggests that rather than advocating early ANC initiation, perhaps early recognition is more important, as it may result in improved behaviours such as reduced alcohol or smoking, and taking prenatal vitamins.

All of this leads to the question: does it even matter when a woman books or how many ANC visits she has? Perhaps, it is not the number or timing of ANC that matters, but rather the content of care. One methodological study based in India developed a composite ANC utilization score that combined timing, frequency and content of ANC visits (54). They tested it on poor to middle-income women and found that a higher score was related to using trained assistance at birth and having safe delivery care. In a more recent study conducted in Belgium, a tool based on timing and content of ANC was developed to describe whether ANC was 'adequate' (55). The tool considered whether the pregnancy had adequate initiation of care (before 14 weeks), adequate number of visits at term gestation, and adequate content of care (number and timing of ultrasounds, blood pressure checks, and blood tests). Both of these tools need further exploration and could be used to explore maternal, infant, and delivery outcomes in LMIC settings.

Additionally, it has been pointed out that a life-course approach to investigating birth outcomes might be more appropriate. Lu *et al*. suggest that outcomes, like low birth weight might actually be determined by risk factors that occur early in the life of the mother (56). The function of the mother's organs may be determined *in utero*, rendering

ANC ineffectual in preventing low birth weight. This indicates that the approach for improving birth outcomes needs to be intergenerational in scope.

Finally, there might be need for more rigorous studies to be conducted on alternative forms of ANC that loosely resemble the standard model of care that is commonly espoused. A recent study in U.S. examined this question by investigating different maternal and neonatal outcomes that result when women used Group Antenatal Care (57). This study demonstrated that Group Antenatal Care[2] was associated with high antenatal attendance, lower preterm birth and high breastfeeding initiation (57). Investigating the effects of alternative forms of prenatal care on birth and maternal outcomes might be particularly important in LMIC settings where people might already be practising different or supplementary forms of care. Epidemiological studies have the potential to shed light on these practices and, if they are shown to be effective, advocate for interventions that are commensurate with them.

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Part C: Manuscript

The association between timing of initiation of antenatal care and stillbirths: A retrospective cohort study of pregnant women in Cape Town, South Africa

Stillbirths and late gestation at booking

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1 Abstract

Objective

To determine if the timing of the first ANC visit influences the risk of a stillbirth.

Design

Secondary analysis of a retrospective cohort of pregnant women.

Setting

Peninsula Maternal and Neonatal Service, a public perinatal service in Cape Town, South Africa.

Population

Women of all ages, initiating ANC, and delivering within the PMNS system.

Main Outcome Measures

The main exposure, gestation at first ANC visit, was analysed as a continuous (in weeks) and categorical (in trimesters) variable. The primary outcome was stillbirths.

Methods

Differences in maternal characteristics, by retention status, were investigated using chi-square tests. Descriptive statistics for maternal characteristics were calculated by stillbirth status and level of exposure. Logistic regression, adjusting for maternal characteristics, was conducted to determine the risk of stillbirth.

Results

Of the 34,671 women who initiated ANC, 27,713 women (80%) were retained until delivery. The population stillbirth rate was 4.3 per 1000 births. The adjusted models indicated there was no significant effect of gestation at first ANC visit on stillbirth outcomes when analysed as a continuous variable (OR 1.01; 95% CI: 0.99-1.04) or in trimesters (2nd Trimester OR 0.78, 95% CI: 0.39-1.59; 3rd Trimester OR 1.03, 95% CI: 0.50-2.13). Being black (OR 2.01; 95% CI: 1.31-3.07) and mother's age (OR 1.03; 95% CI: 1.00-1.07) were predictors of stillbirths in both of the adjusted models.

Conclusion

The timing of a woman's first ANC visit may not be an important determinant of stillbirths on its own. It may be more important for a woman to have better content of care, incorporating recently established, effective biomedical interventions.

Keywords

Stillbirths, Antenatal Care, Timing of ANC

2 Introduction

In recent years the International Stillbirth Alliance (ISA), has brought increased attention to stillbirths and has called for renewed interest in and research on stillbirth prevention[1]. Currently stillbirths do not feature in the UN Millennium Development Goals or in the Global Burden of Disease. The lack of attention given to stillbirths in local and international arenas can be attributed to the fallacious view that stillbirths are not preventable [2]. Worldwide there are approximately 2.65 million third-trimester stillbirths and most of the burden (98%) is in low and middle-income countries (LMICs) [3]. In South Africa, 20,000 pregnancies result in stillbirths each year [4]. Approximately 1.02 million of worldwide stillbirths are intrapartum and can be prevented by influencing women not to delay in accessing critical, skilled care at birth [5]. Most antepartum stillbirths can be prevented by limiting maternal infections in pregnancy, treating hypertension in mothers, and monitoring fetal growth restriction and congenital abnormalities in the fetus [3]. Specifically, in South Africa, 20% of intrapartum and 10% of antepartum stillbirths can be attributed to hypertensive disease in pregnancy [3]. This suggests that by improving utilisation of antenatal care (ANC) in LMICs we can eliminate many of the causes of stillbirths.

Until recently the standard model of ANC in South Africa called for primigravidae women to come in for a visit a total of 12-14 times during her pregnancy: a visit every six weeks until 24 weeks, every two weeks until 28 weeks, and weekly thereafter [6]. This schedule of visits continues to be prescribed irrespective of the fact that the schedule is quite burdensome for resource-constrained hospitals and impoverished mothers. Recent randomised controlled trials suggest that in LMICs a schedule of ANC visits reduced to three to five visits is sufficient for mothers to have a safe delivery and give birth to healthy infants [7-10]. In one prospective, multi-site study of LMICs, mothers who did not have any ANC visits had a significant increase in risk of a stillbirth. [11].

What remains unclear in the literature is at what point in the gestation of a fetus a woman should present for her first ANC visit in order to produce a healthy infant. While the medical community suggests that women should present for their first ANC visit between eight and 12 weeks[12], it is not uncommon for women in Sub-Saharan Africa to have it in the second or third trimester [13]. In Finland, having the first ANC visit after 16 weeks has been associated with more caesarean sections, labour inductions, preterm births, as well as lower birth weights and 1-minute APGAR scores[14]. Another study conducted in the U.S, demonstrated that mothers who initiated after month seven had an increased risk

of congenital malformations [15]. Contrary to these results are a few other studies that have shown that the timing of the first ANC visit has little or no effect on birth outcomes, such as birth weight [16-18]. Studies that measure the effect of the timing of first the ANC visit on birth outcomes are few and have conflicting results, demonstrating their inconclusivity. This is true particularly concerning the occurrence of stillbirths.

Given the importance of increasing utilisation of ANC for prevention of stillbirths, the primary objective of this study was to determine if the timing of the first ANC visit, in terms of the gestation of the fetus, influences the risk of having a stillbirth [+]. A secondary objective of the study was to investigate if other maternal characteristics are risk factors for stillbirths.

3 Materials and methods

This study uses data obtained from the CRADLE database, which stores information on pregnancies and infants for the Peninsula Maternal and Neonatal Service (PMNS). The PMNS is a local, public and community based perinatal service for Cape Town, South Africa residents that contains 41 different primary, secondary, and tertiary health facilities. The statistical analysis was performed for a retrospective cohort of women who gave birth between 01 January 2007 and 31 December 2009.

3.1 Population

The study included women of all ages who had their first ANC visit and delivery within the PMNS system. The integrity of the entire database could not be guaranteed because it was not collected and captured by trained researchers. Additionally, the database was not in full use by all of the health care facilities at all points in time. Therefore, the inclusion/exclusion criteria (see figure 1) were chosen because of the higher degree of completeness and presumed accuracy. Women and their pregnancies were excluded from the analysis if they: did not give birth between 01 January, 2007 and 31 December, 2009; did not initiate ANC between 01 April, 2006 and 31 March, 2009; did not have a first

[+] See Appendix C for more tables that investigate the risk of these additional outcomes: caesarean section (yes/no), 1-minute APGAR scores (normal/abnormal), and birth weight (low/normal). These analyses also investigate the risk of gestation at first ANC visit as a 6-level variable.

ANC visit at one of the pre-selected clinics; did not deliver at one of the pre-selected hospitals; were multiple births; or were preterm. Furthermore, pregnancies were also excluded if their: calculated gestation week for the first ANC visit was missing, <6 weeks or >42 weeks; gestation at delivery was <28 weeks; gestation week at first ANC visit was >37 weeks; and race was missing.

3.2 Measures

The main exposure of interest is gestation at first ANC visit, defined as the gestation weeks of the fetus at the first ANC visit. This variable is analysed both as a continuous (in weeks) and categorical (in trimesters: 6-12 weeks/13-26 weeks/27-42 weeks) variable in parallel analyses. It was calculated using information in the database on the expected delivery date (EDD) at the first ANC visit. When gestation could not be calculated using an EDD based on an ultrasound, the EDD based on abdominal palpation was used. If both were missing or inaccurate, it was based on the last menstrual period. The only outcome variable in this study was the presence or absence of a stillbirth. By definition, all the stillbirths in this analysis occurred after 28 weeks.

Five additional explanatory variables, comprising of maternal characteristics, were analysed as potential confounders: Maternal Age (continuous, years); smoking status of mother (yes/no/missing); parity (Nulliparous/Multiparous); and education level of mother (none or primary/ secondary or tertiary/ missing). Race (White, Asian, Other/Coloured/Black) was also analysed because it is considered to be a good proxy for socio-economic status in South Africa, as it is often predictive of the health opportunities for individuals. 'Coloured' is a term referring to people of mixed-race ancestry in South Africa. Additionally, the first ANC visit facility, first ANC visit year, and delivery facility were also used in preliminary descriptive analyses to see if they might be potential effect modifiers.

3.3 Statistical analysis

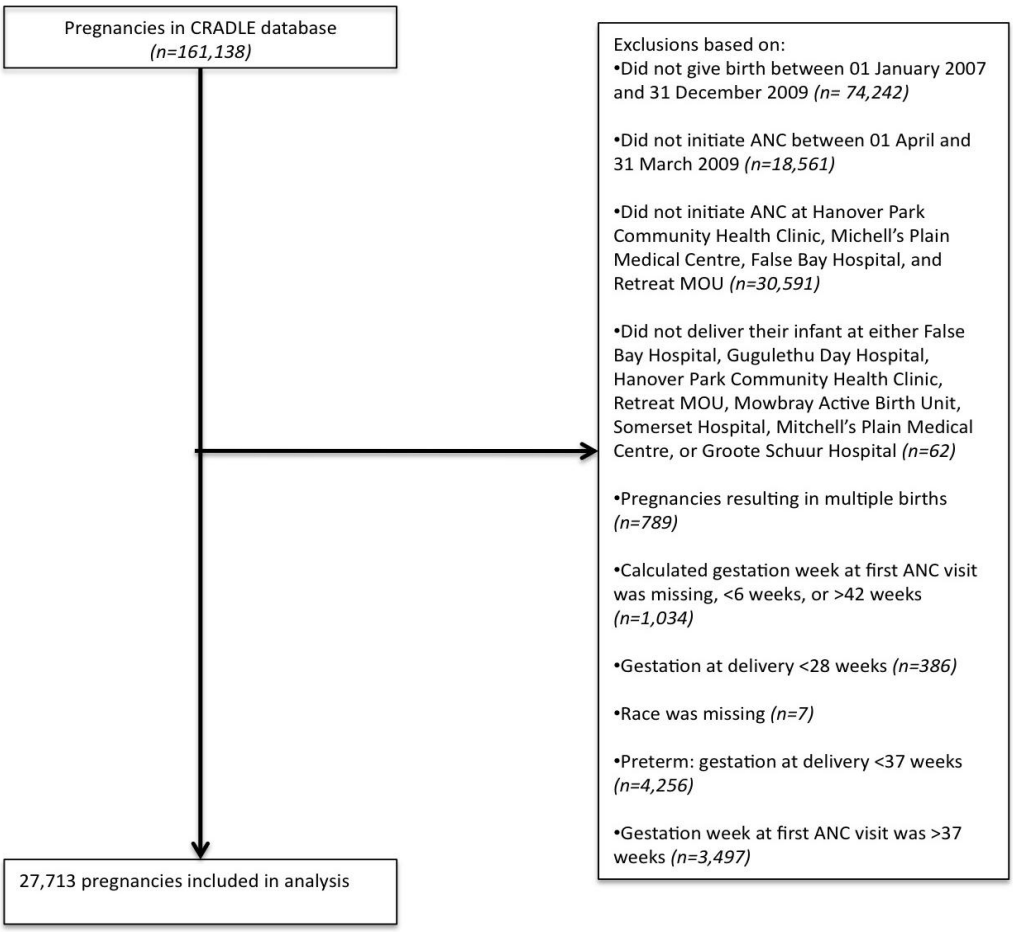
The study resulted in a sample size of 27,713 pregnancies, which included all of the remaining pregnancies that met the inclusion/exclusion criteria.

All analyses were conducted with Stata statistical software, version 11.0 (Stata-Corp Inc., College Station, Texas, USA). A descriptive analysis using chi-square tests was done to determine if maternal characteristics, as well as

gestation at first ANC visit, varied among those who were retained in the study and those who were lost-to-follow-up. Descriptive statistics were also calculated for maternal, first ANC visit, and delivery characteristics by gestation at first ANC visit (trimesters) and the stillbirth status of the pregnancy. For the one continuous, non-parametric variable (Maternal Age), the Wilcoxon Rank test and Kruskal-Wallis Rank tests were calculated. Finally, two different logistic regression models were calculated to determine if the risk of having a stillbirth was influenced by gestation at first ANC visit (in continuous and trimester form). The models were adjusted for the five confounders previously described. The stillbirth rate was calculated by dividing the number of stillbirths by the sum of live births and stillbirths, then multiplying the total by 1000.

This study was approved by the institutional review board of University of Cape Town, Health Research Ethics Committee before the analysis commenced.

Figure 1: Flow chart of participants in retrospective cohort of pregnancies in CRADLE



4 Results

Of the 34,671 pregnancies that initiated ANC, 27,713 were retained until delivery: 20.1% were lost-to-follow-up. Table 3 provides a detailed look at the differences in maternal and first ANC visit characteristics by lost-to-follow-up status. There were significant differences between the two groups for all variables except maternal age. Those that were lost-to-follow-up were more inclined to be nulliparous (46.6% vs. 43.0%), be black (38.7% vs. 33.0%), be non-smokers (20.7% vs. 24.2%), book at Hanover Park Hospital (50.8% vs. 24.1%), book in 2006 (24.4% vs. 10.1%), and initiate ANC in the first and second trimesters (11.2% vs. 7.3% and 61.5% vs. 60.1%, respectively).

Table 3:Comparison of baseline variables for those retained and those lost-to-follow-up

Explanatory Variable		**Retained N (%)**	**Lost-to-Follow-up N (%)**
Total		27,713 (79.9)	6,958 (20.1)
Parity	Primi/Multiparous	15,795 (57.0)	3,717 (53.4)
	Nulliparous	11,918 (43.0)	3,241 (46.6)
Educational Level	None or Primary	1,299 (4.7)	393 (5.7)
	Secondary or Tertiary	17,285 (62.4)	4,085 (58.7)
	Missing	9,129 (32.9)	2,480 (35.6)
Race	White, Asian, Other	532 (1.9)	140 (2.0)
	Coloured	18,046 (65.1)	4,126 (59.3)
	Black	9,135 (33.0)	2,692 (38.7)
Smoking	No	13,580 (49.0)	3,323 (47.8)
	Yes	6,704 (24.2)	1,441 (20.7)
	Missing Data	7,429 (26.8)	2,194 (31.5)
First ANC Visit Facility	False Bay	1,528 (5.5)	191 (2.8)
	Hanover Park	6,673 (24.1)	3,536 (50.8)
	Mitchells Plain	12,659 (45.7)	1,675 (24.1)
	Retreat MOU	6,853 (24.7)	1,556 (22.4)
First ANC Visit Year	2006	2,788 (10.1)	1,699 (24.4)
	2007	10,094 (36.4)	2,663 (38.3)
	2008	11,946 (43.1)	1,913 (27.5)
	2009	2,885 (10.4)	683 (9.8)
Gestation at First ANC Visit (3 categories)	1st Trimester	2,026 (7.3)	778 (11.2)
	2nd Trimester	16,641 (60.1)	4,278 (61.5)
	3rd Trimester	9,046 (32.6)	1,902 (27.3)
Gestation at First ANC Visit (continuous)	Mean (sd)	23.0 (7.2)	21.8 (7.3)
Maternal Age	Mean (sd)	25.4 (6.0)	25.6 (6.2)

SD, Standard Deviation
∗ Wilcoxon Rank test

Tables 4 and 5 provide a breakdown of maternal, first ANC visit and delivery facility characteristics by trimester and stillbirth status, respectively. Only 7.3% (n=2,026) of births had a first ANC visit take place in the first trimester—the recommended time period, while 60.1% (n=16,641) occurred in the second trimester and 32.6% (n=9,046) in the third trimester. Women initiating ANC in the third trimester had a tendency to be multiparous, be less educated, have a lower maternal age, be black, and be non-smokers, book and deliver in Mitchell's Plain Hospital, and book in 2007 and 2008. The stillbirth rate was 4.3 per 1000 births during the study time period. In pregnancies resulting in stillbirths, the mothers were often multiparous, had no or primary education, had a higher median age, were black, were non-smokers, initiated ANC in False Bay and Mitchell's Plain hospitals, initiated ANC in 2007, and delivered in Mowbray Maternity Hospital and Groote Schuur Hospital.

Table 6 (A and B) examines the odds of having a stillbirth when gestation at first ANC visit is a continuous variable and when it is categorised into trimesters. Gestation at first ANC visit, when analysed continuously and in trimesters, has no significant effect on the stillbirths. Although the results are not significant, each week increase in first ANC visit results in a 1% (95% CI: 0.99-1.04) increase in the risk of a stillbirth. Using a logit-transformed Lowess smooth curve, Figure 2 also demonstrates this slight increase in odds for stillbirths when first ANC visit happens towards the end of pregnancy. Accordingly, initiating ANC in the second trimester has a protective effect on stillbirths (OR: 0.78; 95% CI: 0.39-1.59), while initiating in the third trimester is harmful (OR: 1.03; 95% CI: 0.50-2.13). The maternal age and race both had a significant effect on stillbirths in both analyses. Pregnancies of black women had twice the odds (OR: 2.01; 95% CI: 1.31-3.07 and OR: 2.03; 95% CI 1.33-2.10, for models 1 and 2, respectively) of having a stillbirth in both models. In both analyses, a one-year increase in maternal age resulted in 3% increased odds (95% CI: 1.00-1.07) of stillbirths.

Table 4:Maternal, first ANC visit and delivery characteristics for women who booked in the first, second and third trimesters of their pregnancy

Variable Name	Gestation at First ANC Visit		
	1st Trimester (6-12 Weeks)	2nd Trimester (13-26 Weeks)	3rd Trimester (27-42)
Number of Observations (%)	2,026 (7.3)	16,641 (60.1)	9,046 (32.6)
Parity (n) (%)			
Nulliparous	822 (40.6)	7,563 (45.5)	3,533 (39.1)
Primi/Multiparous	1,204 (59.4)	9,078 (54.6)	5,513 (60.9)
Educational Level (n) (%)			
None or Primary	99 (4.9)	706 (4.2)	494 (5.5)
Secondary or Tertiary	1,333 (65.8)	10,606 (63.7)	5,346 (59.1)
Missing	594 (29.3)	5,329 (32.0)	3,206 (35.4)
Maternal Age			
Median (IQR)	25 (22-30)	25 (21-29)	24 (21-29)
Race (n) (%)			
Coloured	1,641 (81.0)	11,398 (68.5)	5,007 (55.4)
Black	340 (16.8)	4,943 (29.7)	3,852 (42.6)
White, Asian, Other	45 (2.2)	300 (1.8)	187 (2.1)
Smoking (n) (%)			
Non-smoking	968 (47.8)	8,190 (49.2)	4,422 (48.9)
Smokers	591 (29.2)	4,118 (24.8)	1,995 (22.1)
Missing	467 (23.1)	4,333 (26.0)	2,629 (29.1)
First ANC Visit Facility (n) (%)			
False Bay	68 (3.4)	763 (4.6)	697 (7.7)
Hanover Park	758 (37.4)	4,041 (24.3)	1,874 (20.7)
Mitchell's Plain	634 (31.3)	7,176 (43.1)	4,849 (53.6)
Retreat MOU	566 (27.9)	4,661 (28.0)	1,626 (18.0)
First ANC Visit Year (n) (%)			
2006	390 (19.3)	1,919 (11.5)	479 (5.3)
2007	654 (32.3)	5,980 (35.9)	3,460 (38.3)
2008	798 (39.4)	7,031 (42.3)	4,117 (45.5)
2009	184 (9.1)	1,711 (10.3)	990 (10.9)
Delivery Facility (n) (%)			
False Bay Hospital	31 (1.5)	348 (2.1)	308 (3.4)
Gugulethu	2 (0.1)	24 (0.1)	12 (0.1)
Hanover Park	458 (22.6)	2,779 (16.7)	1,429 (15.8)
Mitchells Plain	313 (15.5)	4,105 (24.7)	3,104 (34.3)
Retreat MOU	240 (11.9)	2,509 (15.1)	949 (10.5)
Mowbray Maternity Hospital	283 (14.0)	2,839 (17.1)	1,603 (17.7)
Somerset Hospital	172 (8.5)	969 (5.82)	354 (3.9)
Groote Schuur Hospital	527 (26.0)	3,068 (18.4)	1,287 (14.2)

IQR, Inter-quartile Range

∗ Kruskal-Wallis Rank test

Table 5: Maternal, first ANC visit and delivery characteristics of pregnancies that resulted in stillbirths and live births

Variable Name	Outcomes	
	Stillborn	Alive
Number of Observations (%)	119 (0.4)	27,594 (99.6)
Parity (n) (%)		
Nulliparous	50 (42.0)	11,868 (43.0)
Primi/Multiparous	69 (58.0)	15,726 (57.0)
Educational Level (n) (%)		
None or Primary	9 (7.6)	1,290 (4.7)
Secondary or Tertiary	78 (65.6)	17,207 (62.4)
Missing	32 (26.9)	9,097 (33.0)
Maternal Age		
Median (IQR)	26 (21-31)	25 (21-29)
Race (n) (%)		
Coloured	56 (47.1)	17,990 (65.2)
Black	59 (49.6)	9,076 (32.9)
White, Asian, Other	4 (3.4)	528 (1.9)
Smoking (n) (%)		
Non-smoking	71 (59.7)	13,509 (49.0)
Smokers	26 (21.9)	6,678 (24.2)
Missing	22 (18.5)	7,407 (26.8)
First ANC Visit Facility (n) (%)		
False Bay	15 (12.6)	1,513 (5.5)
Hanover Park	21 (17.7)	6,652 (24.1)
Mitchell's Plain	58 (48.7)	12,601 (45.7)
Retreat MOU	25 (21.0)	6,828 (24.7)
First ANC Visit Year (n) (%)		
2006	9 (7.6)	2,779 (10.1)
2007	51 (42.9)	10,043 (36.4)
2008	50 (42.0)	11,896 (43.1)
2009	9 (7.6)	2,876 (10.4)
Delivery Facility (n) (%)		
False Bay Hospital	3 (2.5)	684 (2.5)
Gugulethu	0 (0.0)	38 (0.1)
Hanover Park	6 (5.0)	4,660 (16.9)
Mitchells Plain	9 (7.6)	7,513 (27.2)
Retreat MOU	5 (4.2)	3,693 (13.4)
Mowbray Maternity Hospital	33 (27.7)	4,692 (17.0)
Somerset Hospital	3 (2.5)	1,492 (5.4)
Groote Schuur Hospital	60 (50.4)	4,822 (17.5)

IQR, Inter-quartile Range

∗ Mann-Whitney Wilcoxon test

Table 6: Odds ratios for stillbirths and maternal characteristics: A) using gestation at first ANC visit as a continuous variable and B) using gestation at first ANC visit in trimesters.

A

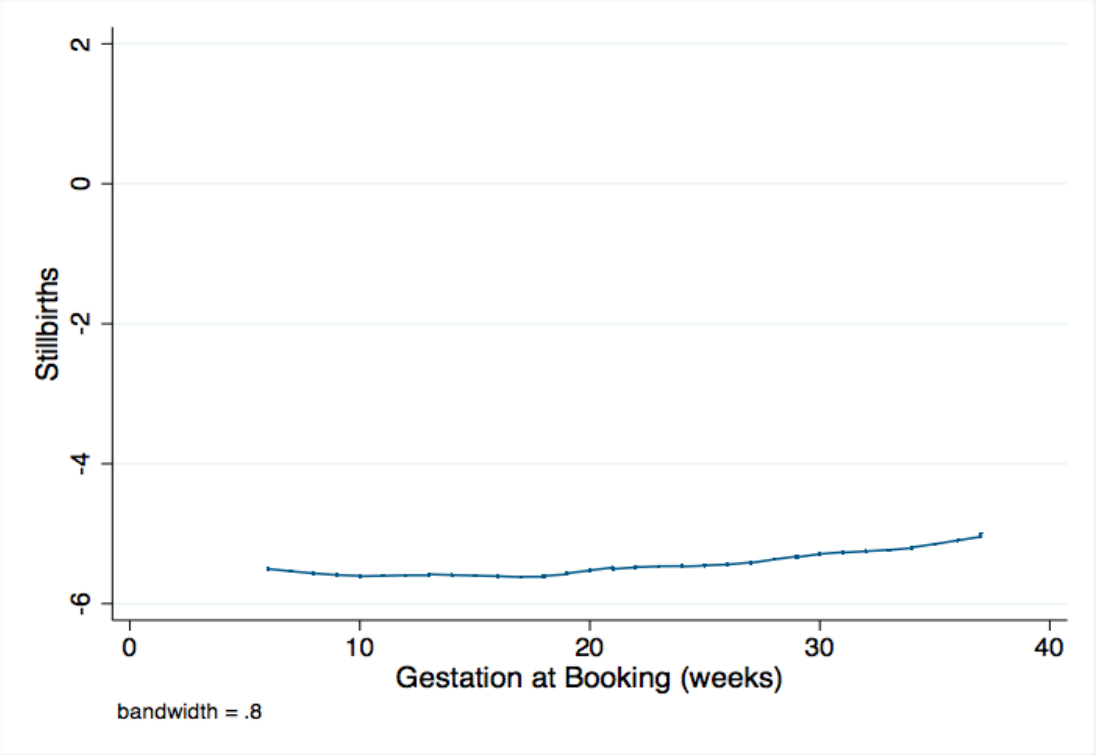
Variables	OR (95% CI)
Number of observations	27,713
Gestation at First ANC Visit (continuous)	1.01 (0.99-1.04)
Parity	
Nulliparous (ref)	1.00
Primi/Multiparous	1.20 (0.77-1.86)
Education	
None or Primary (ref)	1.00
Secondary or Tertiary	0.68 (0.34-1.37)
Missing	0.76 (0.32-1.84)
Maternal Age (continuous)	1.03 (1.00-1.07) *
Race	
Coloured (ref)	1.00
Black	2.01 (1.31-3.07) *
White, Asian, Other	2.43 (0.86-6.83)
Smoking	
Non-smoking (ref)	1.00
Smoking	1.10 (0.66-1.84)
Missing	0.61 (0.30-1.25)

B

Variables	OR (95% CI)
Number of observations	27,713
Gestation at First ANC Visit (Trimesters)	
1st Trimester (ref)	1.00
2nd Trimester	0.78 (0.39-1.59)
3rd Trimester	1.03 (0.50-2.13)
Parity	
Nulliparous (ref)	1.00
Primi/Multiparous	1.20 (0.77-1.86)
Education	
None or Primary (ref)	1.00
Secondary or Tertiary	0.68 (0.34-1.38)
Missing	0.77 (0.32-1.85)
Maternal Age (continuous)	1.03 (1.00-1.07) *
Race	
Coloured (ref)	1.00
Black	2.03 (1.33-2.10) *
White, Asian, Other	2.42 (0.86-6.82)
Smoking	
Non-smoking (ref)	1.00
Smoking	1.10 (0.66-1.84)
Missing	0.61 (0.30-1.25)

OR, Odds Ratio
*Indicates a significant OR at 5% significance

Figure 2: Pattern for increasing gestation at first aNC visit using a logit transformed Lowess smooth



5 Discussion

The results presented from this retrospective cohort of women in Cape Town, South Africa demonstrated that there appears to be no significant effect of the gestation at first ANC visit on the odds of having a stillbirth, after adjusting for maternal characteristics. This finding does not seem to support many of the messages produced in stillbirth literature on the value of ANC for preventing stillbirths. Indeed, Chopra *et al.* claim that 24% of stillbirths and neonatal deaths in South Africa could be prevented every year if family and communities took action to prevent them by using ANC, for example [4]. Reductions in stillbirth mortality can be achieved through ANC by increasing detection and management of hypertensive disease, fetal growth restriction and gestational diabetes as well as referring women to appropriate and skilled care for delivery when caesarean sections or inductions would be appropriate [19]. Additionally, health care providers can advise mothers on the prevention of malaria during pregnancy, prescribe folic acid supplements, test and treat syphilis [20], and encourage the use of balanced protein energy supplements [21], which are all said to improve stillbirth outcomes. Moreover, screening for congenital abnormalities as a part of ANC may help to reduce rates[22]. The results of this study indicate that initiating ANC early, on its own, does not seem to matter so much as ensuring that some of these effective interventions take place at some point in the antenatal period.

The stillbirth rate produced by this study, 4.3 per 1000 births, remains unacceptably high, although it is less than the South African national rate of 20 per 1000 births [23]. This may be partially explained by the fact that the health care facilities in the PMNS are located in an urban area where transport to the delivery facility is more accessible and frequent, and referrals can easily be made to secondary or tertiary hospitals when complications arise [24]. Predictably, most stillbirths occurred at Mowbray Maternity Hospital and Groote Schuur Hospital, which are secondary and tertiary hospitals, respectively. The lower stillbirth rate observed in Cape Town is consistent with the overall rate observed in high-income countries: less than 4 per 1000 total births [3]. In these countries, stillbirths often result from an inability to detect and manage fetal growth restriction when placental failure occurs, as well as maternal infections, congenital abnormalities [3], and other placental pathologies [25]. This suggests that the occurrence of stillbirths observed in Cape Town may not be due to inadequate ANC, but rather some of the same causes described in literature about high-income countries. Unfortunately, the causes of stillbirths could not be verified because the integrity of this data was lacking in the dataset.

This study contributes to what is known about the relationship between the initiation of ANC and birth outcomes and it is the only known study to investigate how delay in first ANC visit influences the occurrence of stillbirths. Perhaps more importantly, this study points to a methodological concern that arises when trying to operationalise 'adequate' ANC. While this study would seem to indicate that the timing of the first ANC visit does not matter for stillbirths, a more plausible scenario is that timing matters, but needs to be taken in conjunction with the number of ANC visits and the receiving of the recommended content of care. In fact, a study of health care facilities in Chicago demonstrated that a majority of women utilizing ANC at these facilities had less than 80% of the recommended content during ANC. The same study also demonstrated that less adherence to recommended content was associated with more preterm births and lower birth weights [26]. Another study, conducted in Canada, indicated that health care facilities often meet recommendations for medical management of pregnancy, but neglect the advice and education component of ANC [27].

Future studies could attempt to investigate the risk of stillbirths and other birth outcomes by utilising scoring tools that combine information on all three indicators —timing, number, and content— which are typically used independently of each other to describe 'adequate care'. It has been suggested that the adequacy of ANC should be operationalised with as many of the following as possible: timing of initiation of ANC, number and spacing of visits, adherence to

recommended schedule, content of medical care, type and training of service provider, setting of care, content of ancillary and educational services, and quality of the ANC provider system [28]. One such tool, developed in Belgium, operationalised 'adequate' ANC by considering whether: the first ANC visit occurred before 14 weeks; the recommended number of visits occurred at term gestation; and the appropriate number and timing of ultrasounds, blood pressure checks and blood tests were conducted [29]. A study conducted in India tested a tool like this on a population of poor and middle-income mothers and they found that a higher score resulted in more women using trained assistance at birth and safe delivery care [30]. Studies using tools such as these to analyse the risk of various birth and delivery outcomes are lacking, particularly in LMICs.

It is possible that the timing of first ANC visit is less important in preventing adverse birth outcomes than the time at which a mother recognizes she is pregnant. A U.S. study investigated whether 'time-lag'—delay in ANC after recognition of the pregnancy by the mother—was associated with preterm births, low birth weight, ICU admission, or infant mortality [31]. The study found that time-lag did not adversely affect birth outcomes; however, it was associated with early recognition of pregnancy [31]. The authors suggested that early recognition might result in improved behaviours such as reduced alcohol drinking or smoking, and encourage women to take prenatal vitamins [31]. Another study demonstrated that late recognition of pregnancy by mothers increased the odds of preterm births, low birth weights, and admission into neonatal intensive care units [32]. Studies like these could also shed light on stillbirth rates.

Investigating adequacy of care or early recognition of pregnancy, on their own, may not be sufficient for measuring risk of stillbirths or other birth outcomes. This is particularly true in places like Cape Town or high-income countries where stillbirth rates are relatively low. Approaches need to become more intergenerational in scope and take on a life course approach [33]. Lu *et al*. argue, using low birth weight as an example, that some birth outcomes are influenced by the function of a mother's reproductive organs, which may be determined *in utero* [34]. This approach may be a more valuable way of explaining fetal growth restriction, which is a typical cause of stillbirths among women living in high-income counties or where the stillbirth rates are relatively low.

While providing insight into a key determinant of stillbirths, this study has a couple of important limitations. First, the dataset used for the analysis already existed prior to the commencement of this study and so the data were not collected and entered by healthcare facility staff in a standardised way. Therefore the quality of many variables, and information

on participants from particular facilities and years, were not accurate and could not be used, which ultimately restricted this analysis, both in terms of sample size and variables that could be used to shed light on stillbirths. For instance, data on the causes of stillbirths were largely missing and often inaccurately coded. Additionally, the number of total ANC visits, as well as indicators of the content of each visit (e.g. which blood tests were done and when), was not available, thus precluding the possibility of creating an ANC adequacy scoring tool.

Secondly, the analysis of those who were lost-to-follow-up after the first ANC visit shows that most of the maternal characteristics and the exposure of interest are differential with respect to their retention status, potentially indicating that selection bias and informative censoring occurred. However, this may be partially accounted for by the fact that the sample size was so large that any small, clinically meaningless difference in the two groups was seen as significantly different, particularly for the gestation at first ANC visit variable. Moreover, some of the largest differences occurred for the first ANC visit facility and delivery facility variables. This may be explained by the fact that some facilities were worse than others about entering delivery data into the CRADLE database, therefore artificially making it look as though they had more loss-to-follow-up.

Despite these limitations, the study had a few key strengths. While it is possible that lost-to-follow-up may occur differentially for many explanatory variables, the overall rate of loss-to-follow-up was only 20%, allowing us to maintain a large sample size. Additionally, our large sample size ensured that most of our calculations were powered enough to detect real measures of effect. The fact that our exposure of interest (both forms) had such small confidence intervals and still overlapped with the null, demonstrates that we can confidently accept that gestation at first ANC visit has little effect on stillbirths. Furthermore, our large, population-based study ensures that the results are moderately generalisable to women with singleton, full-term births and utilising public hospitals in urban South Africa.

6 Conclusion

The study results have substantial implications for researchers investigating the use of ANC as a determinant of stillbirths and, potentially, other birth and delivery outcomes. Ideally, future research should aim to include a combination of indicators for ‘adequate’ ANC usage, in addition to beginning to explore life course determinants. Finally, ANC messages promoted by the government and other public health professionals in South Africa should

encourage clinicians to enrich their content of care and implement established effective interventions during ANC, rather than continuing to espouse hard and fast rules about number and timing of visits.

7 Acknowledgements

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8 Disclosure of Interests

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

9 Contribution to Authorship

RB, GP and LM contributed to the conception and design of the study. RB performed the statistical analysis and wrote the paper. GP and LM provided ongoing supervision and assisted with interpretation throughout the duration of the study and writing process.

10 Ethics

Ethics approval for the CRADLE study was obtained from the University of Cape Town Faculty of Health Sciences Research Ethics Committee (IRB00001938) (HREC REF: 162/2011).

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Part D: Appendices

1 Appendix A: Letter of approval from the research ethics committee

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
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11 May 2011

HREC REF: 162/2011

Ms R Beauclair
c/o A/Prof L Myer
Cider,
Public Health & Family Medicine

Dear Ms Beauclair

PROJECT TITLE: ADVERSE OUTCOMES ASSOCIATED WITH DELAYS IN ANTENATAL CARE: A RETROSPECTIVE COHORT STUDY OF PREGNANCIES IN CAPE TOWN, SOUTH AFRICA.

Thank you for your thoughtful response.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Approval is granted for one year till the 15 May 2012.

Please submit a progress form, using the standardised Annual Report Form (FHS016), if the study continues beyond the approval period. Please submit a Standard Closure form (FHS010)if the study is completed within the approval period.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Federal Wide Assurance Number: FWA00001637.
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2 Appendix B: Instructions for authors of articles in the BJOG: International Journal of Obstetrics and Gynaecology

Instructions for Authors

- Please refer to the Equator network website to find the appropriate good reporting flowchart and checklist to accompany your study.

Submission of manuscripts

Submissions to BJOG must be made online through Allentrack: http://bjog.allentrack.net. Paper manuscripts and email submissions are not accepted. Authors must register on the site, and use their login and password to access their Home Page (please avoid creating duplicate accounts, any problems accessing your AllenTrack Home Page please e-mail: bjog@editorialoffice.co.uk). From their Home Page authors will have access to the status of their manuscripts throughout the editorial process and, therefore, they should retain their login and password for future reference. It is essential that the email address for the Corresponding Author is entered correctly and is updated via the Author's Home Page if it becomes invalid at any time, as all correspondence regarding the submission will go to this email address.

Before submitting your manuscript please read both these instructions to authors and the BJOG editorial policies. Once you have logged into AllenTrack click on 'Submit Manuscript'. After reading the instructions on this page you will need to select the appropriate article type at the bottom of the page and click 'Continue'. You will be asked to enter specific information about the manuscript (e.g. title, type of manuscript, clinical category) prior to being asked to upload the actual manuscript files. There are also publication ethics questions to be answered. You will upload manuscript files from your computer as the last stage of the submission process.

Once your files are uploaded to the database, they will be converted by the system to PDF files that can be viewed, downloaded and printed. Manuscript files and your Cover Letter should be in MS Word or RTF format (**we do not currently accept Word 2007 docx files, please save these files in compatibility format before submitting**). Table files can be submitted as Excel files or MS Word files. Figures must be submitted separately from the text as TIFF, EPS, PDF or JPEG files. They should be in order and clearly labelled. Converting most files takes under ten minutes, but sometimes a large file will take longer. Conversion time also depends on the speed of your connection. The system will ask you to confirm that all files have converted correctly - please check your files to make sure that the system has

converted each element properly. Your paper will be considered officially submitted only after the system receives this confirmation when you click on Approve the Converted Files. If your submission is not correct, the file will be returned to your Home Page for you to make any necessary corrections, as detailed in an email frombjog@editorialoffice.co.uk. Please follow the instructions below to increase the chances of your paper passing this initial quality control stage first time, avoiding delays to your submission. Once a paper has been correctly submitted through the online system, it is assigned a tracking number and is accessed by the Editor in Chief for his assessment.

Supporting Information (online only)

Please note that the length of papers in the printed journal is restricted, and authors are encouraged to consider selecting information for publication on the web only version, as supporting information. Supporting Information must be important, ancillary information that is relevant to the parent article but which is not essential in the print edition of the journal. All supporting information must be referred to in the manuscript, and labelled Table S1, Table S2, Figure S1, Video S1 etc. Please do not include supporting information within the main manuscript file, but upload as separate file(s). Videos will be included as supporting information. For further instructions, click here.

Writing style and terminology

Manuscripts should be written in clear concise English. 'Fetus' and 'fetal' should be spelt without 'o', and 'ise' spellings are preferred to 'ize' spellings. Numbers one to ten should be spelled out; for more than ten people, objects, days, months, etc., use Arabic numerals. 'Women' is generally preferred to 'patients' when reporting on obstetrics. 'Termination of pregnancy' is preferred to 'therapeutic abortion' and 'miscarriage' is preferred to 'spontaneous abortion'. Authors should always use the generic names of drugs unless the proprietary name is directly relevant. Any specialised equipment, chemical or pharmaceutical product cited in the text must be accompanied by the name, city and country of its manufacturer. Please refer to this paper for terminology of lower urinary tract function:http://onlinelibrary.wiley.com/doi/10.1002/nau.10052/pdf and this paper for early pregnancy events http://humrep.oxfordjournals.org/content/20/11/3008.full.pdf.

Layout of manuscripts

All manuscripts should be double-spaced in an A4-sized document. The manuscript text must be arranged consecutively in the following sequence for **main research articles**, **surgical techniques**, **short**

communications and **systematic reviews**: 1. Title Page; 2. Abstract (if required); 3.Main Body of Text; 4. Acknowledgements; 5. Disclosure of Interests; 6. Contribution to Authorship; 7. Details of ethics approval; 8. Funding; 9. Reference List and 10. Table/Figure caption List.

1.Title page

The title page should include the following information:

• full title of the paper (The title should include the methodology at the end of the title after a colon e.g. "Transcutaneous electrical nerve stimulation in labour pain: a systematic review")

• names of all co-authors, with their addresses, please include the department/division (Maximum 2 affiliations per author. If an author has moved to new institutions, the new institution should be used and it should be clear in the article where the research took place.)

• name and contact details (address, telephone number and email address) of the corresponding author responsible for checking proofs and distributing offprints

• a shortened running title of no more than 60 characters for continuation pages

2. Abstracts

A full structured abstract of no more than 250 words is required for **main research articles**, subdivided into the following sequential sections: **Objective**; **Design**; **Setting**; **Population or Sample**; **Methods**;**Main Outcome Measures**; **Results**; **Conclusions**; and **Keywords**. For **Systematic Reviews**, the abstract should be subdivided into the following sequential sections: **Background**; **Objectives**; **Search Strategy**; **Selection Criteria**; **Data Collection and Analysis**; **Main Results**; **Conclusions**; and**Keywords**.

Short communications, non-systematic **reviews** and **surgical techniques** require a 100-word 'block' style, **non-structured abstract**.

Help to improve the search engine ranking of your paper by optimizing your title and abstract, see this webpage for tips: http://authorservices.wiley.com/bauthor/seo.asp

3. Main body of text

The text of **main articles** and **short communications** should be subdivided under the headings: Introduction; Methods;

Results; Discussion and Conclusion. **Case reports** should be in sections under the headings: Case report and Discussion. **Commentaries** and **Reviews** should have headings appropriate to the article. Any abbreviations or acronyms used should be defined at first use in the main body of the article.

4. Acknowledgements

Include, for example, funding for OnlineOpen publication, or funding for writing or editorial assistance. Also include contributors who do not qualify as authors (see the Editorial policies for the criteria for authorship), with their contribution described.

5. Disclosure of Interests

These include relevant financial (for example patent ownership, stock ownership, consultancies, speaker's fees, shares), personal, political, intellectual (organizing education) or religious interests. Please note that a competing interest should not prevent someone from being listed as an author if they qualify for authorship. If there is doubt about whether interests are relevant or significant, it is prudent to disclose. To read more about conflicts of interests, click here.

6. Contribution to Authorship

A paragraph explaining each author's contribution: their role in the conception, planning, carrying out, analysing and writing up of the work should be detailed. Authors' initials should be used as appropriate.

Please note: To qualify for authorship, an individual must meet all the criteria set out in the journal's editorial policies. All authors must accept responsibility for the paper as published.

7. Details of Ethics Approval

Any reports of studies or trials involving human or animal subjects, or medical records should contain a statement, in this Details of Ethics Approval section, that the procedures of the study received ethics approval from the relevant regional or institutional ethics committee responsible for human experimentation or complied with regulations governing experimentation using animals. The name of the ethics committee/IRB, date of approval and reference number must be included in this section. If there was no ethics committee, institutional review board or similar available locally, please refer to the BJOG Editorial Policies. For authors based in the UK, you might find this National Research Ethics Service flyer useful (please refer to the table for the differences between audit/service evaluation and

research).

8. Funding

Funding for any type of publication, for example by a commercial company, charity or government department, should be stated here. This applies to all types of papers (including, for example, research papers, review papers, letters, editorials and commentaries).

9. References

BJOG follows the conventions of the Vancouver reference list system in which references are numbered consecutively in the order in which they are first mentioned in the text. References should be identified as superscripts within the text, table headings and figure captions. Information from submitted manuscripts, which have not yet been accepted, should be cited as unpublished observations. As a guideline for the citation style of the varied types of sources, contributors should consult the Uniform Requirement for Manuscripts Submitted to Biomedical Journals. An article with up to six authors should include all authors. If an article has more than six authors, only the first six need be given, followed by 'et al'.

We recommend the use of a tool such as Endnote or Reference Manager for reference management and formatting.

EndNote: http://www.endnote.com/support/enstyles.asp

Reference Manager: http://www.refman.com/support/rmstyles.asp

10. Table/Figure Caption List

Digital artwork files for reproduction should preferably be high quality, low compression JPEG, TIFF or EPS, but we may be able to use other formats (see click here for the graphics resource for authors. Please note: BJOG cannot accept .zip files). BJOG publishes figures in colour.

11. Word Count

The word count for an article does not include the abstract, references, tables or figures.

Study design and statistics

The design of investigations, methods of analysis and the source of data should be described in sufficient detail to

permit the study to be repeated by others, and must include specification of all statistical methods. Measurements should be expressed in SI units with the exception of haemoglobin (g/dL) and blood pressure (mmHg). If human participants were involved, manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and appropriate informed consent of each. If experimental animals were used, the materials and methods (experimental procedures) section must clearly indicate that appropriate measures were taken to minimize pain or discomfort, and details of animal care should be provided.

Good reporting guidelines

For a better understanding of the reporting guidelines, please refer to the EQUATOR Network website:http://www.equator-network.org/ the resource centre for good research reporting. Any paper reporting the results of a questionnaire survey should include a copy of the questionnaire used, together with the manuscript. The reporting guidelines which are valuable for desiging your, include:

CONSORT statement, checklist and flow diagram for RCTs

PRISMA statement, checklist and flow diagram for systematic reviews and meta-analyses

MOOSE checklist is required for meta-analysis of observational studies

STARD flow diagram and checklist are required for evaluations of diagnostic tests (diagnostic accuracy studies)

STROBE observational studies in epidemiology (cohort, case-control, and cross-sectional studies)

STREGA genetic association studies

TREND statement and check list for nonrandomized controlled trials.

COREQ statement and check list for qualitative research (focus groups and interviews)

SQUIRE check list for quality improvement studies

REMARK check list for tumour marker prognostic studies

ORION infection control intervention studies

STRICTA controlled trials of acupuncture

ORION infection control intervention studies

RedHot homeopathic treatments.

Types of articles

Commentaries

Commentaries on subjects of current interest or controversy are welcome. They should be no more than 1800 words with 10–12 references. A ‘Disclosure of interests’ section should be included after the main body of text and before the references.

Mini Commentaries

Mini Commentaries are by invitation only, usually written by an editor or referee. They will relate specifically to a single paper, usually no more than 500 words, with integral (i.e. appearing where mentioned in the text) and truncated references (include the first author 'et al', Journal Name, year of publication, volume number and pages numbers) . There should be no separate reference list. A ‘Disclosure of interests’ section should be included at the end. Mini commentaries are attached to the article to which they refer, and therefore do not appear separately in indexing services, such as PubMed.

Short communications

Short communications (2000-3000 words) are usually reports of smaller studies and are only permitted one table or one illustration and should have no more than six references. A block abstract of no more than 100 words should be included.

Surgical techniques

Surgical techniques are descriptions of new or innovative techniques and allow authors more scope to illustrate their work: ten or more illustrations may be allowed, at the Editor's discretion, accompanied by informative text of up to 1800 words. A block abstract of no more than 100 words should be included.

Case Reports

We do not publish case reports unless they highlight important innovations with wide applicability, or previously unpublished complications of new techniques or medications. Over the last year 98% of case reports were rejected. Case reports do not require an abstract and should be no more than 1800 words. Only one table or illustration is permitted. Authors must confirm in their manuscript that they have obtained the written permission of those whose 'case' is being presented. You may wish to use this form to gain consent for publication: consent form. Please DO NOT submit this form to BJOG.

Main research article

A main article of between 4000 and 5000 words may present the outcome of a large trial, case control, observational or retrospective study; these must have a full structured abstract (see above).

Randomised controlled trials (RCT)

Randomised controlled trials require (a) a copy of the ethics approval (or an explanation as to why ethics approval was not received/evidence that it was not required), (b) a completed CONSORT flowchart(submitted as Figure 1) and CONSORT checklist (for Editor/Reviewer reference only) (c) a copy of the original protocol upon which the trial was based. Additionally, the clinical trial registration number should be included along with the name of the trial at the end of the abstract. Clinical trials should be registered in free to access, public clinical trial registries (for example,: www.actr.org.au, www.clinicaltrials.gov (free),www.ISRCTN.org, www.umin.ac.jp/ctr/index/htm, www.trialregister.nl or one of the WHO primary registries:http://www.who.int/ictrp/network/primary/en/index.html) before the first patient is recruited. These trial registries will all require the 20 Minimal Registration Data set of 20 items.

Trial registration: Studies that commenced before 1st July 2005 - all randomised trials must have been registered, but registration can be retrospective (i.e. registration can be done after the trial has been completed).

From 1st July 2005 – all randomised phase III trials (trials that compare new treatments with the best currently available treatment (the standard treatment) started after this date must have been registered prospectively (i.e. before or at commencement). Prospective registration is not required for Phase I trials (no more than 50 participants, often called 'pilot studies') or phase II trials (randomised but no more than 100 participants). However, trials should still be registered retrospectively.

From 1st July 2008 - any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes must have been registered prospectively (includes phase I and phase II trials and non-randomised studies of interventions).

Systematic review

A PRISMA (formerly QUOROM) statement and checklist are required for systematic reviews.Systematic reviews are welcome. They should be critical assessments of current evidence covering a broad range of topics of concern to those working in the field of obstetrics and gynaecology. Systematic reviews should be 4000-5000 words (abstracts to be structured as above).

N.B. For advice on writing systematic reviews consult: The Cochrane Reviewers' Handbook

Letters to the Editor

We are pleased to publish letters relating to papers published recently in BJOG (we do not publish research letters or stand-alone comments not referring to papers in BJOG). Letters should be no more than 500 words, contain no more than four references and must be in a separate file to the covering letter. The letter must include the names of the persons who wish to be published signatories, and their affiliations. Please include a title for the letter, which will usually contain the title of the paper about which a comment is made. Criteria for acceptance include timeliness in relation to the topic/published paper, the significance of the points made, and whether the letter is well written.

Appeals

The purpose of the appeal procedure is to allow the editor in chief or his deputy to assess the appropriateness of the editorial handling of the paper. It is not intended to trigger a review of the opinions of the referees or editors, as it would be inappropriate for a single individual (i.e. the editor-in-chief or their deputy) to overturn the majority view of referees and consulted editors.

Post acceptance issues

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Authors should advise the publisher (BJOG@wiley.com) of corrections, apologies and retractions to the publisher who will publish them as the next available opportunity. The Editor in Chief may by consulted as appropriate.

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The standards for the editorial process are in accordance with the Committee on Publications Ethics Code of Conduct.

References

The requirements for preparation of manuscripts submitted to BJOG are in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: http://www.icmje.org/manuscript_1prepare.html/, please see the sections 'General Considerations Related to References' and 'Reference Style and Format' .

Resources__

BJOG Author Brochure PDF

We have released a new version of the BJOG Author Brochure (2009) to provide authors with useful tips and links and to explain the BJOG peer review process. A list of the Scientific Editors and their specialities is also included. An understanding of publication ethics is important for all authors writing and submitting a paper, so this brochure makes both an interesting read and a useful reference.

The Library of Health Research Reporting

This page is regularly updated and includes the following resources:

- Reporting guidelines

- Guidance on scientific writing
- Guidance developed by editorial groups
- Research ethics, publication ethics and good practice guidelines
- Examples of editorials introducing reporting guidelines
- Examples of good research reporting
- Examples of guidelines for peer reviewers
- Useful and interesting presentations

EQUATOR Network resource for authors

This page can help you with:

- Planning and conducting your research
- Writing up your research
- Ethical guidelines and considerations

3 Appendix C: Additional Tables

3.1 Univariate Analyses

Table 7: Summary statistics for numerical variables

Variables	Observations (n)	Missing (n)	Mean	SD	Median	IQR	Range	Shapiro-Wilks p-value
Gestational Age at Delivery	35,473	0	38.8	2.2	40	38-40	28-45	0.0000
Maternal Age	35,466	7	25.5	6.1	25	21-29	11-57	0.0000
Gestation at Booking	35,859	0	25.0	8.5	24	18-31	6-42	0.0000
Parity	35,473	0	1.03	1.2	1	0-2	0-10	0.0000
APGAR Score	33,555	2,930	8.4	1.2	9	8-9	0-10	0.0000
Birth weight	35,473	0	3041.7	586.7	3080	2740-3400	200-6820	0.0000

SD, Standard Deviation
IQR, Inter-quartile Range

Table 8: Frequencies of categorical variables

Variable	Categories	Frequency (%)
Gestation at Delivery (Preterm)	Full term (>=37 weeks)	31,215 (88.0)
	Preterm (<37 weeks)	4,258 (12.0)
Gestation at Booking (Trimesters)	1st (6-12 Weeks)	2,290 (6.5)
	2nd (13-26 Weeks)	18,601 (52.4)
	3rd (27-42 Weeks)	14,582 (41.1)
Gestation at Booking (6 categories)	6-11 Weeks	1,678 (4.7)
	12-17 Weeks	5,892 (16.6)
	18-23 Weeks	8,832 (24.9)
	24-29 Weeks	8,110 (22.9)
	30-35 Weeks	5,667 (15.98)
	36-42 Weeks	5,294 (14.9)
Maternal Age	<20 years	5,996 (16.9)
	20-29 years	20,720 (58.4)
	30-39 years	8,102 (22.8)
	>=40 years	655 (1.9)
Parity	Nulliparous	14,798 (41.7)
	Primi/Multiparous	20,675 (58.3)
Education Level	None	70 (0.2)
	Primary	1,571 (4.4)
	Secondary	20,484 (57.8)
	Tertiary	68 (0.2)
	Missing	13,280 (37.4)
Race	Black	11,571 (32.6)
	White	157 (0.4)
	Coloured	23,238 (65.5)
	Asian	73 (0.2)
	Other	427 (1.2)
	Missing	7 (0.1)
Smoking	Yes	8,370 (23.6)
	No	15,993 (45.1)
	Missing	11,110 (31.3)
Booking Facility	Hanover Park Community Health Clinic	8,288 (23.4)
	Mitchell's Plain Medical Centre	16,174 (45.6)
	False Bay Hospital	2,240 (6.3)
	Retreat MOU	8,771 (24.7)
Booking Year	2006	3,130 (8.8)
	2007	13,262 (37.4)
	2008	15,349 (43.3)
	2009	3,732 (10.5)
Birth Weight	Low	4,831 (13.6)
	Normal	30,642 (86.4)
APGAR Score (1 min)	Low	1,320 (3.7)
	Normal	31,223 (88.0)
	Missing	2,930 (8.3)
Caesarean Section	Yes	6,144 (17.3)
	No	29,329 (82.7)
Still birth	Yes	444 (1.25)
	No	35,029 (98.8)
Delivery Facility Level of Care	Primary	20,577 (58.0)
	Secondary	7,728 (21.8)
	Tertiary	7,168 (20.2)
Delivery Facility	False Bay Hospital	881 (2.5)
	Gugulethu	44 (0.1)
	Hanover Park	5,734 (16.2)
	Mitchells Plain	9,427 (26.6)
	Retreat MOU	4,491 (12.7)
	Mowbray Maternity Hospital	5,909 (16.7)
	Somerset Hospital	1,819 (5.1)
	Groote Schuur Hospital	7,168 (20.2)

Tables 7 and 8 explore summary statistics for numerical variables and frequencies for categorical variables. Most variables have distributions and frequencies that would be expected for the variables, except for the continuous version of gestation at booking, where there is a disproportionate amount of women booking between 36 and 42 weeks. Additionally, it appears that there are smaller proportions of people booking in 2006 and 2009, however this is expected and reflects the fact that deliveries were limited to those occurring from 2007-2009.

3.2 Idiosyncrasies in Gestation at Booking

Table 9: Exploring reasons for excess bookings at 40 weeks

	Gestation at Booking (weeks)				
	37	**38**	**39**	**40**	**41**
n	679	736	1,217	1,618	243
Mean Mother's Age (sd)	25.61 (6.6)	25.91 (6.0)	25.48 (6.2)	25.53 (6.0)	25.72 (5.9)
Booking Facility n (%)					
False Bay	97 (14.3)	125 (17.0)	134 (11.0)	117 (7.2)	47 (19.3)
Hanover Park	117 (17.2)	116 (15.8)	250 (20.5)	423 (26.1)	22 (9.1)
Mitchell's Plain	305 (44.9)	299 (40.6)	591 (48.6)	776 (48.0)	92 (37.9)
Retreat MOU	160 (23.6)	196 (26.6)	242 (19.9)	302 (18.7)	82 (33.7)
Delivery Facility n (%)					
False Bay	32 (4.7)	39 (5.3)	38 (3.1)	30 (1.9)	10 (4.1)
Gugulethu	1 (0.2)	0 (0.0)	2 (0.2)	2 (0.1)	0 (0.0)
Hanover Park	85 (12.5)	97 (13.2)	217 (17.8)	382 (23.6)	13 (5.4)
Mitchell's Plain	219 (32.3)	213 (28.9)	482 (39.6)	573 (35.4)	60 (24.7)
Retreat MOU	89 (13.1)	98 (13.3)	125 (10.3)	204 (12.6)	36 (14.8)
Mowbray Maternity Hospital	76 (11.2)	74 (10.1)	92 (7.6)	162 (10.0)	22 (9.1)
Sommerset Hospital	25 (3.7)	10 (1.4)	21 (1.7)	33 (2.0)	4 (1.7)
Groote Schuur Hospital	152 (22.4)	205 (27.9)	240 (19.7)	232 (14.3)	98 (40.3)
Median Gestation at Delivery (IQR)	39 (38-40)	39 (38-40)	40 (38-40)	40 (38-40)	40 (38-40)
Mean Gestation at Delivery (sd)	38.59 (2.0)	38.57 (1.9)	38.87 (2.0)	39.03 (2.0)	39.31 (1.7)
Normal Vaginal Deliveries n (%)					
Yes	544 (80.1)	574 (78.0)	1,031 (84.7)	1,388 (85.8)	161 (66.3)
No	135 (19.9)	162 (22.0)	186 (15.3)	230 (14.2)	82 (33.7)
Stillbirths n (%)					
Yes	6 (0.9)	12 (1.6)	12 (1.0)	19 (1.2)	4 (1.7)
No	673 (99.1)	724 (98.4)	1,205 (99.0)	1,599 (98.8)	239 (98.4)
Low Birth Weight n (%)					
Yes	102 (15.0)	100 (13.6)	152 (12.5)	202 (12.5)	21 (8.6)
No	577 (85.0)	636 (86.4)	1,065 (87.5)	1,416 (87.5)	222 (91.4)
Caesar n (%)					
Yes	107 (15.8)	129 (17.5)	136 (11.2)	168 (10.4)	67 (27.6)
No	572 (84.2)	607 (82.5)	1,081 (88.8)	1,450 (89.6)	176 (72.4)
Low APGAR					
Yes	22 (3.2)	24 (3.3)	39 (3.2)	44 (2.7)	10 (4.1)
No	581 (85.6)	611 (83.0)	1,002 (82.3)	1,319 (81.5)	204 (84.0)
Missing	76 (11.2)	101 (13.7)	176 (14.5)	255 (15.8)	29 (11.9)

SD, Standard Deviation
IQR, Inter-quartile Range

Table 9 investigates potential reasons for the disproportionate number of 38 to 40-week gestations at booking. There is a higher proportion of women who book at 40 weeks who have normal vaginal deliveries. These women also tend to book and deliver at Hanover Park and Mitchell's Plain hospitals.

3.3 Bivariate analyses with gestation at booking categorized into six categories

Table 10: Predictor variables by gestation at booking (6 levels)

Variable Name	Gestation at Booking					
	6-11 Weeks	12-17 Weeks	18-23 Weeks	24-29 Weeks	30-35 Weeks	36-42 Weeks
Number of Observations	1,678 (4.7)	5,892 (16.6)	8,832 (24.9)	8,110 (22.9)	5,667 (16.0)	5,294 (14.9)
Parity n (%)						
Nulliparous	669 (39.9)	2,631 (44.7)	4,123 (46.7)	3,493 (43.1)	2,125 (37.5)	1,757 (33.2)
Primi/Multiparous	1,009 (60.2)	3,261 (55.4)	4,709 (53.3)	4,617 (56.9)	3,542 (62.5)	3,537 (66.8)
Parity						
Mean (sd)	1.04 (1.1)	0.92 (1.1)	0.89 (1.1)	0.99 (1.2)	1.15 (1.3)	1.27 (1.3)
Educational Level n (%)						
None	0 (0.0)	7 (0.1)	16 (0.2)	20 (0.3)	18 (0.3)	9 (0.2)
Primary	91 (5.4)	269 (4.6)	362 (4.1)	354 (4.4)	317 (5.6)	178 (3.4)
Secondary	1,121 (66.81)	3,740 (63.48)	5,552 (62.86)	5,202 (64.14)	3,150 (55.58)	1,719 (32.47)
Tertiary	5 (0.3)	11 (0.2)	14 (0.2)	15 (0.2)	14 (0.3)	9 (0.2)
Missing	461 (27.5)	1,865 (31.7)	2,888 (32.7)	2,519 (31.1)	2,168 (38.3)	2,279 (63.8)
Mother's Age						
Mean (sd)	26.44 (5.9)	25.77 (5.9)	25.22 (5.9)	25.26 (6.1)	25.29 (6.3)	25.67 (6.2)
Mother's Age n (%)						
<20 years old	196 (11.7)	859 (14.6)	1,532 (17.4)	1,494 (18.4)	1,067 (18.8)	848 (16.0)
20-29 years old	976 (58.2)	3,547 (60.2)	5,217 (59.1)	4,663 (57.5)	3,208 (56.6)	3,109 (58.7)
30-31 years old	475 (28.3)	1,381 (23.4)	1,974 (22.4)	1,806 (22.3)	1,259 (22.2)	1,207 (22.8)
>=40 years old	31 (1.9)	105 (1.8)	109 (1.2)	147 (1.8)	133 (2.4)	130 (2.5)
Race n (%)						
Coloured	1,373 (81.8)	4,630 (78.6)	6,036 (68.3)	4,657 (57.4)	3,194 (56.4)	3,348 (63.2)
Black	276 (16.5)	1,149 (19.5)	2,643 (29.9)	3,294 (40.6)	2,368 (41.8)	1,841 (34.8)
Asian	4 (0.2)	11 (0.2)	15 (0.2)	20 (0.3)	12 (0.2)	11 (0.2)
White	10 (0.6)	38 (0.6)	33 (0.4)	22 (0.3)	19 (0.3)	35 (0.7)
Other	15 (0.9)	64 (1.1)	105 (1.2)	115 (1.4)	72 (1.3)	56 (1.1)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.0)	2 (0.0)	3 (0.1)
Smoking n (%)						
Non-smoking	798 (47.6)	2,775 (47.1)	4,256 (48.2)	4,164 (51.3)	2,604 (46.0)	1,396 (26.4)
Smokers	522 (31.1)	1,627 (27.6)	2,235 (25.3)	1,924 (23.7)	1,289 (22.8)	773 (14.6)
Missing	358 (21.3)	1,490 (25.3)	2,341 (26.5)	2,022 (24.9)	1,774 (31.3)	3,125 (59.0)
Gestational Age at Delivery						
Mean (sd)	38.67 (2.2)	38.87 (2.1)	38.85 (2.1)	38.75 (2.4)	38.57 (2.5)	38.80 (2.0)
Gestational Age at Delivery n (%)						
Preterm (<37 weeks)	197 (11.7)	561 (9.5)	913 (10.3)	1,000 (12.3)	914 (16.1)	673 (12.7)
Full term (>=37 weeks)	1,481 (88.3)	5,331 (90.5)	7,919 (89.7)	7,110 (87.7)	4,753 (83.9)	4,621 (87.3)
Booking Facility n (%)						
False Bay	54 (3.2)	281 (4.8)	396 (4.5)	416 (5.1)	461 (8.1)	632 (11.9)
Hanover Park	664 (39.6)	1,538 (26.1)	2,078 (23.5)	1,772 (21.9)	1,160 (20.5)	1,076 (20.3)
Mitchell's Plain	511 (30.5)	2,173 (36.9)	3,841 (43.5)	4,214 (52.0)	3,043 (53.7)	2,392 (45.2)
Retreat MOU	449 (26.8)	1,900 (32.3)	2,517 (28.5)	1,708 (21.1)	1,003 (17.7)	1,194 (22.6)
Booking Year n (%)						
2006	330 (19.7)	896 (15.2)	921 (10.4)	626 (7.7)	226 (4.0)	131 (2.5)
2007	539 (32.1)	2,012 (34.2)	3,180 (36.0)	3,047 (37.6)	2,231 (39.4)	2,253 (42.6)
2008	648 (38.6)	2,422 (41.1)	3,777 (42.8)	3,596 (44.3)	2,557 (45.1)	2,349 (44.4)
2009	161 (9.6)	562 (9.5)	954 (10.8)	841 (10.4)	653 (11.5)	561 (10.6)
Delivery Facility n (%)						
False Bay Hospital	22 (1.3)	115 (2.0)	179 (2.0)	193 (2.4)	189 (3.3)	183 (3.5)
Gugulethu	2 (0.1)	8 (0.1)	11 (0.1)	9 (0.1)	9 (0.2)	5 (0.1)
Hanover Park	377 (22.5)	968 (16.4)	1,357 (15.4)	1,252 (15.4)	882 (15.6)	898 (17.0)
Mitchells Plain	227 (13.5)	1,123 (19.1)	2,094 (23.7)	2,357 (29.1)	1,870 (33.0)	1,756 (33.2)
Retreat MOU	173 (10.3)	876 (14.9)	1,354 (15.3)	898 (11.1)	525 (9.3)	665 (12.6)
Mowbray Maternity Hospital	234 (14.0)	935 (15.9)	1,546 (17.5)	1,642 (20.3)	1,025 (18.1)	527 (10.0)
Somerset Hospital	153 (9.1)	401 (6.8)	537 (6.1)	393 (4.9)	211 (3.7)	124 (2.3)
Groote Schuur Hospital	490 (29.2)	1,466 (24.9)	1,754 (19.9)	1,366 (16.8)	956 (16.9)	1,136 (21.5)

SD, Standard Deviation

Table 10 looks at the relationship between the predictor variables and gestation at booking when its categorized into 6 levels. Parity, mother's age, race, gestational age at delivery, booking facility, booking year, and delivery facility are all associated with gestation at booking, indicating they could be potential confounders. The proportion of women booking in each of the categories who were nulliparous gradually increases until the 18-23 weeks and then decreases. Additionally, the mean mother's age gradually decreases for each gestation at booking category until 18-23 weeks and then increases again. The table also shows that a larger proportion of women booking between 30-35 weeks are

preterm, compared to the other booking categories, which indicates that most may have been unbooked pregnancies.

3.4 Bivariate analyses for outcome variables not included in the manuscript

Table 11: Exposure and predictor variables versus caesarean sections, stratified by preterm status

Variable Name	All Gestations at Delivery		37+ Weeks at Delivery		<37 Weeks at Delivery
	Caesar	No Caesar	Caesar	No Caesar	Caesar
Number of Observations (%)	6,144 (17.3)	29,329 (82.7)	5,080 (16.3)	26,135 (83.7)	1,064 (25.0)
Parity n (%)					
Nulliparous	2,597 (42.3)	12,201 (41.6)	2,174 (42.8)	10,875 (41.6)	423 (39.8)
Primi/Multiparous	3,547 (57.7)	17,128 (58.4)	2,906 (57.2)	15,260 (58.4)	641 (60.2)
Parity					
Median (IQR)	1 (0-2)	1 (0-2)	1 (0-2)	1 (0-2)	1 (0-2)
Educational Level n (%)					
None	12 (0.2)	57 (0.2)	12 (0.2)	53 (0.2)	1 (0.1)
Primary	277 (4.5)	1,294 (4.4)	222 (4.4)	1,119 (4.3)	55 (5.2)
Secondary	3,994 (65.0)	16,490 (56.2)	3,343 (65.8)	14,927 (57.1)	651 (61.2)
Tertiary	17 (0.3)	51 (0.2)	13 (0.3)	51 (0.2)	4 (0.4)
Missing	1,843 (30.0)	11,437 (39.0)	1,490 (29.3)	9,985 (38.2)	353 (33.2)
Mother's Age					
Mean (sd)	26.82 (6.1)	25.17 (6.0)	26.83 (6.0)	25.19 (6.0)	26.75 (6.3)
Mother's Age n (%)					
<20 years old	663 (10.8)	5,333 (18.2)	531 (10.5)	4,665 (17.9)	132 (12.4)
20-29 years old	3,549 (57.8)	17,171 (58.6)	2,947 (58.0)	15,423 (59.0)	602 (56.6)
30-39 years old	1,780 (29.0)	6,322 (21.6)	1,472 (29.0)	5,615 (21.5)	308 (29.0)
>=40 years old	152 (2.5)	503 (1.7)	130 (2.6)	432 (1.7)	22 (2.1)
Race n (%)					
Coloured	3,362 (54.7)	19,876 (67.8)	2,728 (53.7)	17,519 (67.0)	634 (59.6)
Black	2,642 (43.0)	8,929 (30.4)	2,229 (43.9)	8,136 (31.1)	413 (38.8)
Asian	11 (0.2)	62 (0.2)	10 (0.2)	52 (0.2)	1 (0.1)
White	48 (0.8)	109 (0.4)	39 (0.8)	99 (0.4)	9 (0.9)
Other	77 (1.3)	350 (1.2)	70 (1.4)	328 (1.3)	7 (0.7)
Missing	4 (0.1)	3 (0.0)	4 (0.1)	1 (0.0)	0 (0.0)
Smoking n (%)					
Non-smoking	3,629 (59.1)	12,364 (42.2)	3,068 (60.4)	11,371 (43.5)	561 (52.7)
Smokers	1,307 (21.3)	7,063 (24.1)	1,024 (20.2)	6,108 (23.4)	283 (26.6)
Missing	1,208 (19.7)	9,902 (33.8)	988 (19.5)	8,656 (33.1)	220 (20.7)
Booking Facility n (%)					
False Bay Hospital	686 (11.2)	1,554 (5.3)	592 (11.7)	1,359 (5.2)	94 (8.8)
Hanover Park	958 (15.6)	7,330 (25.0)	775 (15.3)	6,615 (25.3)	183 (17.2)
Mitchell's Plain	2,773 (45.1)	13,401 (45.7)	2,273 (44.7)	11,973 (45.8)	500 (47.0)
Retreat MOU	1,727 (28.1)	7,044 (24.0)	1,440 (28.4)	6,188 (23.7)	287 (27.0)
Booking Year n (%)					
2006	503 (8.2)	2,627 (9.0)	433 (8.5)	2,449 (9.4)	70 (6.6)
2007	2,205 (35.9)	11,057 (37.7)	1,809 (35.6)	9,810 (37.5)	396 (37.2)
2008	2,720 (44.3)	12,629 (43.1)	2,248 (44.3)	11,216 (42.9)	472 (44.4)
2009	716 (11.7)	2,016 (10.3)	590 (11.6)	2,660 (10.2)	126 (11.8)
Gestation at Booking					
Mean (sd)	23.95 (8.4)	25.22 (8.5)	23.91 (8.5)	25.05 (8.5)	24.13 (8.3)
Gestation at Booking-trimesters n (%)					
1st Trimester	497 (8.1)	1,793 (6.1)	406 (8.0)	1,620 (6.2)	91 (8.6)
2nd Trimester	3,432 (55.9)	15,169 (51.7)	2,870 (56.5)	13,773 (52.7)	562 (52.8)
3rd Trimester	2,215 (36.1)	12,367 (42.2)	1,804 (35.5)	10,742 (41.1)	411 (38.6)
Gestation at Booking n (%)					
6-11 Weeks	360 (5.9)	1,318 (4.5)	295 (5.8)	1,186 (4.5)	65 (6.1)
12-17 Weeks	1,193 (19.4)	4,669 (16.0)	999 (19.7)	4,332 (16.6)	194 (18.2)
18-23 Weeks	1,535 (25.0)	7,297 (24.9)	1,285 (25.3)	6,634 (25.4)	250 (23.5)
24-29 Weeks	1,432 (23.3)	6,678 (22.8)	1,187 (23.4)	5,923 (22.7)	245 (23.0)
30-35 Weeks	890 (14.5)	4,777 (16.3)	696 (13.7)	4,057 (15.5)	194 (18.2)
36-42 Weeks	734 (12.0)	4,560 (15.6)	618 (12.2)	4,003 (15.3)	116 (10.9)
Delivery Facility n (%)					
False Bay Hospital	6 (0.1)	875 (3.0)	6 (0.1)	799 (3.1)	0 (0.0)
Gugulethu	0 (0.0)	44 (0.2)	0 (0.0)	42 (0.2)	0 (0.0)
Hanover Park	1 (0.0)	5,733 (19.6)	1 (0.0)	5,291 (20.3)	0 (0.0)
Mitchells Plain	0 (0.0)	9,427 (32.1)	0 (0.0)	8,754 (33.5)	0 (0.0)
Retreat MOU	0 (0.0)	4,491 (15.3)	0 (0.0)	4,128 (15.8)	0 (0.0)
Mowbray Maternity Hospital	2,317 (37.7)	3,592 (12.3)	2,068 (40.7)	2,957 (11.3)	249 (23.4)
Somerset Hospital	618 (10.1)	1,201 (4.1)	554 (10.9)	1,005 (3.9)	64 (6.0)
Groote Schuur Hospital	3,202 (52.1)	3,966 (13.5)	2,451 (48.3)	3,159 (12.1)	751 (70.6)

SD, Standard Deviation
IQR, Inter-quartile Range

Table 12: Exposure and predictor variables versus low birth weight, stratified by preterm status

Variable Name	All Gestations at Delivery		37+ Weeks at Delivery		<37 Weeks at Delivery
	Low Birth Weight	Normal Birth Weight	Low Birth Weight	Normal Birth Weight	Low Birth Weight
Number of Observations (%)	4,831 (13.6)	30.642 (86.4)	1,806 (5.8)	29,409 (94.2)	3,025 (71.0)
Parity n (%)					
Nulliparous	2,082 (43.1)	12,716 (41.5)	826 (45.7)	12,223 (41.6)	1,256 (41.5)
Primi/Multiparous	2,749 (56.9)	17,926 (58.5)	980 (54.3)	17,186 (58.4)	1,769 (58.5)
Parity					
Mean (sd)	1.06 (1.3)	1.02 (1.2)	0.99 (1.2)	1.02 (1.2)	1.10 (1.3)
Educational Level n (%)					
None	3 (0.1)	67 (0.2)	0 (0.0)	65 (0.2)	3 (0.1)
Primary	271 (5.6)	1,300 (4.2)	91 (5.0)	1,250 (4.3)	180 (6.0)
Secondary	2,538 (52.5)	17,946 (58.6)	975 (54.0)	17,295 (58.8)	1,563 (51.7)
Tertiary	4 (0.1)	64 (0.2)	2 (0.1)	62 (0.2)	2 (0.1)
Missing	2,015 (41.7)	11,265 (36.8)	738 (40.9)	10,737 (36.5)	1,277 (42.2)
Mother's Age					
Mean (sd)	25.68 (6.5)	25.42 (6.0)	25.83 (6.5)	25.43 (6.0)	25.60 (6.5)
Mother's Age n (%)					
<20 years old	890 (18.4)	5,106 (16.7)	314 (17.4)	4,882 (16.6)	576 (19.0)
20-29 years old	2,627 (54.4)	18,093 (59.1)	992 (54.9)	17,378 (59.1)	1,635 (54.1)
30-39 years old	1,185 (24.5)	6,917 (22.6)	450 (24.9)	6,637 (22.6)	735 (24.3)
>=40 years old	129 (2.7)	526 (1.7)	50 (2.8)	512 (1.7)	79 (2.6)
Race n (%)					
Coloured	3,503 (72.5)	19, 735 (64.4)	1,363 (75.5)	18,884 (64.2)	2,140 (70.7)
Black	1,270 (26.3)	10,301 (33.6)	428 (23.7)	9,937 (33.8)	842 (27.8)
Asian	11 (0.2)	62 (0.2)	4 (0.2)	58 (0.2)	7 (0.2)
White	16 (0.3)	141 (0.5)	4 (0.2)	134 (0.5)	12 (0.4)
Other	29 (0.6)	398 (1.3)	7 (0.4)	391 (1.3)	22 (0.7)
Missing	2 (0.0)	5 (0.0)	0 (0.0)	5 (0.0)	2 (0.1)
Smoking n (%)					
Non-smoking	1,740 (36.0)	14,253 (46.5)	663 (36.7)	13,776 (46.8)	1,077 (35.6)
Smokers	1,438 (29.8)	6,932 (22.6)	528 (29.2)	6,604 (22.5)	910 (30.1)
Missing	1,653 (34.2)	9,457 (30.9)	615 (34.1)	9,029 (30.7)	1,038 (34.3)
Booking Facility n (%)					
False Bay Hospital	286 (5.9)	1,954 (6.4)	84 (4.7)	1,867 (6.4)	202 (6.7)
Hanover Park	1,022 (21.2)	7,266 (23.7)	371 (20.5)	7,019 (23.9)	651 (21.5)
Mitchell's Plain	2,170 (44.9)	14,004 (45.7)	838 (46.4)	13,408 (45.6)	1,332 (44.0)
Retreat MOU	1,353 (28.0)	7,418 (24.2)	513 (28.4)	7,115 (24.2)	840 (27.8)
Booking Year n (%)					
2006	321 (6.6)	2,809 (9.2)	136 (7.5)	2,746 (9.3)	185 (6.1)
2007	1,828 (27.8)	11,434 (37.3)	654 (36.2)	10,965 (37.3)	1,174 (38.8)
2008	2,142 (44.3)	13,207 (43.1)	815 (45.1)	12.649 (43.0)	1,327 (43.9)
2009	540 (11.2)	3,192 (10.4)	201 (11.1)	3,049 (10.4)	339 (11.2)
Gestation at Booking					
Mean (sd)	25.35 (8.5)	24.94 (8.5)	24.77 (8.5)	24.87 (8.5)	25.70 (8.5)
Gestation at Booking n (%)					
1st Trimester	314 (6.5)	1,976 (6.5)	123 (6.8)	1,903 (6.5)	191 (6.3)
2nd Trimester	2,374 (49.1)	16,227 (53.0)	954 (52.8)	15,689 (53.5)	1,420 (46.9)
3rd Trimester	2,143 (44.4)	12,439 (40.6)	729 (40.4)	11,817 (40.2)	1,414 (46.7)
Gestation at Booking n (%)					
6-11 Weeks	231 (4.8)	1,447 (4.7)	86 (4.8)	1,395 (4.7)	145 (4.8)
12-17 Weeks	740 (15.3)	5,152 (16.8)	313 (17.3)	5,018 (17.1)	427 (14.1)
18-23 Weeks	1,140 (15.3)	7,692 (25.1)	470 (26.0)	7,449 (25.3)	670 (22.2)
24-29 Weeks	1,084 (22.4)	7,026 (22.9)	396 (21.9)	6,714 (22.8)	688 (22.2)
30-35 Weeks	935 (19.4)	4,732 (15.4)	279 (15.5)	4,474 (15.2)	656 (21.7)
36-42 Weeks	701 (14.5)	4,593 (15.0)	262 (14.5)	4,359 (14.8)	439 (14.5)
Delivery Facility n (%)					
False Bay Hospital	72 (1.5)	809 (2.6)	29 (1.6)	776 (2.6)	43 (1.4)
Gugulethu	4 (0.1)	40 (0.1)	2 (0.1)	40 (0.1)	2 (0.1)
Hanover Park	523 (10.8)	5,211 (17.0)	226 (12.5)	5,066 (17.2)	297 (9.8)
Mitchells Plain	903 (18.7)	8,524 (27.8)	443 (24.5)	8,311 (28.3)	460 (15.2)
Retreat MOU	517 (10.7)	3,974 (13.0)	285 (15.8)	3,843 (13.1)	232 (7.7)
Mowbray Maternity Hospital	898 (18.6)	5,011 (16.4)	358 (19.8)	4,667 (15.9)	540 (17.9)
Somerset Hospital	297 (6.2)	1,522 (5.0)	114 (6.3)	1,445 (4.9)	183 (6.1)
Groote Schuur Hospital	1,617 (33.5)	5,551 (18.1)	349 (19.3)	5,261 (17.9)	1,268 (41.9)

SD, Standard Deviation
IQR, Inter-quartile Range

Table 13: Exposure and predictor variables versus low APGAR score, stratified by preterm status

Variable Name	All Gestations at Delivery		37+ Weeks at Delivery		<37 Weeks at Delivery
	Low APGAR	Normal APGAR	Low APGAR	Normal APGAR	Low APGAR
Number of Observations (%)	1,320 (4.1)	31.223 (95.9)	957 (3.1)	28,179 (90.3)	363 (8.5)
Parity n (%)					
Nulliparous	773 (58.6)	12,874 (41.6)	612 (64.0)	11,681 (41.5)	161 (44.4)
Primi/Multiparous	547 (41.4)	18,249 (58.5)	345 (36.1)	16,498 (58.6)	202 (55.7)
Parity					
Mean (sd)	0.69 (1.0)	1.02 (1.2)	0.59 (0.9)	1.01 (1.2)	0.96 (1.1)
Educational Level n (%)					
None	3 (0.2)	55 (0.2)	3 (0.3)	52 (0.2)	0 (0.0)
Primary	59 (4.5)	1,353 (4.3)	46 (4.8)	1,185 (4.2)	13 (3.6)
Secondary	782 (59.2)	18,354 (58.8)	578 (60.4)	16,702 (59.3)	204 (56.2)
Tertiary	4 (0.3)	59 (0.2)	4 (0.4)	57 (0.2)	0 (0.0)
Missing	472 (35.8)	11,402 (36.5)	326 (34.1)	10,183 (36.1)	146 (40.2)
Mother's Age					
Mean (sd)	24.99 (6.2)	25.42 (6.0)	24.67 (6.1)	25.45 (6.0)	25.83 (6.4)
Mother's Age n (%)					
<20 years old	270 (20.5)	5,306 (17.0)	205 (21.4)	4,699 (16.7)	65 (17.9)
20-29 years old	741 (56.2)	18,273 (58.5)	539 (56.3)	16,592 (58.9)	202 (55.7)
30-39 years old	286 (21.7)	7,078 (22.7)	197 (20.6)	6,381 (22.6)	89 (24.5)
>=40 years old	23 (1.7)	566 (1.8)	16 (1.7)	507 (1.8)	7 (1.9)
Race n (%)					
Coloured	732 (55.5)	20,726 (66.4)	505 (52.8)	18,526 (65.7)	227 (62.5)
Black	563 (42.7)	9,906 (31.7)	433 (45.3)	9,108 (32.3)	130 (35.8)
Asian	1 (0.1)	68 (0.2)	0 (0.0)	59 (0.2)	1 (0.3)
White	9 (0.7)	139 (0.5)	7 (0.7)	124 (0.4)	2 (0.6)
Other	15 (1.1)	378 (1.2)	12 (1.3)	357 (1.3)	3 (0.8)
Missing	0 (0.0)	6 (0.0)	0 (0.0)	5 (0.0)	0 (0.0)
Smoking n (%)					
Non-smoking	715 (54.1)	14,201 (45.5)	544 (56.8)	13,061 (46.4)	171 (47.1)
Smokers	278 (21.1)	7,456 (23.9)	190 (19.9)	6,538 (23.2)	88 (24.2)
Missing	327 (24.8)	9,566 (30.6)	223 (23.3)	8,580 (30.5)	104 (28.5)
Booking Facility n (%)					
False Bay Hospital	150 (11.4)	1,887 (6.0)	124 (13.0)	1,675 (5.9)	26 (7.2)
Hanover Park	150 (11.4)	7,437 (23.8)	93 (9.7)	6,798 (24.1)	57 (15.7)
Mitchell's Plain	560 (42.4)	14,411 (46.2)	397 (41.5)	13,009 (46.2)	163 (44.9)
Retreat MOU	460 (34.9)	7,488 (24.0)	343 (35.8)	6,697 (23.8)	117 (32.2)
Booking Year n (%)					
2006	121 (9.2)	2,813 (9.0)	97 (10.1)	2,631 (9.3)	24 (6.6)
2007	497 (37.7)	11,642 (37.3)	357 (37.3)	10,481 (37.2)	140 (38.6)
2008	555 (42.1)	13,497 (43.2)	408 (42.6)	12,118 (43.0)	147 (40.5)
2009	147 (11.1)	3,271 (10.5)	95 (9.9)	2,949 (10.5)	52 (14.3)
Gestation at Booking					
Mean (sd)	24.29 (8.5)	24.78 (8.5)	24.28 (8.6)	24.66 (8.5)	24.32 (8.2)
Gestation at Booking-trimesters n (%)					
1st Trimester	100 (7.6)	2,055 (6.6)	70 (7.3)	1,865 (6.6)	30 (8.3)
2nd Trimester	717 (54.3)	16,675 (53.4)	530 (55.4)	15,253 (54.1)	187 (51.5)
3rd Trimester	503 (38.1)	12,493 (40.0)	357 (37.3)	11,061 (39.3)	146 (40.2)
Gestation at Booking n (%)					
6-11 Weeks	67 (5.1)	1,502 (4.8)	50 (5.2)	1,361 (4.8)	17 (4.7)
12-17 Weeks	258 (19.6)	5,307 (17.0)	189 (19.8)	4,901 (17.4)	69 (19.0)
18-23 Weeks	324 (24.6)	7,949 (25.5)	238 (24.9)	7,281 (25.8)	86 (23.7)
24-29 Weeks	287 (21.7)	7,177 (23.0)	202 (21.1)	6,457 (22.9)	85 (23.4)
30-35 Weeks	217 (16.4)	4,882 (15.6)	148 (15.5)	4,242 (15.1)	69 (19.0)
36-42 Weeks	167 (12.7)	4,406 (14.1)	130 (13.6)	3,937 (14.0)	37 (10.2)
Delivery Facility n (%)					
False Bay Hospital	17 (1.3)	806 (2.6)	14 (1.5)	746 (2.7)	3 (0.8)
Gugulethu	0 (0.0)	37 (0.1)	0 (0.0)	36 (0.1)	0 (0.0)
Hanover Park	17 (1.3)	5,245 (16.8)	15 (1.6)	4,915 (17.4)	2 (0.6)
Mitchells Plain	52 (3.9)	8,701 (27.9)	36 (3.8)	8,226 (29.2)	16 (4.4)
Retreat MOU	54 (4.1)	4,019 (12.9)	45 (4.7)	3,765 (13.4)	9 (2.5)
Mowbray Maternity Hospital	369 (28.0)	5,163 (16.5)	301 (31.5)	4,428 (15.7)	68 (18.7)
Somerset Hospital	70 (5.3)	1,630 (5.2)	57 (6.0)	1,422 (5.1)	13 (3.6)
Groote Schuur Hospital	741 (56.1)	5,622 (18.0)	489 (51.1)	4,641 (16.5)	252 (69.4)

SD, Standard Deviation
IQR, Inter-quartile Range

Tables 11-13 analyse the relationship between predictor variables and the different outcome variables: caesarean section, low birth weight, and low 1-minute APGAR scores. Frequencies are presented for all births and stratified according to whether or not the birth was preterm. Table 11 shows that education, mother's age, race, smoking status, booking facility, delivery facility, and gestation at booking are all associated with having a caesarean section, indicating

they could be potential confounders. A majority of women who did not have caesarean sections were in the younger two age groups. Additionally, women who do not have caesarean section tend to book later in their gestation.

Table 12 demonstrates that education, race, booking year, gestation at booking and delivery facility are all associated with birth weight. A greater proportion of low birth weight infants are coloured and booked in the 3rd trimester— specifically, 30-35 and 36-42 weeks— compared to normal birth weight infants. A smaller proportion of low birth weight infants booked in 2007 compared to normal birth weight infants. A greater proportion of preterm infants are low birth weight infants who had a low birth weight compared to full term infants. Preterm infants also had a lower mean gestation at booking among low birth weight infants.

Table 13 suggests that parity, race, booking facility, smoking, and delivery facility may confound the relationship between gestation at booking and low 1-minute APGAR scores since they are all associated with low 1-minute APGARs. A higher proportion of pregnancies that result in low APGAR scores occur among nulliparous mothers. Preterm infants also have a higher proportion of low APGAR scores compared to full term infants.

Based on the stratified analyses, the sample-size was limited to full term pregnancies since preterm pregnancies are usually associated with adverse outcomes. Additionally, the excess of pregnancies that booked at 40 weeks, made it hard to continue to look at preterm status as an outcome or predictor variable.

3.5 Additional Regression Analyses

Table14 shows the crude analysis for odds of stillbirths when gestation at booking was categorized into six levels. In both the unadjusted model and the different adjusted models, no category of gestation at booking ever produces a significant OR. This only reinforces the findings presented in Part C: Manuscript. In the adjusted model, booking at any time in the pregnancy is protective of stillbirths. Black people have twice the risk of having a stillbirth compared to coloured people (OR 2.01; 95% CI: 1.31-3.08). Additionally, each year increase in a mother's age results in a 3% increase in odds of a stillbirth (OR 1.03; 95% CI: 1.00-1.07).

Table 14: Crude models for odds of stillbirths using GAB (6 levels)

Variables	Model 1	Model 1	Model 3	Model 4	Model 5	Model 6
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
n	27,713	27,713	27,713	27,713	27,713	27,713
Gestation at Booking						
6-11 Weeks (ref)	1.00	1.00	1.00	1.00	1.00	1.00
12-17 Weeks	0.75 (0.32-1.80)	0.75 (0.32-1.80)	0.76 (0.32-1.81)	0.77 (0.32-1.84)	0.75 (0.31-1.78)	0.75 (0.32-1.79)
18-23 Weeks	0.69 (030-1.60)	0.69 (0.30-1.60)	0.70 (0.31-1.63)	0.73 (0.31-1.68)	0.65 (0.28-1.50)	0.65 (0.28-1.52)
24-29 Weeks	1.13 (0.50-2.54)	1.13 (0.50-2.54)	1.14 (0.51-2.56)	1.18 (0.53-2.65)	0.97 (0.43-2.19)	0.98 (0.43-2.21)
30-35 Weeks	1.07 (0.46-2.49)	1.07 (0.46-2.48)	1.08 (0.46-2.51)	1.13 (0.49-2.64)	0.92 (0.39-2.15)	0.93 (0.39-2.18)
36-37 Weeks	0.94 (0.30-2.98)	0.94 (0.30-2.98)	0.99 (0.31-3.14)	1.02 (0.32-3.25)	0.85 (0.27-2.70)	0.87 (0.27-2.76)
Parity						
Nulliparous		1.00	1.00	1.00	1.00	1.00
Primi/Multiparous		0.98 (0.68-1.41)	1.00 (0.69-1.45)	1.29 (0.83-1.99)	1.19 (0.77-1.84)	1.20 (0.77-1.86)
Education						
None or Primary (ref)			1.00	1.00	1.00	1.00
Secondary or Tertiary			0.66 (0.33-1.32)	0.70 (0.35-1.41)	0.67 (0.33-1.35)	0.68 (0.34-1.37)
Missing			0.51 (0.24-1.08)	0.54 (0.26-1.14)	0.53 (0.25-1.11)	0.76 (0.32-1.84)
Mother's Age (continuous)				1.04 (1.00-1.07)	1.03 (1.00-1.07)	1.03 (1.00-1.07)
Race						
Coloured (ref)					1.00	1.00
Black					1.97 (1.35-2.87)	2.01 (1.31-3.08)
White, Asian, Other					2.44 (0.88-6.79)	2.41 (0.86-6.79)
Smoking						
Non-smoking (ref)						1.00
Smoking						1.10 (0.66-1.84)
Missing						0.61 (0.30-1.26)

OR, Odds Ratio

Tables 15-17 show crude adjusted models for low birth weight, caesarean sections, and low 1-minute APGAR scores. In each of the tables, the analysis of caesarean sections is limited to nulliparous women, since a common indication for caesarean sections is having a previous caesarean section. Table 15 analyzes the odds of each outcome when gestation at booking is analysed continuously. There is a 1% increase in odds of having a low birth weight infant for each week increase in the gestation at booking (OR 1.01; 95% CI: 1.00-1.02). For each week increase in gestation at booking there is also a 1% decrease in odds of having a caesarean section and low 1-minute APGAR score (OR 0.99; 95% CI: 0.98-1.00 and 0.98-0.99, respectively).

Table 16 shows that there is no significant effect of gestation at booking on odds of having a low birth weight infant, although the third trimester appears to have a harmful effect (OR 1.13; 95% CI: 0.92-1.38). Additionally, booking in the second trimester reduces a woman's odds of having a caesarean section by 15% compared to first trimester (OR 0.85; 95% CI: 0.70-1.02) and doing so in the third trimester reduces a woman's odds by 20% (OR 0.80; 95% CI: 0.65-0.97). Furthermore, booking in the third trimester is also protective of low 1-minute APGAR scores, although not significantly (OR 0.77; 95% CI: 0.59-1.02).

Finally, Table 17 demonstrates that when gestation at booking is broken down into six levels, there is no significant effect on low birth weight or low 1-minute APGAR scores. However, there is a significant protective effect of booking at 18-23 weeks or 30-35 weeks on having caesarean sections (OR 0.77; 95% CI: 0.62-0.97 and OR 0.76; 95% CI: 0.59-

0.97, respectively). It is likely that there was not sufficient power in each of the levels of gestation at booking, to produce significant results.

Table 15: Crude models for odds of birth and delivery outcomes using GAB (continuous)

Variables	Low Birth Weight	Caesarean Sections	1-minute APGAR Scores
	OR (95% CI)	OR (95% CI)	OR (95% CI)
n	27,713	11,918	26,083
Gestation at Booking (continuous)	1.01 (1.00-1.02)	0.99 (0.98-1.00)	0.99 (0.98-0.99)
Parity			
Nulliparous	1.00		1.00
Primi/Multiparous	1.48 (1.31-1.67)		2.80 (2.36-3.33)
Education			
None or Primary (ref)	1.00	1.00	1.00
Secondary or Tertiary	0.83 (0.66-1.05)	0.93 (0.69-1.25)	0.69 (0.50-0.94)
Missing	1.08 (0.82-1.42)	1.30 (0.93-1.82)	1.17 (0.82-1.68)
Mother's Age (continuous)	1.03 (1.02-1.04)	1.08 (1.07-1.10)	1.02 (1.01-1.03)
Race			
Coloured (ref)	1.00	1.00	1.00
Black	0.66 (0.58-0.75)	1.62 (1.45-1.82)	1.58 (1.35-1.85)
White, Asian, Other	0.40 (0.24-0.67)	1.49 (1.07-2.07)	1.20 (0.74-1.95)
Smoking			
Non-smoking (ref)	1.00	1.00	1.00
Smoking	1.47 (1.29-1.68)	0.84 (0.73-0.97)	0.94 (0.77-1.14)
Missing	1.09 (0.89-1.33)	0.39 (0.33-0.48)	0.48 (0.37-0.62)

OR, Odds Ratio

Table 16: Crude models for odds of birth and delivery outcomes using GAB (trimesters)

Variables	Low Birth Weight	Caesarean Sections	1-minute APGAR Scores
	OR (95% CI)	OR (95% CI)	OR (95% CI)
n	27,713	11,918	26,083
Gestation at Booking			
1st Trimester (ref)	1.00	1.00	1.00
2nd Trimester	1.00 (0.82-1.21)	0.85 (0.70-1.02)	0.85 (0.66-1.10)
3rd Trimester	1.13 (0.92-1.38)	0.80 (0.65-0.97)	0.77 (0.59-1.02)
Parity			
Nulliparous	1.00		1.00
Primi/Multiparous	1.48 (1.31-1.67)		2.82 (2.37-3.35)
Education			
None or Primary (ref)	1.00	1.00	1.00
Secondary or Tertiary	0.84 (0.66-1.05)	0.93 (0.69-1.26)	0.69 (0.50-0.94)
Missing	1.08 (0.82-1.42)	1.30 (0.93-1.82)	1.17 (0.82-1.68)
Mother's Age (continuous)	1.03 (1.02-1.04)	1.08 (1.07-1.10)	1.02 (1.01-1.03)
Race			
Coloured (ref)	1.00	1.00	1.00
Black	0.66 (0.58-0.75)	1.60 (1.43-1.79)	1.56 (1.33-1.82_
White, Asian, Other	0.40 (0.24-0.67)	1.48 (1.06-2.05)	1.19 (0.73-1.93)
Smoking			
Non-smoking (ref)	1.00	1.00	1.00
Smoking	1.47 (1.29-1.68)	0.84 (0.73-0.97)	0.93 (0.77-1.13)
Missing	1.09 (0.89-1.34)	0.39 (0.32-0.48)	0.48 (0.37-0.61)

OR, Odds Ratio

Table 17: Crude models for odds of other birth and delivery outcomes using GAB (6 levels)

Variables	Low Birth Weight	Caesarean Section	1-minute APGAR Scores
	OR (95% CI)	OR (95% CI)	OR (95% CI)
n	27,713	11,918	26,083
Gestation at Booking			
6-11 Weeks (ref)	1.00	1.00	1.00
12-17 Weeks	1.02 (0.80-1.31)	0.91 (0.72-1.15)	1.00 (0.73-1.38)
18-23 Weeks	1.09 (0.86-1.29)	0.77 (0.62-0.97)	0.81 (0.59-1.11)
24-29 Weeks	1.09 (0.86-1.39)	0.80 (0.64-1.01)	0.75 (0.54-1.03)
30-35 Weeks	1.17 (0.91-1.51)	0.76 (0.59-0.97)	0.87 (0.62-1.21)
36-37 Weeks	1.32 (0.96-1.82)	0.84 (0.60-1.17)	0.82 (0.52-1.31)
Parity			
Nulliparous	1.00		1.00
Primi/Multiparous	1.48 (1.31-1.67)		2.82 (2.37-3.35)
Education			
None or Primary (ref)	1.00	1.00	1.00
Secondary or Tertiary	0.83 (0.66-1.05)	0.93 (0.69-1.26)	0.69 (0.51-0.95)
Missing	1.08 (0.82-1.42)	1.30 (0.93-1.82)	1.18 (0.82-1.69)
Mother's Age (continuous)	1.03 (1.02-1.04)	1.08 (1.07-1.09)	1.02 (1.01-1.03)
Race			
Coloured (ref)	1.00	1.00	1.00
Black	0.66 (0.58-0.75)	1.62 (1.45-1.81)	1.58 (1.35-1.85)
White, Asian, Other	0.40 (0.24-0.67)	1.48 (1.07-2.06)	1.20 (0.74-1.95)
Smoking			
Non-smoking (ref)	1.00	1.00	1.00
Smoking	1.47 (1.29-1.68)	0.84 (0.73-0.97)	0.94 (0.77-1.14)
Missing	1.09 (0.89-1.33)	0.40 (0.33-0.48)	0.48 (0.37-0.62)

OR, Odds Ratio