ADVERSE OUTCOMES OF PREGNANCY IN POTCHEFSTROOM, SOUTH AFRICA

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A Research Report submitted to the Faculty of Health Sciences, University of Witwatersrand, in partial fulfilment of the requirements for the degree of Masters in Medicine in the speciality of Community Health

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Declaration

I, Ziyanda Vundle, declare that this report is my own work. It is being submitted for the degree of Masters in Medicine in Community Health, as applicable, in the University of Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this university or any other university.

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Ziyanda Vundle

On the 30th day of October 2009

Dedication

To my mother, Nokwazi Zettie Vundle, who has been the my pillar of strength throughout my life; who has nurtured and guided me; who has instilled in me discipline, responsibility, independence and self sufficiency; while making sure that I remain true to myself and my roots, and achieve my successes with humility.

To my siblings, Daluxolo, Lungile and Fezeka, who supported me during my quests for successes; who sacrificed their desired achievements to ensure my successes and who continue to provide a family unit that I would never trade for anything.

I have met and continue to meet different people from all walks of life who inspire me in different ways. All of these people contribute to the values and principles by which I live. These values and principles have made me who I am and continue to mould me, and have contributed directly or indirectly to the successes of my life.

To you all, I am eternally grateful, I value your individual contributions with the unique level of appreciation that they deserve; and I value the collective nature of intellectual and emotional resources that your contributions continue to provide.

Enkosi! Nangamso! Zanga iinkomo zenu zingazala amathokazi!

ABSTRACT

Introduction

Adverse outcomes of pregnancy are global health problems that are much more pronounced in developing countries. The risk factors associated with adverse outcomes of pregnancy are multifactorial. In South Africa, the population prevalence and associated risk factors of maternal and perinatal mortality are routinely documented, but there are gaps in the data on other pregnancy adverse outcomes. This study was aimed at determining the prevalence rates and related risk factors of preterm births and pregnancy loss in an urban population in South Africa.

Methods

The study was a cross-sectional analytical community study of women 18 to 49 years of age, living in the Potchefstroom municipality. It was conducted from August 2007 to April 2008. Participants were selected using a systematic random sampling strategy; 1 210 women participated. An adapted reproductive health questionnaire was used to collect socio-demographic, environmental, occupational and reproductive health data.

Results

Prevalence of pregnancy loss and preterm births were estimated to be 5.6% [95% CI: 5.57% - 5.63%] and 13.4% [95% CI: 13.36% - 13.44%], respectively. Pregnancy loss was associated with psychological stress and working during pregnancy; preterm birth was associated with White, Coloured and Indian race, primary and high school education, psychological stress and chronic disease; and antenatal care use was protective against both pregnancy loss and preterm birth.

Conclusion

The prevalence of pregnancy loss found in this study was lower than would be expected in the general South African population; while the preterm birth prevalence, although lower than that of other developing and middle income countries, could be improved. Generally, there are common risk factors for pregnancy loss and for preterm births. Some of the existing evidence on risk factors was supported by the findings of this study. Improvement of surveillance and health information systems for pregnancy loss and preterm births would provide essential information on the burden of these outcomes in South Africa and would subsequently guide policy, research and prioritisation of effective control programmes.

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CHAPTER ONE

1. INTRODUCTION

1.1. Background

Reproductive health has often been described as a crucial aspect of general health, and as being central to human development.[1] The definition of reproductive health as "the state of complete physical, mental, and social well being and not merely the absence of disease or infirmity, in all matters related to the reproductive system and to its functions and processes" was adopted in the Programme of Action of the International Conference on Population and Development (ICPD) in 1994, and was endorsed by the United Nations General Assembly.[1-3] Embodied in this definition is the right of women to access appropriate health care services that will enable them to progress safely through pregnancy and child birth while providing them with the best chance of delivering a healthy infant.[2]

One of the commitments of the World Health Organisation's (WHO) work on reproductive health is to ensure that women who choose to have children, have their desired number of children safely and healthily.[1] This commitment, which is further emphasized in the Millennium Declaration adopted in 2000, can also be found in goal five of the Millennium Development Goals (MDG).[4] This goal recognises that adequate maternal health services are essential in improving overall maternal health and reducing maternal mortality. [4] Despite these commitments made by the international community to

make pregnancy safer, pregnancy related problems still persist with greater burdens experienced by the developing countries.[5]

Pregnancy is a normal and unique physiological state that involves at least two individuals – the woman and the unborn child. Most women desire to be pregnant at some point in their lives.[6, 7] Once pregnancy has occurred, diagnosis thereof rarely poses a problem as the signs and symptoms of pregnancy are usually evident, even to the expectant mother.[8] While, in most cases, having a baby is a positive and fulfilling experience, pregnancy and childbirth can also be associated with a spectrum of adverse outcomes such as physical and emotional suffering, ill health or even death for both mother and child.

1.2. Problem statement

Adverse outcomes of pregnancy in developing countries, such as South Africa, far outweigh those of developed countries where most pregnancies are planned, complications are few and outcomes are generally favourable for both mother and infant.[9] Pregnancy adverse outcomes that have been reported include: foetal loss (abortions, stillbirth), preterm birth, low birth weight or small for gestational age, congenital abnormalities, childbirth complications, and perinatal and/or maternal death.[10] The extremes of this spectrum of adverse outcomes of pregnancy are the death of a mother and the child. These worst outcomes are often recorded and monitored at global and regional levels, with many commitments and interventions targeted at addressing and reducing them.

However, there seems to be a lack of data related to quantifying the extent and factors associated with non-mortality related adverse outcomes of pregnancy at a regional and or broader global level, especially in developing countries like South Africa. Non-mortality related adverse outcomes of pregnancy are often precursors of the mortality related adverse outcomes of pregnancy, and their associated risk factors are often the same as those of the mortality related adverse outcomes of pregnancy. Therefore, in order to fully address the mortality outcomes, there needs to be insight into the extent of non-mortality related adverse outcomes of pregnancy and their associated risk factors. This study was aimed at determining the prevalence and related risk factors for adverse outcomes of pregnancy, focusing specifically on preterm birth and pregnancy loss.

1.3. Motivation for the study

In South Africa, the population prevalence of some of these adverse pregnancy outcomes is routinely documented in publications such as "Saving Babies: A Perinatal Care Survey of South Africa", "Saving Mothers: A confidential enquiry into maternal deaths" and "Every death count: Saving the lives of mother, babies and children in South Africa." [7, 11-13] However, these publications report maternal and perinatal mortalities, and factors associated with these mortalities; they do not report on other adverse outcomes of pregnancy. The South African Demographic and Health Survey (SADHS) measures other aspects of reproductive health such as fertility, contraceptive use, and maternal mortality, but also does not report on other adverse pregnancy outcomes.[14]

When other adverse outcomes of pregnancy are reported in these publications, they are often reported as exposures that contribute to the mortality outcomes. Therefore, the figures usually reflect the contributions of these outcomes to the mortality outcomes. An illustration of this can be seen in the "Saving Babies: A Perinatal Care Survey of South Africa" report where a mention on preterm births is in relation to how many of the perinatal deaths are attributed to preterm births.[7] This study presented here aimed to address some of these gaps in the data by determining the prevalence rates and related risk factors of foetal adverse outcomes of pregnancy in an urban population in South Africa. The findings of this study provide relevant information on adverse outcomes of pregnancy, at a population level, for targeted planning of maternal and child health services, to make pregnancy safer and to improve foetal outcomes.

1.4. Literature review

The literature review for this study was done using Google, Google Scholar and PubMed search engines. Combinations of search words were used and, in general, each variable and outcome was searched separately for most of the exposures and outcomes of interest. The literature review was initially limited to resources published in the last 10 years. However, due to limited information on the topics of interest published in the last decade, the review was extended to include publications in the last 20 years. The resources used for reference included scientific journal articles, policy documents, guidelines, reports and other resources that could be accessed through the university subscriptions, either electronically or by requesting hard copies of what could not be accessed electronically.

Worldwide, approximately 210 million women become pregnant annually; 130 million of these pregnancies result in live infant births, while the remaining 80 million result in foetal loss (stillbirths or abortions).[15] Pregnancy loss can occur at any stage of pregnancy and, although its classification is complex, pregnancy loss can generally be classified into early embryonic loss, early foetal loss and late foetal loss.[16] This classification includes miscarriages that occur before clinical detection (usually in the first 12 weeks of gestation), clinically detected miscarriages (from 12 to 24 weeks of gestation), and stillbirths (after 24 weeks of gestation).[16] Fetuses may die in utero, before onset of labour, because of pregnancy complications or maternal diseases. However, no particular cause can be identified for many antepartum intrauterine deaths.[17]

Despite the broader classification of pregnancy loss, reports on prevalence and risk factors for pregnancy loss are often in reference to either miscarriages or stillbirths, but never to the two outcomes combined. Stillbirths can occur either before onset of labour (antepartum death) or during labour (intrapartum death). In 2000, the stillbirth rate was estimated to be 24 per 1000 births worldwide and 32 per 1000 births in Africa.[17] In South Africa, the stillbirth rate was estimated to be 18 per 1000 births.[17] Approximately 10% to 20% of all pregnancies are estimated to result in foetal loss due to spontaneous abortion.[18,19] The majority (50% to 60%) of these spontaneous abortions are as a result of chromosomal abnormalities and single gene mutations, while the remainder are associated with structural uterine abnormalities, endocrine abnormalities, immunologic factors, genital infections, cigarette smoking, alcohol use, psychological stress, various environmental and occupational exposures, and advanced maternal age.[20]

Even though spontaneous abortions account for a much higher percentage of reproductive failure than do congenital malformations, a very high proportion of spontaneously aborted foetuses are malformed or defective. Congenital abnormalities occur during the embryonic or foetal developmental stages, and occur in 3% to 6% of the general population.[21, 22] These congenital abnormalities occur as a result of a combination of factors. More than 65% to 75% of congenital abnormalities are due to unknown causes; genetic causes account for 20% to 25% of these, while maternal disease states, maternal infections, mechanical factors, problems of constraint, chemicals, drugs, and physical agents account for 10%.[22-24]

Once the infant has been born alive, it still faces numerous challenges that may influence its chances of survival, depending on the size of the infant at birth and the timing of delivery. Low birth weight is the result of either preterm birth or restricted foetal growth (intrauterine growth retardation). Birth weight is affected, to a great extent, by the mother's own foetal growth, her nutritional and developmental milestones from birth to pregnancy, and as her body composition at conception. More than 20 million infants worldwide, representing 15.5% of all births, are born with low birth weight, 95.6% of which are in developing countries. The level of low birth weight in developing countries (16.5%) is more than double that in developed regions (7%). In South Africa, low birth weight was estimated to be 15% in 2000.[25]

Preterm births, on the other hand, have been estimated to be as high as 12.8% in developed countries like the United States. [26] In South Africa, the prevalence of preterm births as an outcome has not been estimated. However, spontaneous preterm birth as a risk factor for perinatal death has been estimated to account for 80% of all immaturity related perinatal deaths in South Africa.[7] The aetiology of preterm birth is multifactorial and include premature contractions, premature rupture of membranes and maternal or foetal indications. Factors contributing to preterm birth include psychosocial factors, sociodemographic factors, socioeconomic factors (such as income and education), maternal lifestyle and behavioural factors (such as cigarette smoking), exposure to environmental pollutants (such as pesticides and other toxicants), work related psychological stress and ergonomic related stressors (such as lifting of heavy loads).[17, 27]

Low birth weight and preterm births are important adverse outcomes of pregnancy as they are both significant in determining neonatal morbidity and mortality, inhibited growth and cognitive development, and chronic diseases later in life.[28]

Maternal mortality remains a major adverse outcome of pregnancy, especially in developing countries. According to the WHO, approximately eight million women suffer pregnancy related complications and half a million die every year, worldwide.[6,29,30] These statistics are worse in developing countries where it has been estimated that one in 16 women die of pregnancy related complications, compared to one in 2 800 women in developed countries.[6,11,31] Each year in Africa, 30 million women become pregnant, 700 000 die of pregnancy related causes, 3 100 newborns die and another 2 400 are

stillborn.[11] In South Africa, a confidential enquiry into maternal deaths, in the period 2002 to 2004, estimated that complications of pregnancy and childbirth lead to 1 600 maternal deaths; literature published in 2006 estimated that these complications lead to 20 000 stillbirths and 22 000 neonatal deaths annually.[32]

Adverse outcomes of pregnancy can be broadly categorized into maternal and foetal outcomes. Maternal adverse outcomes include ectopic pregnancy, medical conditions resulting from pregnancy (e.g. postpartum infection, thrombo-embolism), psychiatric conditions (postnatal psychosis, postnatal depression), physical disabilities (e.g. symphysis pubis dislocation), injuries to the genital tract, and maternal death. Foetal adverse outcomes include miscarriage/spontaneous abortion, stillbirth, congenital abnormalities, preterm birth, low birth weight, and neonatal death.

The focus of this study was to examine foetal adverse outcomes of pregnancy only, with specific focus on pregnancy loss and preterm births. As the literature review revealed a significant gap in scientific information on the estimates and risk factors of these outcomes, the results of this study provided much needed information on these often neglected adverse outcomes in South Africa.

Risk factors for adverse outcomes of pregnancy

Risk factors contributing to adverse outcomes of pregnancy are multifactorial and can be broadly categorized into maternal and health system risk factors.

a. Maternal risk factors

Maternal age

Both advanced maternal age and teenage or adolescent pregnancy are risk factors for adverse pregnancy outcomes. Advanced maternal age is defined as the age of an expected mother of 40 years or more at delivery. The older the pregnant woman, the more likely she is to have pre-existing medical conditions such as diabetes, hypertension, other endocrine diseases and other medical conditions. In addition, the risk of chromosomal abnormalities increases with increasing age. Many studies have shown an increased risk of preterm births, spontaneous abortions, ectopic pregnancies and stillbirths with increasing age, irrespective of reproductive history.[28,33] Advanced maternal age has become an increasingly important factor in recent years as more women postpone child bearing as a result of social, educational and economic factors.[33] Teenage and adolescent pregnancy, on the other hand, is also an independent risk factor for adverse outcomes of pregnancy, particularly foetal growth retardation and preterm birth.[35,36] The risks associated with teenage and adolescent pregnancy are often a consequence of biological immaturity complicated by socioeconomic deprivation.[36]

Medical history

Pre-existing maternal medical conditions and conditions acquired during pregnancy (e.g. hypertension, diabetes, syphilis, HIV/AIDS) increase the risk of adverse outcomes of pregnancy for both mother and infant.[17,28] Pre-eclampsia affects around three percent of pregnant women and accounts for 25% of all babies with low birth weight.[37] A review of the literature reveals that the incidence of gestational diabetes varies from one to five percent, while pre-existing diabetes accounts for 0.2% to 0.3% of all diabetes in pregnancy.[38] Failure to diagnose diabetes early and poor diabetes management in pregnancy is associated with increased risk of foetal loss, congenital abnormalities and other neonatal complications.[38] Sexually transmitted infections, such as syphilis, still pose a heavy burden on health in developing countries, such as South Africa, and are associated with adverse outcomes of pregnancy, including spontaneous abortions, distortion of the morphology of the fallopian tubes (which increases the risk of ectopic pregnancy), stillbirths and congenital malformations.[39] The national syphilis and HIV seroprevalence in 2007 amongst pregnant women attending antenatal care in South Africa was estimated at 2.9% and 28%, respectively.[40] HIV infected women are more likely than uninfected women to experience adverse pregnancy outcomes such as foetal loss, preterm birth, low birth weight, congenital abnormalities and perinatal and maternal morbidity and mortality.[12,40,41] There is also growing evidence of an independent association between psychological stress and adverse outcomes of pregnancy.[42]

Obstetric factors

Previous obstetric history plays a major role in the occurrence or recurrence of certain adverse outcomes. For example, women with previous histories of ectopic pregnancies, abortions or preterm births have an increased risk of having another ectopic pregnancy, abortion or preterm birth in their next pregnancy, compared to women without a prior history of these events.[8, 39]

Lifestyle and behavioural factors

Lifestyle and behaviours may negatively affect the developmental process of the foetus in a number of ways.[43] Lifestyle choices, such as cigarette smoking and alcohol consumption, have been shown to negatively affect the developing foetus, resulting in a number of adverse outcomes of pregnancy, including preterm births, pregnancy loss and congenital malformations.[19,24,44] Socio-cultural factors often influence the different health seeking behaviours of women and these are also likely to influence birth outcomes.[45] There are a number of examples of this. Opting for family planning has been shown to reduce adverse outcomes by reducing the frequency of high risk pregnancies and unsafe abortions. Planned pregnancies have fewer complications and more favorable outcomes for both mother and infant than unplanned pregnancies. Unplanned pregnancies have a higher risk of preterm birth, low birth weight, and infant and maternal morbidity and mortality. Antenatal care attendance reduces the risk of preterm births, low birth weight and perinatal deaths.[9, 45, 46]

Socioeconomic factors

In most instances, however, the above-mentioned health seeking behaviours are influenced by more than just individual choices or socio-cultural practices. Health seeking behaviours can be influenced by other socioeconomic factors, such as income, education, employment, health systems and other determinants of health.[47] Individual family and neighbourhood income have been shown to have an impact on pregnancy outcomes; lower income quintiles are associated with an increased risk of adverse pregnancy outcomes.[47] Although income level is often used as a surrogate measure for socioeconomic status, level of education and employment status are also important socioeconomic factors that influence pregnancy outcomes. Women with low levels of education and those who are unemployed are more likely to experience adverse pregnancy outcomes.[48]

Environmental and occupational exposures

Although employment can be viewed as a means to improve the livelihoods of the women by improving their socioeconomic status, it may also pose a threat to pregnancy outcomes. Occupational exposures such as certain chemicals, ergonomic factors, and work stress have been associated with an increased risk of adverse pregnancy outcomes.[49, 50] In addition; the occupational environment often has an impact on the general environment through emissions of by-products into the environment.[19]

b. Health system risk factors

Prenatal and delivery care have been identified as important determining factors for adverse outcomes of pregnancy.[45] The rationale for providing antenatal care is to screen pregnant women to detect early signs of, or risk factors for, abnormal conditions or diseases during pregnancy, and to follow this detection with effective and timely intervention to improve the health and well being of both mother and child.[45,51] Diseases such as anaemia, syphilis, HIV and preeclampsia can be detected during antenatal care and managed timeously to prevent adverse outcomes of pregnancy associated with these conditions.[12, 51] Studies have illustrated an association between antenatal care and reduction in the occurrence of adverse outcomes of pregnancy such as premature birth, low birth weight and intrauterine death.[10,51,52] Antenatal care has also been linked to an opportunity of delivery assisted by a skilled health care worker.[51] However, this seems not to be the case in Sub-Saharan Africa where the levels of antenatal care use are consistently higher than those of delivery care by skilled health professionals.[51] This discrepancy has been attributed to a number of factors, including the quality of antenatal care provided and antenatal care focused maternal health programmes at the detriment of delivery care or care for the management of obstetric complications.[51]

In addition to antenatal care, attendance by a skilled birth attendant and access to emergency obstetric care during pregnancy, delivery and the perinatal period have been shown to decrease maternal and perinatal morbidity and mortality.[30,53] A model of continuum of care, proposed through the “making pregnancy safer initiative”, emphasises the principle that all women should have the highest attainable standard of health,

through the best possible care before and during pregnancy, childbirth, and the postpartum period.[54] Implementation of this model is vital in reducing maternal and perinatal morbidity and mortality at different levels through access to family planning, antenatal care, care provided by a skilled birth attendant at delivery, and access to postnatal services.[54] Key factors for prenatal and delivery care are the availability, affordability, accessibility and acceptability of good quality health care during pregnancy and the perinatal period.

2. AIMS AND OBJECTIVES

2.1 Aims of the study

The aim of this study was to determine the prevalence and related risk factors of selected foetal adverse outcomes of pregnancy, in the Potchefstroom municipality from August 2007 to March 2008.

2.2 Objectives of the study

1. To describe the participants in the study according to demographic, lifestyle, socioeconomic, medical and obstetric characteristics.
2. To determine the prevalence of selected adverse outcomes of pregnancy, viz. pregnancy loss and preterm birth.
3. To investigate maternal factors associated with these adverse pregnancy outcomes, such as:
   - Demographic
   - Lifestyle
   - Socioeconomic
   - Medical and obstetric factors.
4. To make recommendations for a public health intervention.

CHAPTER TWO

METHODS

2.1 Setting

The study was conducted in the Potchefstroom municipality in the North West Province of South Africa. Potchefstroom is a major city with approximately 128 357 people, with the female population accounting for 51% (65 225) of its general population.[55] Women of reproductive age (15 to 49 years) account for 58% (38 184) of the female population.[55] Potchefstroom is predominantly a university town but is also home to industries such as engineering, constructions and agriculture.

2.2 Study design

The study was a cross-sectional study of women living in the Potchefstroom municipality. This study is the second of two parts of a larger epidemiological reproductive health project of the Epidemiology unit of the National Institution for Occupational Health (NIOH). The first part of the project is focused on determining the distribution of fecundity –using the concept of *time to pregnancy* (TTP) – in a South African population, and a description of fertility and contraceptive use in the population.

2.3 Study population

The study population comprised women of reproductive age from the ages of 18 to 49 years, living in the Potchefstroom municipality in 2007. For the purpose of this study the

women were stratified according to race and selected to ensure inclusion and adequate representation of all race groups in the municipality. The race classification is as per race groups in Potchefstroom registered with statistics South Africa.

2.4 Sampling and sample size determination

The sample size calculation for this study was done by evaluating the expected prevalence of the outcomes in the larger reproductive health study. In order to increase the power of the study and to enable measurement of most adverse outcomes, prevalence of pregnancy adverse outcomes reported in developed countries was used as they have lower rates compared to developing countries. The prevalence of pregnancy adverse outcomes in developed countries ranges from 3% to 12.8% (3% to 6% for congenital abnormalities, 0.6% for stillbirths, 7% for low birth weights, 10% to 20% for spontaneous abortions and 12.8% for preterm births).[17-19,21,22,25,26] Therefore, the median prevalence of 7% for pregnancy adverse outcomes was used to calculate the sample size.

Sample size calculation, based on an estimated prevalence of 7% for pregnancy adverse outcomes with +/-1.5% precision at a 95% confidence level, led to a sample size of 1 079. To ensure reliable stratum-specific estimates for the different racial groups, the Indian and Coloured women were oversampled by 20% as they are the minority groups in this population. This led to an effective sample size of 1 093.

To achieve the required sample size, sampling was initially planned to be done without replacement; while accounting for non responders. We selected a non response rate of 20%. This led to a probable sample size of 1 312. However, systemic random sampling

without replacement was not feasible in the field due to some logistical difficulties such as absence of eligible women in a selected household, refusal to participate by eligible women in a selected household, and refusal of access to enter a selected household. Therefore, to achieve an effective sample size of 1 093, the sampling strategy used was systemic random sampling with replacement. This means that the adjacent household was selected in the case of an unsuccessful interview on the first selected household. The following household was identified using the sampling interval and the replacement household as a reference point. This process was carried out in all the wards until all consenting eligible women in each ward, within the specific sampling intervals were interviewed. The total number of women who participated in the study was 1 210.

Table 1: Racial distribution of women of reproductive age in the Potchefstroom population, the required sample and the participants of the study

Race Group	Population [55] N (%)	Required Sample N (%)	Participants N (%)
African	27 286 (71.5)	771 (70.5)	779 (64.4)
White	8 305 (21.7)	234 (21.4)	241 (19.9)
Colored	2 458 (6.4)	83 (7.6)	159 (13.1)
Indian	135 (0.4)	5 (0.5)	31 (2.6)
Total	38 184 (100)	1 093 (100)	1 210 (100)

Sampling in this study was designed to be representative of the Potchefstroom population of women of reproductive age. This study employed a sampling strategy at various levels. First, all 21 wards in the municipality were included in the study. Second, a systematic random sampling strategy was used in all the 21 wards to select households. To ensure

racial representation, the wards were stratified according to race as they serve well as a proxy for race. In wards that were of mixed race, sampling was done proportionally, according to the number of participants, per race group, that would be required from that ward. Therefore, the number of women sampled in each ward was proportional to the number of eligible women in each race group within the ward. Systematic random sampling was then carried out in each of the 21 wards to select the households.

Households were the sampling units used for the study, where a household included all the persons who occupy a house, apartment, group of rooms or a single room that is considered a housing unit. For each ward, a sampling interval (SI) was calculated (SI = number of households/sample size); this number was different for each ward. The first assessed house was the random starting point from which other households were systematically selected. After the first household has been assessed, every nth house along the same street in a straight line was then assessed according to the SI. All eligible women within each selected household were offered the opportunity to participate in the survey.

2.5 Inclusion criteria

All women in the reproductive age group (18 to 49 years) living in the Potchefstroom district area during the period of the study and who had a history of having been pregnant, or were pregnant at the time of the interview, were included.

2.6 Exclusion criteria

Women who had no history of pregnancy were excluded from the study. Women in the reproductive age 15 to 17 years were also excluded as they were under the legal consenting age

2.7 Measurement

Data collection

The data for the study were collected from August 2007 to April 2008. A European Reproductive Questionnaire (ERQ) adapted, in collaboration with a United Kingdom expert (Prof. Michael Joffe), for the South African population, was piloted in this community. The ERQ focused mainly on fertility factors; its adaptation included the addition of variables that were of interest in this study. A pilot study was done in 2006 in the same population to assess the practical logistical planning for the main study; 150 volunteers participated. The pilot study also included taking urine and blood samples to measure pesticide levels in the participants. Sample collection proved to be logistically difficult and was not included in the main study. The field experiences of administering the pilot questionnaire led to the main study questionnaire being refined.

The questionnaire used in this study is part of the full reproductive health questionnaire used in the larger study (Appendix 2), which has been translated and back translated (English – Setswana/ Afrikaans) by two translators. The questionnaire was administered in the language best understood by the participant (English, Setswana or Afrikaans). The team involved in the administration of the questionnaires included the research team and

trained interviewers. The interviewers, who were members of the community and individuals usually employed by Potchefstroom University in their research projects, were trained by the research team during the pilot study. They were retrained during the main study and continuously monitored throughout the data collection period.

The questionnaire was used to collect the following information (see Appendix 2).

- Reproductive history
- Socio-demographic information
- Environmental and occupational information

Variables

a. <u>Outcome variables</u>

Pregnancy outcome - the end-point of a pregnancy, including live term birth, live preterm birth or foetal loss (still births and miscarriages).

Adverse pregnancy outcome –outcome other than a live term birth, viz. live preterm birth, still birth and miscarriage.

Live term birth –birth of a live infant occurring after 37 completed weeks of pregnancy

Live preterm birth –birth of a live infant occurring prior to 37 completed weeks of pregnancy.[56]

Pregnancy loss –occurrence of either a miscarriage or a stillbirth.

Miscarriage –spontaneous termination of pregnancy (spontaneous abortion) before 24 weeks of gestation.

Stillbirth – occurs when a foetus which has died in the womb or during labour or delivery exits its mother's body. The term is often used in distinction to live birth and

miscarriage and it is reserved for death of a foetus after reaching the mid second trimester to full term. This includes any foetal death from 20 or 24 weeks of gestation, depending on a particular country's guidelines or resources. For the purposes of this study, stillbirth was defined as foetal death after 24 weeks of gestation.

b. Exposures / explanatory variables

Tobacco use - any intake of cigarettes, cigars, snuff or combination thereof.

Pesticides use –exposure to any from of insecticides in the house, garden and or from domestic animals.

Alcohol consumption – intake of any form of alcohol**.**

Gravidity – total number of pregnancies that a woman has had.

Contraceptive use – choice of pregnancy prevention mechanism, such as oral contraception, injectable contraceptive, intrauterine contraceptive device, condoms, natural rhythm methods.

Most recent pregnancy exposures - These were participants' exposures during their last pregnancy, which included maternal age (at time of pregnancy), antenatal care, chronic diseases, tobacco consumption, alcohol consumption, pesticide exposure, employment and psychological stress.

Teenage pregnancy at the most recent pregnancy - a pregnancy that occurred when the participant was younger than 20 years of age.

Advanced maternal age at the most recent pregnancy - a pregnancy that occurred when the participant was 40 years of age or older.

Psychological stress - significant emotional stress such as death of a close relation, divorce or loss of source income.

c. Variables for risk factor analysis

The exposure variables included in the risk factor analysis were as follows:

1. Maternal age –expressed as a categorical variable
2. Race – according to the four race group
3. Level of education – expressed as a categorical variable
4. Level of income - expressed as a categorical variable
5. Gravidity - expressed as a categorical variable
6. Working during pregnancy (actively participating in employment activities during pregnancy) - expressed as a binary variable
7. Pesticide exposure during pregnancy - expressed as a binary variable
8. Tobacco use during pregnancy - expressed as a binary variable
9. Alcohol intake during pregnancy – expressed as a binary variable as well as a categorical dose response variable.
10. Psychological stress exposure during pregnancy - expressed as a binary variable.
11. Chronic diseases during pregnancy - expressed as a binary variable
12. Antenatal care attendance - expressed as a binary variable

The outcome variables included in the risk factor analysis were all binary variables and were as follows:

1. Live term birth

2. Live preterm birth
3. Pregnancy loss

2.8 Data management and analysis

Data were entered into Microsoft Excel. Cleaning, reliability and reproducibility studies were performed using Microsoft Excel and Epi Info statistical software. Data analysis was performed using STATA version 10.

Descriptive analysis was performed to describe the demographic and lifestyle, socioeconomic and obstetric characteristics of the participants at the time of the interview, and the relative proportions of these characteristics.

A total of 1 210 women participated in the study. Eighty three participants were excluded from the analysis due to the unreliability of information provided by one of the interviewers (upon monitoring, investigation and reliability checks, it was discovered that this particular interviewer made up some of the information). A further 53 participants were excluded from the analysis as they had never been pregnant. Therefore, the number of participants included in the initial descriptive analysis was 1 074.

The prevalence of adverse outcomes (preterm births and pregnancy loss) was calculated using the weighted prevalence's of the outcomes in the different racial groups. The prevalence of outcomes was calculated separately for each racial group with the sum of the weighted prevalence's presenting the total average prevalence for that particular outcome:

- **Prevalence of pregnancy loss** for Black women [ppl (B)] was calculated as (the number of pregnancy losses amongst Black participants / total number of births amongst Black participants) * population proportion of Black women. Prevalence of pregnancy loss for White [ppl (W)], Coloured [ppl(C)] and Indian [ppl (I)] women were calculated in the same manner.
- **Weighted prevalence of pregnancy loss** = ([ppl(B) + ppl(W) + ppl(C) + ppl(I)])* 100 (presented as a percentage)
- **Prevalence of preterm births** for Black women [ppb (B)] was calculated as (the number of **preterm births** amongst Black participants / total number of births amongst Black participants) * population proportion of Black women. Prevalence of preterm births for White [ppb (W)], Coloured [ppb(C)] and Indian women [ppb (I)] were calculated in the same manner.
- **Weighted prevalence of preterm births** = ([ppb(B) + ppb(W) + ppb(C) + ppb(I)])* 100 (presented as a percentage)

The total number of births is usually used as the denominator for calculating stillbirth rates. This number represents all viable births. In this study, we used the total number of all births in each race group, viable or not, as the denominator to calculate the rate of all pregnancy loss (viable or not). The participants that were pregnant at the time of the interview (n = 43) were excluded from the denominator. Therefore, the denominator used to calculate the prevalence was the same for each pregnancy outcome, but different for each race group.

Demographic characteristics:

Race (analysed according to the four race groups in Potchefstroom) and age (analysed according to five age categories).

Lifestyle characteristics:

Tobacco use (in the form of cigarettes, cigars, snuff or any combination. Participants answered “yes” or “no” to the question on tobacco use, rather than the dose or intake of the tobacco),

Use of pesticides (in the house, garden or from domestic animals). Analysis looked at whether the participants answered “yes” or “no” to the question on pesticide exposure regardless of where the exposure happened, rather than the dose).

Socioeconomic characteristics:

Employment (yes or no), household monthly income (analysed according to five categories), highest level of education (analysed according to four categories), type of dwelling, source of water and electricity access (yes or no).

Obstetric characteristics: gravidity (analysed according to five categories), contraceptive use and whether the most recent pregnancy was planned or not.

As most of the participants’ characteristics were expressed as either a binary and or categorical variable, descriptive analysis mainly described the proportional distributions of the different characteristics. Since age could be expressed as both a continuous and a categorical variable, it was also described in terms of range, mean and standard deviation.

Seventeen more participants were excluded from other analyses due to incomplete data on most exposure variables. The number of participants included in the risk analysis was 1 014. Analysis focused on maternal risk factors, as our exposure variables of interest. The selection of exposure variables was based on the exposures during the most recent pregnancy leading to an outcome and according to biological plausibility.

Risk analysis was performed in three phases:

Chi square analysis was used to compare differences in the outcomes between groups of women according to the explanatory variables:

1. Demographic variables - maternal age and race
2. Socioeconomic variables - level of education, level of income and employment during pregnancy (actively participating in employment activities during pregnancy)
3. Lifestyle variables - pesticide exposure, tobacco use and alcohol intake during pregnancy.
4. Obstetric and medical variables – gravidity, psychological stress exposure, chronic diseases during and antenatal care attendance during pregnancy.

Chi square test analysis was performed to assess differences in proportions of the explanatory variables between the three different outcomes individually and then combined (live term birth = 0, preterm birth =1, pregnancy loss = 2). A p value of 0.05 or less was considered to show a statistically significant difference in the distribution of the explanatory variable proportions between and the outcome groups.

Univariate regression analysis, using simple logistic regression where the outcome variables were dichotomous and the exposure variable was either dichotomous or polytomous, was used to calculate crude odds ratios. Crude odds ratios greater than one with confidence intervals that were not inclusive of one were considered to be statistically significant. Crude odds ratio less than one with confidence intervals that were not inclusive of one were considered to show statistical significance in the protective effect of the exposure variable against the outcome.

For multivariate regression analysis, a combination of automatic variable selection [we selected pr (0.15) for backward selection and pe (0.10) for forward selection], stepwise regression (using backward elimination and forward selection methods) and logistic regression modelling, was performed to examine determinants of each adverse outcome while controlling for confounding factors. P values of 0.05 or less were considered to show a statistical significance in determining adverse outcomes. Adjusted odds ratios were the measures of association used.

Adjusted odds ratios greater than one with confidence intervals that was not inclusive of one were considered to show statistical significance in the association of individual exposure variables to each adverse outcome; and adjusted odds ratios of less than one with confidence intervals that were not inclusive of one were considered to show statistical significance in the protective effect of the exposure variable.

2.9 Permission and ethical clearance

1. Research approval was granted by the Human Research Ethics Committee of the University of Witwatersrand, Johannesburg (ethics clearance number M070330; appendix 1).
2. The North West Department of Health Research Committee was also approached for permission to conduct the study in Potchefstroom.
3. Community leaders and the general community were informed of the study through local media (radios and news papers), and posters distributed throughout the city.
4. An information sheet, together with a written consent form (explaining the reasons for the study and what was expected of the participant) was given to the participant (appendix 3).. This was accompanied by verbal explanation and permission, requested by the interviewer.
5. Participants' confidentiality was maintained
6. Provisions to refer participants with urgent medical needs to the nearest public health facility were made.

2.10 Student's role in the study

The student was part of the research team and was involved in all the phases and processes of the study. She contributed during the questionnaire adaptation process, during the pilot phases of the study, during training of interviewers and towards data collection for the main study. The student was the primary investigator for this master's project, and was assisted by her supervisors.

CHAPTER THREE

RESULTS

3.1 Descriptive Analysis

There were 1 074 women included in the descriptive analysis.

a. Lifestyle and demographic characteristics

The women ranged in age from 18 to 58 years at the time of the interview with a mean age of 34 years and a standard deviation of 8.9. The majority were 25 to 34 years and 35 to 44 years, accounting for 38% and 32% of the total, respectively. Very few (5%) were older than 49 years (Figure 2).

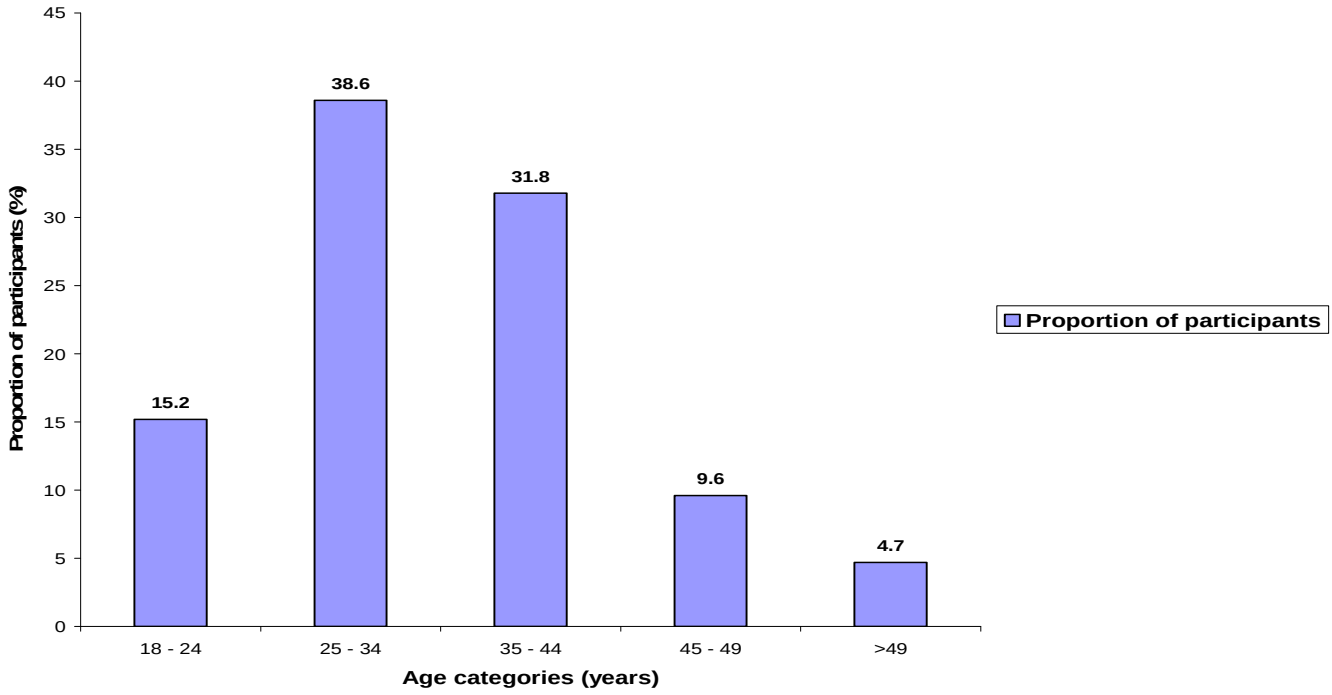

Figure 1: Age distribution of study participants at the time of the interview

[N = 1074]

The race distribution of the participants included in the analysis was similar to that of women of reproductive age in Potchefstroom (Figure 3). The majority of the women (63.3%) were Black.

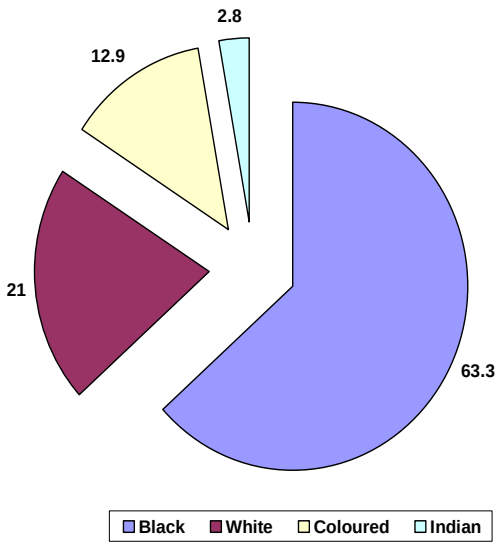

Figure 2: Distribution of study participants by race groups (%); [N = 1074]

The lifestyle characteristics of interest were tobacco and pesticide use. There were 376 (35%) participants who were tobacco users and 796 (74.1%) used pesticides in their homes.

b. Socio-economic characteristics

Only 397 women (37%) were employed. The majority of participants (62%) had a total household monthly income of less than R 2 500, which was the lowest income level in our questionnaire; had been to high school (with or without obtaining a Matric certificate) (59%); had formal household dwellings (62%) and had access to electricity (92%). The

source of water was almost equally split between in-house tap water and communal tap (Table 2).

Table 2: Socio-economic characteristics of study participants

Socio-economic variable	Number of participants	Percent (%)
Income level		
Less than 2500	660	62.1
2500 to 4999	131	12.3
5000 to 10000	106	10.0
10000 to 19999	100	9.4
20000 and more	66	6.2
Total	1 063	100
Education level		
No schooling	31	2.9
Primary school	194	18.1
Secondary school	637	59.3
Tertiary education	212	19.7
Total	1 074	100
Household dwelling		
Formal	665	62.1
Informal	397	37.1
Flat/Hostel/other	9	0.8
Total	1 071	100
Water access		
In-house tap	473	44.1
Communal tap	599	55.8
Total	1073	100
Electricity access		
No	82	7.6
Yes	991	92.4
Total	1073	100

*The total numbers (and respective percentages) projected in this table, for each characteristic, differ as they reflect the discrepancies in the number of respondents for each characteristic.

c. Obstetric history characteristics

The majority (71%) of the participants had used contraceptives at some point in their lives. Most of the participants reported having used either oral or injectable contraceptives. Only 105 (14%) participants reported condom use (as a sole contraceptive method or in addition to other contraceptive methods). The majority of women (54%) did not plan their most recent pregnancy. However, some race groups were more likely to have planned their pregnancies than others (69% of White women, 49% of Coloured women and 43% of Indian women, compared to only 38% of Black women).

All the participants included in the analysis had been pregnant; 43 (4%) were pregnant at the time of the interview. The number of pregnancies (previous and current) ranged from one to eight (Table 3).

Table 3: Distribution of number of pregnancies per study participant

Number of pregnancies	Number of participants	Percent (%)
1	328	30.5
2	359	33.4
3	223	20.8
4	102	9.5
5 or more	62	5.8
Total	1074	100

d. Maternal characteristics during the most recent pregnancy

Maternal age at the most recent pregnancy was recorded for 1 071 participants. Three participants had missing maternal age data. The majority were aged 20 to 29 years [563 (52.6%)], and 30 to 39 years [349 (32.6%)]. Only 131 (12.2%) were teenagers at the time of the last pregnancy, while 28 (2.6%) were of advanced maternal age. The average maternal age was 27 years with a standard deviation of 6.24.

Most participants received antenatal care (90.9 %) with the first antenatal visit occurring in the first (48.9%) and second trimesters (42.1%).

Chronic diseases during pregnancy (such as hypertensive disorders, hypotension, diabetic disorders, HIV infection, asthma and other diseases) were reported by 170 (15.9%) participants. The majority of these participants (63.6%) reported having hypertensive disorders (hypertension, preeclampsia) during their most recent pregnancy. Psychological stress was reported by 329 (30%) participants. The majority of participants did not use alcohol or tobacco during pregnancy (83% and 87%, respectively). Almost a third of participants (29%) reported having used pesticides during pregnancy, while a quarter (42%) reported being employed during pregnancy. Lifestyle characteristics of participants during their most recent pregnancy are shown in detail in table 4.

Table 4: Distribution of Lifestyle characteristics of study participants during their most recent pregnancy

Lifestyle exposures	Number of participants	Percent (%)
Pesticides exposure during pregnancy		
No	744	70.7
Yes	309	29.3
Total	1053	100
Tobacco use during pregnancy		
No	883	82.9
Yes	182	17.1
Total	1065	100
Daily alcohol intake during pregnancy		
More than 5 drinks	20	1.9
3 to 4 drinks	39	3.6
1 to 2 drinks	86	8.0
None	925	86.5
Total	1070	100

*The total numbers (and respective percentages) projected in this table, for each characteristic, differ as they reflect the discrepancies in the number of respondents for each characteristic.

e. Outcomes of the most recent pregnancy

The majority of participants (824) had a pregnancy that resulted in a live term birth, while some (147) had a live preterm birth and even fewer (60) had a pregnancy loss. Preterm births occurred more commonly among Indian (28.6 %) and White (21.6) participants, while pregnancy loss was more common among White (9.5) and Coloured (7.5) participants. Some participants (43) had missing outcomes data as they were still pregnant at the time of the interview (Figure 3). Table 5 illustrates the racial distribution of these outcomes.

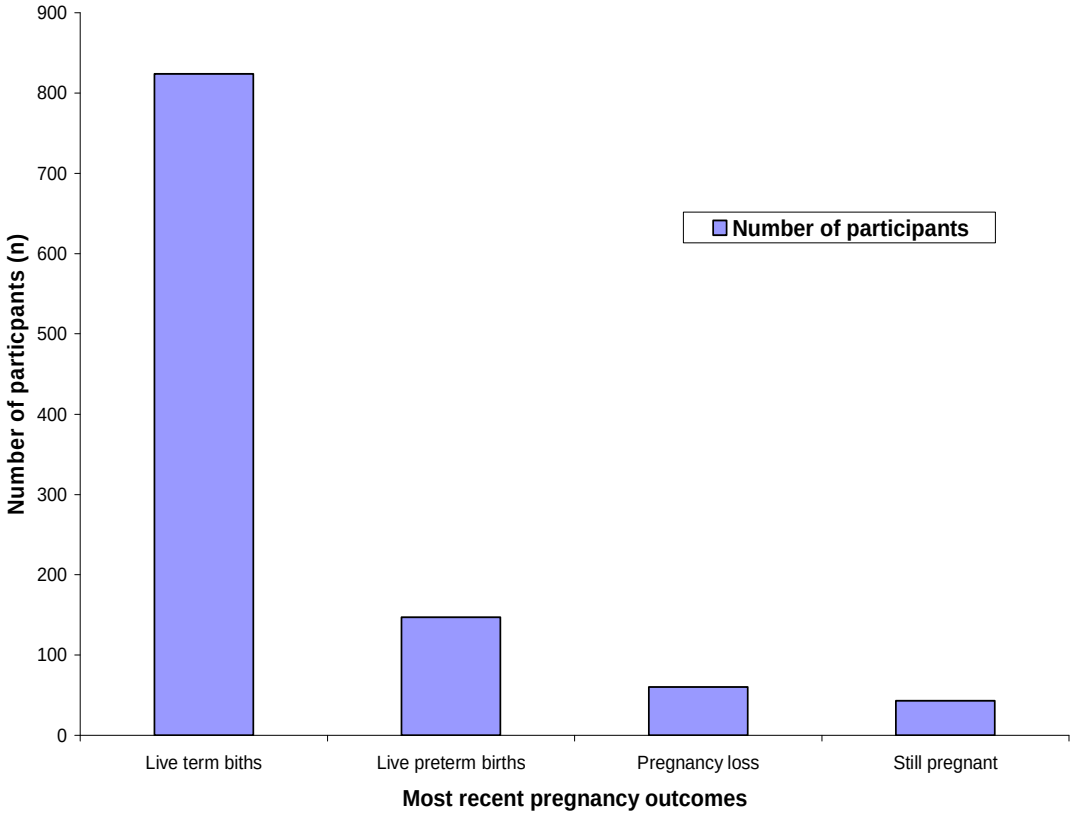

Figure 3: Distribution of participants according to the most recent pregnancy outcomes; [n = 1074]

Table 5: Racial distribution of most recent pregnancy outcomes

Race group	Live term births [n (%)]	Live preterm births [n (%)]	Pregnancy loss [n (%)]	Total births [n (%)]	Population weight (%)
Black	554 (85.5%)	67 (10.3)	27 (4.2)	648 (100)	71.5
White	153 (68.9)	48 (21.6)	21 (9.5)	222 (100)	21.7
Coloured	99 (74.4)	24 (18.1)	10 (7.5)	133 (100)	6.4
Indian	18 (64.3)	8 (28.6)	2 (7.1)	28 (100)	0.4
Total	824 (79.9)	147 (14.3)	60 (5.8)	1031 (100)	100

Weighted prevalence of pregnancy loss

= 5.6% [95% Confidence interval: 5.57% - 5.63%]

Weighted prevalence of live preterm births

= 13.4% [95% Confidence interval: 13.36% - 13.44%]

3.2 Distribution of risk factors for adverse outcomes of the most recent pregnancy

Chi square test analysis was performed to determine the difference in the distribution of risk factors for each adverse outcome (preterm births and pregnancy loss). Risk factor analysis excluded the participants that were pregnant at the time of the interview and the participants that had missing information on most of the risk factors. Therefore, there were 1014 participants included in the risk factor analysis.

a. Demographic and lifestyle factors

There was a statistically significant difference in the distribution of race ($p<0.001$) amongst the women that had a preterm birth and those that had a pregnancy loss outcome. Furthermore, Chi Square test analysis showed a statistically significant difference in the distribution of pesticide use amongst the women that had a pregnancy loss outcome ($p = 0.022$); while this difference was not statistically significant amongst the women that had a preterm birth outcome and when the two outcomes were combined. There was no statistical significant difference in the distribution of maternal age, alcohol intake and tobacco amongst both adverse outcomes. Therefore, Chi square test analysis of demographic and lifestyle factors showed that race and pesticide use were significant risk factors for pregnancy loss, while race alone was a significant risk factor for preterm birth. Maternal age, alcohol intake, and tobacco use were not shown to be significant risk factors in this analysis. Table 6 summarises of the results of the combined outcomes' analysis.

Table 6: Distribution of lifestyle and demographic factors by pregnancy outcomes

Pregnancy exposure variables	Pregnancy outcomes [n (%)]			Chi-square	P-value
	Live term birth	Live preterm birth	Pregnancy loss		
	807 (79.6)	147 (14.5)	60 (5.9)		
Maternal age (years)					
≤ 19	99 (78.6)	19 (15.1)	8 (6.4)		
20 - 29	433 (81.7)	71 (13.4)	26 (4.9)		
30 - 39	252 (76.4)	55 (16.7)	23 (7.0)	6.02	0.421
≥40	23 (82.1)	2 (7.1)	3 (10.7)		
Race					
Black	546 (85.2)	66(10.3)	29(4.5)		
White	144(67.9)	47(22.2)	21(9.9)		
Coloured	99(73.9)	26(19.4)	9(6.7)	38.33	<0.001
Indian	18(66.7)	8(29.6)	1 (3.7)		
Pesticides use					
No	583 (80.6)	105 (14.5)	35 (4.8)	5.28	0.071
Yes	224 (77.0)	42 (14.4)	25 (8.6)		
Alcohol intake					
No	725 (79.5)	136 (14.9)	51 (5.6)		
Yes	82 (80.4)	11 (10.8)	9 (8.8)	6.77	0.149
Tobacco use					
No	673(79.8)	122 (14.5)	48(5.7)	0.46	0.794
Yes	134 (78.4)	25 (14.6)	12(7.0)		

b. Socio-economic factors

There was a statistically significant difference in the distribution of income level ($p < 0.001$) amongst the women that had a preterm birth outcome; while there was no statistically significant difference in the distribution amongst the women that had a pregnancy loss outcome. There was a statistical significant difference in the distribution of education level for both preterm birth ($p = 0.001$) and pregnancy loss ($p = 0.01$) outcomes. Furthermore, there was a statistically significant difference in the distribution of employment during pregnancy amongst the women that had a pregnancy loss outcome ($p = 0.022$); while this was not statistically significant amongst those that had a preterm birth outcome. Combined Chi Square test analysis of all the socioeconomic factors showed a statistically significant difference in the distribution of the socioeconomic factors when the adverse outcomes were combined (p value < 0.05). Therefore, Chi square test analysis of socioeconomic factors showed that all the socioeconomic factors were significant risk factors for both adverse pregnancy outcomes. (Table 7)

Table 7: Distribution of socio-economic risk factors by pregnancy outcomes

Socio-economic variables	Pregnancy outcomes [n (%)]			Chi - square	P-value
	Live term birth 807 (79.6)	Live preterm birth 147 (14.5)	Pregnancy loss 60 (5.9)		
Education level				26.74	<0.001
No Schooling	29 (93.6)	0	2 (6.5)		
Primary School	151 (82.1)	19 (10.3)	14 (7.6)		
Secondary school	491 (81.6)	87 (14.5)	24 (4.0)		
Tertiary	136 (69.0)	41 (20.8)	20(10.2)		
Income level(in Rands)				31.1	<0.001
<2500	526 (83.1)	76 (12.0)	31 (4.9)		
2500 -4999	107(84.9)	14 (11.1)	5 (4.0)		
5000 -10000	65 (65.7)	25 (25.3)	9 (9.1)		
10000 -19999	70 (73.7)	16 (16.8)	9 (9.5)		
≥20000	39 (63.9)	16 (26.2)	6 (9.8)		
Employed				7.97	0.019
No	484(81.8)	83 (14.0)	25 (4.2)		
Yes	323 (76.5)	64 (15.2)	35 (8.3)		

c. Obstetric and medical factors

There was a statistically significant difference in the distribution of chronic diseases ($p = 0.007$) amongst the women that had a preterm birth outcome; while this was not seen amongst the women who experienced a pregnancy loss outcome. There was a statistical significant difference in the distribution of psychological stress amongst the women for both preterm birth ($p = 0.037$) and pregnancy loss ($p < 0.001$) outcomes. Chi Square test analysis revealed a statistically significant difference in the distribution of antenatal care use ($p < 0.001$) amongst the women that had a pregnancy loss outcome; while there was no statistically significant difference in the distribution amongst the women who had a preterm birth outcome. Chi Square test analysis of gravidity showed no statistically significant difference in the distribution of gravidity amongst the women for both adverse outcomes. Combined Chi Square test analysis showed a statistically significant difference in the distribution of most obstetric and medical risk factors amongst the women for both adverse outcomes, except gravidity ($p < 0.05$) (Table 8).

Table 8: Distribution of obstetric and medical risk factors by pregnancy outcome

Obstetric and Medical variables	Pregnancy outcomes [n (%)]			Chi-square	P-value
	Live term birth 807 (79.6)	Live preterm birth 147 (14.5)	Pregnancy loss 60 (5.9)		
Gravidity					
1	248 (80.5)	40 (1	20 (6.5)		
2	272 (81.0)	3.0)	17 (5.1)		
3	162 (77.1)	47 (14.0)	13 (6.2)		
4	80 (80.0)	35 (16.7)	5 (5.0)	3.22	0.920
≥ 5	45 (75.0)	15 (15.0)	5 (8.3)		
		10 (16.7)			
Psychological stress					
No	586 (83.1)	94 (13.3)	25 (3.6)	27.77	<0.001
Yes	221 (71.5)	53 (17.2)	35 (11.3)		
Chronic diseases					
No	688 (81.0)	112 (13.2)	49 (5.8)	7.70	0.021
Yes	119 (72.1)	35 (21.2)	11 (6.7)		
Antenatal care use					
No	60 (65.2)	17 (18.5)	15 (16.3)	21.56	<0.001
Yes	747 (81.0)	130 (14.1)	45 (4.9)		

In summary, there were statistical significant differences in the distributions of race, education level and psychological stress amongst the women who had a preterm birth outcome as well as those who had a pregnancy loss outcome. Distribution of maternal age, tobacco use, alcohol intake and gravidity showed no statistically significant differences.

3.3 Associations between maternal factors and preterm birth outcome for the most recent pregnancy

Univariate analysis showed that race, education level, income level and chronic diseases were associated with preterm birth. White, Coloured and Indian women were at least twice as likely to have a preterm birth compared to Black women, and this was statistically significant. Women who had chronic diseases during pregnancy were also almost twice as likely to have a preterm birth outcome compared to those that had no chronic diseases during pregnancy; and this was statistically significant. Having primary and secondary school education was also a risk factor for preterm birth when compared to no schooling (crude OR >2). Some income levels were more likely to be risk factors for preterm birth than others. Maternal age, tobacco use, alcohol intake, pesticide use, employment, psychological stress, gravidity and antenatal care use showed no statistically significant association with preterm birth. These results are summarised in Table 9.

Table 9: Risk Factors associated with live preterm births

Pregnancy exposures	Crude Odds Ratio	95% Confidence Interval
Maternal age (years)		
≤19	Reference	
20 - 29	0.9	0.5 – 1.5
30 - 39	1.1	0.6 – 2.0
≥40	0.5	0.1 – 2.1
Race		
Black	Reference	
White	2.8	1.8 – 4.2
Coloured	2.2	1.3 – 3.6
Indian	3.7	1.5 – 8.8
Pesticides	1.0	0.7 – 1.5
Daily alcohol intake	0.8	0.4 – 1.5
Tobacco use	1.0	0.6 – 1.6
Education level		
No Schooling	Reference	
Primary School	2.2	1.2 – 3.9
Secondary school	3.1	2.0 – 4.6
Tertiary	0.00	
Income level(in Rands)		
<2500 omitted	Reference	
2500 -4999	0.9	0.5 - 1.7
5000 -10000	2.7	1.6 – 4.5
10000 -19999	1.7	0.9 -3.0
≥20000	2.8	1.5 – 5.3
Employed	1.1	0.8 – 1.6
Gravidity	1.1	0.9 – 1.2
Psychological stress	1.4	1.0 – 2.1
Chronic diseases	1.8	1.2 -2.7
Antenatal care use	0.6	0.4 -1.1

3.4 Associations between maternal factors and pregnancy loss outcome for the most recent pregnancy

Univariate analysis showed that race, pesticide use, employment and psychological stress were associated with pregnancy loss, while antenatal care use was protective against pregnancy loss. White women were twice as likely to have a pregnancy loss compared to other women of other races. Women who used pesticides and those that were employed during pregnancy were also twice as likely to have a pregnancy loss outcome compared to those who did not. Being psychologically stressed during pregnancy carried a three times greater risk of having a pregnancy loss outcome compared to not being psychologically stressed. Women who used antenatal care were protected against pregnancy loss by 30%. Maternal age, education level, income level, tobacco use, alcohol intake, gravidity and chronic diseases showed no statistically significant association with pregnancy loss. These results are summarised in table 10.

Table 10: Risk Factors associated with pregnancy loss

Pregnancy exposures	Crude Odds Ratio	95% Confidence Interval
Maternal age (years)		
≤19	Reference	
20 - 29	0.7	0.3 – 1.7
30 - 39	1.1	0.5 – 2.5
≥40	1.8	0.4 -7.1
Race		
Black	Reference	
White	2.3	1.3 -4.2
Coloured	1.5	0.7 – 3.3
Indian	0.8	0.1 – 6.2
Pesticides	1.8	1.1 -3.1
Daily alcohol intake	1.6	0.8 – 3.4
Tobacco use	1.3	0.7 – 2.4
Education level		
No Schooling	Reference	
Primary School	1.2	0.3 – 5.5
Secondary school	0.6	0.1 – 2.7
Tertiary	1.6	0.4 – 7.4
Income level(in Rands)		
<2500 omitted	Reference	
2500 -4999	0.8	0.3 – 2.1
5000 -10000	1.9	0.9 – 4.2
10000 -19999	2.0	0.9 – 4.4
≥20000	2.1	0.9 – 5.3
Employed	2.1	1.2 – 3.5
Gravidity	1.0	0.8 – 1.3
Psychological stress	3.5	2.0 – 5.9
Chronic diseases	1.2	0.6 -2.3
Antenatal care	0.3	0.1 – 0.5

3.5 Determinants of adverse outcomes

Multivariate analysis was performed in stages for each individual outcome and for the combined adverse outcome. Automatic variable selection using forward, backward selection and stepwise regression methods were used to determine the best fit logistic regression model for of the determinants of both pregnancy loss and preterm birth, while controlling for confounding.

Analysis of preterm birth revealed that race (White, Coloured and Indian), education level (primary and high school) and psychological stress exposure had a statistically significant association with preterm birth, while antenatal care attendance protected against preterm birth. Chronic diseases, in addition to these four exposure variables, formed the best fit logistic regression model for preterm birth.

Being White, Coloured or Indian increased the odds of having a preterm birth outcome by at least twice as much compared to being Black; primary and secondary school education increased the odds of preterm birth by more than five times compared to other levels of education; and the odds of having a preterm birth outcome were almost twice as much for women who had psychological stress or chronic diseases than for those who did not. Antenatal care use decreased the odds of preterm birth by 50%.

Analysis of pregnancy loss revealed that being employed and psychological stress were associated with pregnancy loss; while antenatal care attendance protected against pregnancy loss. These three exposure variables formed the best fit logistic regression model for pregnancy loss.

When the two outcomes were combined into one outcome, named 'adverse outcome', the results of the analysis were similar. Race (being White, Coloured and Indian) and psychological stress exposure had a statistically significant increased risk of adverse outcome, while antenatal care attendance was protective. Chronic diseases exposure in addition to these three exposure variables formed the best fit logistic regression model for adverse outcomes. These results are summarized in table 11.

Table 11: Summary of determinants of adverse pregnancy outcome for the most recent pregnancy

Outcome	Risk Factors	Characteristic	Multivariate analysis	
			Adjusted OR	95 % CI
Pregnancy loss	ANC use		0.2	0.1 - 0.4
	Psychological Stress		3.8	2.2 - 6.5
	Employment		2.3	1.3 - 3.9
Preterm birth	Race	White	2.5	1.5 - 4.3
		Coloured	2.3	1.4 - 3.8
		Indian	3.6	1.5 - 8.9
	Education	Primary	6.4	3.0 - 1.3
		Secondary	8.1	4.7 - 1.4
	Stress		1.5	1.0 - 2.2
	ANC use		0.5	0.3 - 0.98
	Chronic disease		1.8	1.2 - 2.9
Adverse outcomes	Race	White	3.0	2.0 - 4.3
		Coloured	2.2	1.4 - 3.4
		Indian	3.3	1.4 - 7.9
	Stress		2.0	1.5 - 2.8
	ANC use		0.4	0.2 - 0.6
	Chronic disease		1.6	1.1 - 2.4

CHAPTER FOUR

4.1 DISCUSSION

This was a population-based analytical cross-sectional survey whose aims were to determine the prevalence of selected adverse outcomes of pregnancy (pregnancy loss and preterm birth) in women in the Potchefstroom municipality; and to identify the risk factors associated with these adverse outcomes. Reporting of the prevalence of pregnancy loss and preterm birth as a percentage rather than per population is in accordance with common practice in literature.[17, 18, 33, 57]

Our study found a prevalence of 5.6% for pregnancy loss and 13.4% for preterm birth. Psychological stress and working during pregnancy were independent risk factors for pregnancy loss while antenatal care use was protective against pregnancy loss. White, Coloured or Indian race, having a primary or secondary school education, psychological stress, and chronic diseases were risk factors for preterm birth, while antenatal care use protected against preterm birth.

Prevalence of pregnancy loss

The outcome measure of pregnancy loss in this study was a combination of stillbirths and miscarriages due to the limitation of subjective reporting of pregnancy loss as either stillbirth or miscarriage. In 2000, the WHO estimated stillbirths in South Africa to be 18 per 1000 births, which is the same amount estimated by the Perinatal Care survey.[13] Data on miscarriages that are available in the literature refer to clinically recognised

miscarriages which have generally been estimated to occur in 10% to 20% of all pregnancies[18,19], with 1% to 3 % of women experiencing recurrent miscarriages.[17] Our results could not be directly compared with these figures due to the differences in the outcomes being measured. In addition, the outcomes measured in this study focused on the most recent pregnancy for which such a denominator has not been estimated in the general population. The common practice in the literature is to estimate prevalence for a specific point or period in time. However, the prevalence of pregnancy loss found in this study is still much lower than that previously reported for either miscarriages or stillbirths.[7, 17, 20] The prevalence of pregnancy loss could be influenced by a number of factors, including contraceptive use which impacts on rate of pregnancy, recognition of pregnancies when they occur, reporting of pregnancies, the denominator used to calculate the prevalence and the exposures that predispose to pregnancy loss.

In this study, the percentage of women who had ever used contraception was 71%, similar to that in the general South African population.[58] Contraceptive use, therefore, did not explain the low prevalence of pregnancy loss. Pregnancy rates have not been estimated in South Africa or in this study. Therefore, the possibility that the rate of pregnancy in the study population was lower than that in the general South African population could not be established. Planning of pregnancy and education in reproductive health matters, such as the menstrual cycle and symptoms of pregnancy, could influence the ability of women to recognize when pregnancy has occurred. This would cause women who had recognized the occurrence of pregnancy and experienced a pregnancy loss to be more likely to report it as such, compared to women who were not aware of

their pregnancy status. The majority of participants in this study were Black women who were also the least likely to have planned their pregnancies. Therefore, these women could have missed recognizing a pregnancy loss and thus not reported it as such, which would contribute to the low prevalence of pregnancy loss found in this study. The knowledge of fertile period which influences the ability of women to recognize the occurrence of pregnancy has been estimated to be very low in the South African population (12%), [58] but this was not established in this study.

The above-mentioned factors apply primarily to early miscarriages. Late miscarriages and stillbirths would be evident regardless of circumstances related to the pregnancy. A seemingly low prevalence of pregnancy loss could have also been due to a larger denominator used than what is usually used in literature.

Prevalence of preterm births

The prevalence of preterm births as on outcome, in a population study, has never been estimated in South Africa. Preterm births have been established to be the major cause of perinatal deaths, with an estimated 80% of all perinatal deaths being attributed to preterm births.[7] The prevalence of preterm births in developed countries is around 12.3%;[59] while a hospital study done in Tanzania found the prevalence of preterm births to be 17%.[60] A population study done in 2004 in Brazil, a middle income country, estimated preterm birth prevalence to be between 16% and 17%.[57] The Tanzanian study was hospital based which limits comparability with our study due to the selection biases inherent in hospital based studies. The prevalence of preterm births estimated in our study is lower than that

of developing and middle income countries, but higher that of developed countries or what is viewed to be an acceptable level.[57, 59, 60] In the United States, for example, the acceptable preterm birth rate set out in the Health People 2010 objectives was no more than 7.6%.[27]

The high prevalence of preterm births estimated in this study could be influenced by a number of factors including gestational age measurements and exposures that predispose women to preterm births. Gestational age was based on the recall of the participants; measurements were not taken and no verification from clinical documents was done. As the majority of pregnancies were not planned, the date of conception and/or delivery may have been inaccurately estimated, resulting in a differential misclassification of outcomes. Therefore, the preterm births could have been misclassified.

Risk factors for pregnancy loss and preterm births

Several factors were associated with preterm births and pregnancy loss in this study: race, psychological stress, pesticides, working during pregnancy, chronic diseases, education level and income level. Antenatal care use was a protective factor.

Most studies have shown that Black women are more likely to experience adverse outcomes due to differential exposures to protective and risk factors during pregnancy, such as antenatal care, socioeconomic status and lifestyle background.[61,62] This study, however, contradicted these previous findings; White women were found to be at a higher risk of pregnancy loss and preterm birth compared to the other race groups, while

Indian and Coloured women were more likely to experience preterm births than Black women. Being White was an independent risk factor for pregnancy loss even on multivariate regression analysis. We argue this point with caution, recognising the possibility that different cultural practices and educational backgrounds might have an influence in the recognition and reporting of pregnancy loss. As most pregnancies (69%) amongst the White women were planned, compared to the Black women (38%), it is possible that the White women would have been more likely to recognise a pregnancy loss, especially early miscarriages, than the Black women. The same argument can be used for better estimation of conception and or delivery date, and thus the acknowledgement of a preterm birth.

Some studies support our findings of psychological stress being an independent risk factor for pregnancy loss and preterm birth.[42, 44] Psychological stress has been shown to challenge the maintenance of pregnancy through a number of processes. It has been shown to affect the nervous, endocrine and immune systems, the equilibrium of which is mandatory for pregnancy maintenance.[42] When the equilibrium of these systems is disturbed, the resultant failure of pregnancy maintenance can result in a wide range of adverse pregnancy outcomes, ranging from miscarriages to still births as well as preterm births. A study that evaluated the impact of stress after the World Trade Centre disaster found maternal stress to be associated with adverse pregnancy outcomes such as birth defects, low birth weight, preterm delivery, and early onset preeclampsia.[44]

Pesticide exposure has been shown to be associated with adverse pregnancy outcomes, including miscarriages and preterm birth.[44] Women can be exposed to pesticides in many areas of their lives. In our study we focused on exposures from the house environment, domestic animals and from the garden, either at home or at work. We found an association between pesticide exposure and pregnancy loss. This association was, however, lost when we controlled for other risk factors. We found no association between pesticide exposure and preterm birth. This result is not surprising as another study has also shown similar conflicting results.[63]

Being employed during pregnancy may be a risk factor in pregnancy in a number of ways, depending on the types of exposures associated with the working environment, such as physical exertion, chemical exposures, psychological stress and other work exposures. Many studies have reported the association between employment during pregnancy and adverse pregnancy outcomes, with specific mention of physical exertion and ergonomic factors related to the work.[49, 50, 64] Even though this study did not analyse the details of the different types of work exposures to which participants could have been exposed, being employed during pregnancy was a significant independent risk factor for pregnancy loss even after controlling for other risk factors. Some studies, however, have reported that being employed during pregnancy is protective against preterm birth as it acts as a mode of improving socioeconomic status.[61,65] In this study, however, the socioeconomic status associated with being employed was not determined.

Results that pose the biggest confusion are the associations found between maternal level of education and preterm birth, and household income level and preterm birth. Women who had a primary or a high school education had an increased risk of preterm births, compared to women with no schooling. The women with average to higher household monthly income also had a higher risk of having preterm births, compared to those in the lower income brackets. These associations were not statistically significant for pregnancy loss. Our findings regarding maternal education and income level contradict previous studies which found lower maternal education and lower income to be associated with adverse pregnancy outcomes.[47,48] Our data did not enable us to explain these different findings. Even though the population in our study was representative of the general population in Potchefstroom, these results could have been affected by reporting bias. We recognise the possibility that educational background might have an influence in the recognition and reporting of pregnancy outcomes; better educated women might have recognised and reported the adverse outcomes more than the less educated.

Having a chronic disease during pregnancy was a significant risk factor for preterm birth; 14, 8% of the participants reported having had a chronic disease during pregnancy, which increased the risk of adverse outcome almost two-fold. A number of medical conditions, such as hypertensive disorders, diabetes, hypotension and asthma have been associated with an increased risk of preterm birth and stillbirths.[28,66] Our study, however, did not find any statistically significant associations between chronic diseases and pregnancy loss.

The graveness of maternal mortality caused by life threatening complications that can rarely be prevented by antenatal care has overshadowed other important benefits of antenatal care, specifically foetal and neonatal benefits, such as increased growth, reduced risk of infection and improved chances of survival.[45] A debate on the impact of antenatal care on pregnancy outcome concluded that appropriate strategies of information, education and communication lead to or reinforce desirable behaviour and outcome.[51] The results of our study indicate that antenatal care attendance is a significant protective factor against pregnancy loss and preterm birth. Similar findings have been reported[10, 45, 51, 52]

The association between maternal age, tobacco use, alcohol intake, and adverse pregnancy outcomes found in this study is contrary to some previous reports but supportive of others.[19,35,67] Teenage pregnancy is a risk factor for adverse pregnancy outcomes and is often associated with preterm births, especially for the first pregnancy.[35] Increased maternal age is also associated with increased risk of adverse pregnancy outcomes including pregnancy loss and preterm births; advanced maternal age is associated with medical conditions and other exposures that pose an increased risk for adverse pregnancy outcomes.[19,67] In most studies, cigarette smoking and alcohol intake during pregnancy increase the risk of adverse outcomes including preterm births and miscarriages, but this was not illustrated in this study.[19, 44, 63]

4.2 BIASES AND LIMITATIONS

The prevalence of adverse outcomes and their associated risk factors are point population estimates. Therefore, the lack of temporality between exposures and outcomes and causal relationships could not be evaluated.

There may have been recall bias in this study. Data Women were asked to recall circumstances surrounding previous pregnancies. Women who had adverse pregnancy outcomes might have recalled their prior circumstances more clearly than those with good pregnancy outcomes. Those whose infants experienced medical problems at birth might be more inclined to report them as preterm infants and vice versa. This kind of information bias would lead to differential misclassification resulting in exaggeration of odds ratios or finding an association where none exists.

Another limiting factor is incompleteness of data. Nineteen participants were excluded from statistical analysis due to incomplete data. Some of these participants refused to answer questions related to risk factors such as alcohol intake, smoking and pesticide use during pregnancy. Exclusion of these participants could have resulted in selection bias and thus impacted on our results.

CHAPTER FIVE

5.1 CONCLUSIONS

This study found a pregnancy loss prevalence of 5.6% (a combined prevalence for spontaneous abortions and stillbirths) which is lower than expected in the general South African population. The preterm birth prevalence of 13.4% was lower than that of other developing and middle income countries, and could be improved upon.[57,60] These prevalences' are the weighted prevalences' and therefore can be generalized to the Potchefstroom population. However, generalization to the general South African population could not be made as the study was limited to an urban community that is not representative of the general South African population. This is the first community study in South Africa to estimate prevalences' of preterm birth and pregnancy loss at a population level.

There are common risk factors for pregnancy loss and preterm births. Our study supported some of the evidence for these risk factors (psychological stress, pesticides, working during pregnancy, chronic diseases, and antenatal care use as a protective factor), but contradicted the evidence for others (race, education level and income level). Further research is needed to investigate these contradictions.

5.2 RECOMMENDATIONS

No issue is more central to global well-being than maternal and perinatal health. Every individual, every family and every community is intimately involved with pregnancy and the success of childbirth at some point.

In order to understand and effectively address perinatal and neonatal morbidity and mortality, there needs to be an understanding about, and processes need to be put in place to address, the issues related to preterm births. In addition to addressing stillbirths, attention needs to be directed towards addressing spontaneous abortions as they may cause equal emotional and economic burdens to the communities as do stillbirths.

The following public health interventions can be applied to address the prevalence and risk factors associated with preterm births and pregnancy loss in South Africa:

Improving surveillance programmes for reproductive and maternal health outcomes

Even though stillbirth rates are estimated regularly, lack of detailed data on pregnancy loss in the population may lead to an undermining of the extent of the health problem. Miscarriages often cause emotional stress for the individual or couple wishing to have a baby and therefore cannot be neglected. Improvement of health information systems at facility level to capture all clinically visible miscarriages, while encouraging women who had miscarriages at home to report to the nearest health facility would provide much

needed information on the extent of pregnancy loss in South Africa and would subsequently guide policy, research and prioritization of effective control programmes.

The prevalence of preterm birth is not routinely assessed in the population. Estimating the extent of preterm birth as an outcome, rather than as a cause of perinatal death, deprives public health officials of the relevant information needed to effectively address child health issues in an effort to reduce perinatal morbidity and mortality. In areas where there is a lack of access to quality health care, preterm births can be an economic burden on households as more finances would be directed towards the health care needs of the premature infant.[59] This could lead to a vicious cycle of general deterioration in the livelihood and health of households and communities.[59] Therefore, estimating preterm births, as an outcome, should be a public health priority as preterm births have a large bearing on whether South Africa achieves millennium development goal four of reducing childhood mortality. Again, this could be achieved through improved surveillance of preterm births,

Health promotion and health education programmes

Education and increase in awareness of reproductive health matters such as the menstrual cycle, fertile window period and family planning in order to empower women and couples to decide on their desired number of children; increase in awareness of signs and symptoms of pregnancy to enable women to appropriately estimate their conception and delivery dates; encouragement of women to present timeously for the full range of maternal health care services; as well as the general

promotion of healthy lifestyles programmes that advocate smoking cessation, responsible alcohol use, healthy eating and adoption of regular moderate exercise should be emphasized in pregnancy as well and appropriately tailored for maternal health care needs. These programmes would empower women and reduce avoidable risk factors that predispose them to adverse pregnancy outcomes.

Strengthening health systems and health policy

The above-mentioned programmes will be fruitless if health systems are not equipped to cope with the expected increase in health care needs. Therefore, better capacity building of health systems to increase the availability, accessibility, affordability and acceptability of quality maternal health services, such as family planning, antenatal care, delivery care and emergency obstetric care, should be incorporated into programme planning.[30, 45, 51, 53] Health systems should also be equipped to provide this maternal health care model of continuum of care.

Health systems operations need to be guided by health policies that will direct the implementation of the above-mentioned educational and health promotion programmes, at home, at work and in the community; provide monitoring and evaluation strategies that will inform the progress and continuous development of the health care systems; and ensure continuous research into these adverse outcomes to reduce the prevalence, control the risk factors and better manage them.

5.3 FUTURE RESEARCH AREAS

1. Potchefstroom's population is not representative of the general South African population. Therefore, a population based survey, representative of the general South African population, to determine the prevalence and related risk factors of preterm birth in South Africa is still necessary.

2. A hospital based study to determine the prevalence and related risk factors of miscarriages that present to health facilities would assist in providing essential data on this important outcome even though it would still be an underestimate.

3. A qualitative study to look into knowledge, attitudes and practices on reproductive health matters in the different race groups might be instrumental in understanding some of the differences between the race groups.

4. A qualitative study to look into knowledge, attitudes and practices on reproductive health matters in the different socioeconomic clusters might be instrumental in understanding the factors influencing some of the results that are in contradiction to general scientific knowledge such as levels of education and income.

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APPENDICES

Appendix 1: Ethics clearance certificate and Postgraduate approval letter

Appendix 2: Study questionnaire

Appendix 3: Consent form and Information sheet

Appendix 4 : Analytical tables