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THE EFFECT OF MATERNAL WEIGHT ON OBSTETRIC OUTCOME

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Declaration

I, Mokgadi Johannah Nchinyani declare that the work on this report is original and has not been submitted for another degree or examination at this or any other institution. Part of this research report was presented as e-poster at the Royal College of Obstetrician and Gynaecology (RCOG) world congress held in Cape Town (20 – 22 March 2017).

.....

(Signature of candidate)

...20th.....day of...JUNE.....20...18.....in .....JOHANNESBURG

Dedication

The work of this report is dedicated to my husband Fhedzisani, my son Mahlatse and my daughter Moraka, and my parents Botsamang and Sebolaishi for their support and sacrifices during my studies. I will also like to dedicate this report to Helen Mashao my children's Nanny, for being a mother to my children while I was studying.

*Pr*esentation arising from the study (Poster number EP345)

20 – 22 March 2017	**Royal College of Obstetrician and Gynaecology world congress in South Africa, Cape Town.** **e-poster**	**Cape Town International Convention Centre**

Abstract

Background

In a demographic health survey done in South Africa (2008), 25% of adults were classified as overweight and 20% were obese. Maternal obesity has been recognized as a risk factor for poor outcomes, such as gestational diabetes mellitus (GDM), fetal macrosomia, pre-eclampsia, stillbirth and post-term pregnancy in mothers and their babies. The main objective of this study was to describe the proportion of women with different BMI and obesity classes and the associated outcomes in pregnant women in Soweto between March 2011 and August 2012.

Methods

This is a cross-sectional study using secondary data collected between (March and June) 2011 and (March and August) 2012 in two randomised controlled trials assessing the efficacy of trivalent inactivated influenza vaccine. Pregnant women were recruited at Chris Hani Baragwanath Academic hospital and at midwife obstetric units in Soweto and mothers and babies were followed up for 24 weeks postpartum.

For this study we used data collected at the baseline and delivery visits. Pregnant women aged between 18 and 39 years were included in the study. Ethics approval for this study and both previous studies was obtained from Human Research Ethics Committee (M101106, M101107 and M151033).

Results

Of the 2310 women recruited between 20 and 36 weeks gestation, 488 were excluded from the study (no heights/weights recorded).The median maternal age was 25.4 years [IQR 22-30; range 18.2- 38.3]. The median parity was 1[IQR 0-1; range 0- 4] and median gravidity was 2[IQR 1-2; range1- 5]. More than 99% (1817) of the women enrolled on the trials were black, 0.2% (3) coloured and 0. 1% (1) was Indian. HIV infection was present in 172(9.6%) women. The proportion of women in different BMI categories is as follows; underweight - 18(1%), normal weight- 516(28.3%), overweight- 649(35.6%) and obese - 639(35.1%). The median gestational age at birth was 38.7[IQR 37.1- 40.0; range 28.3- 42.7] weeks. The median systolic BP was 112 mmHg [IQR 104-121; range 89 – 142] and the median diastolic BP was 70 mmHg [IQR 62 – 75; range 50- 91]. More women in the obese group had experienced a previous miscarriage (93; 14.6%) compared to women of normal weight (52; 10.1%; p= 0.09). There was no difference in BMI of women who had suffered a previous neonatal death (55; 3.0%) or stillbirth (37; 2.0%; p=0.55). Obese women (468; 38.2 %) were significantly

more likely to be referred to hospital for delivery than women of normal weight (325; 26.5; p=0.00).

Women with an increased BMI (overweight or obese) were more likely to require caesarean section overweight (187; 28.8%), obese (232; 36.3%) (p- =0.00) than the other categories; underweight (4; 22.1%), normal weight (112; 21.7%). The mean birth weight in the different BMI categories was; underweight 2.7 kg(±0.3), normal weight 2.9 kg(±0.5), overweight 3.0 kg(±0.5) and in obese group 3.1 kg(±0.5), with p=0.00. The mean birth length in the different BMI categories was; underweight 48.1 cm(±3.0), normal weight 49.3 cm(±3.7), overweight 49.6 cm(±4.0) and in the obese group 50.0 cm(±4.1), with p = 0.01. The mean one minute Apgar scores 8 (±1.2) and five minute 9 (±0.9) and there was no difference in APGAR scores with different BMI categories. Women in obesity Class III were older and had more ultrasound examinations (39; 55%) compared to women in Class I (143; 36.8%).

Conclusion

Obese women were more likely to be delivered by caesarean section and had a history of poor obstetric outcome. Obesity was associated with increased systolic and diastolic blood pressures; however, this was not clinically significant. Obese women were more likely to be having a hospital delivery than women delivering at MOUs.

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List of abbreviations

AIDS : Acquired immune deficiency syndrome

ARV : Antiretroviral

BMGF : Bill and Melinda Gates Foundation

BMI : Body Mass Index

BP : Blood Pressure

CEO : Chief Executive Officer

CHBAH : Chris Hani Baragwanath Academic Hospital

CHC : Community health centres

CMJAH : Charlotte Maxeke Johannesburg Academic Hospital

cm : Centimetre

COC : Combined oral contraception

CI : Confidence Interval

GDM : Gestational Diabetes Mellitus

GWG : Gestational Weight gain

HREC : Human Research Ethic Committee

HIV : Human Immunodeficiency Virus

IM : Intramuscularly

IOM : Institute of Medicine

IQR : Interquartile Range

Kg : Kilogram

NICU : Neonatal Intensive Care Unit

OR : Odds Ratio

PCOS : Polycystic Ovarian Syndrome

PPH : Post-Partum Haemorrhage

RMPRU : Respiratory and Meningeal Pathogens Research Unit

SA : South Africa

SADHS : South African Demographic Health Survey

TOL : Trial of Labour

UK : United Kingdom

WHO : World Health Organisation

WITS : University of the Witwatersrand

Definition of terms

Gestational Diabetes mellitus	Diabetes first diagnosed in pregnancy
Gestational hypertension	Hypertension diagnosed in pregnancy after 20 weeks gestation without proteinuria
Joel-Cohen Incision	Transverse skin incision placed 3 cm below the line joining anterior superior iliac spine (ASIS), the subcutaneous tissue is incised only in three most medial centimetres and lateral tissues are separated manually
Large for gestational age	Weight, length, or head circumference that lies above 90th percentile for that gestational age
Macrosomia	Birth weight of greater than 4000g - 4500g or greater than 90% for gestational age
Miscarriage/Abortion	Spontaneous abortion of pregnancy occurring before 28 weeks gestation
Parity	Number of previous birth including stillbirth(at 28 weeks or later)
Post-term	Pregnancy duration of 42 gestational weeks and more
Pfannenstiel Incision	Transverse skin incision, two finger-breadths above the symphysis pubis and extended in the direction of the anterior superior iliac spine(ASIS) and ends 2-3cm medial ASIS on both sides
Pre-eclampsia	Hypertension diagnosed in pregnancy after 20 weeks with signs of other organ damage
Preterm labour	Labour before 37 completed weeks

Morbidly obese	Body mass index of ≥40 kg/m² or more
Obesity	Body mass index of ≥30 kg/m²
Neonatal death	Death of a live born viable neonate between birth and 28 days of life
Stillbirth	Fetal death occurring at 28 weeks >1000g or later (WHO definition)
Viability	Pregnancy more than 28 completed weeks

1.1 Introduction

Obesity and overweight has become a major health problem,[1] and the rising prevalence is a global concern. The prevalence of obesity has more than doubled worldwide between 1980 and 2014. More than 1.9 billion adults (≥ 18 years) were overweight and over 600 million adults were obese in 2014.[2]

The body mass index (BMI) is commonly used to classify weight categories. BMI is a simple index of weight in kilograms divided by height squared (kg/m²). The World Health Organisation (WHO) classifies BMI as (i) underweight: BMI <18.5kg/m^2, (ii) normal weight: BMI between 18.5 to 24.9 kg/m², (iii) overweight: BMI between 25 to 29.9 kg/m²; and (iv) obese BMI ≥30 kg/m².[3] It further classifies obesity as class I (BMI 30 to 34.9 kg/m²), class II (BMI 35 to 39.9 kg/m²), and class III (BMI >40 kg/m²).[3]

In the USA, 24.5% of women of childbearing age (20-44 years) are overweight and 23% are obese. Of the obese women 10.3% had a BMI of more than 35 (class II and III).[4] The prevalence of obesity amongst pregnant women attending antenatal clinic in a study conducted between February 2006 and September 2006 at the Johannesburg General hospital (renamed Charlotte Maxeke Academic Johannesburg Hospital) was 44%. Of a total of 767 women.[5] A systematic review of the prevalence of obesity in pregnant women in 16 studies in African countries, was between 6.5 % and 50.7 %.[6]

An increased BMI in pregnant women is recognized as a risk factor for adverse outcomes for both women and their babies.[7] Obesity has been shown to be associated with poor pregnancy outcomes including increased rates of caesarean delivery, pre-eclampsia, gestational diabetes mellitus (GDM), fetal macrosomia, stillbirth, and post term pregnancy.[8] Injuries in neonates born to mothers with a high BMI may be central nervous system, peripheral nervous system or skeletal. The risk of birth injuries was highest in vaginal delivery.[9]

The prevalence and the effects of obesity in pregnant women in Soweto are largely unknown. This study therefore aims to describe the proportion of women with different BMI's, classified using the WHO classification in pregnancy. The maternal and fetal outcomes in BMI and obesity classes will also be described.

The guidelines for maternity care in South Africa 2015, recommend the measurement of Mid-upper arm circumference (MUAC) with increased vigilance for hypertension and gestational diabetes if this exceeded 33cm.[10] However, the basic antenatal care (BANC) handbook advises that women with weight less than 45 kg or more than 85 kg should be referred for evaluation by obstetrician.[11] These guidelines are not clear on the BMI at which women should be referred to a hospital for delivery.

1.2 Literature review

1.2.1 Prevalence and physiology of obesity

The prevalence of obesity worldwide has nearly doubled in the last 20 years. In 2008, 10% of men and 14% of women in the world were obese. Morbid obesity was found in 7.6% of women aged 20-39 in the US in 2007-2008,[9] and more than half of the pregnant women were overweight or obese.

In South Africa, an increase in BMI is a concern with more than 29% of men and 56% of women being classified as overweight or obese.[12] Nearly 30% of South African women aged 30 and 59 years are obese. The mean BMI is lower in other African countries as seen in table 1.2.1.

Table 1.2.1: **Mean BMI in African countries categorised by age (adapted from International Obesity) Task Force: Global Burden of Disease Analyses 2002)[13]**

Country	**Mean BMI in kg/m²**		
Age (years)	**15-29 years**	**30-44 years**	**45-59 years**
South Africa	24.4	28.5	29.9
Nigeria	21.0	21.8	20.3
Zimbabwe	21.3	23	23.5
Ethiopia	18.9	18.6	17.3
Ghana	21.8	22.4	22
Kenya	21.7	22.3	22
Tanzania	21.8	22.3	21.6

Developed countries have a higher prevalence of obesity.[14] Currently many developing countries are experiencing a double burden of malnutrition, with increasing prevalence of maternal obesity as well as underweight. In countries like Burundi and Madagascar the prevalence of overweight and obesity is 40% and the prevalence of stunting is 50%.[15] In a Meta-analysis of 16 African studies, including countries such as Nigeria, South Africa, Zimbabwe, Egypt and Tanzania the prevalence of obesity was between 6.5% and 50.7%. Fifteen studies used BMI and one study used maternal weight with a cut-off point of ≥ 90Kg.[6]

Weight gain during pregnancy is normal and expected, largely due to the physiological changes including the increasing mass of developing fetus with an average weight of 3.4 kg, enlarging placenta (0.6 kg at term), increasing amniotic fluid volume (0.8 kg), increased

maternal blood volume and extracellular fluid (1.5 kg), increased uterine muscle mass (1.0 kg), breast tissue (0.5 kg) and increased maternal adipose tissue (3.3 kg).[16]

The rate at which weight is gained varies by trimester. The total gain during the first trimester is minimal (1-1.5 kg). An increase of 0.5 kg per week is expected between 20-30 weeks gestation. After 36-38 weeks the weight gain plateaus until delivery.[17]

In practice maternal weight is usually measured at every antenatal visit. However, there is some evidence that suggest that this does not improve pregnancy outcome.[17] Women with low BMI < 20 kg/m² and women with a high BMI >30 kg/m² are more likely to benefit from routine weighing during antenatal care, to prevent and intervene in the cases of fetal growth restriction and macrosomia.[18]

Abeysekera et al. looked at the alteration in energy homeostasis in pregnancy. They found that energy requirements of pregnancy are met without increasing energy intake and that total energy expenditure increases significantly throughout pregnancy. This occurs primarily due to increase in cardiovascular, respiratory and renal demands, increased tissue synthesis and requirements of the feto-placental unit. Body fat accumulates during pregnancy, even in undernourished women to prepare the mother for increased demands during labour and the postnatal period.[19]

Pre-pregnancy weight loss can improve pregnancy outcome in women with high BMI. Lifestyle and behavioural modification such as diet and exercise can decrease postpartum weight loss. Exercise alone was shown not to improve weight loss.[20]

1.2.2 General risk associated with obesity

Increased BMI is associated many conditions which are leading causes of deaths. There is a large financial burden and increased costs of chronic illness associated with overweight and obesity. The concerns of increased BMI have emerged as the global issue demanding attention from researchers and health workers.[21]

The metabolic syndrome is a condition which is associated with an increasing BMI. About 30% of middle-aged people in developed countries have features of the metabolic syndrome. The risk of developing hypertension was five times higher with obesity.[22]

Overweight and obesity are associated with:

- Coronary heart disease
- Type 2 diabetes
- Dyslipidaemia

There is a 10% risk of all cancers among obese non-smokers.[22] Cancers associated with obesity:

- Breast
- Colorectal
- Oesophageal
- Pancreas

The risk of endometrial cancer in overweight and obese individuals is 30% more than in normal weight women.[22] Endometrial cancer is the fourth most common cancer in women. Obesity has long been linked with the risk of endometrial cancer, with its association with high levels of oestrogen.[24]

In a systematic review on the relationship between depression and weight, it was found that the risk of depression was increased in obese people. In addition to that depression was found to be predictive of being obese.[25]

1.2.3 Reproductive health risk associated with obesity

High BMI is also associated with reproductive health abnormalities. Adverse reproductive health outcomes include menstrual irregularities which are typically due to anovulation. The development of polycystic ovary syndrome (PCOS) may be induced by metabolic abnormalities, like insulin resistance. Even in obese women with a regular cycle, anovulation contributes to subfertility.[26]

Obesity is an independent risk factor for spontaneous abortion among women who undergo infertility treatment.[27]It is difficult to obtain true incidence of the risk of miscarriage among obese women who conceive spontaneously. Many obese women experience early pregnancy loss before becoming aware that they were pregnant.[26] There is an association between

obesity and increased risk of first trimester miscarriage and recurrent miscarriage. Theories to explain the association include hyperlipidaemia leading to vascular inflammation and obesity associated sleep apnoea with subsequent desaturation events have been postulated, but remain unconfirmed.[28]

There is an extensive body of literature that supports the relationship between increasing maternal weight and hypertensive disorders of pregnancy. There is also a link between obesity and pre-eclampsia.[8] In obese individuals increased blood pressure is associated with adipose tissue that surrounds the kidney, resulting in renal compression.[29] A Norwegian study, found that maternal obesity was associated with large for gestational age infants in pre-eclamptic women delivering at term.[30]

The Triennial UK confidential Enquiry into Maternal and Child health 2003-2005 showed that 50% of women who died during pregnancy or 42 days postnatal were either overweight or obese.[31]

The National Committee for Confidential Enquiries into Maternal death (NCCEMD) in SA in the 2011-2013 report recommended that women with a BMI ≥40kg/m² should preferably be managed at a regional hospital, due to the increased risks associated with high BMI e.g. thrombosis, gestational diabetes, macrosomic babies, difficult caesarean section (both surgical and anaesthesia) and postpartum haemorrhage.[32]

1.2.4 Antenatal complications

Pregnancy can be complicated by pre-eclampsia and gestational diabetes mellitus (GDM). Observational studies demonstrate the link between obesity and pre-eclampsia with a reported 2.5 to 3.2 fold increased risk.[33] A meta-analysis and systematic review found the overall risk between increased BMI and GDM to be 3.8(CI 95%; 3.3 – 4.3) times higher compared to non-obese women.[34] The risk of venous thromboembolism (VTE) is increased 4- to -5-fold among all pregnant women. In obese women there is a 1.7 to 5.3fold increased risk of VTE. It is currently unknown if increasing level of obesity increases the risk of VTE.[35]

Obesity may cause difficulty in accurately assessing the fundal height, and hence lead to overestimation of the fetal weight. Abdominal sonographic visualisation of the fetus is often difficult in obese women due to distortion through a thick adipose tissue layer.[36] Fetal

malformation such as neural tube defects and major cardiac anomalies tend to occur more commonly in obese women.[17]

1.2.5 Intrapartum complications

Increased maternal BMI is associated with a range of intrapartum complications. In a study in the UK, it was found that women with increased BMI without additional risk factors had an increased risk of maternal intrapartum interventions, including augmentation of labour with oxytocin and intrapartum caesarean section. Duration of active phase of labour (from 4cm to 10 cm cervical dilatation) was prolonged for both overweight and obese women, compared to women of normal weight (7.7, 7.9, and 6.2 hours, respectively).[37.38]

In extremely obese women with BMI more than 40 kg/m² attempting trial of labour (TOL), BMI was an independent predictor of caesarean delivery. The underlying mechanisms for failed TOL in maternal obesity remains largely unknown.[39] Weight gain in excess of that recommended in pregnancy may contribute to the high rate of caesarean delivery in obese women, with increased risk of macrosomia leading to difficult delivery.[40]

There are potential challenges associated with anaesthesia and a higher risk of anaesthesia-related complications in obese women compared to women with normal weight.[41] It may be technically difficult to administer spinal or epidural anaesthesia in overweight and obese women because of obscured landmarks, difficulty with positioning the woman and excessive adipose tissue. General anaesthesia poses a greater risk, including difficult intubation due to excessive tissue and oedema .[42]Women with a BMI≥40kg/m^2 at first antenatal visit should have an obstetric anaesthesia consultation (RCOG).[31]

In women with increased BMI it is difficult to interpret fetal heart rate and monitor uterine contractions because of adiposity.[41] Of those infants born to obese women 10% weigh more than 4 kg, which increases the risk of shoulder dystocia during labour.[17]

Few studies support a link between obesity and operative vaginal delivery. One small case-control study in India showed a statistically significant increase in instrumental deliveries among obese women.[8]

1.2.6 Difficulty with caesarean delivery

Obese pregnant women are at an increased risk of excessive bleeding at caesarean section. Operative time of longer than 2 hours, wound infection and endometritis have also been shown to be associated with an increased BMI.[13] Obese women may require specific resources, such as additional blood products, a large operating table, and extra personnel to assist with the delivery. These are challenges related to morbidly obese women during caesarean section. The operating table should be constructed in a way to allow a 10 to 15 degree tilt to reduce hypotension and its consequences.[43]

Some practitioners have suggested using vertical skin incisions or higher transverse incisions on the abdomen to decrease the rate of wound complications and to increase operative access. The use of Pfannenstiel incision in the moist region below the panniculus in an obese woman remains the subject of debate.[43] However, vertical skin incisions have been associated with increased adverse outcome such as wound dehiscence and infections.[8]

A study conducted at Tygerberg Hospital in Cape Town, SA assessed the time of skin incision-to-delivery in obese women. They analysed 1120 women delivered by caesarean section over 6 months in 2010. The types of skin incision used for the delivery was Pfannenstiel (88.4%), Joel-Cohen (4.3%) and midline incision (7.3%). The Joel-Cohen incision provided the fastest delivery time followed by Pfannenstiel incision and then the midline incision. The study concludes that skin incision-to-delivery time was significantly extended amongst repeat procedures and increased progressively with increased maternal BMI.[44]

While comparing Joel-Cohen skin incision and Pfannenstiel skin incision, it was found that Joel-Cohen was superior to Pfannenstiel. The Joel-Cohen was associated with shorter operating times, less blood loss and less postoperative pain.[45] Also the time to mobilise out of bed and detects bowel sound and to pass gas was significantly shorter in Joel-Cohen incision.[46]

1.2.7 Fetal and neonatal complications

Higher rates (OR 1.6; CI 95%, 1.1 to 2.3) of preterm delivery (<32 weeks) in obese women, than for women of normal weight have been reported.[47] A large Swedish cohort study

reported a greater risk (OR 2.2; CI 95%, 1.2 to 4.1) of antepartum stillbirth among obese women.[47]

Maternal obesity is associated with significantly increased 1.4(CI 95%, 1.1 to 1.7) risk for low (4-6) Apgar score at birth and neonatal death.[48] Data concerning NICU admission are difficult to interpret and may reflect local guidelines, as knowledge regarding the association between maternal obesity and adverse neonatal outcomes are limited.[9]

Maternal obesity is not a risk for fetal aneuploidy; obesity is associated with increasing maternal age. When using serum biochemical screening for aneuploidy and neural tube defects, it is important to accurately record maternal weight as it has been shown to alter the levels of serum analysis. Maternal serum Alpha-Fetoprotein, levels of human chorionic gonadotropin (HCG) and plasma-associated pregnancy protein-A (PAPP-A) with Neural tube (NT) measurements are used as combined tests to provide risk assessments for trisomy 21 and trisomy 18.[49]

1.2.8 Postpartum complications

The incidence of post-operative endometritis is three times higher in obese women compared to normal weight women. Post-operative wound infection is found to be double in obese women.[43] Due to abdominal wall distortion by a large pannus, this presents difficulties during surgery. Retrospective data suggest vertical incision is associated with increased wound complication and may not improve lower segment visualization.[50]

Pregnancy increases the risk of thrombo-embolic events due to decreases in venous return, hypercoaguable state and immobility. The risk is higher with increasing BMI and surgical management of the obese women.[51] In an Australian study the risk of VTE was found to be higher at 37.5% after caesarean delivery and 75% were seen in women with high BMI.[40] In an American retrospective study over nearly a decade, they found a 14-fold increase in maternal deaths from pulmonary embolism in women undergoing caesarean delivery compared with vaginal delivery and obesity was identified as a risk factor.[40]

A retrospective cohort study showed that there is a significant risk of postpartum haemorrhage (PPH) in women of high BMI. The volume of distribution for uterotonics in

obese women is increased and the difficulty in palpating the fundus and performing bimanual massage probably contribute to this risk.[8] Women in obesity class III had a twofold (1.8 %) increased risk of postpartum haemorrhage secondary to uterine atony. The risk of postpartum haemorrhage in women with BMI of 40kg/m² or higher was increased at 5.2% [OR 1.23, CI; 1.04 – 1.45] compared to women of normal weight at (4.4%).[52]

Post-partum urinary stress incontinence is more common (OR 1.6; CI 95% 1.1 to 2.4) in obese women than in women with normal BMI but it also dependant on the mode of delivery and parity. Prolonged hospital stays are more common in obese women than women with normal weight (34.9% vs 2.3%) after both caesarean and vaginal delivery.[43]

1.2.9 Management of obesity

Management of reproductive complications associated with increased BMI starts preconception with weight control strategies, involving healthy eating and physical activity. Weight loss is not recommended during pregnancy, even for those who are overweight or obese.[53] Use of correct size cuff for the blood pressure (BP) measurement is important. A cuff that is too small for the women leads to over-estimation of actual BP reading.[31]

At the first antenatal visit the body mass index should be determined and the pregnant woman can be counselled regarding the benefit of appropriate weight gain.[16] There are no South African guidelines regarding weight gain in pregnancy. In 2009 the Institute of Medicine (IOM) published guidelines on optimal Gestational Weight Gain (GWG), based on the pre-pregnancy BMI and is independent of age, race, parity, smoking history and ethnic background.[16,54] The IOM recommends GWG of 12.7-18.2 kg in underweight women, 11.4-15.9 kg in normal weight women, 6.8- 11.3 kg in overweight and 5.9-9.1 kg in obese women.[16]

There is limited recommendation for weight reduction during pregnancy and its safety is not substantiated. Some observational studies have indicated that some obese pregnant women may intentionally lose weight.[55]

Bariatric surgery pre-pregnancy is associated with reduced risks of gestational diabetes and large-for-gestational-age infants.[56] However, it is not recommended during pregnancy, as it is associated with nutritional deficiencies including iron, vitamin B12, folate, vitamin D and

calcium.[53] During pregnancy, women with gastric band should be monitored by general surgeon to adjust the band if necessary.[53]

A systematic review looking at the risk of caesarean section after bariatric surgery found conflicting outcomes. In women who had a delivery both before and after bariatric surgery, the percentage of women who underwent caesarean delivery because of labour dystocia decreased from 5.6% to 2.1 %.[40] Bariatric surgery is not an indication for caesarean section without an obstetric indication.[41]

1.3 Problem statement

Obesity has become a global epidemic,[12] with morbid obesity of pregnant women becoming very important in perinatal medicine. In SA, where under-nutrition, poverty, and infectious diseases, such as HIV/AIDS and Tuberculosis are realities, the problem of obesity could be viewed as less pressing.[56] In 2002, of the 10% of South African women surveyed in the SADHS, aged 15-24 years were already obese.[56] In the South African Birth-to-Twenty cohort, it was found that girls had increasing level of overweight and obesity throughout childhood compared to boys.[10]

Obesity in pregnancy is associated with an increased risk of miscarriage, antenatal problems, and intrapartum complications. There is also an increase in poor neonatal outcomes.

The prevalence of obesity and the problems associated with it are unknown in Soweto. This study will therefore attempt to describe the proportion of women within each BMI category and obesity classes. We will also describe the fetal and maternal outcomes in these women.

1.4 Objectives:

The main objective of the study is to describe the weight in pregnant women attending two community health clinics (CHC's) in the Johannesburg Metropolitan area over 2 years (2011-2012) and the effect of weight on pregnancy outcomes.

1. To determine the distribution of maternal BMI in pregnancy according to normal, overweight and obese.
2. To describe maternal and neonatal outcomes associated with different WHO categories of BMI; associated maternal co-morbidities, labour outcomes, mode of delivery and birth weights.
3. To describe maternal and neonatal outcomes associated with different WHO categories of obesity (Class I, Class II and Class III); associated maternal co-morbidities, labour outcomes, mode of delivery and birth weights.

2.0 Methods

2.1 Study setting:

Soweto has an estimated population of 1.5 million in 2017.[57] It is an urban, low-income community, where the population is mostly dependent on public hospital for health care services.

CHBAH is a tertiary hospital in Soweto and had 21 449 deliveries in 2011 and 22 029 in 2012. CHBAH is one of three teaching hospitals affiliated to the University of the Witwatersrand; CHBAH was a referral hospital for 7 MOUs in the south of Johannesburg at the time of this study.

It offers high risk maternity care and has several sub-speciality services. It has a feto-maternal unit and multidisciplinary clinics for medical maternal disorders such as gestational diabetes, hypertension, cardiac disorders and poor obstetric history. Pregnant women have a risk assessment at their first antenatal visit and low risk patients are referred to MOUs. Intermediate risk patients have their antenatal care at MOU, but delivery at hospital. High risk patients are referred to CHBAH for antenatal care and delivery. Patients that develop labour related complication such as poor progress, antepartum haemorrhage or fetal distresses are referred to CHBAH. Women with a BMI of > 40 kg/m^2 should be referred to hospital according the maternity guidelines 2015.[10]

2.2 Study design and study population:

This was a cross-sectional study with a secondary data analysis. The data were collected in the MATFLU trials in 2011 and 2012. The two studies were randomised, double-blind, placebo controlled trials of trivalent inactivated influenza vaccine (IIV3), conducted in Soweto .[58] The enrolment of HIV- uninfected pregnant women was initiated at four antenatal clinics before the onset of the 2011 influenza season (3rd March until 4th August) and the 2012 season (6th March until 2nd July). HIV-infected pregnant women were not recruited in the first study, but were include in the second study. In 2011, the participants were recruited at Lillian Ngoyi clinic, Diepkloof clinic, Mofolo clinic, CHBAH and RMPRU. In 2012, participants were recruited from the same clinics, with the addition of Michael Maponya clinic.

Women were enrolled from when TIV was available for the season. – TIV formulation is changed annually, after a decision on strains to be included in vaccine is made at WHO meetings. Once strains have been selected, pharmaceutical companies manufacture vaccines. The vaccines are then tested and released upon approval by the Medicine Control Council (MCC).

2.3 Inclusion criteria:

The inclusion criteria from the MATFLU trial listed below.

1. Aged 18 to less than 39 years at trial enrolment.
2. Enrolment between 20 and 36 weeks gestation (was also a period of BMI calculations).
3. The ability to understand and comply with the planned study procedures.

2.4 Exclusion criteria:

The exclusion criteria from MATFLU trial listed below.

1. Planned delivery outside the designated trial centres
2. Patient with pre-existing medical condition such as hypertension, pre-eclampsia, patients on corticosteroids, uncontrolled major psychiatric disorder and fetal anomalies were excluded from the original MATFLU trials. As a result they were also excluded from our study. The inclusion and exclusion criteria from MATFLU trials (Appendix 1).

   Women without heights and weights measurements were also excluded from this study secondary analysis.

2.5 Sample size:

The original Matflu trials enrolled 2310 pregnant women (2116 HIV-uninfected and 194 HIV-infected women). We included all the Matflu participants who had a weight and a height recorded. A systematic review of 29 African studies used sample sizes of between 80 and 78 545 pregnant women, with most (22/29) of the studies in this review had sample sizes below

1822.[6] The convenient sample size used in this secondary analysis is larger than the sample size utilized for most other similar analyses.

2.6 Data collection:

The following definitions were used in the MATFLU trial:

A Stillbirth: Fetal death occurring at 28 gestational weeks or later.

Miscarriage: The spontaneous abortion of pregnancy occurring before 28 gestational weeks.

A list of the variables utilised for the MATFLU are included in Appendix 2 and Appendix 3.

Variables used for this study:

Data that were collected for the MATFLU study included routinely collected information that is needed for routine antenatal care and data specific for the study. Data were collected by trained research personnel with experience in data collection and research.

Gestational age staging of the mother at enrolment was undertaken using the most reliable method for best gestational age in order of superiority of staging by fetal ultrasonography (undertaken as part of the standard of care), the last menstrual period of the mother and physical examination by palpation of fundal height.

For the purpose of the study we used the WHO categories of BMI .[3] BMI of 18.5 to <25.0 kg/m² as normal weight, 25 to <30.0 kg/m² as overweight and 30 kg/m² and more as obese. Obesity was further classified using the WHO classes into class I (30 to <35.0 kg/m²), class II (35 to <40.0 kg/m²) and class III (≥40 kg/m²).[3]

MATFLU trial data were double entered into MS Access electronic databases and entries were compared for accuracy and completeness.

Variables collected:

Weight and height were collected, and BMI and Obesity classes were calculated/

Demographics and antenatal data:

- Age
- Gravidity
- Parity
- Maternal HIV infection status,
- Weight and height at trial enrolment - Maternal height and weight were taken from the antenatal card. Patients were weighed wearing indoor clothing, but without shoes. Blood pressure was measured with patients sitting with an electronic machine.
- Gestational age at delivery
- Blood pressure at first screening
- Ultrasound performed (yes or no)

Prior contraception history:

- Non-Hormonal (Barrier/ IUCD/ None)
- Hormonal (COC, IM such as Depo Provera)

Past obstetric history:

- Miscarriage
- Stillborn
- Neonatal death

Birth place:

- Hospital
- MOU

Mode of delivery

Fetal outcome:

- Live birth
- Birth weight
- Birth length
- Head circumference
- Gestational age at birth

- Apgar score at 1 and 5 minutes
- Neonatal admission
- Neonatal discharge
- Neonatal death

2.7 Data analysis:

The Data variables utilised for this study were exported from the MATFLU MS Access database into a CSV file, converted into Microsoft Excel for cleaning of certain variables, and then exported to STATA 14.2(stataCorp, 4905 Lakeway Drive College Station, Texas 77845 USA).

Categorical variables were described using frequencies and percentages and continuous variables were described using means with standard deviation and median with IQR. Both the means and medians for some variables were presented in the results because this provided more information regarding the dispersion. New variables were created for the calculation of BMI, underweight, overweight and obesity. In the comparison of hormonal contraception versus non –hormonal we added no contraception use on the Non -hormonal contraception group. A new variable was created for different classes of obesity. For the purpose of the study we used BMI of 18.5 to <25.0 kg/m² as normal weight, 25 to <30.0 kg/m² as overweight and 30 and more as obese. Obesity was further classified into class I (30 to <35.0 kg/m²), class II (35 to <40.0 kg/m²) and class III (≥40 kg/m²).

Chi-square test or the Fisher exact test was used for comparison between categorical variables. The T-test/Anova/Kruskall Wallis was used to compare continuous variables. A p-value of less than 0.05 was considered statistically significant.

2.8 Ethical considerations:

Permission to perform the MATFLU trials was obtained from Human Research Ethics Committee (HREC) of the University of the Witwatersrand (HREC reference numbers: 101106 for HIV negative trial and 101107 for HIV positive trial). Permission to use these data was obtained from Professor Shabir Madhi (principal investigator, MATFLU trials) and Dr Clare Cutland (lead trial co-ordinator, MATFLU trials) (appendix 4 and 5). Dr Cutland is a co-supervisor for this MMed.

Permission to perform the study for this MMed, was obtained from University of Witwatersrand Human Research Ethics Committee (HREC), approval number M151033 (Appendix 6).

2.9 Funding:

The MATFLU trials were funded by a grant from the Bill and Melinda Gates Foundation (BMGF), grant number OPP1002747.

3.0 Results

In this chapter I will describe the total population and compare the clinical factors for each category of BMI and different classes of obesity of the same comparisons.

A Cohort of 2310 women was recruited onto the Matflu trials between 3rd March and 4th August 2011, and 6th March and 2nd July 2012. Of these, 78.9% (1822) of participants were analysed for this study; 488 had to be excluded as weight and/ or height measurements was not recorded.

The mean maternal age was 26.3 (±5.3) and the median age was 25.4 [IQR 22-30] with a range of 17.5- 39.8. There were 1817 (99.7%) Black women, 3 (0.2%) Coloured women and 1 (0.1%) Indian woman.

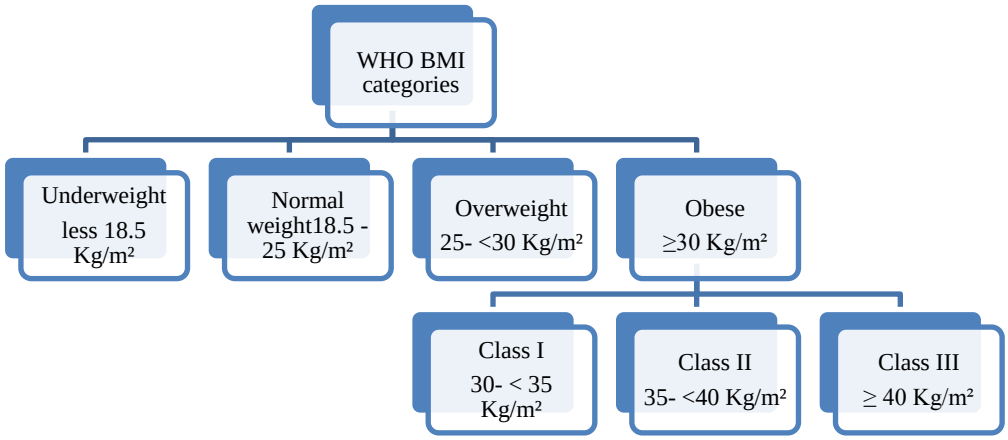

Figure 3.0 WHO categories and classes of BMI

3.1 Recruitment site

The figure below demonstrates the site of recruitment. There were 527 (28.9%) women who were recruited at CHBAH (high risk antenatal) and the others from MOUs (low risk antenatal- Michael Maponya, Lillian Ngoyi, Diepkloof and Mofolo) and the RMPRU (low risk antenatal women who heard about the MATFLU trial and wanted to participate, and would then delivered at one of the trials designated delivery sites).

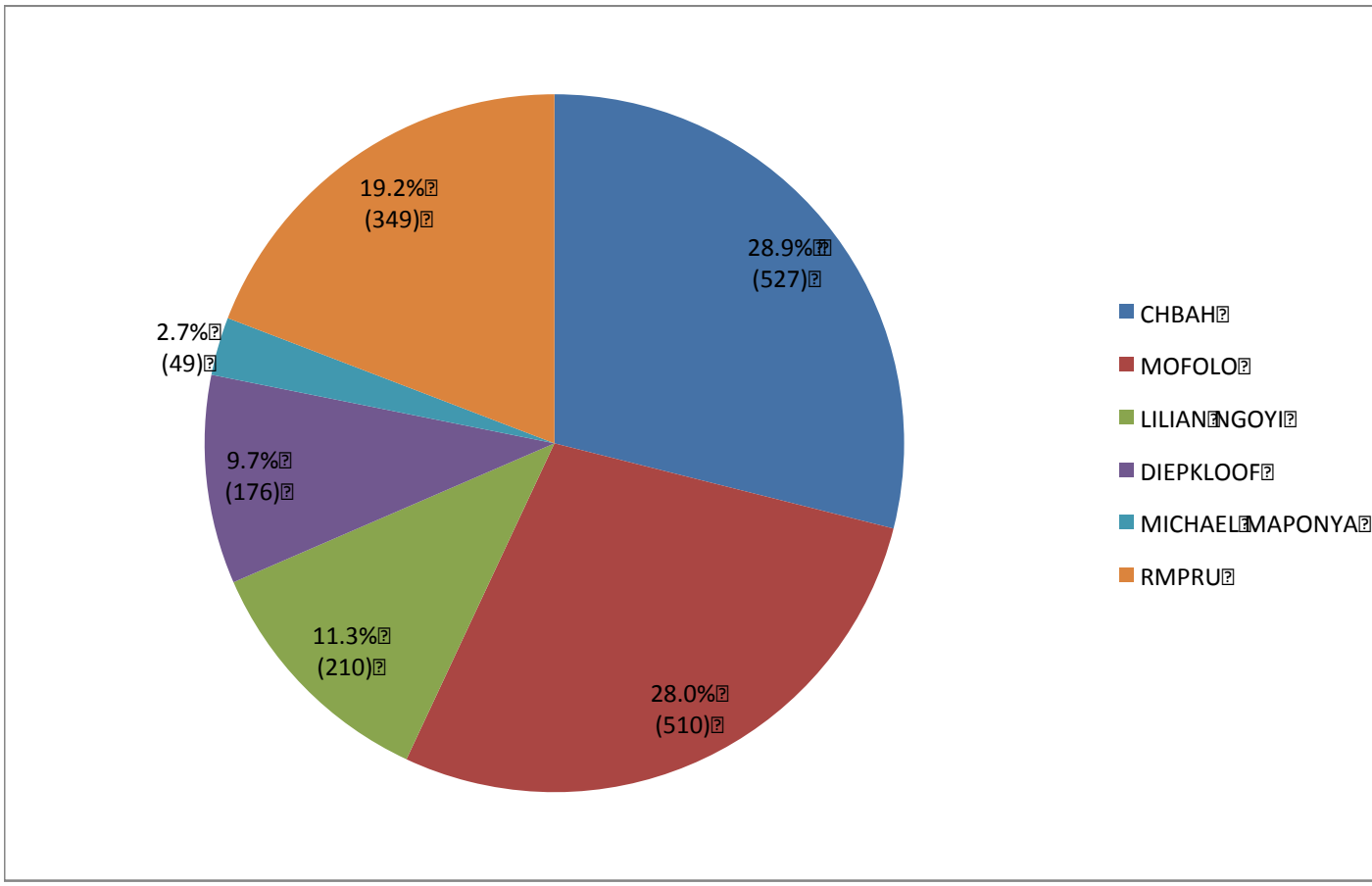

Figure 3.1 A description of the site at which pregnant women were recruited

3.2 History of contraception

A total of 931 (51.1%) women had used hormonal contraception prior to this pregnancy. Combined oral contraception (266; 14.6%) and injectable contraception (665; 36.4%) were the methods used for hormonal contraception. Eight hundred and seventy three (48%) women reported the use of non-hormonal contraception including condom use and intrauterine contraceptive devices. The table below is a comparison of past use of hormonal contraception and different categories of BMI. Women who were obese were more likely to have used hormonal contraception. There were 18 women in whom contraception use was unknown.

Table 3.2 Contraception use prior to the index pregnancy (n=1804)

Maternal BMI Total 1804	**Underweight N=18(1%)**	**Normal weight N=515(28.5%)**	**Overweight N=638(35.4%)**	**Obese N=633(35.1%)**	**p-value**
Non-Hormonal* n=873 (48.4%)	11 (61.1%)	295 (57.3 %)	313 (49.1%)	254 (40.1%)	0.00**
Hormonal n=931 (51.6%)	7 (38.9%)	220 (42.7%)	325 (50.9%)	379 (9.9%)	

*This category includes women who were none users ** Fischer exact

3.3 Antenatal characteristics

The median parity was 1 [IQR 0-1] with a range of 1-4 and the median gravidity was 2 [IQR 1-2] with a range of 1-5. The median maternal height was 160 cm [IQR 155-164] with a range of 143-176 cm and the median weight was 70 kg [IQR 62-82] with a range of 47-115 kg.

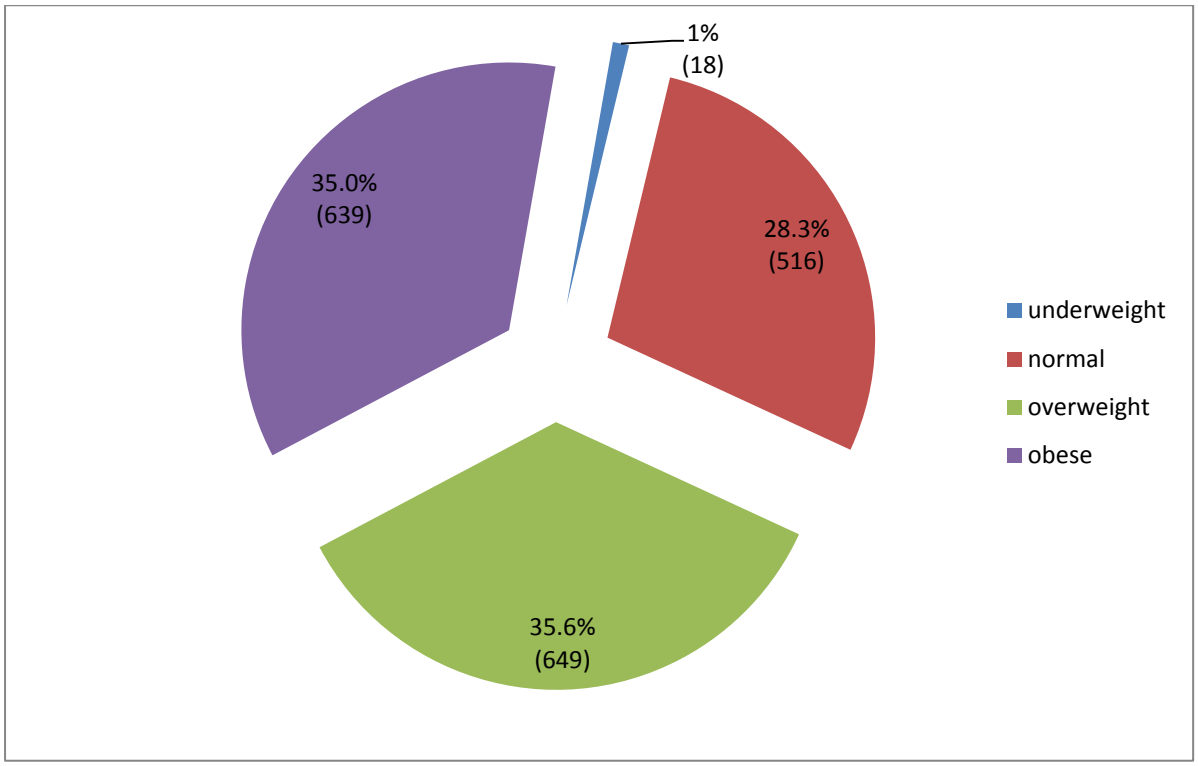

Figure 3.3 Distribution of BMI categories in pregnant women

Figure 3.3 shows the different BMI categories. The majority of women are in the normal weight, overweight and obese category.

Women in the obese category were more likely to be older and have higher gravidity and parity, compared to women of normal weight, Table 3.3.1 below. There was no difference in gestational age at delivery between different maternal BMI categories.

Table 3.3.1 A comparison of Maternal and pregnancy characteristics by BMI (n=1822)

Maternal characteristic Median (IQR; range	Total population N= 1822	Underweight N=18 (1.0%)	Normal weight N=516 (28.3)	Overweight N=649 (35.6%)	Obese N=639 (35.0%)	P- value
Maternal Age Median	25.4 [IQR 22-30; 17.5-39.8]	21.8 (19.5-23.8)	23.3 (20.8-27.4)	25.3 (22.2-29.6)	28.2 (24.1-32.2)	0.00**
Parity median	1 [IQR 0-1;1-4]	0(0-1)	0(0-1)	1(0-1)	1(0-2)	0.00**
Gravidity median	2 [IQR 1-2; 1-5]	1(1-2)	2(1-2)	2(1-3)	2(2-3)	0.00**

*Anova **Kruskal-Wallis

Table 3.3.2, mean systolic BP and the mean diastolic BP in the obese category was higher, p=0.00.There was no significant difference in HIV status between women in different BMI categories. HIV status of one participant was unavailable. Two hundred and forty six (39.3%) of obese women had an ultrasound as did 144 (28.5%) of women in normal weight category.

Table 3.3.2 A comparison of some antenatal characteristics and BMI category

Antenatal Factors	Underweight N=18 (1.0%)	Normal weight N=516 (28.3%)	Overweight N=649 (35.6%)	Obese N=639 (35.0%)	p- value
HIV status					
HIV Pos 172(9.4%)	1(5.6%)	42(8.1%)	68(10.5%)	61(9.6 %)	0.59**
HIV Neg 1649(90.1%)	17(94.4%)	474(91.9%)	581(89.5 %)	577(90.4 %)	
Ultrasound Yes	5(27.8%)	144(28.5%)	197(31.0%)	246(39.3%)	0.00**
Blood pressure Systolic BP Mean(SD)	107.6(±14.4)	109.9(±11.7)	113.0(±12.0)	116.3(±12.0)	0.00*
Diastolic BP Mean(SD)	65.7(±12.7)	66.8(±9.1)	69.5(±9.0)	70.7(±8.5)	0.00*

*Anova ** Fisher's test

3.4 Past obstetrics history

There were 37(2.0%) women with history of a previous stillborn. There were none in the underweight group, 10 (1.9%) in the normal weight group, 10(1.5%) in the overweight group and 17(2.7%) in the obese group and this was not statistically different across the groups with p=0.551. A total of 218(12.0 %) women had a history of miscarriage. The highest proportion of miscarriages was seen in the obese category with 93(14.6%) women with a previous miscarriage, followed by 2 (11.1%) in the underweight group, 71(10.9%) in the overweight category and, 52(10.1%) women in the normal weight group, and this was not statistically different across the groups with p=0.086. There were 55 (3.0%) patient with a previous neonatal death, 2(11.1%) in the underweight group, 11(2.1%) in the normal weight group, 24(3.7%) in the overweight group and 18(2.8%)) in the obese group and this was not statistically different across the groups with p=0.09.

3.5 Comparison of antenatal characteristics with WHO classes of obesity

Obese women were classified into WHO classes of obesity. Of the obese women, 400 (62.6%) women were in class I, 167 (26.1%) were in class II and 72 (11.2%) were in class III. A comparison of women in different classes of obesity, demonstrated a statistically significant difference between maternal age with Obesity classes (p=0.04) as shown in table 3.5. The mean parity and gravidity was also significantly higher from class I to class III. There was no difference in terms of gestational age between the different classes of obesity at delivery.

Blood pressure at booking was significantly elevated within different classes of obesity. There was no difference in past medical history between different WHO classes of obesity. Obese women were more likely to have an ultrasound as shown in table 3.5, more women in class I had an ultrasound done compared to women in class III and the difference was significant p=0.01.

Table 3.5 Comparison of antenatal characteristics with WHO classes of Obesity

Characteristics	Total population N=639	Obese Class I N=400 (62.6%)	Obese Class II N=167(26.1%)	Obese Class III N=72 (11.3%)	p- value
Maternal age	28.2[IQR 24.1-32.2]	28.0 [23.5-21.8; 17.2-39.6]	28.4[IQR 24.3-32.7; 17.8-38.2]	28.8[25.8-33.6; 19.5-39.1]	0.04 *
Median Parity	1(0-2;0-5)	1 (0-2 ;0-5)	1 (1-2; 0-5)	1 (1-2; 0-5)	0.01 *
Median gravidity]	2[2-3;1-7]	2 (2-3;1-6)	2(2-3;1-6)	2(2-3; 1-7)	0.009 *
Systolic BP in mmHg Mean(SD)		115(±11.8)	116.9(±12.1)	120.6(±12.0)	0.00*
Diastolic BP in mmHg Mean(SD)		70.2(±8.3)	70.7(±8.4)	73.8(±9.4)	0.00*
HIV status (+)		39(9.8%)	17(10.2%)	5 (6.9%)	0.76**
Past medical history		24 (6.0%)	10 (6.0%)	1 (1.4%)	0.29**
Ultrasound		143 (36.8%)	64 (38.3%)	39(55.7%)	0.01**

*Kwallis ** fisher's exact

3.6 Gestational age at delivery

The overall mean gestational age at delivery was 38.3(±2.7) weeks. The mean gestational age in the underweight group was 37.5(±2.4) weeks, 38.1(±2.7) weeks in the normal weight group, 38.3(±2.7) weeks in the overweight group and 38.4(±2.6) weeks in the obese group.

3.7 Place of birth and different BMI categories

Delivery site data for two participants was incomplete. Obese women were most likely to deliver at hospital as shown in the table 3.7.

Table 3.7 Place of birth and different BMI categories n=1820

Place of birth	Overall N=1820	Underweight N=17(1.0%)	Normal weight N= 516(28.4%)	Overweight N= 648(35.6%)	Obese N= 639(35.1%)	p-value
Hospital	1225(67.3%)	15(1.2%)	325(26.5%)	417(34.0%)	468(38.2%)	0.00**
MOU's	595(32.7%)	2(0.5%)	191(32.1%)	231(38.8%)	171(29.0%)	

**Fisher's exact

3.8 Birth place and classes of obesity

Women in different classes of obesity were more likely to be referred and deliver in hospital. There were 118(29.5%) of women in class I obesity who delivered in MOU, low risk antenatal run by midwives and less women in Class III obesity (Table 3.8)

Table 3.8 Birth place and WHO classes of obesity

Place	Overall 639(35.0%)	Obese Class I N=400 (62.6%)	Obese Class II N=167 (26.1%)	Obese Class III N=72 (11.3%)	p-value
Hospital	468(73.2%)	282(70.5%)	123(73.7%)	63(87.5%)	0.008**
MOU	171(26.8%)	118(29.5%)	44(26.3%)	9(12.5%)	

**Fisher's exact

3.9 Mode of delivery and different categories of BMI

Women who were overweight or obese were more likely to deliver by caesarean section than women who were normal or underweight and this was statistically significant p=0.00.The detail on the indications for caesarean section was not available. Details on the mode of delivery for 4 patients were incomplete.

Table 3.9 Mode of delivery

Mode of delivery Total=1818	Underweight N=18(1%)	Normal weight N= 515(28.3%)	Overweight N= 647(35.6%)	Obese N= 638(35.1%)	P=value
NVD n=1283	14(77.7%)	403(78.2%)	460(71.1%)	406(63.6%)	0.00**
Caesarean section n=535	4(22.2%)	112(21.8%)	187(29.0%)	232(36.4%)	
Elective caesarean section n=240	1(5.5%)	39(7.6%)	83(12.8%)	117(18.3%)	0.04**
Emergency caesarean section n=295	3(16.6%)	73(14.1%)	104(16.0%)	115(18.0%)	

**Fisher's exact

3.10 Comparison of mode of delivery with WHO classes of obesity

Normal vaginal deliveries accounted for 406(63.5%) and caesarean section for 232(36.4%) in this group of women. Data for one patient in the obese group was missing. Of those women with class III obesity more women had a caesarean section, and this was more likely to be an elective caesarean section. The information on the indication, difficulty and complications related to each mode of delivery was not available.

Table 3.10 Mode of delivery with WHO classes of obesity

Mode of delivery Total=638	Class I N=400(62.6%)	Class II N=167(26.1%)	Class III N=72(11.3%)	p-value
NVD	27(68.5%)	98(58.7%)	34(47.2%)	0.00**
CS	126(31.5%)	69(41.3%)	37(52.1%)	
Elective	60(15.0%)	35(21.0%)	22(30.5%)	0.00**
Emergency	66(16.5%)	34(20.4%)	15(20.8%)	

****Fisher's exact**

3.11 Perinatal outcome

These are the results of perinatal outcome amongst different categories of BMI. There was an increasing trend of higher birth weight in the obese group. Obese women tend to have longer and heavier babies. There was no significant difference in gender and Apgars scores in different categories of BMI. There were total of 38(2.2%) of multiple pregnancies. There was no significant difference in the APGAR scores at 1 or at 5 minutes across the different classes of BMI.

Table 3.11 Perinatal outcome for different BMI category

Factors Total=1822	Underweight N=18 (1.0%)	Normal weight N=516(28.3%)	Overweight N=649(35.6%)	Obese N=639(35.0%)	p-value
Birth weight (kg)mean (SD)	2.7(±0.3)	2.9(±0.5)	3.1(±0.5)	3.1(±0.5)	0.00*
Birth length (cm) mean (SD)	48.1(±3.0)	49.3(±3.7)	49.6(±4.0)	50.0(±4.1)	0.01*
Head circumference (cm) mean (SD)	33.1(±2.5)	33.9(±2.3)	34.2(±2.3)	34.5(±2.3)	0.00*
Gender					
Male	9(50.0%)	272(55.1%)	317(51.0%)	316(5.0%)	0.49**
Female	9(50.0%)	221(44.8%)	302(48.8%)	304(49.0%)	
Multiple pregnancy	0(0.0%)	6(1.2%)	12(1.9%)	20(3.1%)	0.15**

***Anova ** Fisher's exact**

3.12 Comparison of perinatal outcome with WHO classes of obesity

There was no significant difference between increasing maternal obesity in difference WHO classes and birth weight. The birth length and head circumference at birth did not differ among women in different classes of obesity. The median Apgar at 1 minute was 9 [IQR 9-9; range 0-10]. The median Apgar at 5 minutes was 10[IQR 10-10; range 0-10].The was no significant difference in the APGAR scores at 1 or at 5 minutes across the different classes of obesity.

Women in class I obesity were more likely to have their neonate admitted, but there was no increased difference compared to pregnancy complicated by stillborn delivery which was high between the three classes of obesity.

Table 3.12 Perinatal outcome and classes of obesity

Factors Total =639	Class I N= 400(62.6%)	Class II N=167(26.1%)	Class III N=72(11.3%)	p-value
Birth weight (kg)	3.1(±0.6)	3.2(±0.5)	3.1(±0.5)	0.46*
Birth Length (cm)	49.9(±4.2)	50.3(±4.3)	50(±3.2)	0.69*
Head circumference (cm)	34.4(±2.3)	34.7(±2.4)	34.6(±1.9)	0.45*
Gender				
Male	206(53.2%)	85(52.8%)	25(34.7%)	0.01**
Female	181(46.8%)	76(47.2%)	47(65.3%)	
APGARS				
Neonate discharged	346(86.5%)	149(89.2%)	66(91.7)	0.54**
Neonate admitted	32(8.0%)	11(6.6%)	5(6.9%)	0.48**
Stillbirth delivery	24(6.0%)	8(4.8%)	4(5.7%)	0.98**

***Anova ** Fisher's exact**

3.13 Past obstetrics history in different classes of obesity

The increased risk of poor obstetric history is shown in Table 3.13. Obesity has been associated with increased risk of stillbirth. The total number of patient with previous stillbirth was 17(2.7%). Women in class I obesity had significant history of previous neonatal death. Obese women were more likely to have increased risk of abortions.

Table 3.13 Past obstetric history and classes of obesity

Characteristics	Obese Class I	Obese Class II	Obese Class III	p-value
Total =639	N=400(62.6%)	N=167(26.1%)	N=72(11.3%)	
Stillbirth	13 (3.3%)	1 (0.6%)	3 (4.2%)	0.10**
Neonatal death	11 (2.8%)	4 (2.4%)	3(4.2%)	0.63**
Abortion				
One abortion	49 (12.3%)	22(13.2%)	9 (12.5%)	0.34**
Two abortions	5 (1.3%)	6 (3.6%)	2 (2.8%)	

****Fischer's exact**

4.0 Discussion

4.1 Prevalence of obesity

In this study we found a 35.1% prevalence of obesity among pregnant women in Soweto, similar to a retrospective study done in a Johannesburg Hospital (Now known as Charlotte Maxeke Johannesburg Academic Hospital) in 2006, where 767 pregnant women were enrolled between February and September. The prevalence of normal, overweight and obese pregnant women was 19%, 37% and 38.9% respectively.[6] The prevalence of obesity among non-pregnant women from different ethnic group for example, African, Asian, White and coloured in SA ranged from 19.9% to 34.4%.[5] In a systematic review of maternal obesity across African countries in 16 studies it was found that obesity ranged from between 6.6% and 50.7%. They also found that older and parous women were more likely to be obese and had increased risk of adverse labour.[6]

A retrospective study conducted in 2010 at Dr George Mukhari Academic Hospital, Pretoria, South Africa, enrolled 442 primigravida women attending ANC. The maternal age ranged between 16 and 35 years. They found the overall prevalence of obesity among primigravida to be 30.1%, 19.7% of whom were in WHO class I obesity (30-34 kg/m²) and 6.3% in WHO class II obesity (35-39.9 kg/m²) and there no women classified into class III, which is lower compared to our findings 62.6% class I; 26.1% class II, 11.2% class III respectively). It may be because only primigravida were considered.[59]

Across classes of obesity, women in class III tended to be older and have higher parity compared to women in class I and class II obesity p=0.00 in our study. Kominiarek et al reported that multiparous women were more likely (74.2 % vs. 25.8%) to experience gestational weight loss and low gestational weight gain compared to nulliparous women.[60]

Obesity is a big problem even in non-pregnant women. In a Turkish study, the prevalence of obesity in non-pregnant women was 29.4% and overweight 28.6%. The prevalence of obesity increased with age. In women between the ages of 20 and 29 years, the prevalence of obesity was 8.6% and overweight at 14.4%; women between the ages 30 to 39 years, 22.9% were obese and 28.6% were overweight. Their sample size was bigger than ours at 2728 women. They also looked at the prevalence of obesity in men, and they found 16.5% to be obese.[1]

In a cross-sectional study done in Ghana 2006, published in 2013 the prevalence of obesity among non-pregnant teachers was four times higher in women over 35 years of age, than those of middle age (26-35 years). They recruited 400 female teachers of child-bearing age. The study also showed that there was a positive association between parity, marital status with BMI and waist circumference.[61] Our study found that older age was associated with obesity, and different WHO classes of obesity.

We found that women in class II and class III obesity had bigger babies. However, the difference was non-significant between different class of obesity p=0.46. A systematic review demonstrated that obese women were at increased risk of having a large for gestational age baby at 8-12% in women with class I obesity, 8-14% in women with class II obesity 12-17.5% in women with class III obesity.[62]

4.2 Maternal weight and parity

Women with high parity were most likely to gain weight during pregnancy.[63] We did not examine weight gain in pregnancy. In this study a larger proportion of women with high parity were in the obese group. A study by Harris et al looked at independent association between parity and maternal BMI, and between parity and maternal weight gain. They found that in women of greater parity were associated with excessive weight gain as results from cumulative excess gestational weight.[63]

Kominiarek in a United States study showed a different pattern in multiparous women who were more likely to experience gestational weight loss; however in their study the reasons for gestational weight loss were unknown.[60]

4.3 HIV and obesity

HIV infected women were not recruited in the first study of the MATFLU trial, as a result the overall prevalence in this study is low compared to the study population. The roll out of antiretroviral (ARV) has led to changes in the cause of morbidity and mortality among HIV-infected people. The life expectancy of HIV-infected individual has increased.[64]

In this study we found no difference in BMI or WHO obesity classes among HIV-infected and HIV-uninfected individual. Tate et al looked at HIV infection and obesity. In their study they found that at 24 months at least 20% of their patients that were initially classified as

normal weight had become overweight or obese. They concluded that antiretroviral therapy provided only a limited contribution to weight gain.[64]

4.4 Ultrasound and maternal weight

A large proportion of women in the obese category had an ultrasound. This could be because of difficulty with clinical examination in this group of women or because these women had other indications for an Ultrasound. Dashe et al did a study looking at maternal obesity and limitation to evaluate fetal anatomy by ultrasound. They found that increasing maternal BMI limits the visualisation of fetal anatomy during a standard ultrasound examination at 18 to 24 weeks.[65]

With increasing severity of obesity carrying out an ultrasound examination is a difficult task. Paladini et al reported that the rate of suboptimal visualization was increased with degree of obesity. Despite the use of ultrasound in pregnancy and increasing rate of maternal obesity, there is little evidence in the literature to suggest that the difficulty with the sonar in these patients correlate with finding fetal anomalies .[36]

4.5 Blood pressure and maternal weight

In this study there was statistically significant difference between SBP and DBP in obese women compared with women of normal weight. This was not clinically significant. There were no women who were hypertensive, we did not have serial Blood pressures and Blood pressures at delivery. In a United State study of 6902 women, the association of maternal obesity with BP and the risk of gestational hypertensive disorder. They found that maternal obesity and morbid obesity are strongly associated with increased blood pressure in each trimester, and increased risk of gestational hypertensive disorders such as pre-eclampsia.[66] For each increase in BMI of 5 to 7 Kg/m², there is a corresponding 2-fold increase in the risk of developing pre-eclampsia.[67]

The majority of obesity related risks during pregnancy are related to increasing weight gain during pregnancy. Maternal risks are gestational diabetes mellitus (GDM), hypertension and increased duration of labour. Hypertension in pregnancy is associated with poor perinatal outcome such as preterm delivery and intrauterine growth restriction.[54] It was proposed that

the adipose tissue in obese patient surrounds the kidneys and cause compression resulting in blood pressure increase.[29]

4.6 Poor obstetric history and maternal weight

In this study obese women had higher rates of previous abortion compared to women of normal BMI. The proportion of women with previous stillbirth was also higher in obese women compared to women with normal BMI 2.7% vs. 1.9%. Although there was no statistically significant difference in our study between different categories, we know that increase maternal weight is associated with poor obstetric outcome.

In the Society of Obstetrician and Gynaecology (SOGC) clinical practice guidelines 2010, they reported that the risk of spontaneous abortion was increase in obese women.[68] However, we were not able to say whether the woman was obese at the time of the losses.

4.7 Intrapartum complications and maternal BMI

The women in the overweight and obese category were more likely to be referred to and deliver at hospital, which was a reflection of the maternity care guidelines. There is an increased risk of complications at the time of labour in obese women.[67] In this study obese women were more likely to delivered by Caesarean section compared to women of normal weight and this was statistically significant p=0.00. Maternal obesity influences the success rate of vaginal delivery and attempted vaginal birth after caesarean section.[67]

In a South African study done at Tygerberg hospital in the Western Cape, a prospective study on women undergoing caesarean section from May to November 2010. They found that repeat caesarean section, adhesions, and obesity prolonged the time taken for caesarean section.[44]Obesity not only poses a risk for surgical complications, but also for anaesthetic complications. The techniques for local anaesthesia may be difficult and time consuming in obese women.[43]

In a study done in Iraq, looking at maternal obesity and its relation with the caesarean section a significantly high rate of caesarean section in primigravidae and multigravid women with high BMI was found. Obese women were considered high risk and were managed appropriately during pregnancy.[69]

4.8 Perinatal outcome and maternal weight

The extent of maternal BMI influence on neonatal health prior to pregnancy is not clear. Vinturache et al reported on the impact of maternal pre-pregnancy BMI on perinatal outcome. The outcome they looked at was macrosomia, Apgar score, NICU admission and postnatal hospital stay and maternal BMI prior to pregnancy. They demonstrated that increased maternal BMI before conception had an influence in increasing growth and weight of the infant at delivery.[70]

In this study there was a statistically significant difference in the mean birth weight and the mean birth length between different categories of BMI p=0.00. Obese women tended to have heavier and longer babies. There was no difference in the mean Apgar score at 1 minute p=0.67 and at 5 minutes p=0.76.

4.9 Classes of obesity and mode of delivery

Women in class III category of obesity were most likely to deliver by caesarean section (51.4%). The incidence of caesarean section was higher with increasing BMI, confirming the results of Faucher et al showed in a systematic review 2015. In this systematic review, they looked at the relationship between gestational weight gain and caesarean delivery in obese women. They reported that, caesarean section rate increased with increasing classes of obesity respectively 13 to 37% in class I, 15 to 39% in class II and 17 to 48% in women with class III obesity.[62]

4.10 Limitations

Data used for this study were collected for the MATFLU trials, and some of the variables required for this study were not primary data points in the trial. Several variables, including some demographic factors (marital status, level of education, socio-economic factors such as household income and occupation) were not included in the data collection forms of the MATFLU trials. Family history of selected medical conditions (diabetes mellitus, hypertension and obesity) and lifestyle factors (smoking habits, physical activity and alcohol consumption) were also not collected.

We did not have pre-pregnancy weights and because these women were recruited after 20 weeks and we did not draw any conclusions regarding early pregnancy losses.

Information regarding the intrapartum care, indications for caesarean sections and difficulties of caesarean section was not available. We also did not know the information regarding the reasons for hospital referrals.

In the trial women with pregnancy complications such as hypertension and pre-eclampsia were excluded. We do not know whether the previous poor obstetric history of stillbirth was associated with hypertension and Diabetes. The exclusion of women with medical conditions may have meant that we underestimated the prevalence of obesity. But by excluding the medical conditions we were able to determine the effects of maternal weight without being confounded by the effects of maternal medical conditions. Data were collected over two seasons and this could have affected the results.

4.11 Strength of the study

The women in our study were recruited from Soweto maternity obstetrics units as well as CHBAH. They were not just high risk pregnancies. They are more representative of the population we serve.

Other strengths of the study include the prospective data collection for most required variables under strict guidance of a randomised clinical trial and in accordance with Good Clinical Practice.

4.12 Recommendations

1. All pregnant women with a BMI of >40kg/m² should be referred to hospital, to be evaluated by specialist Obstetrician and Anaesthetist.
2. Periodic education on healthy eating lifestyle and exercise should be emphasized, both pre-and during pregnancy.
3. All women should have an ultrasound in pregnancy, but this is more important for obese women as clinical assessment is difficult albeit with us as well.

Conclusion

In conclusion, the study showed that the prevalence of obesity is high among pregnant women in Soweto. It was also evident that high maternal BMI was associated with poor obstetric history, caesarean section delivery, high systolic and diastolic blood pressure. More women who are obese needing to be referred to a hospital also results in an increase in the use of resources.

It is of paramount importance to educate young women about the importance of maintaining a healthy weight (ideally normal weight) and educate them about the general health risks for woman and their infants and to educate all women about the importance of regular weight checks and knowing the approximate pre-pregnancy weight.

In a country where both undernutrition and obesity are prevalent, we need to develop country specific dietary recommendations in pregnant obese women.

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Appendix 1: Inclusion and Exclusion criteria from the MATFLU trial

	Inclusion criteria		
1	Pregnant woman aged 18 to < 39 years, who has given written informed consent.		
2	Gestational age at enrolment ≥ 20 weeks to < 34 weeks documented by the date of the last menstrual period and corroborated by physical exam		
3	Documented HIV test results from current pregnancy (2 assay for HIV infected, 1 for HIV uninfected used in the MTCT program undertaken within 12 weeks of the study enrolment).		
4	Participant able to attend the scheduled visits and to comply with all trial procedures for herself and her baby		
5	Expected delivery at CHBH or one of the MOUs in Soweto.		
6	Expected stay on the study area until 24 weeks of post-partum age		
	Exclusion criteria		
7	Receipt of TIV other than through the study, during the current influenza season documented by medical history or record.		
8	Receipt of any licenced vaccine≤ 28 days or inactivated licenced vaccine (except for tetanus toxoid within 14 days of study vaccine).		
9	Participants in the nested immunogenicity cohort cannot receive ANY vaccine (including tetanus toxoid within 14 days of study vaccine).		
10	Receipt of a non-licenced agent (vaccine, drug, biologic, device, blood product or medication) ≤ 28 days prior to vaccination in this study, or expects to receive another non-licenced agent before deliver unless study approval is obtained.		
11	Any significant (in the opinion of the site investigator) acute illness and /or oral temperature greater than or equal to 38°c ≤ 24 hours prior to study entry.		
12	Use of anti-cancer systematic chemotherapy or radiation therapy ≤ 48 weeks of the study enrolment, or has immunosuppression as a result of an underlying illness or treatment.		
13	Long term use of glucocorticoids, including oral or parenteral prednisone ≥ 20mg/day or equivalent for more than 2 consecutive weeks(or 2 weeks in total) ≤ 12 weeks of the study entry, or high dose inhaled steroids (> 800mcg/day of beclomethasone dipropionate or equivalent) ≤ 12 weeks before study entry (nasal and topical steroids are allowed).		

14	Women who receive corticosteroids for preterm labour ≤14 days before study entry.		
15	Receipt of immunoglobin or other blood products (with exception of Rho D immune globin) ≤ 12 weeks prior to enrolment in this study or is scheduled to receive immunoglobin or other blood products(with the exception of Rho D immune globin) during pregnancy or for the first 24 weeks after delivery.		
16	Receipt of IL2, IFN, GMCSF, or other immune mediators≤ 12 weeks before enrolment.		
17	Uncontrolled major psychiatric disorder.		
18	History of a severe adverse reaction to previous TIV.		
19	Any condition that would, in the opinion of this site investigator, place the subject at an unacceptable risk or injury or render the subject unable to meet the requirement of the protocol.		
20	Pregnancy complications (in the current pregnancy) such as preterm labour, hypertension or pre-eclampsia.		

Appendix 2: DATA COLLECTION SHEET: screening and demographics

Study no	
Maternal Age	
Race	☐Asian ☐Black ☐Caucasian ☐other
HIV status	☐Negative ☐positive ☐unknown
ARV's	☐Yes ☐No ☐unknown
Past medical history	☐Yes ☐No if yes ….explain
Date of LMP	☐Sure ☐unsure
Ultrasound performed	☐Yes ☐No
Final gestational age at baseline	☐☐weeks ☐days
Contraception used previous to pregnancy	☐Oral ☐injectable ☐barrier ☐none ☐other
Date of first ANC	dd/mm/yy
Hb at booking	
Parity	☐☐ ☐not recorded
Gravidity	☐☐ ☐not recorded
Number of previous neonatal deaths	☐☐ ☐not recorded
Number of previous abortion(spontaneous)	☐☐ ☐not recorded
Number of previous stillbirth	☐☐ ☐not recorded
Maternal Height(m)	
Maternal Weight (Kg) at entry	
Maternal Weight(Kg) at birth	
BMI at entry	
BMI at birth	
Mid upper arm circumference(MUAC)	
Blood Pressure mmHg at booking/ and delivery	

Appendix 3: DATA COLLECTION SHEET: Delivery

Delivery	☐Singleton ☐twin ☐triplet
Place of birth	☐CHBAH ☐Mofolo mou ☐Lillian Ngoyi mou ☐ other
Gender	☐Male ☐female
Birth weight	☐Kg ☐not available
Birth length	☐Cm ☐not available
Birth head circumference	☐Cm ☐ not available
Mode of delivery	☐NVD ☐C/S(☐elective ☐emergency)
Apgar's score	☐1 min ☐not recorded ☐5 min ☐not recorded ☐10 min ☐not recorded
Gestational age	☐Term ≥ 37 weeks ☐preterm ☐☐weeks
Newborn discharge home well after delivery	☐Yes ☐ no
Admitted to neonatal ward	☐Yes ☐ no
Stillbirth(born dead at ≥28 weeks)	☐Yes ☐ no
Miscarriage(born dead at≤28 weeks gestation)	☐Yes ☐ no
Died after delivery	☐Yes ☐ no
Pregnancy/Delivery related complication	☐Yes ☐ no If yes:☐ 1.prolonged rupture of membranes 2.premature delivery 3.antepartum haemorrhage 4. Postpartum haemorrhage 5. Hypertension 6.retained placenta 7.septic wound (episiotomy or Caesar) 8. Other: specify

Appendix 4: Ethics Approval Letter for MATFLU Trial HIV Negative

Wits Clinical Research

8 Blackwood Avenue, Parktown, 2193, South Africa
Tel. +27-11-274-9200, Fax: +27-11-274-9281
Postnet Suite 189, Private Bag x2600, Houghton, 2041

FAXED & COURIE

Prof SA Madhi,

Respiratory and Meningeal Pathogens Research U
Chris Hani Baragwanath Hospital
First Floor, West Wing
Old Potch Rd, Diepkloof, Soweto
2013

Fax: 086 582 7830/9899886

Dear Prof Madhi,

PROTOCOL NO: Maternalflu_HIVneg

PROTOCOL TITLE: Vaccination of HIV-Uninfected Pregnant Woman with Trivalent Influenza Vaccine in the Prevention of Influenza Illness During Early Infancy and in the Mothers: A Randomized Controlled Phase III Trial Evaluating Safety, Immunogenicity and Efficacy

PRC REFERENCE NUMBER:101106

****

Please be advised that your trial application was:

APPROVED

The Expert Reviewer /(s): Prof C Feldman

Also reviewed by: Miss J Bryce-Borthwick: Acting Chairperson Protocol Review Committee
DR ML Likibi: Gauteng Department of Health
Dr B Binkowska: Gauteng Department of Health

Yours sincerely

Acting **MISS JENNIFER BRYCE-BORTHWICK**
Chairperson: Protocol Review Committee
19 January 2011

cc.

Respiratory Meningeal Pathoge	Dr C Cutland	Tel 011 989 9889/	Cell	082 809 6032	Fax 086 573 6646
Bill and Melinda Gates Foundati	Dr C Cutland	Tel 011 989 9889/	Cell	082 809 6032	Fax 086 573 6646

Appendix 5: Ethics Approval Letter for MATFLU Trial HIV Positive

27-JAN-2011 12:22 FROM: TO:00866776604 P.5

Wits Clinical Research

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Reg No.: 97/15443/07

FAXED & COURIE

Prof SA Madhi,

Respiratory and Meningeal Pathogens Research U
Chris Hani Baragwanath Hospital
First Floor, West Wing
Old Potch Rd, Diepkloof, Soweto
2013

Fax: 086 582 7830/9899886

Dear Prof Madhi,

PROTOCOL NO:
Maternalflu_HIVpos_immuno

PROTOCOL TITLE: Trivalent Influenza Vaccine in HIV-Infected Pregnant Women and Kinetics of Transplacental Anti - Influenza Antibody Transfer and Persistence in Young Infants: A Randomized Controlled Phase II Trial Evaluating Safety and Immunogenicity

PRC REFERENCE NUMBER:101107

Please be advised that your trial application was:

APPROVED

The Expert Reviewer /(s): Prof C Feldman

Also reviewed by: Miss J Bryce-Borthwick: Acting Chairperson Protocol Review Committee
DR ML Likibi: Gauteng Department of Health
Dr B Binkowska: Gauteng Department of Health

Yours sincerely

Acting MISS JENNIFER BRYCE-BORTHWICK
Chairperson: Protocol Review Committee
19 January 2011

cc.

Respiratory Meningeal Pathoge	Dr C Cutland	Tel 011 989 9889/	Cell 082 809 6032	Fax 086 573 6646
Bill and Melinda Gates Foundati	Dr C Cutland	Tel 011 989 9889/	Cell 082 809 6032	Fax 086 573 6646
Respiratory Meningeal Pathoge	R Sterley	Tel 011 989 9891/	Cell	Fax 086 573 6646

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Appendix 6: Ethics Approval Letter from the University of Witwatersrand Ethics committee

R14/49 Dr Mokgadi Nchinyani and Dr Claire Cutland

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M151033

NAME: (Principal Investigator)	Dr Mokgadi Nchinyani and Dr Claire Cutland
DEPARTMENT:	Obstetrics and Gynaecology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	The Effect of Maternal Weight on Obsteric Outcome
DATE CONSIDERED:	30/10/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Yasmin Adam
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	21/11/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in June and will therefore be due in the month of June each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 29/11/2016

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES