PREVALENCE OF OVERWEIGHT AND OBESITY IN CHILDREN AGED 5 to 6 YEARS EXPOSED TO GESTATIONAL DIABETES MELLITUS COMPLICATED PREGNANCIES IN THE WESTERN CAPE, SOUTH AFRICA

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SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In partial fulfilment of the requirements for the degree

MASTER OF SCIENCE IN NURSING

Faculty of Health Sciences

Division of Nursing and Midwifery

School of Health and Rehabilitation Sciences

Date of submission: 24 September 2018

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ACKNOWLEDGEMENTS

I would like to thank the following people, without whom I would not have been able to finish this research project and earn my master's degree!

- Supervisors:

Professor Naomi S. Levitt. Thank you for your faith in me and your kind support, insight, and knowledge steered me through the process from beginning to end.

Tawanda Chivese, my supervisor, who always made me feel confident and always kept me motivated and on task and provided positive guidance and feedback during the entire process. Also, thanks for making and sharing your time and patiently assisting me with the interpretation and writing of the study results.

Professor Una Kyriacos. Thanks for being so patient during the review of my research and providing me with sound guidance throughout the process.

- Participants:

To all participants, thanks for your support and giving of your time in support of this sub-study. A big thanks to Groote Schuur Hospital and its management team for allowing us access to the participants' records and the use of the UCT Clinical Research Centre to conduct the sub-study.

- Family:

To my husband Ed and family, thanks for your love, support, sacrifices, and patience and constant encouragement throughout this project.

ABSTRACT

Background: Gestational Diabetes Mellitus (GDM) has been linked with later metabolic abnormalities in offspring due to subsequent overweight and obesity. In Sub-Saharan Africa, there is a paucity of data on the outcomes of children exposed to GDM in utero.

Aims: The primary aim of this sub-study was to investigate the prevalence of overweight and obesity in 5 and 6-year-old children from GDM complicated pregnancies and macrosomia at birth in the same cohort. The secondary aim was to identify risk factors associated with overweight and obesity in these 5 and 6-year-old children.

Outcome measures: The main outcome was the prevalence of overweight and obesity in these children as measured by their age-specific body mass index (BMI) and Z-scores. Additionally, the association between other risk factors, overweight and obesity was investigated.

Methods: A cross-sectional sub-study design was employed nested within a larger study that is investigating the progression to type 2 diabetes in women managed for GDM during 2010 and 2011. Mothers who participated in the larger study were informed about the sub-study and invited to allow their children to participate in the sub-study. Written informed consent was obtained from the mothers for the sub-study. The following data were collected: anthropometric data at birth and pregnancy related information from the mothers' hospital record, additional demographic, social and medical information by questionnaire from the mother and at the research center. In addition, the children were weighed and had their height measured using standardized methods. Anthropometry was standardized using WHO standards. Risk factors for overweight and obesity were tested using a BMI>1 Z-score cut-off, (as a binary variable) in a manual multivariate logistic regression model.

Results: The sub-study recruited 176 participants; 78 boys (44.3%) and 98 girls (55.7%). The mean (SD) Z-scores for the children's anthropometry at ages 5 to 6 years were 0.28 (1.40) for weight, 0.01 (1.07) for height and 0.37 (1.63) for BMI. The overall prevalence of macrosomia at birth (birth weight>4000 gm) was 12.3 % (95% CI 8.2-9.1). The overall prevalence of overweight in the 5 and 6-year-old children was 13.4% (95% CI 8.6-20.4), while the prevalence of obesity was 14.2% (95% CI 9.2-21.2). The combined prevalence of overweight and obesity was 27.6% (95% CI 20.6-35.9). The prevalence of macrosomia (*P*=0.53) or overweight/obesity proportions (*P*=0.37) at ages 5 to 6 years did not differ by gender. In multivariate logistic regression analysis, factors independently associated with the risk of overweight and obesity were: mothers' oral glucose tolerance test 2-hour blood glucose level during pregnancy (AOR=2.06, 95% CI 1.14-3.74, *P*=0.02), birth weight (AOR=1.00, 95% CI 1.00-1.00, *P*=0.01), child's age in years (AOR=0.03, 95% CI 0.002-0.29, *P*=0.004) and number of adults in the house (AOR=0.38, 95% CI 0.17-0.86, *P*=0.02).

Conclusion: This is the first study to report the prevalence of overweight and obesity in children born from GDM complicated pregnancies, in the Western Cape, South Africa. The combined prevalence of overweight and obesity found in 5 and 6-year-old children exposed to GDM in the Western Cape is higher than overweight and obesity in children reported in other South African studies. This can imply a higher tendency towards overweight and obesity in children exposed to GDM which needs further exploration.

Keywords: diabetes, gestational, childhood, fetal macrosomia, obesity, overweight, Z-score (MESH searched 24/07/2017)

ABBREVIATIONS

AGA – Appropriate for Gestational Age

BMI - Body Mass Index

CDC - Centers for Disease Control and Prevention

GDM - Gestational Diabetes Mellitus

GSH - Groote Schuur Hospital

IGT - Impaired Glucose Tolerance

IOTF- International Obesity Task Force

JHNEBP - John Hopkins Nursing Evidence Based Practice

LGA - Large for Gestational Age

NCBI - National Center for Biotechnology Information

NCPP - National Collaborative Perinatal Project

NDDG - National Diabetes Data Group

NGT- Normal Glucose Tolerance

OGDM- Offspring's of Gestational Diabetes Mothers

ONDM - Offspring's of Non-Diabetic Mothers

OT1DM - Offspring's of Type 1-Diabetic Mothers

OGTT - Oral Glucose Tolerance Test

SES - Socio-Economic Status

SOP - Standard Operating Procedures

T1DM - Type 1 Diabetes Mellitus

T2DM - Type 2 Diabetes Mellitus

UNICEF - United Nations Children's Fund

WHO - World Health Organization

CONCEPTUAL DEFINITIONS

Adolescent: This period of development corresponds roughly to the period between the ages of **10 and 19 years**, which is consistent with the World Health Organization's definition of adolescence.

Body Mass Index (BMI): a simple index of weight-for-height that is used to categorize overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters/kg/m² (WHO, 2015).

Chronic medication: The term chronic applied when the course of a disease or diseases lasts for more than three months. Medication used to treat or manage these diseases, prescribed for three months or longer is referred to as “chronic medication”.

Drinker: A person who uses alcohol in any form or amount

Epigenetic alteration: A heritable change that does not affect the DNA sequence but results in a change in gene expression.

Fetal Macrosomia: A condition that take place when the overgrowth of a fetal leads to a large-for-gestational-age (LGA) fetus. According to the National Center for Biotechnology Information (NCBI), it is defined as birth weight over 4,000 grams or above the 90th percentile for population and gender-specific growth curves. Infant macrosomia is commonly seen in gestational diabetes, prolonged pregnancy and pregnancies complicated by pre-existing diabetes mellitus (NCBI, 1987). For purposes of this sub-study the term macrosomia is used and refers to fetal macrosomia.

Gestational Diabetes Mellitus: is diabetes induced by pregnancy but resolved at the end of pregnancy. It does not include previously diagnosed diabetics who become pregnant (pregnancy in diabetics). Gestational diabetes usually develops in late pregnancy when insulin antagonistic hormones peak leading to insulin resistance; glucose intolerance; and hyperglycemia (NCBI, 1992).

Less active: In this sub-study “less active” refers to people with physical activity/exercise of less than once a week.

Low income: In a South African context, it can be defined as Households who reported an annual household income of between R1 and R19 200. According to the Income and Expenditure Survey 2010/2011 (IES 2010/11), the average annual household income for poor households was R25 348.

More active: In this sub-study "more active" refers to people with physical activity/exercise of more than twice a week.

Obesity: Children were classified as obese if their weight-for-height exceeded the 95th percentile for population and gender-specific growth curves (Baptiste-Roberts, Nicholson, Wang & Brancati, 2012). Obesity in adults is defined as a BMI higher than 30 kg/m² (WHO, 2015).

Overweight: Children were classified as overweight if their weight-for-height exceeded the 85th percentile for population and gender-specific growth curves (Baptiste-Roberts et al., 2012). Overweight in adults is defined as a BMI higher than 25 kg/m² (WHO, 2015).

LGA: Infants whose weight is > the 90th percentile for gestational age are classified as LGA.

Macrosomia: is birth weight > 4000 g in a term infant.

Standardized Z-scores: **Z-score** – The deviation of an individual's value from the median value of a reference population, divided by the standard deviation of the reference population (WHO, 1997).

Standardized Z-score classification:

- Overweight = (1 <weight Z-score≤2)
- obese = (>2 weight Z-scores)
- thin = (<-2 weight Z-scores)
- very thin = (<-3 weight Z-scores)
- normal = (1<weight Z-score>2)

Undernutrition: A deficiency of proper nutrition, caused by not having sufficient food or not eating enough food containing substances necessary for growth and health.

WHO BMI cut-offs: The World Health Organisation (WHO) Global Database on Child Growth and Malnutrition uses a Z-score cut-off point of <-1 SD to classify low weight-for-age, low height-for-age and low weight-for-height as moderate and severe undernutrition, and <-2 SD to define severe undernutrition. The cut-off point of >+1 SD classifies high weight-for-height as overweight in children (WHO, 1997). Normal weight: -1.0≤BMI Z-score≤+1.

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Chapter 1 INTRODUCTION

1.1 Background

Gestational Diabetes Mellitus (GDM), is associated with overweight and obesity in children and is usually diagnosed for the first time during pregnancy using an oral glucose tolerance test (Gilmartin, Ural and Repke, 2007). Worldwide, GDM is on the rise, while in Africa, there are scant data on the prevalence of GDM which varies between 0 and 14% (Macaulay, Dunger and Norris, 2014; Mwanri, Kinabo, Ramaiya and Feskens, 2015). In Sub-Saharan Africa, there is a paucity of data on the outcomes of children exposed to GDM in utero. In South Africa, GDM prevalence has been estimated to be as high as 26% (Adam & Rheeder, 2017).

Childhood obesity is one of the most serious public health challenges of the 21st century (WHO, 2016). Globally, the increasing rate of childhood overweight and obesity poses significant public health problems from birth and, if these children remain overweight or obese, throughout their adult lives (Reilly & Kelly, 2011). Overweight and obese children are more likely to develop cardio-metabolic conditions such as type 2 diabetes mellitus (T2DM), cardiovascular conditions, and various cancers at a younger age compared to children who are of normal weight (Ge, Zhang, Schatten and Sun (2014) Swinburn et al., 2011). In Africa, there are no data on the cardio-metabolic outcomes (including overweight and obesity) of children exposed to GDM, despite the fact that GDM prevalence appears to be on the rise.

Convincing evidence demonstrates notable increases in overweight and obesity in low- and middle-income countries (LMIC) (WHO, 2015). In a systematic review of 144 countries, De Onis, Blössner and Borghi (2010) estimated that the prevalence of childhood overweight and obesity worldwide rose from 4.2% (95% CI: 3.2%, 5.2%) in 1990 to 6.7% (95% CI: 5.6%, 7.7%) in 2010. A systematic review by Ng et al., (2014) for the period 1980 to 2013 examined the global, regional and national prevalence of overweight and obesity in children and adults of 188 countries using the international Obesity Task Force (IOTF) criteria. The prevalence of overweight and obesity increased from 29.8% to 38% for women and from 8.1% to 12.9% for children and adolescents worldwide and in developing countries, from 8.1% (7.7-8.6) to 12.9% (12.3-13.5) in 2013 for boys and from 8.4% (8.1-8.8) to 13.4% (13.0-13.9) in girls (Ng et al., 2014). The number of overweight or obese children in Africa has nearly doubled from 5.4 million

to 10.3 million between 1990 and 2014 (WHO, 2016). Furthermore, of the overweight children under 5 years of age in 2014, 48% lived in Asia and 25% in Africa (WHO, 2016).

Several studies have investigated the prevalence of overweight and its associated risk factors in children such as lack of physical activity and unhealthy dietary practices at home and at school (Mwaikambo, Leyna, Killewo, Simba, & Puoane, 2015) that can be improved through government policies (Swinburn et al., 2011).

This study was a sub-study within a larger cross-sectional study which is investigating the prevalence of T2DM and associated risk factors in South Africa 5 years after gestational diabetes mellitus has been diagnosed. In the present sub-study, the aim was to investigate the prevalence of macrosomia at birth and the prevalence of overweight and obesity in the cohort of children of the women in the larger study, aged 5 to 6 years living in the Western Cape of South Africa, exposed to GDM during pregnancy.

1.2 Problem Statement

A review of published national and international studies has identified childhood obesity as a growing public health epidemic that affects children's physical and mental health (WHO, 2014) and if continued into adulthood, results in chronic illness. Despite recent published data on childhood overweight and/or obesity in South Africa, studies do not appear to have addressed this phenomenon in children exposed to GDM during pregnancy, despite the reported high GDM prevalence. This sub-study has attempted to address this gap in knowledge (Burns & Grove, 2011).

1.3 Research Questions

This sub-study investigated three questions:

1. What is the prevalence of overweight at birth of infants delivered at the Groote Schuur hospital during November 2010 and November 2011 who were exposed to GDM during the pregnancy?
2. What is the prevalence of overweight and obesity in the same cohort of 5 and 6-year-old children as assessed in 2016-2017?
3. What are the risk factors associated with overweight and obesity in these 5 and 6-year-old children?

1.4 Aims and Objectives of the sub-study

1.4.1 Aims

The primary aim of the sub-study was to investigate the prevalence of macrosomia at birth from GDM complicated pregnancies in the Western Cape, South Africa and overweight and obesity in the same cohort of 5 and 6-year-old children. The secondary aim was to identify the risk factors associated with overweight and obesity in these 5 and 6-year-old children born from GDM complicated pregnancies.

1.4.2 Objectives

To achieve the above aim, the sub-study addressed the following objectives:

1.4.2.1 To describe the anthropometric characteristics of the infants exposed to GDM during pregnancy in the years 2010 and 2011 at Groote Schuur Hospital (GSH) and in the same cohort of 5 and 6-year-old children.

1.4.2.2 To determine the proportion of macrosomia in the same cohort.

1.4.2.3 To estimate the prevalence of overweight and obesity in the same cohort of 5 and 6-year-old children by calculating the proportion of overweight and obese children using WHO BMI cut-offs as well as standardized Z-scores.

1.4.2.4 To identify factors (child and maternal) associated with increased risk for overweight and obesity in these 5 and 6-year-old children exposed to GDM during pregnancy.

1.4.2.5 To compare the anthropometric measures and the prevalence of overweight and obesity between genders in these 5 and 6-year-old children exposed to GDM during pregnancy.

1.5 Rationale for the sub-study

Apart from describing the prevalence of macrosomia in GDM offspring at birth within a local Western Cape context, this sub-study provides the only data on the prevalence of overweight and obesity in children from GDM complicated pregnancies and factors extraneous to GDM that may increase the risk of overweight and obesity in 5 and 6-year-old children. Identification of these risk factors will help in designing appropriate, context-specific strategies to prevent or counter overweight and obesity in 5 and 6-year-old children.

1.6 Summary

A global increase in childhood overweight and obesity and in GDM, particularly in low- and middle-income countries, with evidence suggesting that preschool children exposed to GDM may have a higher risk for overweight and obesity than non-GDM exposed children is of concern. The paucity of published literature from Africa on macrosomia in GDM exposed newborns as well as overweight and obesity prevalence in 5-6 year olds and the associated risk factors contributing to childhood overweight also encouraged research in these areas. The aim of this sub-study was to investigate the prevalence of overweight and obesity in GDM-exposed 5 and 6-year-old children. The following chapter deals with a review of the pertinent literature that was used to guide the development of the sub-study.

Chapter 2 LITERATURE REVIEW

2.1 Introduction

This chapter provides a review of the literature that was used to guide the development of the sub-study and research instruments and for interpreting the results. The review is a critique of existing research on the prevalence of overweight and obesity in preschool children exposed to GDM and informs the study on appropriate study methods as well as gaps in the literature (Burns & Grove, 2011) where further research is required.

Researchers have documented a vast amount of literature and have concluded that childhood overweight and obesity develops into adult overweight or obesity and can cause serious metabolic conditions and cardiac diseases. A review of the literature addressed the three research questions in this sub-study.

1) What is the prevalence of overweight at birth of infants (macrosomia) exposed to GDM during a pregnancy?
2) What is the prevalence of overweight and obesity in 5 and 6-year-old children exposed to GDM?
3) What are the risk factors associated with overweight and obesity in these children?

2.2 Literature search strategy

The search strategy employed for the sub-study identified studies that focused on the prevalence of overweight and obesity in 5 and 6-year-old children from GDM complicated pregnancies and associated risk factors. The searched dates primarily ranged from 2005 to 2016. The earliest reference (1987) is for a NCBI MESH search. Other relevant but dated sources were included.

The following search filters were used: journal articles, English language, free full text, human, and age limits (infant: birth-23 months, preschool child: 2 to 5 years, child: 6 to 12 years). A detailed and wide search strategy was developed using the following electronic databases: PubMed, Medical Subject Headings (MeSH), Africa-wide Information via EBSCOhost, ScienceDirect, Google Scholar, EBSCOhost and the Cochrane Library. The Boolean operators

‘AND’ and ‘OR’ were used as studies combining childhood overweight associated with GDM were limited. The search terms (keywords) gestational diabetes, fetal macrosomia, Africa, South Africa, Western Cape, childhood overweight, childhood obesity, childhood Z-score and risk factors were used in various combinations.

Searched articles were limited to the English language and human subjects. Studies that did not report or allow computational data of the prevalence of overweight and obesity in 5 and 6-year-old children from GDM complicated pregnancies and associated risk factors were excluded. The term GDM alone resulted in 6 articles while other keywords such as ‘fetal macrosomia’, ‘fetal macrosomia and overweight’, ‘fetal macrosomia and obesity were unsuccessful. The terms ‘GDM and pregnancy’ resulted in 8 articles while the term ‘GDM and fetal macrosomia’ was unsuccessful. The term ‘fetal macrosomia or obesity’ resulted in 130 hits. Combining terms ‘fetal macrosomia or childhood overweight or childhood obesity or risk factors or childhood Z-scores’ resulted in 6,468 articles. The most successful search resulted in 3,327 published papers. Lastly South Africa, Western Cape, Z-score and risk factors were used in different combinations to focus the search.

Search results showed that the published research on children exposed to GDM in utero is limited. Research specific to Africa, South Africa and the Western Cape is even more limited in scope and availability. Reference lists were hand searched for relevant articles, books, and grey literature.. The refined search strategy resulted in a total of 155 articles. This resulted in 54 references that were reviewed and met the study’s criteria for inclusion. Eighty-six studies were excluded because data could not be extracted from the articles to determine the prevalence of overweight and obesity in 5 and 6-year-old children from GDM complicated pregnancies and associated risk factors. Upon closer inspection, another 15 references were excluded because the articles were either ambiguous, dated or did not meet inclusion criteria. Figure 2.1 represents a flowchart of the selected articles from the literature search.

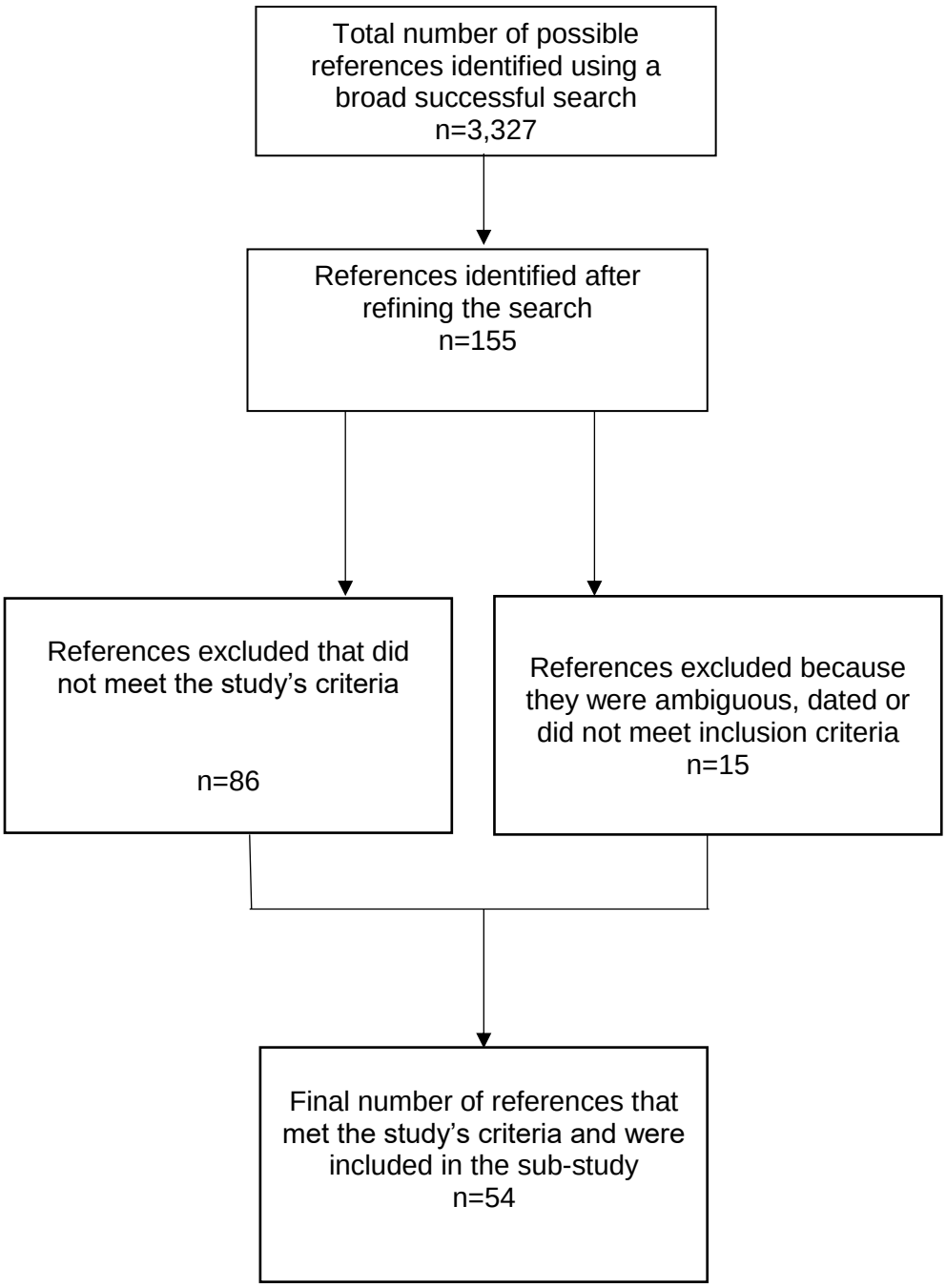

Figure 2.1: Flow diagram of the literature search process

2.3 Assessment of hierarchy of evidence of the reviewed studies

The reviewed studies on GDM and the prevalence of overweight and obesity in preschool children were evaluated by hierarchy of evidence as shown in Figure 2.2.

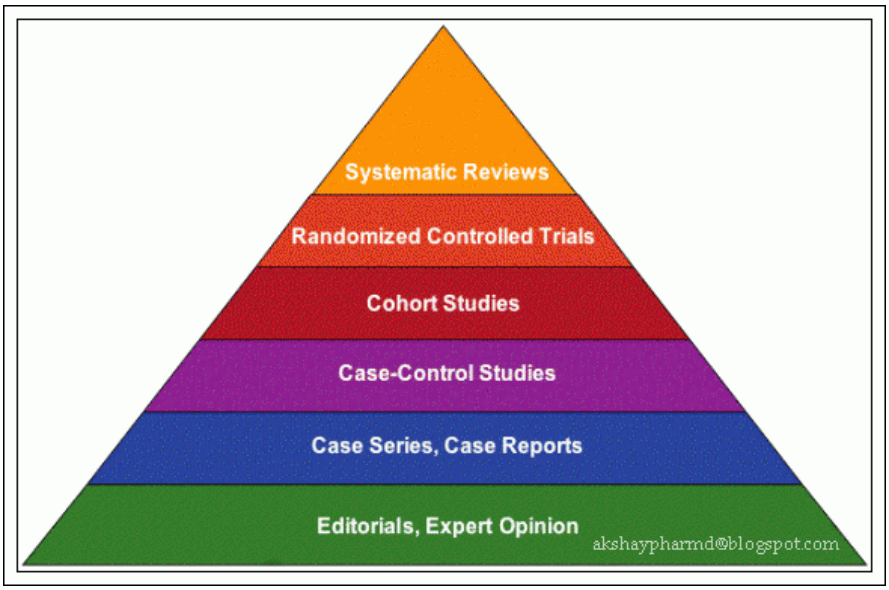

Figure 2. 2: Hierarchy of evidence of the reviewed studies

(Reference: http://3.bp.blogspot.com/-VCmwq8LFAk4/T1-UId5KcGI/AAAAAAAAAog/foLHY3nWBUs/s1600/1.gif)

Systematic reviews at the top of the pyramid are considered to provide the highest levels of evidence, whereas editorials and expert opinion are at the base of the triangle. The study design of the reviewed studies is shown in Table 2.2.

2.4 Assessment of the quality of the reviewed studies

The quality of the reviewed studies regarding GDM exposure and preschool overweight and obesity has been rated according to the Johns Hopkins Nursing Evidence-Based Practice (JHNEBP) Appraisal Tool (Newhouse, Dearholt, Poe, Pugh & White, 2005; Appendix F) as A (high quality), B (good quality) and C (low quality or major flaws (Table 2.1).

Table 2.1: Johns Hopkins Nursing Evidence-Based Practice Appraisal Tool (John Hopkins Medicine, 2005)

A: <u>High quality</u>:	consistent, generalizable results; sufficient sample size for the study design; adequate control; definitive conclusions; consistent recommendations based on comprehensive literature review that includes thorough reference to scientific evidence
B: <u>Good quality</u>:	reasonably consistent results; sufficient sample size for the study design; some control, and fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence
C: <u>Low quality or major flaws</u>:	little evidence with inconsistent results; insufficient sample size for the study design; conclusions cannot be drawn

2.5 Introduction and themes extracted from a review of the published literature

Overweight and obesity are defined as excessive fat growth that presents a risk to a person's health (WHO, 2015). Weight that is higher than that considered as healthy for a given height is described as overweight or obese (CDC, 2016). Body Mass Index (BMI), is used as a screening tool for overweight or obesity in adults. In children BMI is age-and gender-specific and is often referred to as BMI-for-age (CDC, 2016). The WHO has different criteria for identification of overweight and obesity in adults and children.

Overweight and obesity BMI cut-offs are not a good indication of overweight as overweight can develop before these cut-off points are reached (WHO, 2016). For example, children can develop more abdominal fat even if their BMI is within normal limits (WHO 2016). For this sub-study, 5 and 6-year-old participants' weight-for-age Z-scores were compared with the WHO Child Growth Standards to determine if they were overweight or obese. Overweight in children is described as weight-for-height Z-score values with more than 2 standard deviations based on the WHO growth standard median for age and gender (WHO, 2016). Obesity in children is described as children with weight-for-height Z-scores values 3 times above standard deviations from the WHO growth standard median for age and gender (WHO, 2016).

The following themes related to the study focus were extracted:

- GDM, fetal macrosomia and prevalence (research question 1)
    - Background to GDM and fetal macrosomia
    - Prevalence of fetal macrosomia in GDM exposed infants
- Overweight and obesity in children and overweight and obesity in children exposed to GDM (research question 2)
    - Prevalence of overweight and obesity in children
- Risk factors associated with overweight and obesity in children (research question 3)
    - Health risks in overweight and obesity in children and burden on health services
    - Interventions needed for overweight and obesity in children

A discussion of each theme follows and a summary of the themes and the literature is presented in Table 2.2.

2.5.1 GDM, fetal macrosomia and prevalence

2.5.1.1 Background to GDM related to fetal macrosomia and childhood overweight

Diabetes Mellitus is defined as a chronic disease when the body does not make sufficient quantities of the hormone insulin, or when the body cannot efficiently use the insulin it makes (WHO, 2016) to control blood sugar levels. Raised blood sugar levels pose serious health threats and risks to a person with uncontrolled diabetes. The three sub-categories of Diabetes Mellitus: Type 1 (T1DM), Type 2 (T2DM) and Gestational Diabetes Mellitus are described below:

- T1DM: (insulin-dependent diabetes) a condition where the body cannot produce sufficient insulin to control normal blood sugar levels.
- T2DM: (previously named non-insulin dependent or adult-onset diabetes) is caused by the body's improper use of insulin and usually develops in adulthood (WHO, 2016) and seen mostly in adults, but worldwide, since the mid-1990s is occurring more often in children (WHO, 2016; Reinehr, 2013).
- GDM: any degree of glucose intolerance with onset or first recognition during pregnancy (Metzger, Coustan, & Committee, 1998) and diagnosed by using the WHO (2014)

criteria based on a 2-hr 75g Oral Glucose Tolerance Test. Cut offs: for Fasting Blood glucose between 5.1 and 6.9 mmol/L; 1-hr plasma glucose ≥10.0 mmol/L (180mg/dL) and a 2-hr plasma glucose result of 8.5-11.0 mmol/L (153-199 mg/dL) (WHO, 2016).

Why may GDM, a state of glucose intolerance during pregnancy, pose a risk and lead to overweight in children and later in their adult life? A healthy uterine environment is a basis for the normal development of the foetus and child in later life. In GDM the foetus can be exposed to high maternal blood sugar levels that create an imbalance in the uterine environment (Desai, Beall & Ross, 2012). In the Global Diabetes Report (2016), the WHO described high blood sugar in GDM as blood sugars above the normal value, but still below diagnostic values for diabetes (WHO, 2016). GDM has been linked to overweight at birth (fetal macrosomia) in exposed infants by many researchers.

GDM is a commonly expected risk factor associated with infants who are large for gestational age (LGA) also known as fetal macrosomia. Fetal macrosomia is defined as a birth weight above 4,000 grams (Najafian & Cheraghi, 2012). Boney et al., (2005) found that children who were LGA, that is, having a birth weight above the 90th percentile, had been exposed to an intrauterine environment of either high blood sugar levels during uncontrolled diabetes or maternal obesity. A cohort study conducted in Iran showed that diabetes and maternal obesity (an increased BMI) were a major risk factor associated with macrosomia (Najafian & Cheraghi, 2012). Hyperglycemia in utero can cause epigenetic alterations which may subsequently cause overweight and obesity in mothers and their offspring later in life (Ruchat et al 2013).

The mechanism through which GDM leads to both macrosomia and, possibly later childhood overweight and obesity is not clearly understood. However, intrauterine hyperglycemia during GDM may cause fetal hypothalamic changes that lead to leptin resistance (Vrachnis et al., 2012). Data from studies demonstrated that placentas from mothers with GDM had altered DNA methylation patterns within their leptin and adiponectin genes (Ruchat et al., 2013). Cord blood leptin levels from GDM mothers were 29.3 ng/ml compared to 7.9 ng/ml in a control group (Dabelea, 2007). This increase in fetal leptin levels resulted in hyperinsulinemia and leptin resistance which is a forerunner of childhood obesity (Dabelea, 2007; Wright et al., 2009).

Leptin resistance is postulated to be the origin of fetal epigenetics programming that causes obesity and results in metabolic conditions in childhood and later adult life (Vickers, 2007; Desai et al., 2012). The primary function of leptin is to inform the hypothalamus that one is satiated.

As a result of leptin resistance, there is increased fat accumulation in newborns which leads to hyperglycemia and high insulin levels (Desai et al., 2012). During the past decade, the world has witnessed a significant increase (25%) in high birth weight in babies associated with GDM (Desai et al., 2012). These high birth weight babies may have increased health risk factors such as adipose tissue mass and higher rates of obesity and diabetes in later life.

2.5.1.2 Prevalence of fetal macrosomia in GDM exposed infants

Few studies in Africa have investigated the prevalence of GDM as evidenced in two systematic reviews. In the first by Macaulay, Dunger and Norris (2014), data were available from 6 of 54 (11%) African countries. The diversity of population groups and different diagnostic tests used to diagnose GDM indicates the difficulty in determining the prevalence of GDM in African countries and in interpreting data for the South African context. A systematic review by Mwanri et al., (2015) on the prevalence of and risk factors for GDM in 47 sub-Saharan African countries reports a prevalence of 14%. The results indicate a need for earlier screening for GDM and intervention to slow the progression of this disease and its complications in Sub-Saharan Africa (Mwanri et al., 2015). An Iranian cohort study reported that diabetic participants delivered a statistically significant number of macrocosmic babies (39.5%, $P<0.05$) compared to 6.1% in the control-group (Najafian et al., 2012). In Soweto, South Africa, findings from a recent unpublished pilot study (2016) have shown a GDM prevalence of 15%. However, there is limited published data from South Africa and the Western Cape on prevalence of GDM, risk factors associated with developing GDM and the outcomes of GDM on the exposed children.

In some developed countries the prevalence of GDM ranged from 2% (Sweden) to 12.8% (Northern California) (Hunt & Schuller, 2007). In China, between 1999 and 2008 the prevalence of GDM increased from 2.4% to 6.8% (Zhang et al., 2011). Chinese children exposed to GDM in utero had a macrosomia prevalence of 14.0% versus 10.4% in infants not exposed to GDM (Zhao et al., 2015). An increased prevalence of 29% in LGA offspring of GDM (OGDM) mothers in the USA is reported by Boney et al., (2005). Wright et al., (2009) noted a Z-score of 0.26 (0.92) in GDM exposed infants versus 0.18 (0.96) in offspring of NonGDM (ONGDM) mothers. A prevalence of 18% of LGA infants was found when mothers had a fasting glucose of >95 mg/dl versus 8–9% in both treatment groups with a fasting OGTT≤ 95 mg/dl (Hillier et al., 2007). The Gillman, Rifas-Shiman, Berkey, Field & Colditz, (2003) study that investigated overweight

and obesity in GDM exposed children, concluded that infants of GDM mothers had higher birthweights than those of Non-GDM mothers.

Prospective analysis of data from 28,358 USA mothers and their children enrolled in the National Collaborative Perinatal Project from 1959-1965 to determine the effects of GDM on growth patterns of their offspring from birth until age 7, showed that 1.7% of women had GDM (Baptiste-Roberts et al., 2012). Their children had both a higher average birth weight and a 61% greater chance of being medically overweight upon reaching the age of 7 years. A Polish study documented a macrosomia prevalence of 20.6% In OGDM mothers versus 13% in ONGDM mothers (Wroblewska-Seniuk, Wender-Ozegowska & Szczapa, 2009).

2.5.2 Overweight and obesity in children and overweight and obesity children (5-6years old) exposed to GDM

There is limited published research on the prevalence of overweight and obesity in children who had been exposed to GDM. Kim, England, Sharma and Njoroge (2011) were the first to complete a systematic review to investigate the prevalence of overweight and obesity in children exposed to GDM. In a USA study Kim et al., (2011) reported that the prevalence of overweight and obesity in GDM-exposed children was not statistically significant after adjustment for pre-pregnancy BMI (Table 2.2.

A USA cohort study by Gillman et al., (2003) examined the association between birth weight and GDM and adolescent body mass index (BMI) and differentiated between GDM-specific effects and those caused mainly by maternal obesity. A sample of 7,981 girls and 6,900 boys between the ages of 9 and 14 (mean, 11.9 years) showed an increased risk of overweight for children exposed to GDM. The results estimated a 17.1% risk of being overweight and 9.7% were overweight in the GDM exposed children. In the group without GDM, 14.2% were at risk of being overweight and 6.6% were overweight. One major limitation of the Gillman study was recruitment of a study population of 93.6% white participants, which was not reflective of the general population. The strength of the study mainly involved the exclusion of pre-gestational diabetic mothers (Gillman et al., 2003) (Table 2.2).

In another study conducted in the USA, Hillier et al., (2007) examined the prevalence of overweight and obesity in 5 to 7-year-old children exposed to GDM or untreated hyperglycemia compared to overweight and obesity in children with the same ages in non-diabetic mothers.

The risk of obesity in the children whose mothers had an increased fasting glucose of at least 5.3 mmol/l (95 mg/dl) on the Oral Glucose Tolerance Test (OGTT) was nearly double that of the children whose mothers had a normal fasting blood glucose ($p<0.0001$) (Hillier et al., 2007). These study results emphasized the fact that it is not GDM per se, but whether the GDM was treated or not, that increased the risk of overweight or obesity in childhood (Hillier et al., 2007). The strengths of this cohort study were the diverse, large multi-ethnic population and that pre-gestational diabetic mothers had been excluded. The reduction in sample size when some participants resigned from the Kaiser Permanente Medical insurance was documented as a limitation (Hillier et al., 2007).

Results of the cohort study by Baptiste-Roberts et al., (2012) showed that prevalence of overweight in GDM exposed children was higher at 23.3% than 12.6% in non-GDM exposed children. This study included a large diverse population over a 7-year period but had several limitations which included: error in the assessment of gestational age, inability to adjust for unmeasured confounders, possible misclassification of GDM and limited generalizability since participants in the National Collaborative Perinatal Project had been enrolled more than 40 years ago previously (Baptiste-Roberts et al., 2012).

Studies from other countries were also compared with USA studies which dominated this research field. In a German cohort study, researchers investigated the prevalence of overweight and insulin resistance in children aged 2, 8 and 11 years exposed to GDM (Boerschmann, Pflüger, Henneberger, Ziegler & Hummel, 2010). Differences in prevalence of overweight in GDM exposed children compared to overweight in children of T1DM mothers and children of NDM were significant. In children exposed to GDM overweight prevalence was17.2% at age 2, 20.2% at age 8 and 31.1% at age 11 years; higher compared to 15.8%, 11.0%, and15.8% in children of T1DM mothers and 11.4%, 10.3% and 15.5% in children of NDM mothers (Boerschmann et al., 2010). The P values were 0.006 at 2 years, 0.02 at 8 years and 0.01 at 11 years (Table 2.2). The strength of the Boerschmanns' study was that the groups of participants involved were recruited over the same period and were from the same region and ethnicity. This could also be a limitation as study results could not be generalized to the broader population. In contrast, the study was limited because it did not investigate other common risk factors of childhood overweight, such as diet habits during that period in the child's life, physical activity and socioeconomic status (Boerschmann et al., 2010).

In a Polish study, overweight and obesity in children 4 to 9 years old showed no statistically significant differences in BMI (Table 2.2) (Wroblewska-Seniuk et al., 2009). Similarly, a Korean study conducted by Lee, Jang, Park and Cho (2007) concluded that 3 to 4-year-old children exposed to GDM during pregnancy had no significant increase in their BMI when compared to a control group (Lee et al., 2007). In comparison, the BMI of offspring of GDM mothers, who were 5 years old or more remained significantly higher ($P<0.01$) than that of offspring of IGT mothers (Lee et al., 2007).

The results in these studies were not conclusive and could be due to several factors: the use of different glucose loads for the OGTT, the cut off results for OGTT to diagnose GDM not being the same, uncertainty of gestational age when GDM was diagnosed, the criteria to define overweight/obesity in studies were not the same in all studies and inconsistent investigation of additional risk factors.

2.5.2.1 Prevalence of overweight and obesity in children

According to the Centers for Disease Control and Prevention (CDC), BMI is a ratio used to determine childhood overweight and obesity. For children, BMI is age and gender-specific and is often referred to as BMI-for-age. A child's weight status is determined using an age and gender-specific percentile for BMI because children's body compositions vary as they age. Therefore, BMI levels among children are expressed relative to other children of the same age and gender (CDC, 2016). Overweight is defined as a BMI at or above the 85th percentile and below the 95th percentile for children of the same age and gender (CDC, 2016). Obesity is defined as a BMI at or above the 95th percentile for children and teens of the same age and gender (CDC, 2016).

2.5.2.2 Global Prevalence of overweight and obesity in children

The WHO (2014) predicted an increase in childhood overweight in all regions worldwide from 7% in 2012 to 11% in 2025. In 2013, the United Nations Children Fund (UNICEF), WHO and the World Bank estimated that the number of overweight and obese children younger than 5-years old was expected to increase from 32 to 42 million in 3 years from 2000 to 2013 (World Health Organization, 2014). The 2014 Report of the Commission on Ending Childhood obesity indicated that 41 million children under the age of 5 were either overweight or obese (WHO,

2016). The highest number of overweight and obese children were reportedly in Africa (11 million) and Asia (18 million) (World Health Organization, 2014).

In the United States of America (USA), a representative National Health and Nutrition Examination Survey from 2011-2012 identified the obesity rate in children 2 to 5-years old as 8.4% (Ogden, Carroll, Kit, & Flegal, 2014). A 2005 Canadian survey showed that 32.9% of grade 5 students aged 10 in Nova Scotia were overweight and 9.9% were obese (Veugelers & Fitzgerald, 2005). In India the prevalence of obesity between 1976 and 1980 in preschool children of both genders between the age of 2 and 5-years increased by 5% while in boys and girls between the age of 6 and 11 years the increase was 13.1% (Karnik & Kanekar, 2015).

2.5.2.3 Prevalence of overweight and obesity in children in Africa

The prevalence of childhood overweight and obesity in boys in developing countries increased from 8.1% in 1980 to 12.9% in 2013 and for girls from 8.45% to 13.4% as reported by Ng et al., 2014. Athough this was a large study, there were limitations. One very important limitation is that the study included surveys of self-reported weights and heights which resulted in systematic bias. Secondly, some studies were excluded because they did not include national figures (Ng et al., 2014). These authors concluded that obesity had increased over three decades with no national intervention success stories (Ng et al., 2014).

Several African studies have shown a growing epidemic of overweight and obesity among children of different age groups. A cross-sectional study conducted in 26 of 49 countries in Sub-Saharan Africa from 2010 to 2014 reported that overweight and obesity in preschool children from birth to 59 months was estimated at 6.8% (Gebremedhin, 2015) increasingly becoming a public health risk with harmful health risks for adults (Gebremedhin, 2015).

A cross-sectional study conducted in Kenya that included 320 children aged 3 to 6-years old, in public and private schools investigated the prevalence of overweight and obesity and associated risk factors. Childhood overweight and obesity were defined in terms of body mass index Z-scores. This study showed a prevalence of 13.4 % overweight and 6.9 % obesity (Wandia, Ettyang, & Mbagaya, 2014). A cross-sectional study conducted in Tanzania that included 1,722 children from public and private schools aged 7 to14 years, reported a prevalence of obesity of 10.2% and of overweight of 4.5% (Mwaikambo, Leyna, Killewo, Simba

& Puoane, 2015). A 2011 Demographic Health Survey of 2,205 boys and 2,313 girls in Cameroon (Central Africa), (mean age 30.2 months) conducted over a period of eight months reported BMI Z-scores based on the WHO 2006 reference showing a prevalence of 8% for overweight and obesity and 1.7% for obesity alone (Tchoubi et al., 2015).

2.5.2.4 Prevalence of overweight and obesity in children in South Africa

In South Africa, obesity rates among children and adolescents have reached epidemic proportions, with an estimated 1 out of every 5 children suffering from obesity (Van der Merwe, 2012). Recent comparisons of prevalence studies in different regions in South Africa showed a mean prevalence of overweight and obesity of 15% (Rossouw, Grant, & Viljoen, 2012). Somers (2004), reported overweight and obesity prevalence rates among children aged 10 to 16-years old, in the Western Cape and South Africa in general of 8.31% for overweight and 2.97% for obesity

A cross-sectional study conducted by Kruger et al., (2005), showed an overweight and obesity rate of 7.8% in 10 to 15-year old children in the North West province of South Africa. In Mpumalanga, South Africa, a cross-sectional growth survey of 3,511 children and adolescents aged between 1 and 20 years, investigated stunting, overweight and obesity, and metabolic disease risk (Kimani-Murage et al., 2010). For children aged 1 to 5 years, the 2006 WHO Growth Z-scores were used for the estimation; for those older than 6 years the 1977 NCHS/WHO reference was used. The study found a prevalence of overweight and obesity of less than 5% among boys and girls aged 5 to 6 years. Irrespective of the different age groups and criteria used, most studies showed an increase in prevalence of childhood overweight and obesity.

2.5.3 Risk factors associated with overweight and obesity in children

Risk factors associated with childhood overweight and obesity was found to be similar in other published literature. A South African study found that low maternal education and sedentary lifestyle were risk factors that contributed to overweight and obesity in children aged 1 to 9 years (Kruger et al., 2005).

Maternal overweight/obesity itself is a known high-risk factor for development of GDM. A maternal obesity study conducted by Chu and others (2007) showed that overweight pregnant

women had twice the risk while obese pregnant women had four times the risk for developing GDM as compared with normal-weight pregnant women (Chu et al., 2007). Maternal overweight and high birth weight were also found to be high risk factors for developing childhood overweight and/or obesity in other studies (Gebremedhin, 2015; Tchoubi et al., 2015). Exposure to a hyperglycemic intrauterine environment was found to be a risk factor for association with greater adiposity from infancy (Barouki, Gluckman, Grandjean, Hanson, & Heindel, 2012). Desai et al., (2012) suggested that overweight and obesity in children are directly related to exposure to GDM in utero. However, a few limitations of the study were ages of the children were not mentioned and the significance of maternal obesity versus GDM as a leading cause for childhood overweight could not be distinguished.

Risk factors associated with developing GDM include: increased age, smoking, family history of diabetes, obesity, history of previous GDM, history of macrosomia, stillbirth or birth to infant with congenital anomalies (WHO 2016; Gilmartin et al. 2007). The risk for developing GDM is higher in women aged 25 years and older and who are obese (Mamabolo, Alberts, Levitt, Delemarre-van de Waal & Steyn, 2007). Chu et al., (2007) also found that the risk to develop GDM is 2-8 times higher in overweight and obese women compared to normal weight pregnant women. These results were from a meta-analysis that investigated maternal obesity as risk for GDM in different countries including the USA, United Kingdom (UK), Italy, Canada and Australia (Chu et al., 2007).

In a Kenyan prevalence study of childhood overweight and obesity, a higher prevalence of overweight and obesity was reported in private schools, compared to public schools ($p<0.001$) (Wandia et al., 2014). The same study results showed that children of families that owned a television were more overweight or obese compared to those children from families that did not have television ($p<0.002$) (Wandia et al., 2014). In India, risk factors associated with the increasing prevalence of childhood overweight and obesity were identified as the imbalance between energy consumed and energy used (Karnik & Kanekar, 2015). These risk factors can be grouped as behavioral such as watching television while snacking unhealthy foods and environmental factors such as safe side walks, that lead to reduced physical activity (Karnik & Kanekar, 2015).

A Health of the Nation Study was used to determine prevalence of overweight and obesity in a cohort (2001 to 2004) of 10,195 South African primary school children aged 6 to 13 years. The

study showed that gender and ethnicity were the two main factors associated with obesity and overweight. The prevalence of obesity among boys was 2.4% and the prevalence of overweight was 4.8%. Using the method of Cole et al., (2000) to determine cut-off points for overweight and obesity, the prevalence of obesity in girls was 10.9% and 17.5% for overweight (Armstrong, Lambert, Sharwood & Lambert, 2006). A significant difference was demonstrated in overweight and obesity prevalence in black and white girls at ages 6 and 11 years. The percentage of overweight and obesity among black girls increased from 11.95% in 6-year olds to 21.8% in 11-year old girls. Among white girls the prevalence of overweight and obesity was 25.4% for 6-year olds and 14.5% for 11-year olds (Armstrong et al., 2006).

A summary of study designs on prevalence of overweight and obesity in children, macrosomia in GDM exposed newborns versus newborns of Non-GDM mothers, additional risk factors associated with overweight and obesity and quality of evidenceis presented in Table 2.2.

Table 2.2: Summary of study designs on prevalence of overweight and obesity in children,macrosomia in GDM exposed newborns versus newborns of Non-GDM mothers, additional risk factors associated with overweight and obesity and quality of evidence

Author(s)	Country	Study Design	Population, sample size N=Number of GDM and exposed children versus control group	Criteria to measure overweight and obesity	Prevalence (%) of overweight & obesity in OGDM[1] mothers	Prevalence (%) of overweight & obesity in ONGDM[2] mothers	Prevalence (%) of macrosomia in OGDM mothers	Prevalence (%) of macrosomia in ONGDM mothers	Additional risk factors for overweight and obesity	Quality of evidence A=High B=Good C=Low
Systematic Review										
Kim et al., 2011	USA	Systematic Review	12 studies included (3yrs)	BMI > 85th percentile BMI > 95th percentile	No distinction between GDM and maternal obesity as a cause for childhood overweight No clear association between GDM childhood overweight	No distinction between GDM and maternal obesity as a cause for childhood obesity No clear association between GDM childhood obesity	Not measured	Not measured	Maternal Pre-pregnancy Obesity Poor dietary habits and Sedentary lifestyle pre-pregnancy	A
Cohort Studies										

Author(s)	Country	Study Design	Population, sample size N=Number of GDM and exposed children versus control group	Criteria to measure overweight and obesity	Prevalence (%) of overweight & obesity in OGDM[1] mothers	Prevalence (%) of overweight & obesity in ONGDM[2] mothers	Prevalence (%) of macrosomia in OGDM mothers	Prevalence (%) of macrosomia in ONGDM mothers	Additional risk factors for overweight and obesity	Quality of evidence A=High B=Good C=Low
Zhao et al., 2015	China	Observational	2833 (1-10 yrs.) After 5yrs of age documented in our study OGDM=1068 (38%) ONDM=1765 (62%	BMI growth curves for Chinese children[3]	Overweight OGDM=22 % Obesity OGDM=15. 9%	ONDM= 12.1%, ONDM= 9.0%	OGDM= 13.95%	ONDM= 10.42%	Maternal pre-pregnancy obesity Children gender and age. Male children more overweight LGA children were more overweight	A
Baptiste-Roberts et al., 2012	USA	Prospective cohort	OGDM=484 ONDM = 27,874 3-7 years		Overweight OGDM =23.3%	Overweight in ONDM= 12.6%	Not measured	Not measured	Maternal BMI, Pregnancy weight gain, Family income, Race Birthweight	A
Wright et al., 2009	USA	Prospective cohort	Total = 1,238 (3yrs) GDM =51 Normoglycemic = N = 1,035	BMI 85th–95th percentile BMI > 95th percentile	21% 13.7%	17% 8.8%	Not measured	Not measured	Pregnancy weight gain Marital status Income Race Smoking Education	A
Boney et al., 2005	USA	Longitudinal Cohort	GDM= 58 (11yrs) Non-GDM=51(11yrs	BMI > 85th percentile	27.6%	27.5%	44.7%	50.6%	Maternal Pre-pregnancy obesity of the GDM group	A

Author(s)	Country	Study Design	Population, sample size N=Number of GDM and exposed children versus control group	Criteria to measure overweight and obesity	Prevalence (%) of overweight & obesity in OGDM[1] mothers	Prevalence (%) of overweight & obesity in ONGDM[2] mothers	Prevalence (%) of macrosomia in OGDM mothers	Prevalence (%) of macrosomia in ONGDM mothers	Additional risk factors for overweight and obesity	Quality of evidence A=High B=Good C=Low
Gillman et al.,2003	USA	Retrospective cohort	GDM=465, (9-14yrs) Non-GDM 14,416 (9-14yrs)	BMI 85th-95th percentile BMI > 95th percentile	17.1% 9.7%	14.2% 6.6%	Not documented	Not documented	Preexisting maternal obesity Decreased physical activity and Increased energy intake in the children.	A
Hillier et al., 2007	USA	Prospective cohort	GDM =370 (5-7yrs) Non-GDM=7,609 (5-7yrs)	Carpenter and Coustan: BMI > 85th percentile BMI > 95th percentile National Diabetes Data Group: BMI 85th–95th percentile BMI > 95th percentile	34.7%% 20.2% 27.8% 17.3%	23.5% 12.2% 23.5% 12.2%	Not documented	Not documented	Maternal hyperglycemia Ethnicity Maternal age Maternal weight gain	A

Author(s)	Country	Study Design	Population, sample size N=Number of GDM and exposed children versus control group	Criteria to measure overweight and obesity	Prevalence (%) of overweight & obesity in OGDM[1] mothers	Prevalence (%) of overweight & obesity in ONGDM[2] mothers	Prevalence (%) of macrosomia in OGDM mothers	Prevalence (%) of macrosomia in ONGDM mothers	Additional risk factors for overweight and obesity	Quality of evidence A=High B=Good C=Low
Boersch-mann, 2003	Germany	Prospective cohort	GDM= 232 (2, 8 &11yrs) Non-GDM = 341	BMI ≥ 90th percentile	17.2%, 20.2% 31.1%	11.4% 10.3% 15.5%	Not documented	Not documented	Maternal obesity	A
Wroblew-ska-Seniuk et al., 2009	Poland	Prospective cohort	GDM =34 (4-9yrs) Non-GDM =108(4-9yrs)	BMI 85th–95th percentile BMI > 95th percentile	26.5% 8.8%	15.7% 7.4%	20.6%	13%	Pregnancy weight gain family income race.	A

[1] Offspring of Gestational Diabetes Mellitus (GDM) mothers (OGDM)
[2] Offspring of Non-GDM mothers (ONGDM)
[3] BMI growth curves for Chinese children and adolescents at 0–18 years of age, overweight in boys was defined as BMI⩾82nd percentile for age, and obesity was BMI⩾96.3 percentile for age, while in girls' overweight was BMI⩾87.4 percentile for age and obesity was a BMI⩾98th percentile for age.

Studies in Table 2.2 show one systematic review (Fig 2.2), one observational study, five prospective cohort studies, one longitudinal cohort and one retrospective cohort study and the quality of evidence for all is rated an A (high). Surprisingly, there were no cross-sectional studies. Cohort studies are nevertheless also appropriate for descriptions of prevalence of overweight and obesity in children, macrosomia in GDM exposed and non-GDM exposed newborns and risk factors associated with overweight and obesity.

2.5.3.1 Health risks in overweight and obesity in children and burden on health services

The correct management of GDM is crucial to prevent possible maternal and infant complications which include overweight, obesity and metabolic conditions (Reece, Leguizamón & Wiznitzer, 2009). Obesity may lead to insulin-resistant metabolic conditions in affected children as they get older (Ge et al., 2014).

Rossouw et al., (2012) reported that overweight and obesity were the main cause of psychological problems and low self-esteem during childhood and these children have difficulty interacting with others and fitting in with the rest of society (WHO, 2015; WHO, 2016). Low self-esteem, depression and social isolation caused by overweight and obesity in children reduce confidence to participate in physical activities on school grounds or other areas. The global health problem of an increasing number of overweight and obese children is a burden on government resources and health care systems particularly in low-income countries but increasingly in middle-income countries such as South Africa.

Overweight at age 4 to 5 is linked to higher pharmaceutical and medical care costs (Reddy et al., 2012). A national probability survey in the United States conducted by the Agency for Healthcare Research and Quality Children to compare overweight children with normal/underweight children, reported that children who were obese during both years of the Medical Expenditure Panel Study (MEPS) had $194 higher outpatient visit expenditures, $114 higher in prescription drug expenditures, and $12 higher emergency room expenditures. Children who were overweight during both years, or overweight in one year and obese in the other had $79 higher outpatient visit expenditures, $64 higher prescription drug expenditures, and $25 higher emergency room expenditures than normal/underweight children (Trasande & Chatterjee, 2009). The results showed a statistically significant difference (p=0.025) level across all 6-19-year-old children.

2.5.3.2 Interventions needed for childhood overweight and obesity

Early intervention and behavioural change is needed during a child's formative years such as better lifestyle choices, promotion of physical activities, better food choices and avoidance of exposure to high sugar food advertisements for the prevention of childhood overweight and obesity (Desai et al., 2012). In an effort to decrease adult obesity, it is essential to conduct early screening of children to prevent overweight or obesity in adulthood (van der Merwe, 2012). Well-designed studies that produce useful data are needed to develop evidence-based policies for the preventative management of childhood overweight and obesity.

Gillmann et al., (2003) reported physical inactivity, watching television and energy intake as the main contributing factors to childhood weight and that the link between GDM and childhood obesity was largely reduced when maternal obesity was well controlled. This highlights the importance of high maternal BMI as a risk factor for childhood obesity. Overweight in adolescents associated with GDM mothers, had an adjusted OR of 1.1 (95% CI: 0.5-2.3), whereas in participants without a maternal history of GDM, the OR was 1.3 (95% CI: 1.1-1.5) (Gillman et al., 2003) but results were not statistically significant. However, the study did not include a diverse group of participants, 93% of whom were from one ethnic group (Gillmann et al., 2003). Excluding pre-gestational diabetic mothers contributed to the rigour of this study.

Changing behavioural patterns is not easy. One approach is the use of constructs such as The Health Belief Model (HBM) which was developed as a tool to help researchers understand preventative health behavior in a systematic way (Rosenstock, Strecher & Becker, 1988). It was developed in the 1950s by USA social psychologists Hochbaum, Rosenstock and Kegels. Constructs of the HBM (perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, self-efficacy) have the potential to be used to investigate and explain risk factors associated with overweight and obesity in children between 5 and 6 years of age who were exposed to GDM. The HBM also has the potential to explain and predict health behaviors that lead to overweight and obesity in mothers of large for gestational age infants and preschool children exposed to GDM.

2.6 Summary

There is published evidence that childhood overweight and obesity is on the increase. However, studies on the prevalence of overweight and obesity in 5-6-year olds in Africa are

scarce. For this minor study a review of the published literature addressed the three research questions: what is the prevalence of 1) overweight at birth of infants (macrosomia) exposed to GDM during pregnancy; and of 2) overweight and obesity in this cohort 5 to 6 years later; and 3) what are the risk factors associated with overweight and obesity in these children? A South African study showed a GDM prevalence of 15% but there is a paucity of published data from South Africa and the Western Cape in particular on the prevalence of GDM, risk factors associated with developing GDM and the outcomes of GDM on exposed children.

GDM has been linked to fetal macrosomia in exposed infants and during the past decade there has been a significant global increase of high birth weight in babies associated with GDM. The evidence is inconclusive on the difference in the prevalence of overweight and obesity between GDM exposed children and non-GDM exposed children. Risk factors that contributed to overweight and obesity in children include gender and ethnicity, low maternal education and sedentary lifestyle, maternal overweight, high birth weight, exposure to a hyperglycemic intrauterine environment and exposure to GDM in utero.

In Africa, childhood overweight and obesity is on the rise and nearing epidemic proportions. It is clear that more research is needed to determine the prevalence of overweight and obesity in preschool children exposed to GDM during pregnancy, especially in the Western Cape, South Africa.

Chapter 3 METHODS

3.1 Introduction

This is a sub-study of a larger study that is investigating the progression to type 2 diabetes mellitus (T2DM) in women managed for GDM during 2010 and 2011. The sub-study investigated anthropometry and overweight and obesity in the offspring of these women 5 to 6 years after their birth. Due to the lack of local data on the prevalence of overweight and obesity in children exposed to GDM in the Western Cape, South Africa, this sub-study filled a gap in knowledge to enable health professionals to improve patient outcomes with appropriate interventions and to help policymakers formulate appropriate policies to prevent overweight and obesity in high-risk children.

This chapter describes how the sub-study was conducted to achieve the aims and objectives: study outcomes, design, sampling, setting, data collection, management and analysis and ethical guidelines.

3.2 Study Outcomes

3.2.1 Primary outcome

The primary outcome of the sub-study was to investigate the prevalence of macrosomia at birth of infants born from GDM complicated pregnancies in Cape Town during 2010/2011 and the prevalence of overweight and obesity in these children in 2016, at age 5 or 6 years as measured by their age-specific body mass index (BMI) and Z-scores. Overweight and obesity were derived from anthropometric measurements of weight and height.

Overweight and obesity were defined according to WHO growth standards. For this sub-study, Z-scores were defined as a numerical measurement that represented a value that was related to the mean (a score of zero). The Z-score could be positive (above the mean) or negative (below the mean) by a certain deviation (Dinsdale, Ridler & Ells, 2011). The Z-score deviation was used and compared to the WHO 2007 Child Growth Reference Standard to determine if a child was overweight or obese based on the child's calculated BMI expressed as a Z-score or

centile. Overweight was taken as weight and BMI z-scores between 1 and 2 and obesity as weight and BMI Z-scores above 2 (WHO, 2016).

All participants had anthropometric measurements standardized according to the WHO standard for weight based on their defined Z-scores for this sub-study. Calculations of overweight and obesity were based on the following criteria:

1. Weight for age and gender
2. Height for age and gender
3. BMI for age and gender

In addition to weight and height at 5 or 6 years of age, ancillary anthropometric measurements (birth weight, birth length and birth head circumference) were reported from recorded data. Z-scores for all the anthropometric measurements at age 5 or 6 years were reported.

3.2.2 Secondary outcome

The secondary outcome was to identify the risk factors associated with overweight and obesity in 5 and 6-year old children born from GDM complicated pregnancies. Potential factors, maternal (socio-demographic, anthropometric and clinical) as well as child related (clinical and socio-demographic) were measured and tested for their association with risk of overweight and obesity.

3.3 Research Study Design

We used a cross-sectional design to achieve the aims of this research. Cross-sectional studies are appropriate for estimating the prevalence of a condition, and in this case our main aim was to estimate the prevalence of macrosomia, overweight and obesity in these children (Sedgwick, 2014). Additional advantages are that cross-sectional designs are relatively quick and easy (Mann, 2003) and allow one to measure multiple exposures and outcomes at the same time (Sedgwick, 2014).

3.4 Study Setting

The larger study was conducted at the Groote Schuur Hospital (GSH), a referral hospital in an urban setting in the Western Cape. At the time the sub-study was undertaken the larger study was ongoing. GSH is a large government-funded tertiary academic hospital that serves as a referral care center for large population drainage areas in the Western Cape. High-risk pregnant women, including those with GDM, are referred from primary care centers for further management. GSH is one of the two largest referral hospitals in the Western Cape.

3.5 Study Population

The population in the larger study was women managed for GDM during the period November 2010 to November 2011 at GSH. In this sub-study, the population was defined as 5 to 6-year-old offspring of these women, who were resident in the Western Cape of South Africa.

3.6 Sampling and sample size

The total number of women who were managed for GDM at the GSH between November 2010 and November 2011 was 498 (Figure 3.1, flow chart of the PRO2D, larger study and sub-study). Since this population is finite, a total sampling approach was adopted for the larger study, where an attempt was made to trace and recruit all 498 women who were willing to participate in the larger study to limit selection bias. Since data for this sub-study was from the larger study, the same total sampling approach was employed.

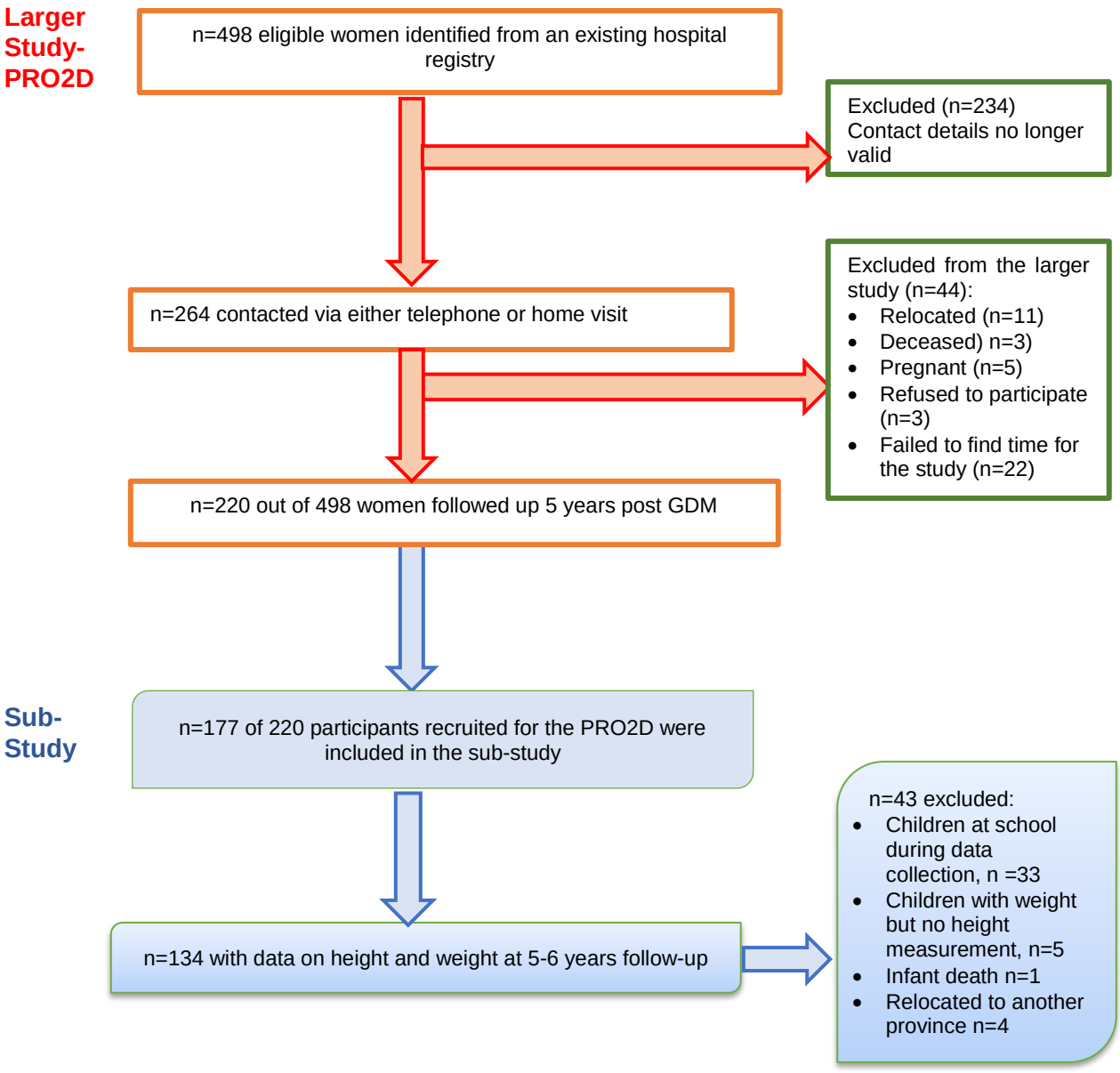

Figure 3.1: Flow chart of the sub-study nested within the PRO2D larger study

Data in Figure 3.1 show that for the sub-study there were n=177 possible mother-child participants, but n=43 were excluded: 33 mothers did not bring their school attending children for the appointment, 5 children had weight but not height measurements, 1 child died during infancy and 4 children moved away to live in another province.

3.6.1 Eligibility Criteria

3.6.1.1 Inclusion Criteria

Child participants for the sub-study were eligible for inclusion if:

a. born from a GDM complicated pregnancy to women managed at the Groote Schuur Hospital between November 2010 and November 2011;

b. aged between 5 and 6 years; and

c. resident in the Western Cape province of South Africa.

3.6.1.2 Exclusion Criteria

Child participants were excluded who:

a. were critically ill or had a terminal illness such as cancer;

b. had congenital malformations.

3.6.2 Sample Size

Although the sub-study used a total sampling approach, a sample size calculation was nevertheless performed to determine whether the primary objective of the sub-study would be achieved. The sample size for the sub-study was calculated using a hypothesized proportion of overweight pre-scholars of 29% found in a study by Baptiste-Roberts et al., 2012 (although these researchers investigated 7-year olds and not 5 to 6-year olds). Using this hypothesized proportion and aiming for a precision of 9% either side of the hypothesized proportion, the estimated sample size for the sub-study was 156 children. This was the minimum sample size required to estimate the prevalence of overweight and obesity. Since the main aim of the study was to estimate prevalence, using data from all the available children would not have affected this objective.

3.7 Data collection

This section deals with the construction and validation of data collection instruments, measurement equipment and standards, data collection procedures, data management and analysis.

3.7.1 Construction of data collection instruments

In the larger study, those mothers who agreed to participate in the study were interviewed using a structured questionnaire (Appendix A). For the sub-study, pertinent data were extracted from those questionnaires using a structured data collection form (Appendix B). The data collection form consisted of two sections: one for maternal information and one for the child's data (age, type of delivery, birth weight, any hospitalizations of the child for ≥ a week). It had sub-sections for specific data, for example, personal information, demographics, and medical history. Additional clinical and medical history data were collected from the mothers' hospital files (Section 3.7.5).

3.7.2 Measurement tools and standards

In the sub-study, all measurements were carried out using standardized techniques and equipment. A balanced digital scale for weight and a fixed wall-mounted stadiometer for height measurements for mother and child were used in a clinical setting. The results were recorded on the questionnaire (Appendix A) and the data extraction form for the sub-study (Appendix B). The weighing scale was calibrated and standardized using the weight of a known mass (a 5 kg weight) prior to weighing the children. A portable stadiometer was used for field visits when required. Each measurement was made according to prescribed standards (Bowring et al., 2012).

3.7.3 Reliability and validity testing

In the larger cross-sectional study, prior to data collection, the principal investigator trained all field staff on the procedure for administering the questionnaire and taking anthropometric measurements. Field staff were also trained on standard operating procedures (SOPs) and given electronic and hard copies thereof. To ensure reliability of anthropometric

measurements, all measurements were taken by competent and trained researchers using the same standards for all participants.

The questionnaire for the larger study was piloted among 20 hospital staff who came from the same neighbourhood as the participants. Their role was to check for any inconsistencies, unclear meanings and any ambiguities in the data. The field staff were trained in anthropometry one month beforehand and coefficients of variation calculated, until the coefficients of variation were very small. For the questionnaire, field staff members were trained using a prepared manual on each section and the questions within the sections. Most of the sections in the questionnaire used in the larger study were from previously validated measuring tools.

To ensure that the study was rigorous and reliable a strict set of procedures and protocols were followed during the data collection phase while using peer reviews and audits throughout the data collection process. At the completion of each questionnaire, a second interviewer double-checked the questionnaire for completeness and obvious errors.

For the sub-study, data extracted from the questionnaire (Appendix A) used in the larger study were recorded on a pre-tested data collection form (Appendix B). In addition, to validate the data collected and improve data reliability, a second investigator rechecked all data on the data collection form.

3.7.4 Recruitment and data collection procedure

3.7.4.1 Structured interviews with participant mothers

In the larger study, all potential participants were first identified from an existing hospital register of all women managed for GDM between November 2010 and November 2011. Those identified and eligible were first contacted telephonically (using a prepared and pretested telephonic script) and recruited for participation in the sub-study. If these mothers were not reached with the first call, a voice message was left, or an alternative number was called if available. If the mother was not reachable, a further three attempts were made to reach her. House visits were also made, to addresses listed in the hospital record to reach mothers whose telephonic contact details might have been out of date.

When contacted, the potential participants (mothers) were informed about the purpose and procedures involved in the larger study and once fully informed, were asked to participate in

the study. If the mothers agreed to participate in the larger study, recruitment of child participants for the sub-study followed by informing the mothers about the purpose and procedures involved in the sub-study. The children were asked to assent to have their height and weight measured. Willing participants (mothers) for the larger study were then invited to bring their children who met the inclusion criteria with them for participation in the sub-study. The mothers were informed that only the children's weight and height would be taken and were given information about the venue.

Following recruitment, data collection for the larger study and the sub-study commenced on 01 May 2016 and ended on 30 April 2017 and took place on the same day as the interview. In cases where children were absent during the data collection process, the mothers agreed to have the children's height and weight taken later. Follow-up calls were made to obtain the missing data. In the larger study, the mothers who had agreed to participate in the study were interviewed using a structured questionnaire (Appendix A). The mother provided information about herself and her child. For the sub-study, pertinent data not obtained from the mothers were extracted from the questionnaires using a structured data collection form (Appendix B).

Clinical and demographic characteristics obtained from the larger study (Appendix A) and interviews included data about the children: ethnicity, type of delivery, breastfeeding and duration, hospitalization, current chronic medication and number of siblings. Maternal data included: age, marital status, number of adults in the house, level of education, employment, number of antenatal visits, BMI at booking, fasting plasma glucose during pregnancy, height, weight, current BMI, history of smoking, electricity in the home, ownership of the home, type of dwelling and availability of tap water.

3.7.4.2 Anthropometric Measurements

Anthropometry refers to the scientific study of the measurements of the human body. In this sub-study, the children's anthropometric measurements were taken (weight and height at ages 5 or 6 years). Before any measurements on children were taken, mothers were asked for written informed consent and they and their children were reassured that no physical discomfort would be caused while taking the child's weight and height. Mothers were informed that they and their children can withdraw their participation from the study at any time during the process without losing incentives for travel. A time for questions was allowed before written consent

was obtained voluntarily from the mother. The mother signed two consent forms: one for herself and one for her child's participation. These forms were retained by the researcher, but the mother was given a copy of both the informed consent and the information sheet with the contact details of the researchers.

Anthropometric measurements of the children and the mothers were taken at the GSH Clinical Research Centre. If the child was not present, arrangements were made for the researcher and a research assistant to obtain the child's anthropometric measurements at either their school or home with the consent of the mother.

Height was measured using a fixed stadiometer. Each child was asked to stand up straight against a wall with their bare heels touching the wall, arms at their side and their heads up by looking straight forward. Measurements were taken to the top of the child's head. The value of each child's height was recorded to the nearest 0.1 cm.

The child's weight was taken using a calibrated electronic scale. Body mass was measured with children wearing light clothes and light, flat shoes (Bowring et al., 2012). If shoes appeared to be heavy or high, the child was asked to remove them before measurement of weight or height was taken. Each child was asked to stand still, with body weight equally distributed on the calibrated scale. When the scale reading stabilized, the body weight was recorded to the nearest 0.1 kg (Bowring et al., 2012). To reduce the risk for error in documenting the anthropometric measurements the weight and height of each child was verbally reported to the mother and research assistant and immediately documented in the file of the participant.

3.7.5 Hospital records review

For purposes of the sub-study data on birthweight, birth length, head circumference and mother's OGTT results at the time of GDM diagnosis were cross-checked against hospital records. Additional data from hospital records included the child's date of birth, and gestational age at delivery. The child's age was verified from the birth certificate when necessary. If needed, the children's Road to Health book given to parents at the birth of a child in South Africa, was used to verify information.

Additional clinical and demographic characteristics of the study participants and selected characteristics of their mothers were obtained from hospital records and data from the larger study (Appendix A):

3.8 Data management and analysis

3.8.1 Data management

Sensitive data such as the participant's name and contact details were treated confidentially, and access restricted. All research data were secured in a locked storage box and in a lockable file cabinet, in a locked room. In addition, electronic data (i.e. computers, memory sticks, CD-ROMS, etc.) were physically secured and password protected.

Data were captured as accurately as possible while data entry errors were minimized by having a co-researcher check each completed questionnaire for errors and omissions. The collected data from the questionnaires were entered onto a Microsoft Office Excel 2016 spreadsheet by using an anonymous identifier for each participant and using double data entry. All data were backed up daily on external media for safe-keeping and prevention of accidental loss.

3.8.2 Statistical Data analysis

Data were captured on Microsoft Excel spreadsheets and analysis was carried out using Stata 14 (StataCorp, 2015). Categorical variables were reported as proportions and frequencies. All data measured were first tested for normality using the Shapiro-Wilks test and histograms. Medians and interquartile ranges (IQR) were reported for skewed measured data, while means and standard deviations (SD) were reported for normally distributed measured data. A two-sided $P<0.05$ was considered as significant while 95% confidence intervals were reported for all estimates.

Z-scores were used to standardize the weight, height and BMI, using WHO growth standards for the ages 5 to 6 years. Mean Z-scores and standard deviations were reported if the Z-sores were normally distributed. If the Z-scores were not normally distributed, the median and interquartile ranges were reported.

The prevalence of overweight and obesity were calculated as a proportion, the total number of overweight/obese children over the total number of participants. To determine the risk factors associated with the outcome (overweight and obesity, treated as a binary variable), the

appropriate hypothesis tests were used, using a 5% significance level. The chi squared test and its variants were used to determine univariate associations between categorical variables and the outcome, defined as overweight or obesity (a binary outcome; either BMI Z-score >1 or BMI ≤1). T-tests, ANOVA and their non-parametric equivalents were used to test univariate associations for numerical data.

Manual logistic regression was used to adjust for multivariate associations as well as confounding factors associated with overweight and obesity. Intelligent manual backward stepwise logistic regression was used with a 0.3 level of significance for entry. Initially, all variables with *P*-values of 0.3 and below were included in the model. Model testing and diagnostics included checking for multicollinearity, model specification, Hosmer Lemeshow goodness of fit test, Lineality assumption between the log odds of overweight and obesity and the covariates as well as checking for influential cases. The Lowes graph to test the Lineality assumption showed some reasonable linear relationship although not satisfactory. We checked for multicollinearity using Variance Inflation factors (VIFs) and the results show VIFs less than 3 (mean 1.46) and this suggested no concern for multicollinearity while the linktest (*P*=0.09) and the Hosmer Lemeshow goodness of fit test (*P*=0.078) suggested that the model fits the data to a reasonable extent. Only one influential case was identified and checking the data of the child reviewed no errors.

3.9 Ethical Considerations

Ethical approval (UCT HREC 656/2015) for the larger study was granted by the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee (Appendix B). Ethical approval for this sub-study (UCT HREC 826/2016) was also granted by this Committee. Approval to gain access to the research site and participants was granted (Appendix C). The legal and regulatory standards and protocols were adhered to as stipulated in the Declaration of Helsinki (2014).

Before the start of the larger study, participant's mothers were briefed about the study and the purpose of the research. The researchers explained to all mothers that no harm will result from the study and that the researchers would always act in their best interests. For the sub-study the mothers were asked for permission to have their children weighed and their height measured, while the children were asked verbally (after explaining the process) for their assent.

It was explained that risk for injury was minimal, and the mother could be present while measurements of the child were being taken. Furthermore, if the child did not want to be weighed, they were not forced to participate. None of the children refused to have their heights and weights measured.

In the parent study, all the mothers were clearly informed that participation in the study was strictly voluntary and anyone could have opted out of the study at any time without any consequences. The mothers were also informed they would receive a stipend for travel costs and food voucher even if the child refuse to be weighted or measured. Mothers of all children signed a written informed consent form prior to participating in the sub-study (see Consent form in Appendix I). All participants' information was protected and secured.

3.10 Summary

In this chapter, a description and discussion of the sub-study methodology was provided. The sub-study was part of a larger cross-sectional study. The study setting, population, eligibility criteria, sampling process, construction of the data collection tool and standards used as well as the processes for data collection, data management and statistical analyses were discussed. Finally, the ethical considerations and the study approval process were covered.

Chapter 4 RESULTS

4.0 Introduction

In this chapter, the results of the sub-study are presented. The primary outcome of the sub-study was to investigate the prevalence of macrosomia at birth of infants born from GDM complicated pregnancies in Cape Town during 2010/2011 and the prevalence of overweight and obesity in these children in 2016, at age 5 or 6 years as measured by their age-specific body mass index (BMI) and Z-scores. Overweight and obesity were derived from anthropometric measurements of weight and height.

The secondary outcome was to identify the possible risk factors associated with overweight and obesity in the same cohort of 5 to 6-year-old children. One hundred and seventy-six participants comprising n=78 boys (44.3%) and n=98 girls (55.7%) were recruited. Clinical and demographic characteristics of the study participants and selected characteristics of their mothers are presented in Table 4.1.

Table 4.1: Clinical and demographic characteristics of the participants and their mothers

Characteristics	Overall, N = 176 (100%)	Boys, N = 78 (44.3%)	Girls, N = 98 (55.7%)	*P*-value
CHILDREN				
Age, median (IQR) years, N=165	5.4 (5.1-5.8)	5.4 (5.0-5.7)	5.5 (5.1-5.9)	0.18
Ethnicity* n (%) N=170				
Black	51 (30.0)	24 (31.6)	27 (28.7)	0.52
Coloured	111 (65.3)	47 (61.8)	64 (68.1)	
White	4 (2.4)	3 (3.9)	1 (1.1)	
Asian	3 (1.8)	1 (1.3)	2 (2.1)	
Other	1 (0.6)	1 (1.3)	0 (0.0)	
Gestational age at birth, median (IQR), weeks, n=174	38 (37-39)	38 (37-39)	38 (37-39)	0.98
Type of Delivery, n (%), N=174				0.75
Vaginal Delivery	78 (44.8)	36 (46.2)	42 (43.8)	
Caesarian Section	96 (55.2)	42 (53.9)	54 (56.3)	
Breastfed, n (%), N=173	137 (79.2)	60 (77.9)	77 (80.21)	0.63
Breastfeeding length, median (IQR), days N=123	51 (12.8-102)	51 (12.8-102)	34 (12.8-102)	0.60
Child history of ever being hospitalized for at least 1 week, n (%), N=166	14 (8.4)	7 (9.3)	7 (7.7)	0.88
Children currently on chronic medication n (%), N=162	8 (4.9)	4 (5.4)	4 (4.6)	0.80
Number of Siblings, median (IQR), N=176	2 (1-3)	2 (1-3)	2 (1-3)	0.51
MATERNAL				
Maternal age at 5-6 years follow-up median (IQR), N=176	36 (32-40)	36 (31-40)	36 (32-40)	0.68
Marital status at 5-6 years follow-up, n (%), N=172				0.97
Single	46 (26.7)	19 (25.0)	27 (28.1)	
Married	113 (65.7)	51 (67.1)	62 (64.6)	
Widowed/Divorced	9 (5.2)	4 (5.3)	5 (5.2)	
Other	4 (2.3)	2 (2.6)	2 (2.1)	
Number of adults in house, median (IQR), N=170	2 (1-3)	2 (1-3)	2 (1-3)	0.97
Mother education, at 5-6 years follow-up, n (%), N=171				0.66
Never went to school	1 (0.6)	0.0	1 (1.1)	
Grade 1 to 7 (Primary school)	15 (8.8)	5 (6.6)	10 (10.5)	
Grade 8 to 10	47 (27.5)	24 (31.6)	23 (24.2)	
Matric	82 (47.6)	36 (48.4)	46 (47.4)	
Tertiary / Diploma	26 (15.2)	11(14.5)	15 (15.8)	

Characteristics	Overall, N = 176 (100%)	Boys, N = 78 (44.3%)	Girls, N = 98 (55.7%)	*P*-value
Mother employment at 5-6 years follow-up, n (%), N= 165				
Employed, salaried	75 (45.5)	34 (47.9)	41 (43.6)	
Self-employed	14 (8.5)	3 (4.2)	11 (11.7)	0.32
Unemployed	63 (38.2)	28 (39.4)	35 (37.2)	
A full-time homemaker	9 (5.5)	4 (4.3)	5 (7.0)	
A pensioner	1 (0.6)	0 (2014)	1 (1.1)	
A student	1 (0.6)	1 (1.4)	0 (0.0)	
Number of Antenatal visits, median (IQR), N=38	7 (3.7-39)	9 (7-11.5)	8 (6.05-10)	0.03*
Maternal BMI at booking median (IQR) N=119	34.7 (28.5-42.5)	35.2 (27.1-42.3)	34.6 (29.7-42.5)	0.73
Mother fasting plasma glucose during pregnancy, mmol/l of measurement median (IQR), N=142	5.7 (5.1-6.4)	5.6 (5-6.4)	5.7 (5.1-6.4)	0.49
Mother OGTT 2 Hour Glucose during pregnancy, mmol/l median (IQR), N=133	8.8 (8.2-9.7)	8.6 (7.9-9.3)	8.9 (8.3-10)	0.08
Mother height, 5-6 years post GDM median (IQR), cm, N=173	161 (157-165)	161 (157-164)	160.7 (157-165.3)	0.64
Mother weight 5-6 years post GDM, median (IQR), kg, N=167	87.7 (74- 107.2)	87.4 (74.1-103.2)	89 (74-109)	0.82
Mother BMI 5–6 years post GDM, median (IQR), kg/m^2, N=167	34.2 (29.2-39.1)	34.2 (28.8-38.6)	34.2 (29.4-40.5)	0.90
Mother smoked at 5-6 years post GDM, n (%) N=170,	57 (33.5)	49 (64.5)	64 (68.1)	0.62
Mothers have electricity in house, n (%) N=172	169 (98.3)	74 (97.)	95 (98.9)	0.43
Mothers own house, n (%) N=164	54 (32.9)	20 (27.0)	34 (37.8)	0.15
Type of house, n (%) N=165:				
Built formal unit	118 (71.5)	50 (67.6)	68 (74.7)	0.20
Informal shack	45 (27.3)	24 (32.4)	21 (23.1)	
Tap-water, n (%) N=172	171 (99.4)	76 (100)	95 (98.9)	0.37
Shared tap-water, n (%) N=168	26 (15.5)	13 (17.8)	13 (13.7)	0.25

Note to table: *A significance level of 0.05 was assigned for statistical significance
* South African race classification
IQR = interquartile range; SD = standard deviation; OGTT = oral glucose tolerance test; GDM = Gestational Diabetes Mellitus

Table 4.1 shows the demographic and some clinical characteristics of the children (at birth and at 5 to 6 years of age) and their mothers. In terms of the South African race classification, the majority of children were Coloured (n=111, 65.2%), 51 (30%) were Black, 4 (2.4%) were White, 3 (1.8%) were Asian and 'Other' accounted for 1 (0.6%). The median gestational age at birth of the children was 38 (37-39) weeks, while during follow-up, the median age of the children

was 5.4 (IQR, 5.1-5.8) years. The number of children who were breastfed was 137 (79.2%) while 8 (4.9%) were taking medications for chronic illnesses. In response to a question in the larger study about the number of children who were hospitalized for at least one week, mothers reported that very few children (n=14, 8.4%) had been hospitalized. More than half of the children (n=96, 55.2%), were delivered via caesarian section.

During pregnancy, the mother's median BMI at booking was 34.9 kg/m^2 (IQR, 28.5-42.7), while their median fasting glucose at GDM diagnosis was 5.7 (IQR, 5.1-6.4) mmol/l and the median 2-hour OGTT result was 8.8 (IQR, 8.2-9.7) mmol/l. The overall median number of antenatal visits for each mother was 8.4 (IQR, 7-11) visits. At 5 to 6 years' post GDM, the median BMI of the mothers was 34.2 (IQR, 29.2-39.1) kg/m^2. At 5 to 6 years post-GDM, more than half (n=113, 65.7%) of the mothers were married, while the majority (n=82, 47.6%) had an educational level of Grade 12 (matric) (the highest level) and 26 (15.2%) had a tertiary education. Seventy-five (45.5%) mothers were employed. Fifty-seven mothers (33.5%) had a history of smoking. The majority (n=169, 98.3%) had electricity in the home which comprised a formal built unit (n=118, 71.5%) and access to their own supply of tap water (n=171, 99.4%). There were no statistically significant differences in most of the variables between the boys' and girls' mothers except in the number of antenatal visits. The median number of antenatal visits for the boys' mothers was 9 (IQR, 7-11.5) during the pregnancy and for the girls' mothers this was 10 (IQR = 8-3) (p=0.03) visits.

Results for the primary outcome of the sub-study are presented in Tables 4.2, 4.3 and 4.4.

4.1 Objective 1: To describe anthropometric characteristics of infants exposed to GDM during pregnancy in the years 2010 and 2011 at Groote Schuur Hospital (GSH) and of the same cohort of 5 and 6-year-old children

Anthropometric measurements at birth (median, IQR) are presented in Table 4.2.

Table 4.2: Anthropometric characteristics at birth

Characteristics	Overall, N =176	Boys, N= 78	Girls, N = 98	*P*-value
Gestational age at birth, median (IQR), weeks, N=174	38 (37-39)	38 (37-39)	38 (37-39)	0.98
Birth weight, median (IQR), gm, N=54	3295 (2985-3600)	3262.5 (2922.5-3595)	3295 (3000-3620)	0.57
Birth length, median (IQR), cm N=54	50 (45-53)	50 (45-52)	51 (47-53)	0.60
Head circumference at birth, median (IQR), cm, N=74	34 (33-35.5)	33 (32-34)	34 (33-36)	0.02*

Note to table: *A significance level of 0.05 was assigned for statistical significance

Gestational age at birth was 38 (IQR, 37-39) weeks (2 missing data), birth weight was 3295 (IQR, 2985-3600) grams (122 missing data), length at birth was 50 (IQR, =45-53) cm (122 missing data) and head circumference was 34 (IQR, =33-35.5) cm (102 missing data). Except for head circumference (p=0.02) there were no statistically significant differences between the boys' and girls' anthropometric measurements at birth,

4.2 Objective 2: To describe anthropometric characteristics of the cohort of children exposed to GDM during pregnancy in the years 2010 and 2011 at Groote Schuur Hospital (GSH) at ages 5 and 6 years

Table 4.3: Anthropometric characteristics of GDM exposed children aged 5 to 6 years

Characteristic	Overall, N = 176	Boys, N= 77	Girls, N = 98	*P*-value
Child Height, mean (SD), cm, n=138	112.14 (5.72)	112.04 (5.84)	112.29 (5.66)	0.78
Z-score for height, mean (SD)	0.013 (1.07)	0.008 (1.08) (	0.017 (1.11)	0.97
Child Weight, median (IQR), kg, n=143	19.3 (18-23)	19.2 (18-21)	19.75 (18-23)	0.50
Z-score for weight, mean (SD)	0.278 (1.40)	0.145 (1.38)	0.390 (1.41)	0.31
Child BMI, median (IQR), kg/m^2, n=138	15.7 (14.5-17.2)	15.7 (14.5-16.7)	15.8 (14.5-18.0)	0.46
Z-score for BMI, mean (SD)	0.365 (1.63)	0.218 (1.72)	0.485 (1.55)	0.35

Note to table: A significance level of 0.05 was assigned for statistical significance

Data in Table 4.3 present anthropometric characteristics of GDM exposed children aged 5 to 6 years, and a comparison between boys and girls. Data for height were normally distributed but not for weight. Measures of central tendency and dispersion of data for height are therefore shown as mean (SD) respectively and for weight as median (IQR) respectively. The mean (SD) height was 112.1 (5.7) cm, median (IQR) weight was 19.3 (18-23) kg and the median (IQR) BMI at 5 and 6-years old was 15.7 (14.5-17.2) kg/m^2. The mean (SD) Z-score for height was 0.013 (1.07), 0.278 (1.40) for weight and 0.365 (1.63) for BMI. Graphic presentation of the data can be found in Appendix D. There were no statistically significant differences between the boys and girls in any of the anthropometric characteristics or their Z-scores at ages 5 to 6 years (Table 4.3).

4.3 Objectives 2 and 3: To describe the proportion of fetal macrosomia and the prevalence of overweight and obesity 5 to 6 years later

Results for the proportion of macrosomia and the prevalence of overweight and obesity 5 to 6 years later are presented in Table 4.4.

Table 4.4: Proportion of macrosomia and prevalence of overweight and obesity at 5 to 6 years of age

Characteristic	Category	Overall, N=138		Boys, N = 75		Girls, N =63		*P*-value
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	
Weight at birth	**Macrosomia** (birth weight>4000 gm), n=171	21 (12.3)	8.2-9.1	8/76 (10.5)	5.3-19.9	13/95 (13.7)	8.0-22.3	0.53
BMI	**Normal** (-1≤BMI Z-score≤1)	93 (69.4)	61.0-76.7	44 (73.3)	60.4-83.2	49 (66.2)	54.4-76.2	0.49
	Overweight, (**BMI** z score more than 1 but less than 2)	18 (13.4)	8.6-20.4	5 (8.3)	3.4-18.9	13 (17.6)	10.4-28.2	
	Obese, (**BMI** Z-score >2)	19 (14.2)	9.2-21.2	9 (15.0)	7.8-26.8	10 (13.5)	7.3-23.6	
	Underweight, (BMI<1)	4 (2.9)	1.1-7.8	2(3.3)	0.8-12.8	2 (2.7)	0.7-10.4	
Weight	**Normal** (-1≤ weight Z-score≤1)	94 (68.1)	59.8-75.4	45(71.4)	58.7-81.4	49 (65.3)	53.7-75.4	
	Overweight, (weight z score more than 1 but less than 2)	17 (12.3)	7.7-19.0	5/63 (7.9)	3.2-18.1	12 (16.0)	9.1-26.4	0.37
	Obese, (weight Z-score >2)	21 (15.2)	10.0-22.3	9 (14.3)	7.4-25.6	12 (16.0)	9.1-26.4	
	Underweight (weight Z-score<1)	6 (4.4)	1.9-9.4	4 (6.4)	2.3-16.1	2 (2.7)	0.6-10.3	
Height	**Normal height** (-1≤height Z-score ≤1)	100 (75.2)	67.0-81.8	44 (73.3)	60.4-83.2	56 (76.7)	65.4-85.2	0.59
	Tall (1<height Z-score ≤2)	4 (3.0)	1.1-7.8	1 (1.7)	2.2-11.5	3 (4.1)	1.2-12.2	
	Too tall (height Z-score >2)	23 (17.3)	11.7-24.8	11 (18.3)	10.3-30.6	12 (16.4)	9.4-27.0	
	short (height Z-score<1)	6(4.5)	2.0-9.7	4(6.7)	2.5-16.9	2 (2.7)	6.6-10.6	

Note to table: A significance level of 0.05 was assigned for statistical significance.

Table 4.4 shows the data on weight (at birth and at ages 5 to 6 years), height (at ages 5 to 6 years) and BMI categories (at ages 5 to 6 years) as categorized using the WHO Z-scores for children. At birth, the overall prevalence of macrosomia was 12.3% (95% CI 8.1%-18. 2%). Using BMI Z-scores, the prevalence of overweight was 13.4% (95% CI 8.5%-20.4%) while the prevalence of obesity was 14.1% (95% CI 9.2%-21.3%). When only weight Z-scores were used, the overall prevalence of overweight dropped slightly to 12.3% (95% CI 7.6%-19.0%), while the prevalence of obesity rose slightly to 15.2% (95% CI 10.1-22.3%). The overall prevalence of children who were tall for their age (1<height Z-score<2) was 3.0% (95% CI 1.1%-7.8%), while the overall prevalence of children who were too tall for their height (height Z-score >2), was 17.3% (95% CI 11.7%-24.8%). There were no significant differences between the boys and girls in the prevalence of overweight and obesity as measured by the Z- scores cut-offs of any of the anthropometric measures (Table 4.4).

4.4 Objective 4: Risk Factors Associated with Overweight and Obesity in Children exposed to GDM

Data for risk factors associated with overweight and obesity in the cohort of 5 and 6-year-old children who were exposed to GDM are presented in Table 4-5.

Table 4.5: Risk factors for overweight and obesity (BMI Z-score ≥1)

Factor	Univariate analysis (showing proportions and medians)			*P*-value	Multivariate analysis		
	Median	Normal weight	Overweight or obese		Adjusted Odds Ratio	95% CI	*P*-value
Child Birth weight (g)	Median (IQR)	3212.5 (2900-3555)	3450 (3175-4050)	0.03	1.002	1.0004-1.0044	0.01*
Child age 5-6 years post GDM	Median (IQR)	5.4 (5.04-5.65)	5.5 (5.09-5.88)	0.18	0.03	0.002-0.29	0.004*
Child Gender, n (%)	Boys	46 (76.7)	14 (23.3)	0.32	0.76	0.15-3.89	0.75
	Girls	51 (68.9)	23 (31.1)		1		
Child Head circumference (cm)	Median (IQR)	34 (32-35)	35 (32.5-36.5)	0.17			
Child Birth length (cm)	Median (IQR)	50 (44-52)	51.25 (47-54)	0.39			
Child Gestational age at birth	Median (IQR)	38 (37-39)	38 (37-39)	0.42			
Child Ethnicity	Black, n (%)	22 (57.9)	16 (42.1)	0.02	4.52	0.7-277.4	0.47
	Coloured, n (%)	71 (80.7)	17 (19.3)		1.15	0.3-40.7	0.94
	White & Others, n (%)	4 (57.1)	3 (42.9)		1		
Type of birth delivery	Vaginal, (n %)	50 (78.1)	14 (21.9)	0.18	0.65	1.2-3.6	0.58
	Caesarian section	46 (67.6)	22 (32.4)				
Child breastfed (any length) days	Yes n (%)	77 (71.9)	30 (28.0)	0.82			
Child on chronic medication at age 5-6 years	Yes n (%)	6 (75)	2 (25)	0.88			
Child hospitalized for at least 1 week since birth	Yes, n (%)	7 (58.3)	5 (41.7)	0.31			
Mother married	Yes n (%)	23 (65.7)	12 (32.4)	0.43			
Maternal age 5-6 years post GDM	Median (IQR)	36 (31-40)	37 (34-41)	0.09	1.01	0.86-1.19	0.88
No. of adults in the house 5-6 years post GDM	Median (IQR)	2 (1-3)	2 (1-2)	0.13	0.38	0.17-0.86	0.02*
No. of siblings in the house 5-6 years post GDM	Median (IQR)	2 (1-3)	2 (1-3)	0.32			
Maternal BMI at booking	Median (IQR)	33.02 (27.1-42.3)	39.16 (33.8-43.7)	0.044	1.002	0.8-1.13	0.84
Mother fasting plasma glucose during pregnancy	Median (IQR)	5.4 (4.9-6.3)	5.8 (5.4-6.6)	0.26	4.13	0.94-18.19	0.06
Mother one-hour plasma glucose during pregnancy	Median (IQR)	9.7 (8.7-10.6)	9.9 (8.4-11.2)	0.32			

Factor	Univariate analysis (showing proportions and medians)			*P*-value	Multivariate analysis		
	Median	Normal weight	Overweight or obese		Adjusted Odds Ratio	95% CI	*P*-value
Mother two-hour plasma glucose during pregnancy	Median (IQR)	8.4 (7.9-9.6)	8.7 (7.9-9.4)	0.001	2.06	1.14-3.74	0.02*
Mother weight 5-6 years post GDM	Median (IQR)	85.3 (72.7-108.5)	97 (75-106)	0.27		0.83-1.11	0.62
Mother height 5-6 years post GDM	Median (IQR)	160.2 (156.4-164.5)	160 (158-166)	0.65			
Mother BMI 5-6 years post GDM	Median (IQR)	33.7 (29.0-41.4)	36.9 (31.9-38.5)	0.27	0.99	0.87-1.13	0.94
Mother number of antenatal visits	Median (IQR)	8 (7-11)	8.5 (6-10)	0.70			
Mother Education: matric and tertiary 5-6 years post GDM	Yes n (%)	58 (65.9)	30 (34.1)	0.03	1.93	0.27-13.82	0.51
Mother Employed 5-6 years post GDM	Yes n (%)	40 (70.2)	17 (29.8)	0.47			
Mother Owns a house 5-6 years post GDM	Yes n (%)	28 (63.6)	16 (36.4)	0.16	0.58	0.10-3.23	0.53
Type of house 5-6 years post GDM	Formal n (%) Informal n (%)	67 (70.5) 25 (75.8)	28 (29.5) 8 (24.2)	0.57			\
Tap-water in home 5-6 years post GDM	Yes n (%)	96 (72.2)	37 (27.8)	0.72			
Electricity in home 5-6 years post GDM	Yes n (%)	94 (71.8)	37 (28.2)	0.37			
Shared tap-water in home 5-6 years post GDM	Yes n (%)	15 (78.9)	4 (21.1)	0.72			
Toilet in home 5-6 years post GDM	Yes n (%)	85 (70.25) 85 (89.5)	36 (29.75) 36 (97.3)	0.14	2.67	0.11-62.31	0.54
Mother ever smoked	Yes n (%)	36 (83.7)	7 (16.3)	0.05	0.38	0.05-2.84	0.38

Note to table: *A significance level of 0.05 was assigned for statistical significance.
Birth head circumference and length were omitted from the multivariate analysis model as there was a significant amount of missing data. Variables with *P*-values greater than 0.3 on univariate analysis were not included in the multivariate logistic regression model.

Data in Table 4.5 show the potential risk factors that were investigated for their association with overweight and obesity, using a BMI Z-score cut-off of 1. All children were categorized as overweight or obese (coded 1) if they had a BMI Z-score cut-off of more than one, while all children with a BMI Z-score less than or equal to 1 were categorized as normal or underweight

(coded 0). Overall, 37/134 (27.6%, 95% CI 20.6%-35.9%) (Table 4.4) children were classified as either overweight or obese at ages 5 to 6 years. Variables in Table 4.5 that had a statistically significant association with overweight and obesity in 5 and 6-year-old children exposed to GDM: birth weight (adjusted OR 1.002, 95% CI 1.0004-1.00, *p*=0.012), age in years (adjusted OR 0.02, 95% CI 0.001-0.29, *p*=0.004), maternal two-hour plasma glucose during pregnancy (adjusted OR 2.06, 95% CI 1.14-3.74, *p*=0.017) and number of adults in the house 5 to 6 years at the time of testing (adjusted OR 0.38, 95% CI 0.17–0.86, *p*=0.020). A potential risk factor was maternal fasting plasma glucose during pregnancy where the *P*-value approached significance (0.06) (Table 4.5).

4.5 Evaluation of the sub-study

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guideline consisting of 22 items for reporting observational studies (EQUATOR Network) was used at the end of the sub-study to standardize and enhance the quality and transparency of reporting (Lachat et al., 2016) (see Appendix G).

4.6 Summary

This chapter presented the results of the sub-study guided by the primary aim of investigating the prevalence of overweight and obesity in children at birth and at ages 5 to 6 years born from GDM complicated pregnancies in Western Cape, South Africa. Further results presented were guided by the secondary aim: to identify the possible risk factors associated with overweight and obesity in the same cohort of 5 to 6-year-old children born from GDM complicated pregnancies. An analysis of the data for each of the four sub-study objectives is presented.

The sub-study recruited 176 participants: 78 boys (44.3%) and 98 girls (55.7%). Anthropometric measurements at birth (Table 4.2) showed a median gestational age at birth of 38 (IQR=37-39) weeks, birth weight of 3,295 (IQR=2,985-3,600) grams, birth length of 50 (IQR=45-53) cm and head circumference at birth of 34 (IQR=33-35.5, *p*=0.02) cm. Missing data for birth weight, length and head circumference was considerable.

Anthropometric characteristics of GDM exposed children aged 5 to 6 years (Table 4.3) showed a mean (SD) height of 112.1 (5.7) cm, median (IQR) weight of 19.3 (8-22.9) kg and median (IQR) BMI of 15.7 (14.5-17.2) kg/m^2. The mean (SD) Z-score for height was 0.01 (1.07), for weight was 0.28 (1.40) and for BMI was 0.37 (1.63).

Data on weight at birth and at ages 5 to 6 years, height (at ages 5 to 6 years) and BMI categories (at ages 5 to 6 years) were categorized using the WHO Z-scores for children. At birth, the overall prevalence of macrosomia (Table 4.4) was 12.3% (95% CI 8.2%-9.1%). Using BMI Z-scores, the prevalence of overweight was 13.4% (95% CI 8.6%-20.4%) while the prevalence of obesity was 14.2% (95% CI 9.2%-21.2%). When only weight Z-scores were used, the overall prevalence of overweight dropped slightly to 12.3% (95% CI 7.7%-19.0%), while the prevalence of obesity rose slightly to 15.2% (95% CI 10.0-22.3%). The overall prevalence of children who were tall for their age (1<height Z-score<2) was 3.0% (95% CI 1.1%-7.8%), while the overall prevalence of children who were too tall for their height (height Z-score >2), was 17.3% (95% CI 11.7%-24.8%).

Overall, 37/134 (27.6%, 95% CI 20.6%–35.9%) children were classified as either overweight or obese at ages 5 to 6 years (Table 4.4). Variables that had a statistically significant association with overweight and obesity in 5 and 6-year-old children exposed to GDM (Table 4.5) were: the number of adults in the house (adjusted OR 0.38, 95% CI 0.17-0.86, *p*=0.02), birth weight (adjusted OR 1.00, 95% CI 1.00-1.00, *p*=0.01), age in years (adjusted OR 0.03, 95% CI 0.002-0.29, *p*=0.004), and maternal two-hour plasma glucose during pregnancy (adjusted OR 2.06, 95% CI 1.14-3.74, *p*=0.02). A potential risk factor was maternal fasting plasma glucose during pregnancy where the *P*-value approached significance (0.06).

Chapter 5 Discussion, Conclusion and Recommendations

5.0 Introduction and main results

The sub-study aims and objectives were achieved. The prevalence of macrosomia at birth in GDM related pregnancies and overweight and obesity in the cohort of children 5 to 6 years later, is of concern. Risk factors associated with overweight and obesity in the participants, a cohort of 5 and 6-year old children, were identified.

The sub-study recruited 176 participants: 78 boys (44.3%) and 98 girls (55.7%). Anthropometric measurements at birth (Table 4.2) showed a median gestational age at birth of 38 (IQR=37-39) weeks, birth weight of 3,295 (IQR=2,985-3,600) grams, birth length of 50 (IQR=45-53) cm and head circumference at birth of 34 (IQR=33-35.5, p=0.02) cm. Missing data for birth weight, length and head circumference was considerable. Anthropometric characteristics of GDM exposed children aged 5 to 6 years (Table 4.3) showed a mean (SD) height of 112.1 (5.7) cm, median (IQR) weight of 19.3 (8-22.9) kg and median (IQR) BMI of 15.7 (14.5-17.2) kg/m2. The mean (SD) Z-score for height was 0.01 (1.07), for weight was 0.28 (1.40) and for BMI was 0.37 (1.63).

At birth, the overall prevalence of macrosomia (Table 4.4) was 12.3% (95% CI 8.2%-9.1%). Using BMI Z-scores, the prevalence of overweight was 13.4% (95% CI 8.6%-20.4%) while the prevalence of obesity was 14.2% (95% CI 9.2%-21.2%). When only weight Z-scores were used, the overall prevalence of overweight dropped slightly to 12.3% (95% CI 7.7%-19.0%), while the prevalence of obesity rose slightly to 15.2% (95% CI 10.0-22.3%). Overall, 37/134 (27.6%, 95% CI 20.6%–35.9%) children were classified as either overweight or obese at ages 5 to 6 years (Table 4.4). Variables associated with overweight and obesity in 5 and 6-year-old children exposed to GDM (Table 4.5) were: the number of adults in the house (adjusted OR 0.38, 95% CI 0.17-0.86, p=0.02), birth weight (adjusted OR 1.00, 95% CI 1.00-1.00, p=0.01), age in years (adjusted OR 0.03, 95% CI 0.002-0.29, p=0.004), and maternal two-hour plasma glucose during pregnancy (adjusted OR 2.06, 95% CI 1.14-3.74, p=0.02).

5.1 Sub-study results compared to existing literature in South Africa and globally

5.1.1 Anthropometric characteristics

A comparison of anthropometric findings from the sub-study with data from other South African studies in the available published literature is not meaningful. First, anthropometric findings amongst children in the South African National Health and Nutrition Examination Survey (SANHANES-1) (Shisana et al., 2014) reflected an age group older (6 to 9 years) than the participants in the sub-study (5 to 6 years) and therefore expected higher values than those for the sub-study. Second, South African and international reviewed studies in Chapter Two did not report anthropometric measurements of children's calculated BMI expressed as a Z-score or centile but instead reported overweight and obesity proportions. Nevertheless, comparative data within the 2012 SANHANES-1 report (Shisana et al., 2014) between national and Western Cape anthropometric measurements are interesting albeit for a larger sample: the national mean weight for 6 to 9 year old boys (n=625/2123) was 24.4 kg (95% CI 23.9-24.9) and the mean height was 123.2 cm (95% CI 122.3-124.0) while data for this group for the Western Cape (n=318) at the time, this was 23.7 kg and 113.6 cm respectively. This can be interpreted to mean that boys in the Western Cape had a comparable weight but were shorter in stature than the national mean. For girls in the Western Cape (n=300), the mean weight was 25.6 kg (national mean 25.4 kg, 95% CI 24.6-26.3, n=2155) and the mean height was 116.5 cm (national mean 123.9 cm, 95%CI 122.8-125.0). This can be interpreted to mean that girls in the Western Cape had a comparable weight but were shorter in stature than the national mean.

An analysis of data by race of 6 to 9 year-olds in the SANHANES-1 survey (Shisana et al., 2014) shows a national mean weight of 24.7 kg for Black boys (n=1629) and 23.7 kg for Coloured boys (n=433) and a mean height of 117.4 cm for Black boys and 116.1 cm for Coloured boys. In this survey, the overall mean weight for Black boys in the Western Cape was marginally higher (.3 kg) than the national average (24.4 kg) but Coloured boys weighed marginally less (.7) than the national average. Both the Black and Coloured boys were shorter than the national average (123.2 cm). The mean weight for Black and Coloured girls was similar (27.0 kg and 27.4 kg respectively) and above the national mean of 25.4 kg but their mean height (118.5 cm for Black girls; 120.6 cm for Coloured girls) was lower than the national mean height of 123.9 cm.

Despite the higher age group in the national survey, the median BMI score in the present sub-study (15.7 kg/m^2, IQR 14.5-17.3) was not very different from the overall BMI for the group of 6 to 9 year-old children (Shisana et al., 2014) of 15.9 kg/m^2 (95% CI 15.7–16.1). In the national survey, the overall BMI in the Western Cape was 17.3 kg/m^2 (95% CI 16.7–17.9) and higher than the national median BMI. Median Z-scores for height, weight and BMI are not reported in the national survey and can therefore not be compared with data from the sub-study.

5.1.2 The proportion of fetal macrosomia in GDM exposed pregnancies in the years 2010 and 2011 at Groote Schuur Hospital (GSH)

The overall prevalence of fetal macrosomia in infants at birth (>4000 gm) exposed to GDM during the pregnancy was 12.3% (8/76, 10.5% among boys; 13/95, 13.7% for girls) (Table 4.4). GDM has been linked to overweight at birth in exposed infants. Infants who had been exposed to an intrauterine environment of either high blood sugar levels during uncontrolled diabetes or maternal obesity were LGA, with a birth weight above the 90th percentile (Boney et al., 2005; Najafian & Cheraghi, 2012). In an Iranian cohort study on macrosomia diabetic participants delivered 39.5% macrosomic babies compared to 6.1% in the control-group ($P<0.05$) (Najafian & Cheraghi, 2012) (Table 2.2).

5.1.3 Prevalence of overweight and obesity in 5 and 6-year-old children

In the sub-study, overweight and obesity were calculated using Z-scores (standard deviation scores). In the Z-score system, the anthropometric value is expressed as a number of standard deviations (SDs) below or above the reference mean or median value WHO, 1997). According to the WHO (1997), “For population-based uses, a major advantage is that a group of Z-scores can be subjected to summary statistics such as the mean and standard deviation” (p.1). Z-scores are gender-independent, so children’s growth status can be determined by combining gender and age groups (WHO, 1997). Few prevalence studies discussed in this sub-section reported using Z-scores, making a comparison of data in the sub-study to the published literature difficult.

In a 2012 SANHANES-1 study, the combined prevalence of overweight and obesity in South African 6 to 14 year old children is reported as 16.7% for Black African boys and 23.5% for Black African girls and for Coloured boys and girls this was lower at 11.8% and 19.9%

respectively. When compared to the earlier 2006 Health of the Nation study conducted by Armstrong et al. of 6 to 13 year olds, the combined overweight and obesity for Black African boys and girls was 9.7% and 17.0% respectively, and for Coloured boys and girls the combined overweight and obesity was 11.7% and 15.5% respectively (SANHANES-1, 2012). As can be seen from these two studies, there is a rising trend in the prevalence of overweight and obesity among South African children. Our study showed that for 5 to 6 year old GDM exposed children there was a combined prevalence of overweight and obesity of 27.6% (Table 4.4). This is nearly double that reported in other South African studies of children of different age groups. Results of the sub-study imply a tendency towards overweight and obesity in children in the Western Cape when exposed to GDM during pregnancy.

According to the National Center for Health Statistics (NCHS) (2016), during the early 1970s, the overweight rate for USA children aged 2 to 19 years, was 10.2% and the obesity rate for the same group was 5.2%. In 2014 the overweight and obesity rates for the same cohort escalated to 16.2% and 17.2% respectively (NCHS, 2016). Despite representing a lower age group, using BMI Z-scores, the prevalence of overweight in the cohort of 5 and 6 year old children in our sub-study was 13.4% and the prevalence of obesity was 14.1%, pointing to a similar trend to the NCHS findings.

5.1.4 Consequences of childhood overweight and obesity

Overweight and obesity are the main cause of psychological problems and low self-esteem during childhood (Rossouw et al., 2012; WHO, 2015; WHO, 2016). Low self-esteem, depression and social isolation caused by overweight and obesity in children can decrease confidence to participate in physical activities. Overweight and obesity are key factors that contribute to poor physical health. Obesity may lead to insulin-resistant metabolic conditions in affected children as they get older (Ge et al., 2014; Gebremedhin, 2015).

Overweight and obesity are key factors that not only contribute to poor health but also make more demands on health systems, particularly in low to medium-income countries, such as South Africa. Although overweight and obesity in children are on the rise worldwide, this is more so in low and- middle-income countries (WHO, 2016). A 6.8% prevalence of overweight and obesity in children has become a public health problem in Sub-Saharan Africa (Gebremedhin, 2015). The tendency to overweight and obesity is not isolated to one group or

even to a few countries and has consequently become a global health problem that is a burden on government resources and their health care systems.

5.1.5 Risk factors (child and maternal) associated with increased risk for overweight in 5 and 6-year old children exposed to GDM during pregnancy

Overall, 37/134 (27.6%) children were classified as either overweight or obese at ages 5 to 6 years (Table 4.4). Variables that had a statistically significant association with overweight and obesity in the 5 and 6-year old children exposed to GDM were: age in years, the number of adults in the house, birth weight, and maternal two-hour plasma glucose during pregnancy. A potential risk factor was maternal fasting plasma glucose during pregnancy where the *P*-value approached significance. Data from the sub-study did not identify ethnicity as a risk factor associated with overweight and obesity in children exposed to GDM during pregnancy even though data were skewed in favour of the Coloured participants (80.7%).

The 2012 SANHANES-1 national survey (Shisana, 2014) reported a prevalence of overweight (16.5%) and obesity (7.1%) among South African girls to be significantly higher than in boys (overweight 11.5%; obesity 4.7%). Girls in the Western Cape had a higher rate (7.2%) of obesity than girls living in the Northern Cape who had an obesity rate of 3.5%.

Univariate analysis of data from the sub-study (Table 4.5) showed that there was a statistically significant difference (P=0.03) between mothers of 5 to 6-year old children of normal weight and those who were overweight or obese if they had completed at least 12 years of schooling (grade 12/matric) and may have completed tertiary level education. However, multivariate analysis of this sub-study data did not identify maternal education as a risk factor associated with overweight or obesity in 5 to 6-year old children. This contrasts with a South African study reporting low maternal education and a sedentary lifestyle as associated risk factors contributing to overweight and obesity in children aged 1 to 9 years (Kruger et al., 2006).

The number of adults in the house was included as part of a number of socio-economic status (SES) variables. SES is a complex measure and cannot be derived from this variable alone. It is very likely that this association is confounded by other (measured and unmeasured) SES variables and requires further investigation. Most of the reviewed studies (Table 2.2), that reported an increase in childhood overweight, indicated a 10-11% difference between

overweight in offspring of GDM mothers and those of non-GDM mothers with pre-existing or maternal overweight as an associated risk factor.

5.2 Critique of the sub-study

5.2.1 Strengths and limitations of the sub-study methods

5.2.1.1 Strengths of the record review process

The sub-study was undertaken in a government sector hospital because in private healthcare settings there may not be standardized and supervised protocols to ensure early screening, diagnosis and treatment to identify GDM and reduce the potential risk of overweight and obesity in childhood. Patient characteristics and outcomes are captured in medical records. For the retrospective review by one reviewer, explicit review criteria were used rather than implicit criteria that made the data collection process more objective and reliable. Start and cutoff dates for the period under review made data collection easier. An expert was available for assistance with interpretation of the data when needed. The layout of the data collection review form facilitated data recording, coding, extraction and analysis with speed and accuracy under field conditions (Kyriacos, 2011).

5.2.1.2 Limitations of record review

The mothers were contacted telephonically to obtain data not found on the record review form of their children. The additional data were then immediately recorded on the data collection document in an Excel Spreadsheet. This data might have been unreliable due to the mother's inability to accurately recall information. The manual process of data extraction from handwritten medical records slowed the process of data collection and might have been expedited if an electronic database was available. Information was not always legible or complete.

5.2.2 Limitations and strengths of the sub-study

Limitations of the sub-study include not reporting the validation results for pilot testing of the questionnaire for the larger study nor for the sections in the questionnaire from already validated measuring tools. Constraints imposed by the school system and working conditions

of mothers prevented all the mothers included in the larger study from bringing their children for measurement of height and weight and this limited recruitment to the sub-study. The absence of a control group may have influenced the results of this sub-study. Single readings for anthropometry were used instead of a mean of three as this was not a major objective of the parent study.

Birth length and head circumference were missing from most of the children's records. Practice guidelines stipulate that birth length and head circumference must be measured and recorded at birth, however, in practice these measurements may not have been measured and recorded by the midwives. This limited interpretation of the data. Missing data were reported but not addressed. The low numbers in some categories (when considering ethnicity) and the known location of the study might risk identification of individuals.

5.2.3 Generalisability of study results

This appears to be the first study to report the prevalence of overweight and obesity in children born from GDM complicated pregnancies in sub-Saharan Africa. The limited scope of the sub-study is appropriate for a minor dissertation. This was therefore not a national but a regional study. Study results therefore, are generalisable only to children exposed to GDM in the Western Cape of South Africa but may not be generalized to children in other regions in the country due to population differences. Even so, data were taken from a limited population of mostly Coloured and Black and residents from the Western Cape, South Africa.

5.3 Conclusions and recommendations

5.3.1 Conclusions

At birth, the overall prevalence of macrosomia found in this sub-study is considered high but cannot be interpreted meaningfully because there are limited published data from South African studies on fetal macrosomia in GDM exposed infants. The combined prevalence of overweight and obesity in 5 to 6-year old children who were exposed to GDM is higher than that in children who had not been exposed to GDM in utero as reported in other South African studies. This implies a tendency towards overweight and obesity in children in the Western Cape region although the data show no statistical significance. Risk factors for overweight and obesity in 5 and 6-year old children exposed to GDM were found to be birth weight, age in years and

maternal two-hour plasma glucose during pregnancy and a potential risk factor was maternal fasting plasma glucose during pregnancy.

5.3.2 Recommendations

5.3.2.1 Recommendations for nursing and midwifery education and practice

Evidence based health education should be provided for pregnant women, in addition to a whole person-centred approach to achieve a healthy lifestyle. Prevention of GDM should be emphasised. Educational content should include risk factors associated with the development of GDM. If GDM is present in pregnancy, education should also include management thereof.

Current guidelines for screening need to be implemented. Early and comprehensive screening methods and techniques need to be implemented and conducted throughout the pregnancy. GDM diagnosed mothers must be monitored regularly to prevent the unborn child from exposure to high blood sugar levels. Curricula for nursing and midwifery programmes should reflect the content as outlined above.

5.3.2.2 Recommendations for policy and healthcare services

It is imperative that increasing maternal overweight and obesity, a modern public health challenge, should be tackled aggressively. Early intervention in the life of a child can have a significant impact on the prevention of childhood overweight and obesity (Desai et al., 2012). Childhood obesity is a strong predictor of adult obesity. In an effort to curb adult obesity, it is essential not only to conduct early screening in children to prevent adulthood overweight or obesity (van der Merwe, 2012) but then when found, to follow-up and monitor these children.

It is recommended that resources should be allocated for large campaigns to ensure maternal and infant health which will require effective and innovative leadership such as the Western Cape Department of Health's First 1000 Days campaign (Western Cape Government, 2017). It is vital that this public health challenge of increasing maternal overweight and obesity be acted on as soon as possible to prevent an epidemic of health problems and risk factors associated with overweight and obesity in the near future. It is recommended that aggressive leadership and effective measures be taken to prevent this epidemic from getting out of control. A first step would be to adhere to the United Nations (UN) Sustainable Development Goals, specifically goal number three – good health and welfare where the goal is to ensure healthy

lives and promote well-being for all at all ages (United Nations Development Programme (UNDP), 2016). By adopting this sustainable development goal the health risks to mother and child can be significantly lowered and some risks may be eliminated.

Although the UN's target goals are long-term in nature, it is vital for all healthcare personnel to be focused and aggressively pursue these goals to prevent children from falling victim to the problem of overweight and obesity. It is recommended that intervention-based research should be conducted in South African schools and other places where large groups of people gather such as churches. Adherence to the Strategic Plan for Prevention and Control of Non-Communicable Diseases 2013-2017 from The South African National Department of Health will also assist in the prevention and control of childhood overweight and obesity.

5.3.2.3 Recommendations for further research

The cycle of childhood overweight and obesity that originates from mothers with GDM associated pregnancies, maternal overweight and obesity, and other related health risk factors in South Africa needs to be investigated. This problem has not been researched adequately to protect future generations of children from overweight and obesity and the long-term effects on their health. A larger, more diverse and inclusive study covering all socio-economic classes, provinces and childhood ages across South Africa is needed. Mothers attending both private and public healthcare facilities need to be included in future studies to improve the diversity among social classes of the South African population.

Regional data is useful, but it is recommended that more South African studies should be conducted on risk factors associated with overweight and obesity in children using larger sample sizes in all provinces and across all socio-economic boundaries. Qualitative research methods should be undertaken to understand perceptions and behavioural patterns. Well designed studies and valid data are needed to develop evidence-based policies for the prevention of childhood overweight and obesity.

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Appendices

Appendix A: Questionnaire used in the parent study

MOTHER PERSONAL INFORMATION		
1	First name	
2	Middle name	
3	Last name	
4	Home address	
5	District	
6	Home phone	
7	Mobile phone	
8	Email address	
9	Mother birthday	MM_____/DD_____ /YYYY_____
Demographics		
10	Place of birth	□ Western Cape □ Cape Town □ Inside South Africa □ Outside South Africa
11	Resides (location)	□ Urban □ Non-Urban
12	Age	Current Age _____ Maternal Age _____
13	Number of adults in household	□ One □ Two □ Three □ Four □ More than Four
14	Marital Status:	□ Married / Domestic Partner □ Divorced □ Widowed □ Single, Never Married

		□ Separated
15	Number of children in household:	□ One □ Two □ Three □ Four □ More than Four
16	Highest Education completed	□ Less than Secondary Schooling □ Graduated Secondary Schooling □ Some Post-Secondary Schooling □ Completed Post-Secondary Schooling
17	Do you own a house	□ Yes □ No
17a	Type of house you live in	□ building □ shack/informal structure
17b	Toilet in house	□ Yes □ No
17c	Shared tap-water with other households?	□ Yes □ No
18	Electricity in house	□ Yes □ No
19	Household Income:	□ Low □ Middle □ High
20	Ethnic Origin (Check One)	□ Black □Colored □ White □ Indian □ Other
21	South African Citizenship	□ Yes □ No
22	Employment status:	□ Employed □ Self-employed □ Unemployed □ A homemaker □ A student

		□ Unable to Work □ Retired
Medical History		
23	How would you say your health is, in general	□ Excellent □ Very good □ Good □ Fair □ Poor
24	Family history	□ Diabetes □ T2DM □ High Blood □ Heart disease □ Cancer □ Other
25	• Do you take tablets for diabetes? • Do you get insulin injections?	□ Yes □ No □ Yes □ No
26	Have you ever been hospitalized for GDM or diabetes?	□ Yes □ No
27	Did you breastfeed this child?	□ Yes □ No

28	Has your general health changed in the past year?	□ YES □ NO □ Not Sure If yes, please explain. _____
29	Last medical examination	□ Last 6 months □ Last year □ Last two years
30	a. At what gestational age were you diagnosed with diabetes b. Results of Fasting blood sugar? c. Results of two-hour blood sugar? d. How was the diabetes managed?	□ Before 20weeks pregnancy □ between 28 and 32weeks pregnancy □ between 36 and 40weeks pregnancy □ normal □ abnormal □ normal □ abnormal □ Diet □ Oral medication □ Insulin □ Combination of diet and other
31	Perception of own weight	□ Underweight □ Normal Weight □ Overweight/Obese
32	Weight	Before pregnancy (kg) _____

		Current Weight (kg) _____
33	Height	_____cm
34	BMI at booking	
35	HbA1c during pregnancy or at booking	
Social History		
36	Do you smoke:	□ Non-Smoker □ Current Smoker □ Smoke When Pregnancy
37	HIV status positive	□ Yes □ No □ Unknown
38	Do you drink alcohol:	□ Non-Drinker □ Current Drinker □ During Pregnancy
39	Rate your physical activity	□ More active □ Less active □ Same as other (Specify) _____
CHILD DATA COLLECTION		
40	First name	
41	Middle name	
42	Last name	
43	Gender	□ Male □ Female
44	Age	□ 5-year old □ 6-year old
45	Ethnic Origin (Check One)	□ Black □ Colored □White

		□ Indian □ Mixed □Other
46	Type of birth/delivery	□ Vaginal □ Caesarean
47	Any complications during birth	□ Yes □ No If Yes, please give detail
48	Anthropological measurements:	Current Weight (kg) _____ Current Height (kg) _____
49	Body Mass Index kg/m^2:	□ Underweight (kg) ___ □ Normal Weight (kg) ___ □ Overweight (kg) ___ □ Obese (kg) ___
50	Previous Hospitalizations	□ Yes □ No If Yes, please give reason _____

This form will gather data on overweight and obesity in 5 to 6-year old children exposed to GDM during pregnancy. This questionnaire will be used to gather personal data on Cape Town 5- and 6-year-old children including necessary information to determine their BMI. Anonymized data will be used by stakeholders, selected organizations, and governmental institutions to design new programs and services that will help prevent future overweight/obesity in children.

Confidentiality: The confidentiality of mother, child and family information is of great concern to the researchers assigned to this study. The research team and assistants promise to comply with all university and state data protection legislation and medical confidentiality guidelines.

Medical information: All medical information will be kept confidential. No information will be disclosed to anyone not involved in the study and without the participant approval.

Research: Anonymized or aggregated data may be used for research or statistical purposes.

Appendix B: Data extraction form for sub-study

Child Questionnaire	
Study ID: PRO2D	**Year of Study:** 2016
Date Form Completed:	
First Author: Magret C Haynes	
Data Extractor: Magret C Haynes	

1. General Information

Participant's Case Number:	
Country of Study:	South Africa
Study Funding Source or Type:	UCTFHS
Potential Conflict of Interest from Funding?	Yes ☐ No ☐ *(If No →Exclude)* Unclear ☐

2. Study Eligibility

2a. Study Characteristics	
2b. Type of study	Cross Sectional Study
2c. Does the Study Design Meet the Criteria for Inclusion?	Yes ☐ No ☐ (*If No →Exclude)* Unclear ☐

3. Study Participants

3a. Description of Participants	5 to 6-year old children exposed to Gestational Diabetes in utero.
3b. Are participants defined as a group having specific social or cultural characteristics?	Yes ☐ No ☐ Unclear ☐ *(Specify in detail)*

3c. How is the geographic boundary defined?	Specify Details: The study population includes only children born in 2010-2011 at Groote Schuur Hospital in Western Cape, South Africa
3d. Do the participants meet the criteria for inclusion?	Yes ☐ No ☐ (*If No →Exclude)*

4. Study Intervention

4a. Intervention Type?	
4b. Intervention Strategy?	History taken from Mother regarding age of child, type of delivery, birth weight, any hospitalizations of the child involved etc. The anthropologic measurements of child will be taken if child and mother agreed to. Measurements: weight and height will be documented to calculate BMI.
4c. Focus of the intervention	Association of overweight
4d. Does the intervention meet the criteria for inclusion?	Yes ☐ No ☐ (*If No →Exclude) Unclear* ☐
4e. Duration of intervention *(Specify Period)*	June 2016 to December 2016
4f. Is the duration of intervention adequate for inclusion?	*Do the outcome measures meet the criteria for inclusion?*

5. Study Outcomes

5a. Identify Outcomes	Overweight ☐ Obesity ☐ List other risk factors
5b. Do the outcome measures meet the criteria for inclusion?	Yes ☐ No ☐ (*If No →Exclude) Unclear* ☐

6. Summary of Assessment for Inclusion

Gender:	Male __ Female __	Delivery Type:	Vaginal ___ Caesarean ___
Age:	_____	Complications with delivery:	Yes __ No __ If Yes, specify details
Ethnicity:	Black ___ Colored ___ White ___ Asian ___ Mixed ___	Birth Weight (Cameron et al.,2014):	Low (less than 2500g) ___ Normal (2500-3999g) ___ Macrosomia (Greater than 4000g) ___
Anthropological measurements:	Current Weight (kg) ____ Current Height (kg) ____	Blood sugar at birth?	Yes __ No __ Was it low, high, or normal? ___
Body Mass Index kg/m^2:	Underweight (kg) ___ Normal Weight (kg) ___ Overweight (kg) ___ Obese (kg) ___	Health Status:	Normal ___ T2DM ___ GDM ___ High Blood Pressure ___
Physical activity:	Yes __ No __	Previous Hospitalizations:	Yes __ No __ If Yes, please give reason for admission.

Appendix C: Ethical Clearance

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 404 7682 • **Facsimile** [021] 406 6411
Email: nosi.tsama@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

13 December 2016

HREC REF: 826/2016

Prof N Levitt
Medicine Dept
Diabetic Medicine & Endocrinology

Dear Prof Levitt

PROJECT TITLE: THE ASSOCIATION BETWEEN OVERWEIGHT AND OBESITY AT BIRTH AT THE AGE 5 TO 6 YEARS AND EXPOSURE TO GESTATIONAL DIABETES MELLITUS (GDM) DURING PREGNANCY IN THE WESTERN CAPE, SOUTH AFRICA (MSc-candidate-M Haynes) SUB-STUDY LINKED TO 665/2015

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

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

Approval is granted for one year until the 30th December 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student M Haynes will be involved in this study.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval before the research may occur.

Please quote the HREC REF in all your correspondence.

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

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 826/2016

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki (2013) guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Appendix D Permission to carry out Research at the Groote Schuur Hospital

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
E-mail : *Bernadette.Eick@westerncape.gov.za*

Professor N. Levitt
Division of Endocrinology
Department of Medicine
J47 – Old Main Building

E-mail: Naomi.Levitt@uct.ac.za / tchivese@gmail.com

Dear Professor Levitt

RESEARCH PROJECT: The Prevelance of Type 2 Diabetes Mellitus & Associated Risk Factors 5yrs After Gestational Diabetes Mellitus In South Africa (PhD Candidate T Chivese)

Your recent letter to the hospital refers.

You are hereby granted permission to proceed with your research and is valid until 30 November 2016.

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No hospital consumables and stationary may be used.
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please introduce yourself to the person in charge of an area before commencing.
f) Please discuss the study with the HOD before commencing.
g) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
h) Confidentiality must be maintained at all times.
i) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
j) Once research is complete, please submit a copy of the publication or report.

I would like to wish you every success with the project.

Yours sincerely

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 29th January 2016

C.C. Mr. L. Naidoo, Professor E. Weimann

G46 Management Suite, Old Main Building,
Observatory 7925

Private Bag X,
Observatory, 7935

Tel: +27 21 404 6288 fax: +27 21 404 6125

www.capegateway.go.v.za

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL

Enquiries: Dr Bernadette Eick
E-mail : *Bernadette.Eick@westerncape.gov.za*

Professor N. Levitt
Division of Endocrinology
Department of Medicine
J47 – Old Main Building

E-mail: Naomi.Levitt@uct.ac.za / tchivese@gmail.com

Dear Professor Levitt

RESEARCH PROJECT EXTENSION: The Prevalence of Type 2 Diabetes Mellitus & Associated Risk Factors 5yrs After Gestational Diabetes Mellitus in South Africa (PhD T. Chivese)

Your recent communication to the hospital refers.

The extension of your research has been approved in accordance with UCT Ethics clearance, until **30 November 2017**.

As previously mentioned:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No hospital consumables and stationary may be used.
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must be maintained at all times.
g) Once the research is complete, please submit a copy of the publication or report.

I would like to wish you every success with the project.

Yours sincerely

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 12 January 2017
BE/vms

C.C. Mr L. Naidoo, Professor E. Weimann

G46 Management Suite, Old Main Building,
Observatory 7925

Private Bag X,
Observatory, 7935

Tel: +27 21 404 6288 fax: +27 21 404 6125

www.capegateway.go.v.za

Appendix E: Anthropometry Graphics

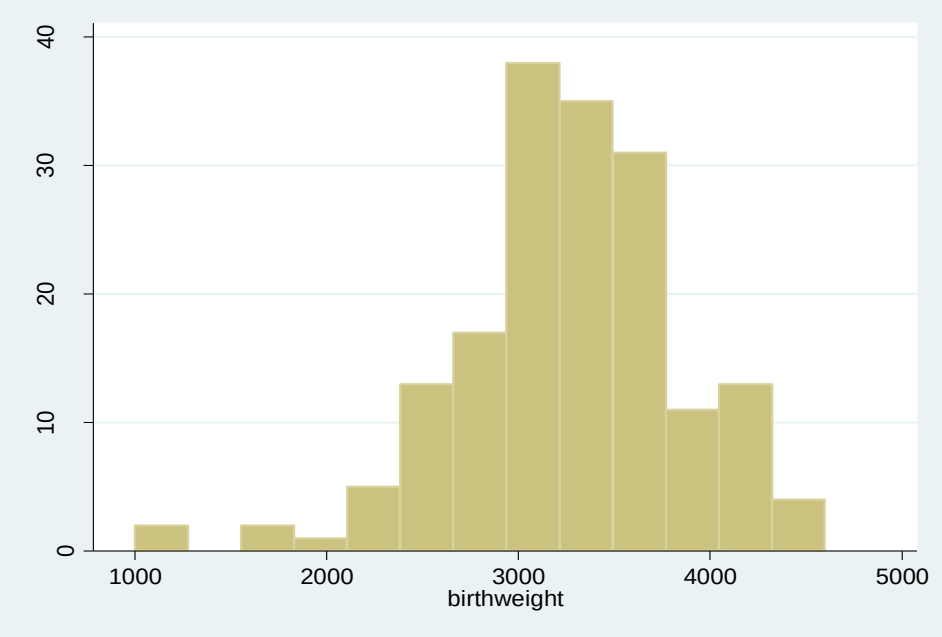

Figure 4. 1: Children's weight at birth, in grams

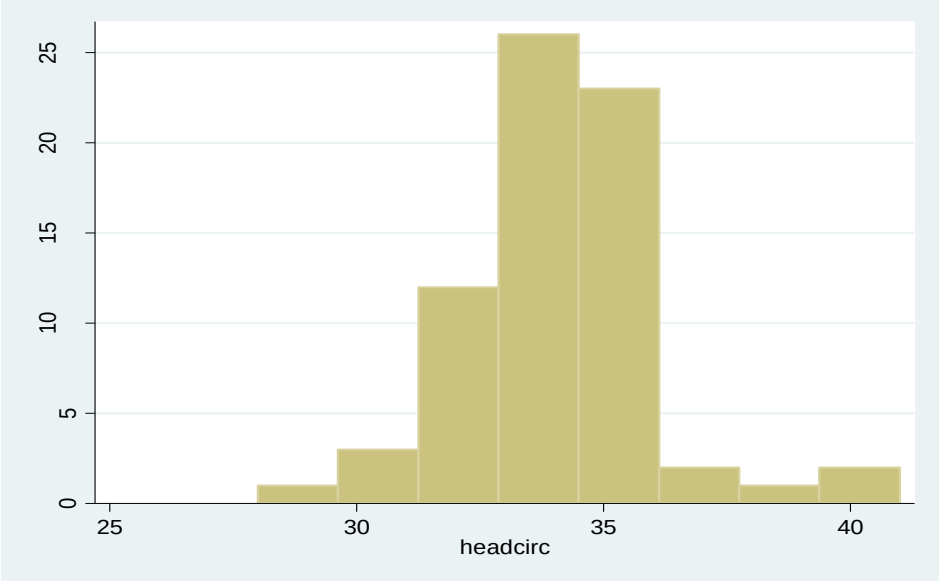

Figure 4. 2: Children ‘s head circumference at birth, in centimeters

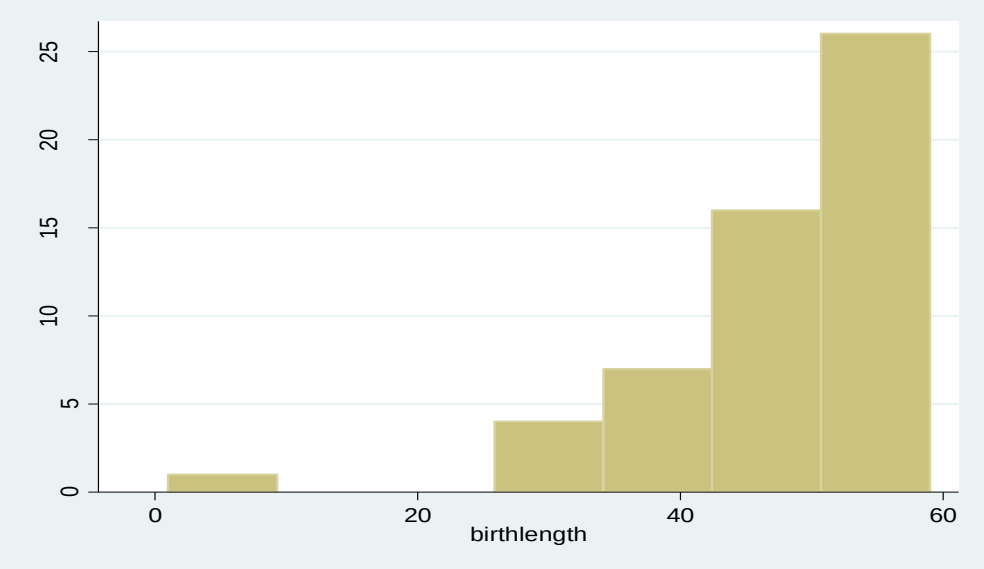

Figure 4. 3: Children’s length at birth, in centimeters

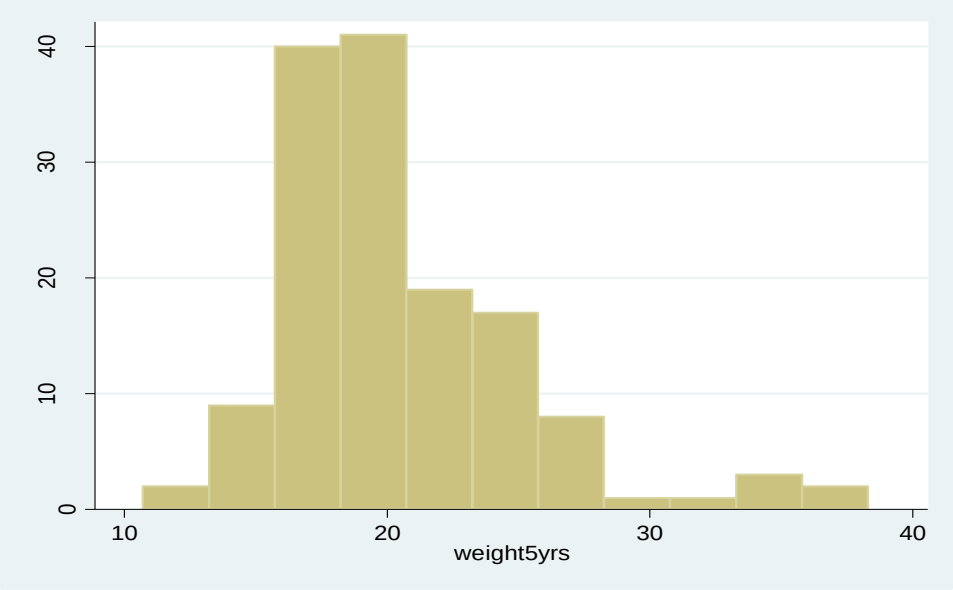

Figure 4. 4: Children's weight at 5 and 6 years of age, in kilograms

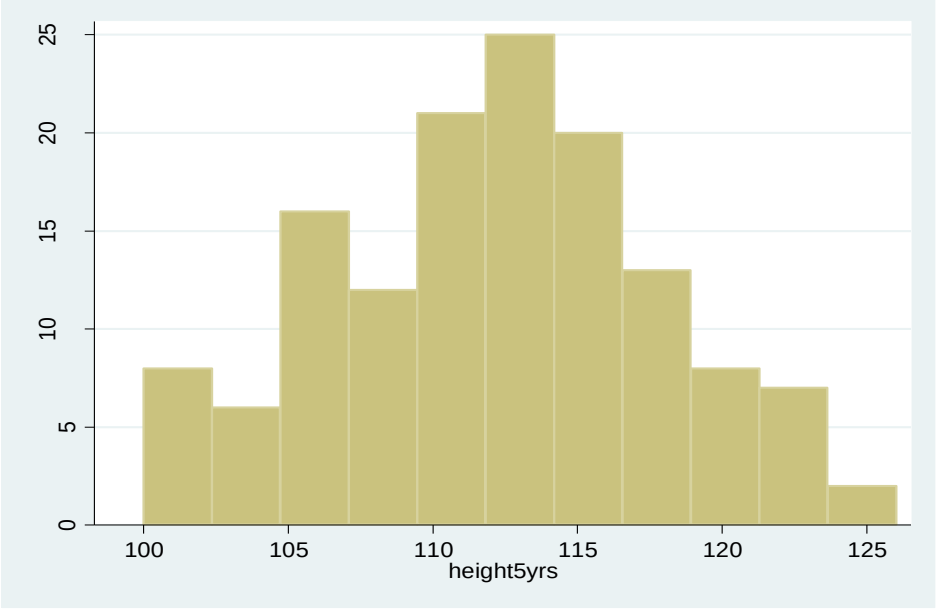

Figure 4. 5: Children's height at 5 to 6 years of age, in centimeters

Appendix F: JHNEBP Evidence Rating Scales

STRENGTH of the Evidence	
Level I	Experimental study/randomized controlled trial (RCT) or meta-analysis of RCT
Level II	Quasi-experimental study
Level III	Non-experimental study, qualitative study, or meta-synthesis.
Level IV	Opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review, clinical practice guidelines)
Level V	Opinion of individual expert based on non-research evidence. (Includes case studies; literature review; organizational experience e.g., quality improvement and financial data; clinical expertise, or personal experience)

QUALITY of the Evidence		
A High	Research	Consistent results with sufficient sample size, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence.
	Summative reviews	Well-defined, reproducible search strategies; consistent results with sufficient numbers of well-defined studies; criteria-based evaluation of overall scientific strength and quality of included studies; definitive conclusions.
	Organizational	well-defined methods using a rigorous approach; consistent results with sufficient sample size; use of reliable **and** valid measures
	Expert Opinion	expertise is clearly evident
B Good	Research	reasonably consistent results, sufficient sample size, some control, with fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence
	Summative reviews	Reasonably thorough and appropriate search; reasonably consistent results with sufficient numbers of well-defined studies; evaluation of strengths and limitations of included studies; fairly definitive conclusions.
	Organizational	Well-defined methods; reasonably consistent results with sufficient numbers; use of **reliable and valid** measures; reasonably consistent recommendations

	Expert Opinion	expertise appears to be credible.
C Low quality or major flaws	Research	little evidence with inconsistent results, insufficient sample size, conclusions cannot be drawn
	Summative reviews	undefined, poorly defined, or limited search strategies; insufficient evidence with inconsistent results; conclusions cannot be drawn
	Organizational	Undefined, **or** poorly defined methods; insufficient sample size; inconsistent results; undefined, poorly defined or measures that lack adequate reliability or validity
	Expert Opinion	expertise is not discernable or is dubious.

**A study rated an A would be of high quality, whereas, a study rated a C would have major flaws that raise serious questions about the believability of the findings and should be automatically eliminated from consideration.* Newhouse R, Dearholt S, Poe S, Pugh LC, White K. The Johns Hopkins Nursing Evidence-based Practice Rating Scale. 2005. Baltimore, MD, The Johns Hopkins Hospital; Johns Hopkins University School of Nursing.© The Johns Hopkins Hospital /The Johns Hopkins University.

Appendix G: STROBE Guideline for reporting observational studies

STROBE Guideline for reporting observational studies

Item	Item No	Recommendation	Application to study Section, Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title on cover page, Abstract pg.v
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract pg.v
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	Chapter 1: Section 1.1 pg 1 Section 1.4, pg 3 Chapter 2, Introduction and themes extracted from a review of the published literature pg. 5-10
Objectives	3	State specific objectives, including any pre-specified hypotheses	1.4.2 Objectives, pg. 3
Methods			
Study design	4	Present key elements of study design early in the paper	In Abstract, pg. v Chapter 3, Section 3.3 pg. 28
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Chapter 3, Section 3.1 & 3.2.1 pg. 27 Section 3.4, pg.29 Fig 3.1 pg. 30 Section 3.7, pg. 32-35
Participants	6	(*a) Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Section 3.5, 3.6, pg. 29, 31
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Section 3.2, pg.27-28 Potential confounders and effect modifiers were not addressed
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of	Section 3.2.1, pg. 27-28 Section 3.8.2, pg.36-37

Item	Item No	Recommendation	Application to study Section, Page
		assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	Section 3.6, pg. 29
Study size	10	Explain how the study size was arrived at	Section 3.6, pg. 29-31
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Grouping was by gender. Section 3.2.1 pg. 27-28 Section 3.2.2 pg. 28 Section 3.7.2 pg. 32-33 Section 3.7.4.2 pg. 34-35
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Section 3.8 (3.8.1, 3.8.2) pg. 36-37
		(*b*) Describe any methods used to examine subgroups and interactions	Section 3.8.2, pg.36
		(*c*) Explain how missing data were addressed	Missing data were reported but not addressed Section 3.7.4.1 p.33 Section 4.1 pg. 43
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Not applicable Not applicable See above
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	Section 3.6, Flow diagram 3.1, pg. 30
		(b) Give reasons for non-participation at each stage	Flow diagram 3.1, pg. 30
		(c) Consider use of a flow diagram	Pg. 30
Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Tables 4.1-4.5, pg. 40-49
		(b) Indicate number of participants with missing data for each variable of interest	Pg. 43

Item	Item No	Recommendation	Application to study Section, Page
		(c) *Cohort study*—Summarise follow-up time (e.g., average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Tables 4.1-4.5, pg. 40-49
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Multivariate analysis Table 4.5, pg. 47-49
		(b) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Section 5.0, pg. 51
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Sections 5.2.1–5.2.2 pg. 56-57
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Sections 5.1.1 – 5.1.5 pg. 52-55
Generalisability	21	Discuss the generalizability (external validity) of the study results	Section 5.2.3, pg. 57
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Sub-study not funded

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix H: Mother's informed consent

Participant Number

Participant information leaflet and Consent Form

Research Title: The prevalence of Type 2 diabetes mellitus and associated risk factors 5 years after gestational diabetes mellitus in South Africa

Principal Investigators: Professor Naomi Levitt, Professor Shane Norris, Professor Christina Zarowsky, Tawanda Chivese

Contact Address: Chronic Disease Initiative for Africa, J47 Room 86, Old Groote Schuur Hospital Building Observatory, 7935, Cape Town

Telephone: +27 21 4066572

Fax: +27 21 4486815

More information: http://www.health.uct.ac.za/fhs/research/groupings/cdia/about

Participant Number:

You are being invited to take part in a research project which asks the question: How many women who had diabetes in their pregnancy have diabetes 5 years later?

This research project is being conducted at the University of Cape Town and the University of the Witwatersrand in Johannesburg. A researcher from the University of Montreal (Christina Zarowsky) will also help with knowledge on how to carry out research properly.

Most women who had diabetes during pregnancy recover from the diabetes after the birth of their babies, but they have a high chance of developing Type 2 diabetes sometime later. Type 2 diabetes is a chronic condition that affects the way your body uses sugar (glucose), your body's source of fuel. If we can find that someone has type 2 diabetes earlier we can start treatment sooner and this may cause fewer long term problems.

Participant Number

We do not know how many women with diabetes during pregnancy end up with type 2 diabetes in South Africa. We also do not know what other factors lead to increased chance of diabetes in this situation. Knowing these factors will enable us to develop better programs to reduce the risk of diabetes in women. Additionally, knowing factors that increase the chance of their children being overweight can help lower the risk of them developing diabetes and heart disease later in their life.

Ethical considerations

This research has been approved by the University of Cape Town Human Research Ethics Committee (Ethics approval number 656/2015). The research will be carried out according to the Declaration of Helsinki, which protects people who take part in research (Fortaleza, Brazil 2013).

You are free to say yes or to say no. If you say no, your medical care will continue just as before, and it will not be held against you. You are also free to withdraw from the study at any point, even if you do agree to take part. If you volunteer to take part in the study, you will only be included if you give written informed consent.

Please ask the study staff any questions about any part of this project that you do not fully understand.

Why have you been invited to participate?

We are inviting all women who live in Cape Town and Soweto who received treatment for diabetes during pregnancy at Groote Schuur Hospital and Chris Hani Baragwanath Hospital to take part in the research.

What will your participation entail?

You have been asked to come to the Groote Schuur Hospital (or Chris Hani Baragwanath Hospital, delete inapplicable) in order to take part in the research. Your participation will be for two and a half hours. You will be asked to complete a questionnaire and have blood taken from a vein in your arm before and after drinking sugar water. In your blood, we will measure glucose, fats and other factors associated with diabetes. We will also store 5ml of your blood, in case we need to retest your blood or carry out additional tests related to the study. We will seek permission from the University of Cape Town Human Research Ethics Committee before we do any additional tests. This stored blood will be destroyed 2 years after the study is finished, if it has not been used.

For the diabetes test, you are requested to fast overnight before the test can be done. We will also measure your blood pressure (BP), height, weight and how wide your waist and hips are. We will also look for information about your pregnancy in your hospital folder. This information will include the sugar level that was in your blood when you were

Participant Number

pregnant, any illnesses you had during the pregnancy, and how much your baby weighed when he/she was born.

An interviewer will ask you some questions using a questionnaire. These question may help us identify a pattern of who is more likely to have diabetes. An example of the questions we are asking is whether you or any of your family members has ever been diagnosed with diabetes.

Will you benefit from taking part in this research?

If any illnesses (such as undiagnosed diabetes or high blood pressure) are identified during the research then you will be referred to a clinic for follow-up and management. You will also be told the results of all the tests that will be done.

Are there any risks involved in your taking part in this research?

We will take blood samples from the forearms. The risk are very small. Some of the potential risks in the blood collection include infection, delayed healing, bruising and some physical pain. The blood samples will be drawn using experienced nurses to minimize the risks.

Your name and personal details will be kept strictly confidential and will not be given to anyone to minimise the risk of improper disclosure of information.

What if Something Goes Wrong?

The University of Cape Town (UCT) has insurance which will compensate you if you suffer injuries or harm during your participation in this research. This compensation will pay for reasonable medical charges and this will be according to the South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI) in the event of an injury or side effect resulting directly from your participation in the trial. You will not be required to prove fault on the part of the University.

The University will not be liable for any loss, injuries and/or harm that you may sustain where the loss is caused by

- The use of unauthorised medicine or substances during the study
- Any injury that results from you not following the protocol requirements or the instructions that the study doctor may give you
- Any injury that arises from inadequate action or lack of action to deal adequately with a side effect or reaction to the study medication

This study has been approved by the University of Cape Town HREC 656/2015
Room: E52 Old Main Building, GSH **Tel:** 021 406 6338 **Fax:** 021 406 6411

Participant Number

- An injury that results from negligence on your part

By agreeing to participate in this study, you do not give up your right to claim compensation for injury where you can prove negligence, in separate litigation. In particular, your right to pursue such a claim in a South African court in terms of South African law must be ensured. Note, however, that you will usually be requested to accept that payment made by the University under the SA GCP guideline 4.11 is in full settlement of the claim relating to the medical expenses.

An injury is considered trial-related if, and to the extent that, it is caused by study activities. You must notify the study doctor immediately of any side effects and/or injuries during the trial, whether they are research-related or other related complications.

UCT reserves the right not to provide compensation if, and to the extent that, your injury came about because you chose not to follow the instructions that you were given while you were taking part in the study. Your right in law to claim compensation for injury where you prove negligence is not affected. Copies of these guidelines are available on request.

If you do not agree to take part, what alternatives do you have?

Not taking part in the study will not change your future care or treatment when you go to hospitals or clinics. You will be treated the same as other women who decide to participate in the study. The researchers are not the same people as your usual doctors.

Who will have access to your medical records and what information will they collect?

All personal information collected will be treated as confidential and access to it will be strictly controlled and limited to the researchers. The information collected from your medical records will include information about your pregnancy, whether you had any illnesses during that pregnancy, the level of sugar in your blood and blood pressure during that pregnancy and whether your child had any problems when they were born. Your name will be removed from all samples and information provided as soon as possible. Only a study number will be used. Your name will never be published anywhere.

Will you be paid to take part in this study and are there any costs involved?

We will give you a R150 food voucher redeemable at Shoprite to thank you for the time you spend during the study. You will not be able to buy alcohol and smoking products using this voucher. We will compensate you for your travelling expenses.

This study has been approved by the University of Cape Town HREC 656/2015
Room: E52 Old Main Building, GSH **Tel:** 021 406 6338 **Fax:** 021 406 6411

Participant Number

Please ensure that you have carefully read and understood this information sheet and been given a copy to keep for yourself.

Contact details of researchers: For any questions or concerns, please feel free to contact the researchers whose details are listed below:

Tawanda Chivese	Email: tchivese@gmail.com
	Tel: 0216505131
Professor Naomi Levitt	Email: Naomi.Levitt@uct.ac.za
	Tel: 0216505110
Professor Shane Norris	Email: san@global.cc.za
Professor Christina Zarowski	Email: czarowsky@gmail.com

You may contact the University of Cape Town Human Research Ethics Committee if you have any questions or concerns your rights and welfare. The contact details are listed below

Email: sumayahariefdien@uct.ac.za

Tel: 021 406 6338

Fax: 021 406 6411

5 This study has been approved by the University of Cape Town HREC 656/2015
Room: E52 Old Main Building, GSH **Tel:** 021 406 6338 **Fax:** 021 406 6411

Participant Number

PARTICIPANT CONSENT

Study Title: The prevalence of Type 2 diabetes mellitus and associated risk factors 5 years after gestational diabetes mellitus in South Africa

By signing this document:

I confirm that I have read the above information and understand it. I confirm that I have had an opportunity to ask questions and I am satisfied with the answers and explanations that have been given to me.

I give my permission for the researchers to use the information in my medical chart for the purposes of this research.

I agree to have left over serum from my blood sample kept and then frozen.

I understand that my participation in this research is voluntary and I am free to withdraw at any time without having to give a reason.

Please tick one of the boxes below:

☐ YES, I would like to take part in this study

☐ NO, I do not wish to take part in this study

Name of research participant: ..... Signature.....
Date: .....

Name of researcher: ..... Signature.....
Date: .....

Name of witness..... Signature.....

Date .....

If participant is not able to write:

Thumbprint of participant .....

Date .....

This study has been approved by the University of Cape Town HREC 656/2015
Room: E52 Old Main Building, GSH **Tel:** 021 406 6338 **Fax:** 021 406 6411

Participant Number

1 **Participant Contact Details**

Forename	
Surname	
Address	
Suburb	
City	
Postcode	
Telephone	
Cell	
Secondary cell	
Next of kin telephone	
Next of kin cell	
Next of kin address	
Date of birth	
Hospital number	

2

3

7 This study has been approved by the University of Cape Town HREC 656/2015
Room: E52 Old Main Building, GSH **Tel:** 021 406 6338 **Fax:** 021 406 6411

Appendix I: Consent for child participation

Participant Number

Consent for Child Participation in research

Research Title: The prevalence of Type 2 diabetes mellitus and associated risk factors 5 years after gestational diabetes mellitus in South Africa

Principal Investigators: Professor Naomi Levitt, Professor Shane Norris, Professor Christina Zarowsky, Tawanda Chivese

Contact Address: Chronic Disease Initiative for Africa, J47 Room 86, Old Groote Schuur Hospital Building Observatory, 7935, Cape Town

Telephone: +27 21 4066572

Fax: +27 21 4486815

More information: http://www.health.uct.ac.za/fhs/research/groupings/cdia/about

Participant Number:

Your child is invited to take part in a research project which asks the question: How many 5 year old children born to women who had diabetes in their pregnancy are overweight?

This research project is being conducted at the University of Cape Town and the University of the Witwatersrand in Johannesburg. A researcher from the University of Montreal will also help with knowledge on how to carry out research properly.

This research will be carried out according to the Declaration of Helsinki, which protects people who take part in research.

Most women who had diabetes during pregnancy recover from the diabetes after the birth of their babies, but their children may be overweight when growing up. This makes it easy for them to become sick with type 2 diabetes and other illnesses like heart disease. Type 2 diabetes is a chronic condition that affects the way your body uses sugar

1 This study has been approved by the University of Cape Town HREC 656/2015
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Participant Number

(glucose), your body's source of fuel. If we can find that someone has type 2 diabetes earlier we can start treatment sooner and this may cause fewer long term problems.

We do not know how many 5 year old children born to women with diabetes during pregnancy are overweight in South Africa. Knowing this will enable us to develop better programs to look after children born to mothers who had diabetes during pregancy. Additionally, knowing factors that increase the chance of their children being overweight can help lower the risk of them developing diabetes and heart disease later in their life.
Please ask the study staff any questions about any part of this project that you do not fully understand. You are free to say yes or to say no. If you say no, your child's medical care will continue just as before, and it will not be held against you. You are also free to withdraw your child from the study at any point, even if you do agree to take part.

Why has your child been invited to participate?

We are inviting all 5 year old children who live in Cape Town and Soweto whose mothers received treatment for diabetes during pregnancy at Groote Schuur Hospital and Chris Hani Baragwanath Hospital to take part in the research.

What will your child's participation entail?

Your child has been asked to come to the Groote Schuur Hospital (or Chris Hani Baragwanath Hospital) in order to take part in the research. The participation will be no more than 30 minutes. You will be asked some questions about your child in a questionnaire. Some of the questions will be to see if your child has been sick, if he/she is taking any medicines for any illness and whether you breast fed your child.

Your child will also be weighed on a scale and have his/her height measured.

Will your benefit from taking part in this research?

If any illnesses (such as your child being too big for their age) are identified during the research then your child will be referred to a clinic for follow-up and management. You will also be told the results of the weight and height measurements of your child.

Are there any risks involved in your child taking part in this research?

Your child will only have his/her height and weight measured. He/she will not have any bloods taken and will not be given any medicines during this study. If your child does not want to have their weight and height measured, we will not force him/her.
Your child's name and personal details will be kept strictly confidential and will not be given to anyone to minimise the risk of improper disclosure of information.

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If you do not want your child to take part, what alternatives do you have?

Not taking part in the study will not change your child's future care or treatment if and when you take him/her to hospitals or clinics. Your child will be treated the same as other children who participate in the study. The researchers are not the same people as your child's usual doctors.

Please ensure that you have carefully read and understood this information sheet and been given a copy to keep for yourself.

Contact details of researchers: For any questions or concerns, please feel free to contact the researchers whose details are listed below:

Tawanda Chivese	Email: tchivese@gmail.com
	Tel: 0216505131
Professor Naomi Levitt	Email: Naomi.Levitt@uct.ac.za
	Tel: 0216505110
Professor Shane Norris	Email: san@global.co.za
Professor Christina Zarowski	Email: czarowsky@gmail.com

You may contact the University of Cape Town Human Research Ethics Committee if you have any questions or concerns about your child's rights and welfare. The contact details are listed below

Email: sumayahariefdien@uct.ac.za

Tel: 021 406 6338

Fax: 021 406 6411

Participant Number

PARENTAL CONSENT

Study Title: The prevalence of Type 2 diabetes mellitus and associated risk factors 5 years after gestational diabetes mellitus in South Africa

By signing this document:

I confirm that I have read the above information and understand it. I confirm that I have had an opportunity to ask questions and I am satisfied with the answers and explanations that have been given to me.

I give my permission for my child (Insert child's name.....) to have their height and weight measured.

I agree to answer question about my child's (Insert child's name.....) health

I understand that my participation in this research is voluntary and I am free to withdraw my child (Insert child's name. .....) at any time without having to give a reason.

Please tick one of the boxes below:

☐ YES, I would like my child (Insert child's name.....) to take part in this study

☐ NO, I do not wish my child (Insert child's name.....) to take part in this study

Name of mother: ..... Signature.....
Date: .....

Name of researcher: ..... Signature.....
Date: .....

Name of witness..... Signature.....
Date .....

If participant is not able to write:

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Participant Number

Thumbprint of participant……

Date ……

Participant Contact Details

Forename	
Surname	
Address	
Suburb	
City	
Postcode	
Telephone	
Cell	
Secondary cell	
Next of kin telephone	
Next of kin cell	
Next of kin address	
Date of birth	
Hospital number	

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