

**Associations between maternal dietary patterns
during pregnancy and early childhood
development in Johannesburg, South Africa**

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By the grace of God alone.

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ABSTRACT

Background and rationale

Pregnancy presents a unique period during which the health and well-being of the offspring can be influenced. Maternal nutrition is known as an important modifiable factor for both fetal and infant growth and development. Dietary pattern analysis allows for the assessment of the diet as a whole. The use of nutrients as variables for dietary pattern analysis rather than foods or food groups are advised as it is universal in consumption and allows for easier comparison between study populations. Studies investigating the associations of maternal dietary patterns during pregnancy with fetal and infant growth and development are limited, with most studies conducted in high-income countries.

The aim of this study was therefore to assess the associations of maternal dietary patterns during pregnancy with fetal and infant growth and development up to the age of 12 months in Johannesburg, South Africa.

Study design and methodology

Generally, healthy women pregnant with a singleton <18 weeks' gestation residing in the city of Johannesburg were enrolled to the Nutrition during Pregnancy and Early Development (NuPED) cohort study between March 2016 and November 2017. Data were collected as part of this prospective study at early (<18 weeks' gestation), mid (± 22 weeks) and late (± 36 weeks) pregnancy, as well as birth. Offspring of the enrolled women were followed up at 6 and 12 months postpartum.

Maternal habitual dietary data was collected at early pregnancy using a validated quantified food frequency questionnaire (QFFQ). *A posteriori* nutrient patterns were determined from 22 nutrients using exploratory factor analysis and *a priori* patterns using the Diet Quality Index – International (DQI-I). Ultrasound-derived fetal growth was described using 418 ultrasound scans at mid ($n = 226$) and late ($n = 192$) pregnancy in terms of biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC), estimated fetal weight (EFW), as well as interval fetal growth (difference between a biometric measure at two time points divided by the difference in gestational age). Infant growth and neurodevelopment were assessed at 6 and 12 months postnatal by anthropometric indices and the Protocol for Child Monitoring – Infant-Toddler (PCM-IT) version, respectively.

Results

A total of 250 pregnant women were enrolled to the NuPED study. Birth data of 203 infants were available, with data of 98 mother-infant pairs available at 6 months and 100 mother-infant pairs available at 12 months postpartum. Based on the *a priori* dietary pattern, the study population followed a borderline low-quality diet. Three distinct nutrient patterns were identified: Pattern 1 “plant protein, iron, thiamine, and folic acid”; pattern 2 “animal protein, copper, vitamin A, and vitamin B₁₂”; pattern 3 “fatty acids and sodium”.

The “plant protein, iron, thiamine, and folic acid” nutrient pattern was associated with higher dietary quality ($p < 0.001$) and was adhered to by women of lower maternal educational level ($p = 0.03$) and socioeconomic status ($p < 0.001$). The pattern was found to be representative of a traditional South African diet and nutrients positively loaded on the factor matrix were representative of the nutrients used in the national food fortification programme. Although the “plant protein, iron, thiamine and folic acid” pattern was found to have a small positive correlation with HC interval growth between mid and late pregnancy ($r = 0.18$, $p = 0.041$), this pattern inversely correlated with adaptive skills, a sub-category to social-emotional development, at 6 months postpartum ($r = -0.339$, $p = 0.009$). These associations may be attributed to the nutrients associated with the pattern being important for brain development; polyunsaturated fatty acids (PUFAs) were though not associated with this nutrient pattern as per the factor matrix and could be explanatory for the poorer scores with regards to adaptive skills.

Nutrient pattern 2 (“animal protein, copper, vitamin A, and vitamin B₁₂”) was not associated with ultrasound-derived fetal growth. Adherence to this pattern was, however, negatively associated with social-emotional development at 12 months postpartum ($p = 0.015$). As with nutrient pattern 1, PUFAs of which the long-chain polyunsaturated fatty acids eicosapentaenoic- (EPA) and docosahexaenoic acid (DHA) are well described to be important for brain development, were not associated with this nutrient pattern as per the factor matrix.

The “fatty acids and sodium” nutrient pattern was significantly associated with lower dietary quality and correlated negatively with FL which is reflective of bone accretion and linear growth at mid-pregnancy ($r = -0.16$, $p = 0.028$). A higher maternal adherence to this pattern was also associated with lower WAZ ($p = 0.005$ and $p = 0.007$) and LAZ ($p = 0.016$ and $p = 0.012$) in the infants at both 6 and 12 months of age. As great number of nutrients were negatively associated with this pattern, the “fatty acids and sodium” patterns probably deprives the fetus of essential nutrients required for optimal growth and development, probably implicating restricted linear growth to commence *in utero* already. Linear growth retardation are well described to be associated with poor early childhood development and these children may later in life present with poorer neurodevelopment.

Conclusion

A higher-quality dietary pattern associated more positively with fetal and infant growth and development, whereas a dietary pattern of poorer quality was associated with poorer development. Although the associations found were small in effect size, our results indicate that the maternal diet may play a role in fetal and offspring growth and development. With various factors influencing child development, ensuring optimal fetal growth and development is crucial rather than relying upon later catch-up growth and development. Nutrition programmes educating South African women of child-bearing age on how to follow a diet of high quality are necessary.

Key words: Dietary patterns, nutrition, pregnancy, fetal growth, infant growth, infant neurodevelopment

ABBREVIATIONS

AC	Abdominal circumference
BMI	body mass index
BPD	biparietal diameter
CDATs	child development assessment tools
DQI-I	Diet Quality Index - International
EFW	estimated fetal weight
FGR	fetal growth restriction
FL	femur length
GWG	gestational weight gain
HC	head circumference
HIV	human immunodeficiency virus
IoM	Institute of Medicine
INTERGROWTH-21 st	International Fetal and Newborn Growth Consortium for the 21 st Century
IQR	interquartile range
kg	kilogram
LBW	low birth weight
NWU	North-West University
NuPED	Nutrition during Pregnancy and Early Development
PCM-IT	Protocol for Child Monitoring–Infant/ Toddler version
QFFQ	quantified food frequency questionnaire
RMMCH	Rahima Moose Mother and Child Hospital
SAMRC	South African Medical Research Council
UNICEF	United Nations Children’s Fund
WHO	World Health Organization

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CHAPTER 1 - INTRODUCTION

1.1 Background information

Millions of children globally are not growing well and not developing to their full potential. According to the State of the World's Children report of 2019 (UNICEF (United Nations Children's Fund), 2019), at least one in three children younger than the age of five years suffers from either stunting, wasting or overweight, and at least one in two from hidden hunger (deficiency of essential micronutrients). Referred to as the triple burden of malnutrition, these three forms of malnutrition (undernutrition, hidden hunger and overweight) are often interwoven within the same community or even household. It is also likely for a child to present with more than one form of malnutrition simultaneously or during the life course (UNICEF, 2019). Each form of malnutrition deprives a child of optimal health and well-being, often having a lifelong effect (UNICEF, 2019). It is well reported in the literature that undernutrition, particularly linear growth retardation (or stunting), is associated with, among others, deficits in cognitive development and educational performance (Grantham-McGregor *et al.*, 2007; Leroy & Frongillo, 2019; Walker *et al.*, 2011; Walker *et al.*, 2007). Hidden hunger and overweight are also known to contribute to poor health, growth and development and the early onset of non-communicable diseases, respectively (Sahoo *et al.*, 2015; Walker *et al.*, 2011; Walker *et al.*, 2007). As indicated by the State of the World's Children report, child malnutrition in the 21st century can be summarised as follows: "More children are surviving, but far too few are thriving. They are not thriving in the crucial first 1000 days when the foundation for healthy, lifelong physical growth and mental development is laid" (UNICEF, 2019).

Poverty is often at the heart of the triple burden of malnutrition (UNICEF, 2019). In defining global indicators for child development, Grantham-McGregor *et al.* (2007) identified early childhood stunting and the number of persons living in extreme poverty as proxy measures for poor childhood development as both factors are associated with inadequate development. Based on these indicators, Lu *et al.* (2016) report that an estimated 250 million children younger than the age of five years in low- and middle-income countries are at risk of not reaching their developmental potential. This is about 43% of all children living in the developing world (Lu *et al.*, 2016). Using, these indicators, among others, Countdown to 2030 - Women's, Children's and Adolescent Health (in partnership with the World Health Organization (WHO), World Bank Group and UNICEF), publish annual early childhood development profiles for each country. According to the 2019 report (Countdown to 2030, 2019), the greatest burden of poor childhood development is concentrated in sub-Saharan Africa as more than 60% of children under five in most of these countries are at risk of not reaching their optimal potential. In South Africa, an estimated 38% of

children younger than the age of five years are at risk of poor development (Countdown to 2030, 2019). Through comprehensive analysis, Fink *et al.* (2016) indicate that the economic burden for a country due to poor early life growth and development is substantial. Using the same algorithm as Fink *et al.* (2016), Countdown to 2030 indicates that the lifetime cost (including the loss of years for educational attainment and costs to the country) of poor childhood development in South Africa is estimated at an annual loss of 174% in adult income when compared with the average adult income in the country (Countdown to 2030, 2019). Malnutrition and poor childhood development hence often contribute to maintaining an intergenerational cycle of poverty (UNICEF, 2019; Walker *et al.*, 2007).

Poor diet is one of the leading contributors to childhood malnutrition (UNICEF, 2019). Although often caused by the poor quality of diets followed by children, the Global Nutrition Report 2020 reiterates the fact that poor diets during pregnancy also contribute towards malnutrition in early life which can, amongst others, compromise physical growth and brain development (Development Initiatives, 2020). This phenomenon of the long-term effect of nutrition and lifestyle during pregnancy (also including nutrition before pregnancy) on the later health of a child is known as the “*early metabolic programming of long-term health and disease*” or the “*developmental origins of health and disease*” (Koletzko *et al.*, 2019). Barker and Osmond (1986) were first to publish comprehensive reports on this in the late 1980s. Much research has since been done to better understand the associations between the early life environment and later health outcomes. With regard to child development, both maternal undernutrition and overnutrition during pregnancy are reported to alter an offspring’s developmental trajectories - possibly contributing towards a child’s failure to reach his/her full developmental potential (Bateson *et al.*, 2004; Oh *et al.*, 2020; Stirrat & Reynolds, 2014). This is likely as fetal growth and development are greatly dependent upon the maternal nutrient supply (Brett *et al.*, 2014; Oh *et al.*, 2020). Georgieff *et al.* (2018) likewise indicate the effect of nutrition during the postnatal period on brain development to be determined by the maternal nutritional status during pregnancy. The importance of maternal nutrition during pregnancy for optimal child development is also acknowledged as part of the nurturing care concept endorsed by the UNICEF, World Bank Group and WHO (WHO *et al.*, 2018). According to the Life-Course Conceptual Framework for early childhood development which depicts the nurturing care concept, maternal nutrition during pregnancy forms part of the foundation upon which the acquisition of skills throughout life is built (Black *et al.*, 2017).

1.2 Rationale for the study

In January 2016, the 2030 agenda for the Sustainable Development Goals, a roadmap to build on the success of the Millennium Development Goals, was implemented. These 17 goals aim to ensure peace and prosperity for all human beings (United Nations, 2016). Of these goals, at least 12 are significant for nutrition – indicating the importance of nutrition in the promotion of health, education, and employment (International Food Policy Research Institute, 2016). Momentum for optimal nutrition is thus strong at present. During the past decade, an unprecedented number of interlinked global nutrition declarations and commitments were made. The World Health Assembly nutrition targets for Maternal, Infant and Young Child Nutrition (adopted 2012) are among these global declarations (International Food Policy Research Institute, 2016). These targets aim to increase exclusive breastfeeding rates by 2025, as well as to reduce the number of infants born with low birth weight (LBW), reduce the rate of stunting, wasting and overweight in children, and reduce the prevalence of anaemia among women of reproductive age (WHO, 2014b). The rationale for these goals is to address the conditions responsible for the majority of the nutrition-related morbidity and mortality during the first 1000 days of life (WHO, 2014a).

A great body of research exists to further understand the associations and to explore interventions to decrease childhood morbidity and mortality. As a part of this, much research has been conducted to date to understand the role of maternal nutrition during pregnancy in offspring well-being. Traditionally, however, nutrition research has focused only on single-nutrient or single-food interactions. As nutrients are not consumed in isolation but as part of a diet comprising different foods in different combinations, Hu (2002) proposed the use of *dietary patterns* as an “alternative and complementary” method to evaluate the effect of the diet as a whole on health outcomes. Consisting of the *a priori* (dietary indices) and the *a posteriori* (for example factor or cluster analysis) methods, the overall study of the diet provides a more predictive approach towards dietary risk factors for poor health outcomes (Hu, 2002). Originally proposed and used to study the associations of the overall diet with cardiovascular disease, it is only in recent years that dietary patterns are being used to study the effect of the maternal diet during pregnancy on offspring health outcomes.

The majority of research studying maternal dietary patterns during pregnancy reports on birth outcomes as an indicator for fetal development. None of these studies, therefore, accounts for the growth trajectories followed by the fetus during pregnancy. Although birth weight is reflective of fetal growth (Kiserud *et al.*, 2018), Bloomfield *et al.* (2006) indicate that birth weight is a “single, cross-sectional summative measurement” which does not account for possible fetal adaptations and variation in growth during pregnancy. Even a birth weight within normal ranges cannot exclude the possibility of variation in fetal growth during gestation (Bloomfield *et al.*, 2006). The

use of at least two ultrasound scans separated in time during the pregnancy is therefore strongly recommended to evaluate fetal growth and development (Bertino *et al.*, 2018; Salomon *et al.*, 2019). Furthermore, studies reporting on the associations between maternal dietary patterns during pregnancy and offspring growth and development are also sparse, with the studies available reporting mainly on the maternal diet as a risk factor for offspring overweight and obesity.

It is important to note that the majority of the research available on the associations between maternal dietary patterns during pregnancy and early childhood development (including both fetal and offspring growth and development) was conducted in high-income countries. In systematic reviews published Kibret *et al.* (2019) and Raghavan *et al.* (2019), respectively, both author groups note that the majority of research was conducted among healthy Caucasian women with access to health care. Research from resource-restricted settings in low-income countries is thus needed to understand fully the impact of the maternal diet on child development (Raghavan *et al.*, 2019). Additionally, all studies, to the student's knowledge, including *a posteriori* dietary patterns, used either foods or food groups to determine the patterns, with no studies including nutrients as variables to determine the empirical dietary patterns. Moskal *et al.* (2014) advocate the studying of nutrient patterns, as nutrients are universal and therefore allow for comparison between populations. Nutrient patterns, since they reflect a combination of nutrients, also contribute towards the studying of nutritional biomarkers and metabolites in epidemiological research (Moskal *et al.*, 2014). *The rationale for this study is hence, first, by means of dietary pattern analysis, to study the associations between the maternal diet and (a) fetal growth, and (b) the growth and development of the offspring up to the age of 12 months.*

Second, the rationale of this study is to explore further the maternal diet of pregnant South African women. As a means to reduce poverty in the country, the South African government commits itself within the National Development Plan for 2030 to ensure adequate nutrition for pregnant women to enhance early childhood development (National Planning Commission (South Africa), 2012). To ensure health services for all pregnant women, the South African government published the updated Guidelines for Maternity Care in 2015 to guide pregnancy-related health care services in primary health care centres (National Department of Health (South Africa), 2015). Although comprehensive with regard to antenatal care, this guideline is limited in dietary guidelines to ensure an optimal diet during pregnancy. Nutrition support, though promoted by this guideline, is the daily supplementation of ferrous sulphate (200mg per day), folic acid (5mg per day) and calcium (1000mg per day) (National Department of Health (South Africa), 2015). Studies reporting on the nutritional status of pregnant women in South Africa are, however, sparse (Hall *et al.*, 2019; Symington *et al.*, 2018), with only four studies (Cormick *et al.*, 2018; Fahey *et al.*, 2019; Krige *et al.*, 2018; Wrottesley *et al.*, 2017) published during the past decade. Although,

based on these studies, it seems that pregnant South African women consume a diet within the acceptable macronutrient ranges (Cormick *et al.*, 2018; Fahey *et al.*, 2019; Krige *et al.*, 2018), none of the research groups explored the quality of the diet followed. Both Cormick *et al.* (2018) and Krige *et al.* (2018), however, report that the maternal diet is deficient in key micronutrients. With South Africa undergoing a rapid nutrition transition (Vorster *et al.*, 2011) which contributes towards the burden of malnutrition within the country (National Department of Health *et al.*, 2017), it is worthwhile to explore further the maternal diet and accordingly investigate possible associations of the maternal diet with fetal and offspring growth and development. This is likely to shed light on whether enough is being done to ensure optimal nutrition among pregnant women, and hence, indirectly, child growth and development. It is envisaged that the results of this study will contribute towards the knowledge base informing nutrition care for pregnant women in South Africa.

1.3 Aim and objectives

The aim of this study is to assess the associations of maternal dietary patterns during pregnancy with fetal and infant growth and development up to the age of twelve months in Johannesburg, South Africa.

The following objectives have been set to reach this aim:

1. Describe and assess the maternal diet of urban South African women during pregnancy by:
 - a) determining maternal *a priori* and *a posteriori* dietary patterns during pregnancy (<18 weeks' gestational age);
 - b) determining the associations between maternal *a posteriori* and *a priori* dietary patterns;
 - c) determining associations of maternal and household characteristics (including but not limited to age, education level, employment, marital status, maternal weight, food insufficiency and insecurity, and maternal depression and fatigue) with *a priori* and *a posteriori* dietary patterns.
2. Assess early childhood development in terms of:
 - a) fetal growth, using fetal ultrasonography (measurements including, but not limited to, biparietal diameter, head circumference, abdominal circumference, and femur length) at <18 weeks', 22 weeks' and 38 weeks' gestation;
 - b) infant growth using anthropometric measurements (including weight, length, mid-upper arm circumference and head circumference) at birth, 6 months and 12 months postpartum; as well as

- c) psychomotor, language and social-emotional development (using the Protocol for Child Monitoring–Infant/ Toddler version) at 6 months and 12 months postpartum; and to
3. Determine the associations between maternal dietary patterns during pregnancy and (a) ultra-sound derived fetal growth, and (b) infant growth and development up to the age of 12 months.

1.4 Overview of the NuPED study

This study is embedded within the NuPED study which was conducted in Johannesburg, South Africa, between March 2016 and June 2019. The NuPED study consists of both a prenatal and a postnatal phase. The protocol of the NuPED study was published by Symington *et al.* (2018) (addendum 1).

In brief, 250 pregnant women were recruited from selected antenatal care facilities within Johannesburg during the pregnancy phase of the study. Women were regarded as eligible for inclusion if they were between the ages of 18 and 39 years, at less than 18 weeks' gestation with a singleton pregnancy, and able to communicate effectively in the local languages (English, Afrikaans, Sotho, Zulu or Xhosa). Eligible women also had to have been born either in South Africa or a neighbouring country (Lesotho, Swaziland, Zimbabwe, Botswana or Namibia). If born in a neighbouring country, the women had to have been residing in South Africa for at least 12 months. Women were excluded if they reported the use of illicit drugs (self-reported) and/or if they smoked (currently or during the past 12 months). The diagnosis of non-communicable disease (hypertension, hypercholesterolaemia, diabetes and renal disease), infectious disease (tuberculosis or hepatitis), or a serious illness (such as lupus, cancer or psychosis) were also considered as exclusion criteria. Women with human immunodeficiency virus (HIV) infection were, however, included in the study to ensure a better representation of the general South African population. Women who complied with the inclusion and exclusion criteria were followed up at Rahima Moose Mother and Child Hospital (RMMCH) for antenatal care, and ultimately, to give birth. Data collection took place during early (<18 weeks' gestation), mid- ($\pm$ 22 weeks' gestation) and late pregnancy ($\pm$ 36 weeks' gestation), as well as at birth.

For the NuPED post-natal phase, infants were enrolled at birth and followed up to the age of 12 months. Recruitment occurred during the pregnancy phase of the study with all enrolled mothers being informed about the continuing leg of the research project at initial recruitment, and again towards the end of their pregnancy. Provided that the mother gave consent for the infant to be included in the post-natal phase, infants were followed up at the Empilweni Services and

Research Unit situated at RMMCH. Data collection during the postnatal phase of the study took place at six weeks, and six and 12 months postpartum.

Ethical approval for both phases was obtained from the Health Research Ethics Committee at the North-West University (NWU) (NWU-00186-15-A1; NWU-00049-16-A1) (Addendum 2), and the University of Witwatersrand (M161045; M161045) (Addendum 3). Permission to perform the research at the relevant clinical setting was also obtained from the Gauteng Health Department (Addendum 4), the City of Johannesburg District Research Committee (Addendum 5), and the Clinical Manager and Head of Department for Obstetrics and Gynaecology at RMMCH, respectively (Addendum 6 and 7). All pregnant women enrolled to the study provided informed consent before any data collection took place (Addendum 8). Consent was again obtained from the mothers before any postnatal data was collected (Addendum 9).

1.5 Research team and contributions

The members of the research team, as well as their contributions to this PhD study, are indicated in table 1.1.

Table 1-1: Research team for the PhD study

Affiliation	Name <i>(Qualification and professional registration)</i>	Role	Relevant expertise and role
North-West University (NWU)	Prof. Marius Smuts (PhD Biochemistry)	Principal Investigator (NUPED Pregnancy and Post-natal studies) Promoter	<i>Expertise:</i> Essential fatty acids and micronutrient nutrition; nutrition during pregnancy and infancy; community-based clinical trials. <i>Role:</i> Overall management of the study, including ethics application and monitoring, funding and resources, and overseeing data collection and analysis. Study supervision of PhD student.

Table 1-1: Research team for the PhD study (continued)

Affiliation	Name <i>(Qualification and professional registration)</i>	Role	Relevant expertise and role
NWU & ETH Zurich	Prof. Jeannine Baumgartner <i>(PhD in Nutrition)</i>	Co-principal investigator (NUPED Pregnancy and Post-natal studies) Co-promoter	<i>Expertise:</i> Essential fatty acids and micronutrient nutrition; Role of essential fatty acid and iron in neurodevelopment and growth; community-based clinical trials. <i>Role:</i> Overall management of the study, including ethics application and monitoring, funding and resources, and overseeing data collection and analysis. Study supervision of PhD student.
NWU & South African Medical Research Council	Prof. Mieke Faber (PhD)	Investigator Co-promoter	<i>Expertise:</i> Dietary data collection and analysis. <i>Role:</i> Providing guidance regarding the capturing and analysis of dietary data obtained for the NuPED pregnancy and post-natal studies. Provide PhD student with guidance on interpreting dietary data for the purpose of the aim and objectives of this study.

Table 1-1: Research team for the PhD study (continued)

Affiliation	Name <i>(Qualification and professional registration)</i>	Role	Relevant expertise and role
NWU	Dr Linda Malan (PhD Nutrition)	Co-principal investigator (NUPED Post-natal study)	<i>Expertise:</i> Essential fatty acids and micronutrient nutrition; role of essential fatty acids and iron in immune development and functioning; community-based clinical trials; laboratory specialist. <i>Role:</i> Overall management of the study, including ethics application and monitoring, funding and resources, and overseeing data collection and analysis.
NWU	Prof. Suria Ellis (PhD Statistics)	Statistician	<i>Expertise:</i> Statistics and data analysis. <i>Role:</i> Assist PhD with statistical analysis and interpretation of results for manuscript 2 (chapter 4).
NWU	Dr Marike Cockeran (PhD Statistics)	Statistician	<i>Expertise:</i> Experience in statistical analysis for nutritional studies. <i>Role:</i> Assist PhD student with statistical analysis and interpretation of results for manuscript 1 (chapter 3).

Table 1-1: Research team for the PhD study (continued)

Affiliation	Name (Qualification and professional registration)	Role	Relevant expertise and role
NWU	Mrs. Cornelia Conradie (M.Sc. Dietetics)	PhD Student	<i>Expertise:</i> Registered dietitian with work experience in the fields of antenatal care and paediatrics; lectures in dietetics modules covering antenatal care (pre-graduate level) and paediatrics (pre- and post-graduate level). <i>Role:</i> Protocol development for this PhD sub-study embedded within the NuPED study; capturing and cleaning of the dietary data; assistance with quality control of the psychomotor development data; statistical analysis (in consultation with Dr M Cockeran and Prof. S Ellis); writing of thesis for the fulfilment of PhD in Nutrition; lead author on all manuscripts.

1.6 Thesis outline

This thesis is presented in article format and is divided into six chapters. The three articles (chapters 3 to 5) are presented according to the format and referencing style of the respective journals' guidelines as specified at the start of each relevant chapter.

Following this introductory chapter, **chapter 2** provides an overview, based on current literature, of the relationship between the maternal diet during pregnancy and early childhood development. Themes covered include the importance of an optimal diet during pregnancy for offspring growth and development, a brief overview of prenatal and postnatal (up to the age of 12 months) growth and development, and the associations between the maternal dietary patterns during pregnancy and early childhood development. To better understand dietary patterns, an overview of this method in assessing dietary intake is given. Lastly, a short overview of the maternal diet in South Africa is given, as well as the key indicators for child development in South Africa.

Chapter 3 presents an article entitled “*A priori and a posteriori dietary patterns among pregnant women in Johannesburg, South Africa: the NuPED study*”. It provides an in-depth description of the maternal dietary patterns during pregnancy and addresses the investigations indicated under objective 1 of this thesis. This article has been published in the peer-reviewed open-access journal *Nutrients* (doi: 10.3390/nu1302565). The published manuscript is provided in addendum 10.

In **Chapter 4** the article “*Maternal nutrient patterns are associated with fetal head circumference and femur length*” is presented. This article describes the associations between maternal dietary patterns during pregnancy and ultrasound-derived fetal development (objective 2a and 3a). It was prepared for submission in the peer-reviewed open-access journal *Maternal and Child Nutrition*.

Chapter 5 is prepared in manuscript format and reports on the associations of maternal dietary patterns during pregnancy and offspring growth and development (objective 2b and c, and 3b). The manuscript is entitled “*Associations between maternal nutrient patterns during pregnancy and offspring growth and development – the NuPED study*” and was prepared according to the author guidelines of the *Journal of Development Origins of Health and Disease*.

Lastly, **Chapter 6** provides a summary of the main findings, a conclusion to the findings, strengths and limitations of the study, as well as recommendations for future research.

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CHAPTER 2 - LITERATURE REVIEW

2.1 Introduction

Optimal development during early childhood is critically important as the trajectories for later health and well-being are established (Britto & Pérez-Escamilla, 2013). The period from conception up to the age of two years, in particular, is regarded as a very sensitive period of development as this is characterised by an enormous amount of change and a high degree of brain plasticity (Black *et al.*, 2017; Britto *et al.*, 2017). The 2020 Global Nutrition Report, however, highlights poor diets during pregnancy and early childhood as the cause of malnutrition during early life, which manifests as compromised growth and development (Development Initiatives, 2020).

In understanding the relationship between the diet during pregnancy and child development, this literature review firstly explores the importance of the maternal diet for optimal early childhood development. Secondly, early childhood development is briefly discussed in terms of prenatal and postnatal development, factors influencing growth and development, as well as methods to monitor growth and development from conception up to the age of 12 months. With dietary patterns regarded as a prominent method in assessing the overall diet, a description of the methodologies used to determine dietary patterns is provided. This review also provides an appraisal of the literature on the associations between maternal dietary patterns during pregnancy and early childhood development. Finally, a brief overview of studies reporting on the maternal diet among South African women is presented, as well as the key indicators for early childhood development in South Africa.

2.2 Maternal nutrition for early childhood development

2.2.1 The Barker and Developmental Origins of Health and Disease hypotheses

Pregnancy is a unique period in life during which the health of the next generation can be influenced (Cetin & Laoreti, 2015). Although the effects of early life events were already noticed and studied during the 1800s, David J.P. Barker and colleagues were the first in the late 1980s to conduct extensive and multiple studies to further understand how such events contribute towards future health outcomes (Barker & Osmond, 1986; Gluckman *et al.*, 2010). During the early 1990s, Hales and Barker (1992) proposed the “thrifty phenotype type” hypothesis suggesting that a nutritionally deprived fetus develops insulin resistance to survive up to birth - resulting in an increased risk of later disease as the nutritional environment is enriched.

Although this model, together with an increased interest and research within this field, evolved to become the Developmental Origins of Health and Disease approach, the Hales-Barker model had its limitations and was later even alleged to be inadequate (Gluckman *et al.*, 2010). Bateson *et al.* (2004), during the early 2000s, reviewed the ultimate cause of developmental outcomes and recommended a new evolutionary model. According to this model the “embryo, fetus or infant draws information from its environment and adjusts its developmental trajectories accordingly” - but, in doing so, brings about probable longer-term consequences (Gluckman *et al.*, 2010)‘.

It is hence thought that cues during early development induce certain growth patterns to prepare the fetus for the environment in which it is likely to live (Bateson *et al.*, 2004). The *maternal nutritional status*, in particular undernutrition, is recognised as affecting the morphology and physiology of the human fetus, hereby altering the trajectory of growth and development (Bateson *et al.*, 2004). Although the Developmental Origins of Health and Disease approach entails the long-term outcomes of the early life environment, further exploring if and how *maternal nutrition during pregnancy, in particular dietary patterns*, influences the growth and development trajectories during early life can be valuable for a deeper understanding of future health outcomes.

2.2.2 The nurturing care concept

Early childhood development is defined as a “maturational and interactive process resulting in an ordered progression of perceptual-motor, cognitive, language, social-emotional and self-regulation skills” (Black *et al.*, 2017). A child will reach its developmental potential once competencies for behavioural, social-emotional, academic and economic accomplishments are acquired (Black *et al.*, 2017).

The attainment of these skills is based upon foundational capacities which are instituted between preconception and early childhood. *Maternal nutrition during pregnancy* is, according to the Life-Course Conceptual Framework for early childhood development (**figure 2-1**), one of the foundational capacities upon which the acquisition of skills from childhood, through to adolescence and into adulthood, are built (Black *et al.*, 2017).

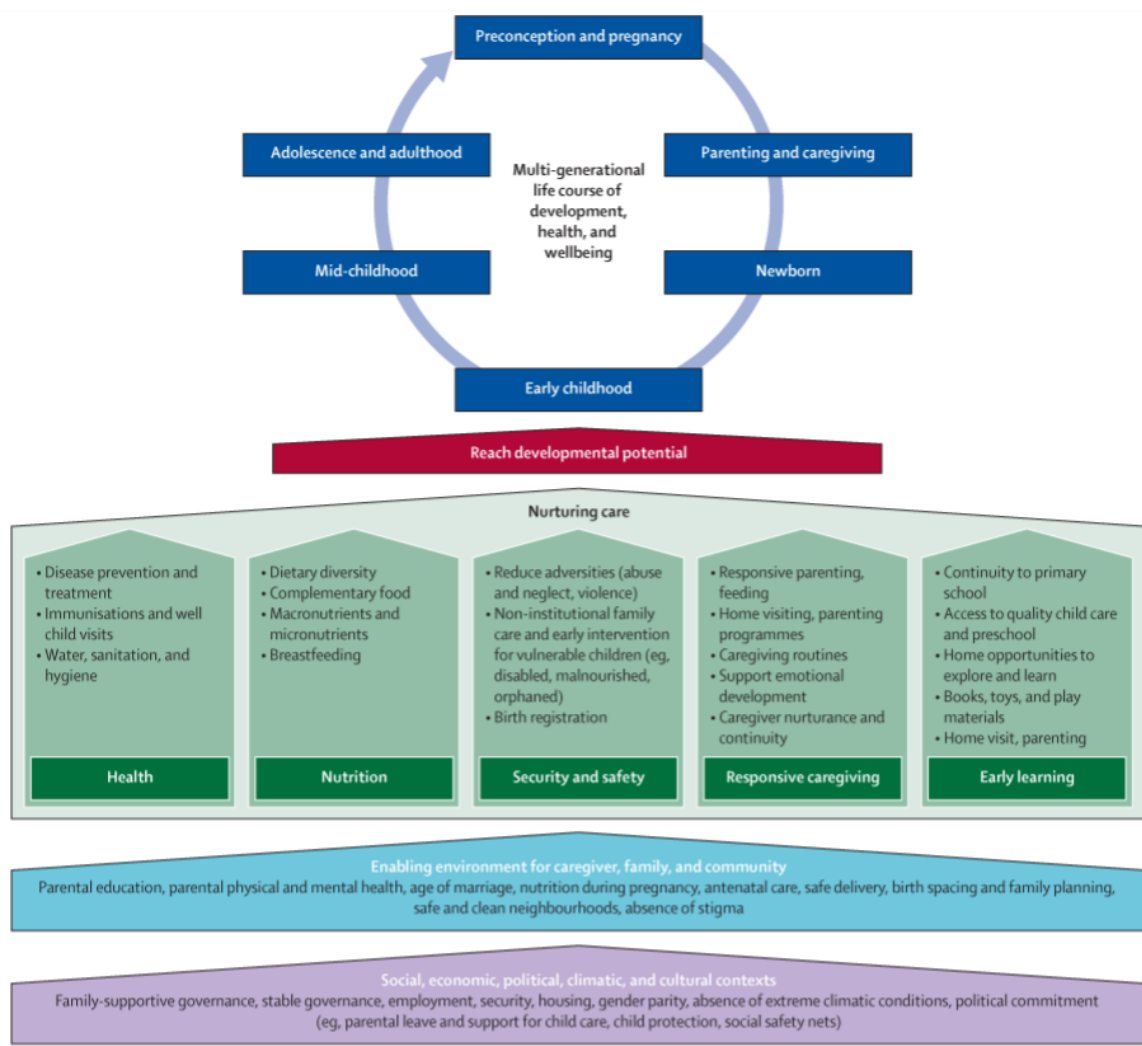


Figure 2-1: Life-Course Conceptual Framework for Early Childhood Development

[Source: Black *et al.* (2017)]

The Life-Course Conceptual Framework for early childhood development forms part of the nurturing care concept – a concept promoted for its ability to support a child in reaching its full developmental potential (Black *et al.*, 2017). This concept emanated from reviews by Walker *et al.* (2007), Walker *et al.* (2011) and Britto *et al.* (2017) (published in the last three *Lancet* Series on early childhood development), which identified the biological and psychological factors, ranging from conception to childhood, that influence child development. These factors can broadly be grouped according to the following five domains: health, nutrition, security and safety, responsive caregiving and early learning (indicated in **figure 2-1**). The 2017 *Lancet* series on early childhood development was among the first to emphasise that these interacting domains are all necessary components for nurturing care.

Nurturing care is characterised as a “stable home environment that is sensitive to children’s health and nutritional needs, responsive, emotionally supportive and developmentally stimulating and appropriate, with opportunities for play and exploration and protection from adversities” (Black *et al.*, 2017). UNICEF, the World Bank Group and the WHO published a Nurturing Care Framework in 2018 which serves as a roadmap for action, providing strategic actions to increase child survival and ensuring conditions in which children can thrive (WHO *et al.*, 2018). Nurturing care is envisaged to transform health and human potential in that it is likely to mediate the development of key brain areas - having lifelong benefits for the child in terms of “increased ability to learn, greater achievement in school and later life, citizenship, involvement in community activities and overall life quality” (Britto *et al.*, 2017; WHO *et al.*, 2018).

2.2.3 Optimal nutrition for positive pregnancy outcomes

Maternal health at the time of conception is likely to determine the success of the pregnancy and the health of the child (Stephenson *et al.*, 2018). Maternal nutritional status, in particular, is an important determinant of embryonic and fetal growth, especially during the time of preimplantation and placental development (Gardiner *et al.*, 2008). With most organs developing between three and seven weeks after the last menstrual period, the period around conception (two to three months before and after conception) is hence regarded as a critical time for fetal development (Gardiner *et al.*, 2008; Stephenson *et al.*, 2018). In a review by Stephenson *et al.* (2018) on the effect of preconception nutrition and lifestyle factors on later health outcomes, the authors highlight the strong relations between preconception nutritional status and maternal and offspring outcomes. By appraising literature, Stephenson *et al.* (2018) indicate that the improvement of the maternal diet during pregnancy has the effect of only a modest reduction in gestational weight gain, with no improvement on maternal and newborn health outcomes. Conversely, healthy dietary patterns up to three years before conception are associated with a decrease in pregnancy complications and preterm birth. There is thus currently a growing unanimity that every effort should be made to ensure a life-course approach to improve the nutrition of women of child-bearing age to ensure optimal maternal and offspring outcomes (Stephenson *et al.*, 2018). Although further exploring the importance of nutrition before pregnancy is beyond the scope of this thesis, Stephenson *et al.* (2018) indicate, regardless, that every effort should be made during pregnancy to ensure optimal maternal nutrition and to correct any nutrient deficiencies.

Rapid and profound physiological changes occur between conception and birth. This warrants an increase in maternal nutritional requirements during pregnancy to maintain elevated maternal metabolism and to support fetal tissue accretion (Mousa *et al.*, 2019). Fetal growth is dependent

on and largely determined by the maternal nutrient supply and the ability of these nutrients (water, glucose, amino acids, fatty acids, vitamins and minerals) to be transported across the placenta into the fetal circulation (Brett *et al.*, 2014; Moore *et al.*, 2018). Should poor maternal diet and lifestyle choices be made, deficiencies in key macro- and micronutrients can have a considerable influence on pregnancy outcomes and the health of the offspring (Mousa *et al.*, 2019). An intergenerational effect is also likely as nutrient deficiencies are likely to affect growth, neurodevelopment, cognition, and the pulmonary and immune function of the offspring. A poor maternal nutritional status, both before and during pregnancy, can hence contribute towards the offspring not reaching full growth and developmental potential (Oh *et al.*, 2020). Adopting healthy behaviours which include optimal nutrition, recommended micronutrient supplementation, and the avoidance of smoking, alcohol and illicit drugs during pregnancy, is strongly recommended to ensure a positive pregnancy outcome and healthy offspring (Procter & Campbell, 2014).

Discerning maternal dietary requirements for optimal fetal growth and development remains difficult owing to gene interactions and the ethical constraints regarding experimental studies during pregnancy (Lowensohn *et al.*, 2016). Addendum 11 provides an overview of recommendations for optimal nutrition during pregnancy as indicated by the Institute of Medicine of the National Academies (IoM) (Institute of Medicine, 2006; Institute of Medicine & National Research Council, 2009). Although more than a decade old, these recommendations are still widely recognised in recent literature (Lowensohn *et al.*, 2016; Mousa *et al.*, 2019; Oh *et al.*, 2020) and by the WHO (WHO, 2016).

Energy recommendations and gestational weight gain

The maternal diet during pregnancy should provide sufficient energy to meet the mother's usual energy requirements, to support the growth of existing maternal tissue (breast tissue, uterus and maternal adipose tissue), and to support the synthesis of new tissue (the fetus, placenta and amniotic fluid) (Mousa *et al.*, 2019). Energy requirements during the first trimester tend not to vary much from requirements before pregnancy. The requirements, however, increase between the 10th and 30th week of gestation, when the maternal and fetal tissue growth is at its greatest (Mousa *et al.*, 2019). Compared with the requirements before pregnancy, energy needs increase only between ten and twenty-five percent during pregnancy – discrediting the old-age belief of “eating for two” (Lowensohn *et al.*, 2016). Energy requirements are greatly dependent upon physical activity levels, pre-pregnancy body mass index and metabolic rate, and therefore vary during pregnancy, as well as between women. To individualise requirements it is suggested that recommendations made be based upon the estimated energy requirement formula (indicated in addendum 11) (Mousa *et al.*, 2019).

Gestational weight gain is greatly determined by energy intake. An inappropriate energy intake (either overconsumption or an insufficient intake) can contribute to poor pregnancy outcomes (Mousa *et al.*, 2019). Overconsumption is associated with an increased maternal weight gain and an increased risk of such conditions as hypertension, gestational diabetes and macrosomia (birth weight >4000g) (Lowensohn *et al.*, 2016). There is also a risk of excessive weight retention twelve months post-delivery (Procter & Campbell, 2014). Insufficient energy intake is, conversely, associated with a decreased birth weight and hence a LBW infant (Lowensohn *et al.*, 2016; Procter & Campbell, 2014). To ensure optimal maternal and child health outcomes, the WHO recommend that women's weight should be within their normal body mass index range (18.5 – 24.9 kg/m²) before conception, and that weight should be gained throughout pregnancy as indicated by the IoM's guidelines for weight gain during pregnancy (see addendum 11) (Institute of Medicine & National Research Council, 2009; WHO, 2016).

Following a healthy diet for positive pregnancy outcomes

The WHO strongly advocate that pregnant women should follow a healthy diet to ensure the optimal intake of all essential nutrients (WHO, 2016). In the mid-1990s, the Food and Agriculture Organization of the United Nations and the WHO embarked on a series of activities to promote the development of country-specific food-based dietary guidelines. These guidelines, which are to be grounded in sound scientific evidence, aim to provoke healthy eating to prevent chronic illnesses and promote overall health (FAO (Food and Agricultural Organization), 2020). The first set of South African food-based dietary guidelines was published in 2001 (Gibney & Vorster, 2001), with an updated version published in 2013 (Vorster *et al.*, 2013). The South African food-based dietary guidelines are discussed in further detail in section 6.1. In 2018, the WHO published a fact sheet on their webpage summarising what a healthy diet entails (WHO, 2018). Although the precise composition of a healthy diet will vary according to age, gender, physical activity levels and the stage within the life-course, the basic principles for a healthy diet for adults necessitate (WHO, 2018):

- A diet rich in whole grains (unprocessed wheat, brown rice, oats and maize), fruits, vegetables, legumes (e.g. lentils and beans) and nuts;
- The consumption of at least 400 grams of fruits and vegetables per day (this amounts to about five portions per day). Within this recommendation, potatoes and sweet potatoes are not regarded as part of the vegetable group;
- Limiting the intake of free sugars, and hence foods and drinks containing sugar added by the manufacturer, the consumer or the cook. Also, limiting all sugar naturally found in fruit juices, fruit juice concentrates, honey and syrups;

- The restriction of fat intake, and choosing unsaturated fats (found in canola and olive oil, fish, avocado and nuts) rather than saturated fats (found in animal fat, cream, cheese, butter and coconut oil) and trans fatty acids (fried and baked food, convenience foods such as pies, pizza, biscuits, and cookies); and
- Limiting the intake of table salt (including discretionary salt usage and that found in processed foods) to one teaspoon per day.

Micronutrient supplementation during pregnancy

A diet that repeatedly lacks food variety (diversity) or sufficient nutrients, increases the risk of micronutrient deficiencies. Micronutrient deficiency is defined as existing when the diet does not meet the body's nutrient requirements to support optimal health, growth and development. Chronic illness and infections can also contribute towards deficiencies as they impede nutrient absorption (Oh *et al.*, 2020).

Micronutrient deficiencies are common in low- and middle-income countries, especially among women and children (Black *et al.*, 2013). During pregnancy, the risk of micronutrient deficiencies is often increased owing to the higher nutritional requirements (Darnton-Hill & Mkpuru, 2015). The WHO hence recommend that all pregnant women use daily oral iron (30 – 60mg of elemental iron) and folic acid (400 µg) supplementation to improve pregnancy outcomes (WHO, 2016). Iron deficiency is one of the most common causes of anaemia and increases the risk of maternal and perinatal mortality and low birth weight (LBW) infants. A deficiency in folic acid is known to cause impaired fetal development as it contributes to neural tube defects and mental retardation (Oh *et al.*, 2020). The WHO recommendations are based mainly on a Cochrane review published by Pena-Rosas *et al.* (2015). The majority of evidence used to recommend iron supplementation is, however, of low quality. Regardless, with iron deficiency and parasite infections being common in low- and middle-income countries, increased coverage of nutritional interventions to prevent maternal anaemia might help decrease morbidity and mortality. Furthermore, the WHO advocates that the availability of iron and folic acid supplementation through the antenatal care providers might encourage pregnant women to engage more with antenatal care services, and hence contribute towards a better pregnancy outcome (WHO, 2016).

Currently, the WHO is not convinced that the routine supplementation of multi-micronutrients improves maternal and perinatal outcomes and it is hence not recommended. A systematic review and meta-analysis newly published by Oh *et al.* (2020) oppose this recommendation by the WHO. When comparing the efficacy and effectiveness of multi-micronutrient supplementation in addressing adverse birth outcomes with that of iron–folic acid supplementation, multi-

micronutrient supplementation had a greater effect on reducing the risk of LBW, small-for-gestational-age infants and stillbirth. Multi-micronutrient supplementation during pregnancy also improved child outcomes as it is associated with a reduced incidence of diarrhoeal episodes and an increased retinol concentration in the offspring (Oh *et al.*, 2020). This review (based on data from 314 articles representing 72 studies) contributes towards the current discourse on whether multi-micronutrient supplementation or iron–folic supplementation should be recommended to pregnant women. The authors of the review conclude that, although they found multi-micronutrient supplementation to have a better outcome, the multi-micronutrient supplementation should be tailored to specific groups and their nutrient needs (Oh *et al.*, 2020).

In accordance with the WHO, the review by Oh *et al.* (2020) confirms that the supplementation of vitamin B₆ (pyridoxine), C, D or E alone does not improve maternal and perinatal outcomes (WHO, 2016). Context-specific single-nutrient supplementation likely to improve maternal and fetal health, however, include daily calcium supplementation (1500 – 2000mg) to reduce the risk of pre-eclampsia, and vitamin A supplementation to prevent night blindness in areas where vitamin A deficiency is a public health concern (Oh *et al.*, 2020; WHO, 2016).

2.3 Early childhood development: prenatal development

2.3.1 Fetal growth and development

During the gestational period (encompassing the embryonic and fetal periods), the zygote (a single cell) is transformed into a multicellular human being through cell division, cell migration, apoptosis, differentiation, cell growth and cell rearrangement (Moore *et al.*, 2015b). The embryonic period begins in the third week after fertilisation. Although the embryo grows only to a crown–rump length of about 30 millimetres and a weight of about five grams, this phase is regarded as the most critical stage of development as basic development of all organ systems occurs at a rapid pace (Arduini *et al.*, 2018; Moore *et al.*, 2015a; Moore *et al.*, 2018). The fetal period commences at week nine after fertilisation and continues throughout the remainder of the pregnancy. It is characterised by the simultaneous and consecutive development of the tissue and organs formed during the embryonic period, resulting in body growth and differentiation of the organs and systems (Blackburn, 2014; Moore *et al.*, 2015b).

Brain development begins soon after conception as the neural plate, which forms the neural tube and eventually the brain and spinal cord, develops approximately 22 days after fertilisation. At about seven weeks' post-fertilisation, the neurodevelopmental process commences with the formation of neurons and glial cells within the neural tube. These neurons migrate to their place

in the brain from where they grow axons and dendrites to form synapses with other neurons (Prado & Dewey, 2014). The brain's functional capacity increases as the neurons and glial cells become more complex and interconnected. This ensures that some fundamental behavioural functions are already present at birth (for example, hearing, touch, taste, pain sensation and, to a lesser extent, vision), with the neural circuits for more intricate behaviours being established. Recognising the importance of prenatal brain development is crucial as preterm development provides the basis for later neurodevelopment (Georgieff *et al.*, 2018).

Although neurogenesis continues throughout the life course, the most rapid brain development occurs between 34 weeks' post-fertilisation and the age of two years (**figure 2-2**) (Nyaradi *et al.*, 2013; Thompson & Nelson, 2001). This rapid growth causes the brain to be vulnerable to biological and psychological factors (Bhutta *et al.*, 2017). Nutrition is regarded as one of the important and controllable environmental factors that influence early brain development (Georgieff *et al.*, 2018). Georgieff *et al.* (2018) and Prado and Dewey (2014) indicate that protein, glucose, long-chain polyunsaturated fatty acids, iron, zinc, copper, iodine, folate, vitamin B₁₂ and choline, in particular, influence key neurodevelopmental processes (this being neuron proliferation; axon and dendrite growth; synapse formation, pruning and function; myelination; and neuron apoptosis). The extent to which deficiencies of these nutrients influence brain development is, however, greatly dependent upon the severity of the deficiency, its timing, and the possibility of recovery. Recent research has indicated that the effect of postnatal nutrition on brain development is greatly reliant upon the fetal nutritional status (Georgieff *et al.*, 2018).

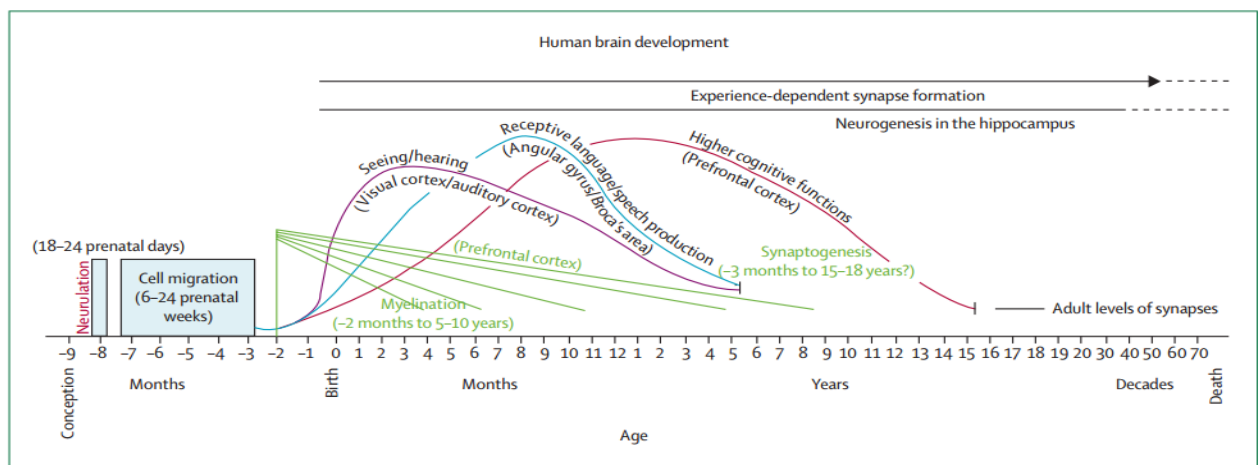


Figure 2-2: Human brain development

[Source: Thompson & Nelson (2001)]

2.3.2 Birth outcome: low-birth weight infants

By the end of the fetal period (40 weeks after the last menstrual period or 38 weeks after fertilisation), the infant typically has a birth length of about 50 cm and a weight of 3400 grams (Blackburn, 2014; Moore *et al.*, 2015b; Villar *et al.*, 2014). An infant born with a weight of less than 2500 grams, irrespective of gestational age, is regarded as a LBW infant (Blencowe *et al.*, 2019). Birth weight is determined by two processes, namely (1) the duration of gestation and (2) the rate of fetal growth (Kramer & Victora, 2001). An infant can thus have a birth weight of less than 2500 grams either as a result of being born too early (preterm birth), or being born too small for its gestational age [fetal growth restriction (FGR)], or a combination of being born too early and too small (Blencowe *et al.*, 2019; Katz *et al.*, 2013; Khan *et al.*, 2018; WHO (World Health Organization), 1977).

Birth weight serves as a prognostic factor for neonatal morbidity and mortality, with a weight at the lower threshold indicating an increased risk (Kramer & Victora, 2001; Malin *et al.*, 2014; UNICEF & WHO, 2019). More than 80% of neonatal deaths are of infants born with a LBW; two-thirds of deaths are due to prematurity and one-third due to FGR (Blencowe *et al.*, 2019). Other than the increased risk of mortality, infants born with a LBW also have an increased risk of stunting and neurodevelopmental impairment during childhood, and non-communicable diseases during adulthood (Blencowe *et al.*, 2019).

Target three of the World Health Assembly's global nutrition targets aims to reduce the prevalence of LBW infants by 30% by 2025 (compared with the prevalence in 2012) (WHO, 2014). A recent systematic analysis of global estimates indicates that the global prevalence of LBW was 14.6% in 2015, amounting to an estimated 20.5 million – or one in every seven – live births. Most of these neonates (91%) reside in low- and middle-income countries, and as many as a quarter of this number in sub-Saharan Africa (Blencowe *et al.*, 2019). Estimates indicate that in South Africa, compared with less than 10% in high-income countries, about 14% of all infants are born with a LBW (Blencowe *et al.*, 2019; UNICEF & WHO, 2019). The global average annual reduction rate was 1.23% between 2012 and 2015, much lower than the 2.74% required to meet the 2025 global target (Blencowe *et al.*, 2019). Owing to this significant shortfall in progress towards meeting this ambitious target, a recent discussion paper by the WHO recommends extending the 2025 LBW target to 2030. Regardless, should current trends continue, the 2025 World Health Assembly's nutrition target for LBW will not be met (UNICEF & WHO, 2019). Every effort should thus be made to enhance current actions addressing the underlying causes of LBW (Blencowe *et al.*, 2019).

To understand LBW, it is important to differentiate between preterm birth and FGR (Kramer & Victora, 2001).

Preterm birth

The WHO defines preterm birth as an infant born before 37 weeks' completed gestation or fewer than 259 days since the first day of the last menstrual period (WHO, 1977). Infants born preterm can further be subdivided according to their gestational age: about 5% of such infants are born extremely prematurely (born at <28 weeks' completed gestation), 15% as severely/very premature (between 28 and 31 weeks' completed gestation), 20% as moderately premature (between 32 and 33 weeks), and 60 – 70% at near-/ late-term (between 34 and 37 weeks' completed gestation) (Goldenberg *et al.*, 2008; WHO, 1977). An infant is regarded as "term" when born after 37 weeks' completed gestation, but before 42 completed weeks (WHO, 1977).

The risk of morbidity and mortality is higher the earlier during gestation an infant is born, with the risk decreasing as the gestational age increases (Chawanpaiboon *et al.*, 2019; Institute of Medicine, 2007). The majority of preterm infants nowadays survive (even infants born severely prematurely) owing to advancements in medical care (Saigal & Doyle, 2008). These infants, nevertheless, face a lifetime of disability as the immature organ system of a preterm infant is not yet able to support life in the extrauterine environment (Institute of Medicine, 2007). The brain and lungs are particularly susceptible to preterm birth and hence an infant born prematurely is at an increased risk of both short- and long-term health problems (Saigal & Doyle, 2008). Short-term health problems include, amongst others, respiratory distress syndrome, bronchopulmonary dysplasia and chronic lung disease, necrotising enterocolitis and feeding intolerance, pneumonia, sepsis, anaemia, congenital or prenatally acquired hearing disorders, and retinopathy of prematurity. Chronic lung disease of prematurity, long-term cardiovascular ill health, visual and hearing impairment, and non-communicable disease are long-term health outcomes of prematurity. Moderate to severe cognitive delay, learning impairments, reduced academic achievement, motor impairment and cerebral palsy are neurodevelopmental disabilities also commonly seen in children born prematurely (Blencowe *et al.*, 2013; Institute of Medicine, 2007). The cut-off point for an infant to be regarded as preterm is, however, thought to be a subjective one, as infants born early term (between 37 and 38 weeks' gestation) also have, compared with full-term infants, a high risk of adverse health outcomes (Blencowe *et al.*, 2013; Chawanpaiboon *et al.*, 2019).

Fetal growth restriction

Fetal growth restriction occurs when the rate of fetal growth decreases to such an extent that it prevents the infant from attaining its growth potential (Brodsky & Christou, 2004). These infants are typically small-for-gestational age and have a birth weight of less than the 10th percentile for gestational age (gender- and population-specific) (Khan *et al.*, 2018). Some infants with FGR experience only mild growth restriction and have a birth weight regarded as appropriate-for-gestational age (birth weight between the 10th and 90th percentile) (Brodsky & Christou, 2004; Khan *et al.*, 2018). In such a case the rate of growth has decreased, causing fetal biometry to shift from a higher to a significantly lower centile without moving below the threshold regarded for normal growth (Bertino *et al.*, 2018).

Not all infants born small, however, have experienced FGR. About 50 – 70% of small-for-gestational age infants are constitutionally small with fetal growth being appropriate for ethnicity and maternal size (Arduini *et al.*, 2018). Should a fetus thus be identified as small-for-gestational age at a prenatal ultrasound, every effort should be made to distinguish between growth restriction and a constitutionally small infant (Bertino *et al.*, 2018). According to the most recent guidelines published by the International Society of Ultrasound in Obstetrics and Gynaecology (Lees *et al.*, 2020), FGR is diagnosed when the AC and/or EFW is below the 3rd percentile for gestational age. Should the biometry be above the 3rd but below the 10th percentile, additional parameters (fetal growth velocity, customised growth charts, Doppler velocimetry and/or biomarkers) must be considered to differentiate between small-for-gestational age and FGR. When considering fetal growth velocity, a drop of more than 50 percent (or two quartiles) in fetal AC and/or EFW centiles between two consecutive ultrasound scans is indicative of FGR. Fetal growth restriction can, furthermore, according to the international Delphi consensus, be classified as being either of early or late onset, based on fetal size, Doppler velocimetry and biomarkers (Lees *et al.*, 2020). The greatest difference between constitutionally small infants and infants with FGR is that infants with FGR are at an increased risk of adverse perinatal and long-term outcomes (Lees *et al.*, 2020).

The hostile environment to which the growth-restricted fetus is exposed, often due to limited maternal-fetal gas and metabolic exchanges, progressively leads to fetal hypoxia. Should the fetal adaptations – including metabolic, hormonal and vascular changes; alterations with regard to cell, tissue and organ growth; alterations in gene expression and molecular pathways; a decrease in cell number; and/ or an imbalance in cell type (Brodsky & Christou, 2004) – to these pathological conditions fail, fetal acidaemia, multi-organ damage, and ultimately, death, is probable. Even if the condition does not become fatal, the epigenetic mechanisms influencing the adaptations contribute to both short- and long-term adverse health effects (Bertino *et al.*, 2018; Brodsky & Christou, 2004; Khan *et al.*, 2018).

The acute neonatal consequences for infants born with FGR include, among others, metabolic (glucose and fatty acid metabolism) and haematological disturbances, disrupted thermoregulation, feeding difficulties, feed intolerance and late-onset sepsis (Brodsky & Christou, 2004; Sharma *et al.*, 2016). The lasting sequelae of FGR include deficits in growth and neurodevelopment (Kramer & Victora, 2001). Most of these infants experience a period of an increased growth velocity together with catch-up growth by the age of two to three years. About 10% of these infants might never reach their optimal growth potential as they often struggle with feeding difficulties – this together with already deficient nutritional stores (Brodsky & Christou, 2004; Levine *et al.*, 2015). Although more significant the earlier the onset or the more severe the growth restriction (Brodsky & Christou, 2004), infants with FGR have an increased risk of delays in motor, cognitive and language development, behavioural problems and poor academic performance (Levine *et al.*, 2015; Sharma *et al.*, 2016). Adults who were born with FGR are also more prone to developing metabolic syndrome (including type 2 diabetes mellitus, hypertension, dyslipidaemia and insulin resistance), cardiovascular diseases, polycystic ovary syndrome and renal insufficiency (Longo *et al.*, 2013).

Determinants of low birth weight in developing countries

The aetiology of LBW is complex and multifactorial as normal fetal growth is an intricate process influenced by various pathological processes (Bertino *et al.*, 2018). A publication by Kramer (1987) is one of the earliest, and possibly most detailed, to identify probable determinants of LBW. Although a rather old publication, it is still viewed as relevant as it was recently named in the UNICEF-WHO Low Birthweight Estimates, Levels and Trends 2000–2015 report (UNICEF & WHO, 2019) to refer the reader to the causes of LBW.

As LBW includes both preterm birth and FGR, it is difficult to separate the determinants (Khan *et al.*, 2018). These factors, however, differ qualitatively and quantitatively: qualitatively in terms of the different ecological determinants for preterm birth and FGR, and quantitatively in terms of the relative risk of the determinants which are the same for preterm birth and FGR (Kramer & Victora, 2001). Recent publications report mainly on the relative risk/ odds ratio of the determinants of LBW as a whole. Johnson *et al.* (2016) report that smoking during pregnancy (both active and passive smoking), substance use, low maternal body mass index and a short interpregnancy interval (< 5 months), increase the risk of LBW among the Welsh population (United Kingdom) (based on data published by 73 studies reporting on the causes of LBW in the Welsh population). Interestingly, an advanced maternal age (35 to 49 years), lack of antenatal medical care, primiparity, illiteracy, low socioeconomic status and delayed conception were reported by Mahumud *et al.* (2017) as carrying the highest risk of LBW in low- and middle-income countries

(based on data from 10 low- and middle-income countries). Regardless, it is well reported in the literature that the determinants of LBW differ between low- and middle-income countries and high-income countries (Brodsky & Christou, 2004; Khan *et al.*, 2018; Kramer, 1987). **Table 2-1** indicates the various determinants of LBW as identified in the literature for low- and middle-income countries.

Table 2-1: Determinant of low-birth-weight in low- and middle-income countries

Determinants of low-birth-weight in low- and middle-income countries	
Maternal factors	
Race/ Ethnicity	Women of black race, compared with other racial groups, have a high risk of preterm birth Asian women tend to be at higher risk of IUGR
Low socioeconomic status	Low educational status and low family income
Young and advanced maternal age	Younger than 16 years and older than 35 years
Short or long inter-pregnancy interval	Less than 6 months' interval, or an interval greater than 120 months
Parity (number of previous pregnancies carried to 20 weeks' gestation and beyond)	None or more than 5
Pregnancy history	Increased risk of preterm birth if previous pregnancy resulted in preterm delivery
Maternal pre-pregnancy weight and height	Body mass index of less than 20 kg/m ² and body weight less than 40kg
Poor maternal nutrition	Low total energy intake and gestational weight gain Low serum levels of iron, folate and zinc increase the risk of preterm birth Moderate to severe maternal anaemia due to iron, folate, vitamin B12 and/ or vitamin A deficiencies)
Toxins	Cigarette smoking (active and passive), excessive alcohol consumption, drug abuse
Strenuous maternal work	Hard physical labour under stressful conditions
Chronic medical illnesses	Hypertension, diabetes mellitus, renal disease, asthma, anaemia, thyroid disease Profound effect with early-onset hypertension and/ or pre-eclampsia
Infections	Malaria, urinary tract infection, rubella, human immunodeficiency virus, herpes virus
Maternal mental health	Psychological and social stress, depression
Multiple gestations	Uterine over-distention is causative of spontaneous preterm birth
Uterine factors	Incompetent cervix and bicornuate uterus
Uteroplacental factors	<i>Abruptio placentae</i> , insufficient uteroplacental perfusion, <i>placenta previa</i>
Poor medical care	A low number and poor quality of antenatal care visits

Table 2-1: Determinant of low-birth-weight in low- and middle-income countries

Determinants of low-birth-weight in low- and middle-income countries	
Fetal factors	
Gender	Male fetuses are at higher risk
Congenital abnormalities and other genetic factors	Chromosomal abnormalities, genetic syndromes, major congenital anomalies, congenital infections, metabolic disorders

Source: Brodsky and Christou (2004), Goldenberg *et al.* (2008), Kramer and Victora (2001), Kramer (1987), Sharma *et al.* (2016)

Even though a low socioeconomic status is identified as a determinant of LBW, the exact mechanism by which it contributes is not clearly understood (Goldenberg *et al.*, 2008). Kramer (1987), after adjusting for other possible causative factors, found no association between socioeconomic status and LBW. It is hence thought that socioeconomic status has an indirect causal effect. Scorgie *et al.* (2015), as part of a qualitative study conducted in a public-sector hospital in Johannesburg, South Africa, published a conceptual framework illustrating the determinants of socioeconomic vulnerability among pregnant women in South Africa. Using in-depth interviews, their study aimed to determine key financial needs experienced by pregnant women, how they prioritise these increased needs, as well as the extent to which their vulnerability is increased should their needs be unmet (Scorgie *et al.*, 2015). An adapted version of the framework by Scorgie *et al.* (2015) is given in **figure 2-3**. The determinants for LBW as listed in table 1 are incorporated within this adapted version to illustrate how socioeconomic vulnerability may contribute towards LBW births among South African pregnant women. Added to the framework of Scorgie and colleagues, is an “increased risk of poor maternal mental health” as part of “women’s experience of pregnancy and postpartum” (under “impact of socioeconomic vulnerability”) as the literature indicates socioeconomic disadvantage to be strongly associated with non-psychotic perinatal mental disorders (Fisher *et al.*, 2012).

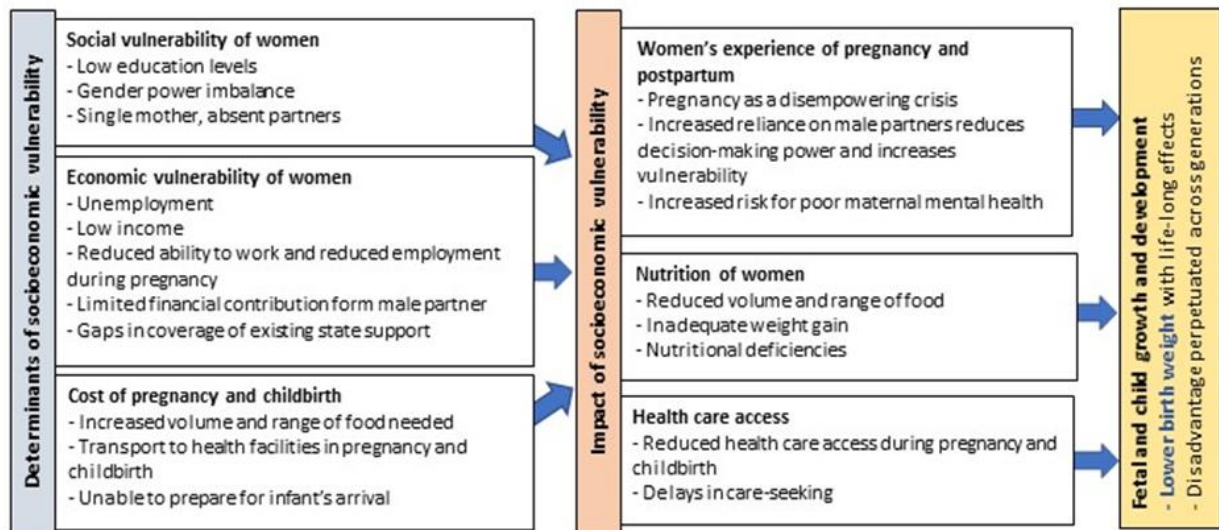


Figure 2-3: Socioeconomic vulnerability as a determinant of low-birthweight births among South African pregnant women

[adapted from Scorgie *et al.* (2015)]

Maternal mental health disorders are thought to increase systemic inflammation related to high levels of psychological and social stress, increasing the risk particularly of preterm birth (Goldenberg *et al.*, 2008). Depression is thought to increase smoking and alcohol and drug usage (Goldenberg *et al.*, 2008). Cigarette smoke contains more than 300 chemicals. Although the precise mechanism by which cigarette smoke influences the fetus is unknown, it is known that both nicotine and carbon monoxide are vasoconstrictors. These two compounds thus reduce the uterine blood flow and hence limit fetal oxygenation and growth (Brodsky & Christou, 2004; Goldenberg *et al.*, 2008). So also, alcohol crosses the placenta and results in concentrations nearly equal to that of the mother. The sensitivity of the fetus to alcohol and thus the extent of the damage is dependent upon the timing of the exposure. A study conducted by Nykjaer *et al.* (2014) in the United Kingdom reported that consuming even less than two units of alcohol per week was associated with a lower birth weight and preterm birth. The fetus was found to be most sensitive towards the effect of alcohol during the first trimester (Nykjaer *et al.*, 2014).

2.3.3 Birth outcome: macrosomia

Although there is as yet no universally accepted definition for macrosomia, it is generally defined as a birth weight of more than 4000g (regardless of the gestational age), or as a large-for-gestational age infant with a birth weight of more than the 90th percentile for age (Akanmode &

Mahdy 2021; Beta *et al.*, 2019; Lewandowska, 2021). Maternal and neonatal complications associated with macrosomia are well reported in the literature. These include, among other complications, emergency Caesarean section, anal sphincter injury and postpartum haemorrhage for the mother, and shoulder dystocia and birth asphyxia for the infant (Beta *et al.*, 2019). Beta *et al.* (2019) report the risk of these complications to be more substantial for the infant than for the mother. In the scope of the Developmental Origins for Health and Disease approach, excessive birth weight is also reported to increase the risk of the development of non-communicable diseases later in life (Lewandowska, 2021).

Possible causative factors for macrosomia included maternal age, maternal height, pre-pregnancy weight and body mass index, gestational weight gain during pregnancy, gestational diabetes, parity, fetal sex, as well as a history of prior macrosomia and gestational diabetes. (Lewandowska, 2021). Using newer prediction indicators, Lewandowska (2021) however, indicates that an excessive pre-pregnancy weight/ body mass index and excessive gestational weight gain are (compared with 26 other possible features) the greatest predictors of macrosomia in infants. This reiterates the importance of women entering pregnancy with a healthy nutritional status (Procter & Campbell, 2014) and of gaining weight throughout pregnancy as recommended by the IoM's guidelines (addendum 11) (Institute of Medicine & National Research Council, 2009).

2.3.4 Monitoring fetal growth: fetal ultrasonography

Screening for disturbances in fetal growth is one of the core components of antenatal care as growth failure is a cumulative process that often begins *in utero* (De Onis, 2017; Papageorgiou *et al.*, 2018). Although birth weight reflects fetal growth and is an indicator of perinatal morbidity and mortality (Kiserud *et al.*, 2018), birth weight is a “single, cross-sectional summative measurement” taken after an extended period of rapid but non-linear growth (Bloomfield *et al.*, 2006). Birth weight thus does not provide insight into the fetal growth trajectories and fetal adaptations made to a potentially inadequate intrauterine environment (Bloomfield *et al.*, 2006). Even a birth weight within normal ranges does not exclude the possibility of variation in fetal growth during gestation (Bloomfield *et al.*, 2006). Bertino *et al.* (2018) strongly emphasise that a longitudinal sequence of fetal biometric measurements should be used to evaluate fetal growth and development. The International Society of Ultrasound in Obstetrics and Gynecology reiterates this as part of its practice guidelines – indicating that fetal growth should be assessed with at least two ultrasound scans separated in time during the pregnancy (Salomon *et al.*, 2019).

The WHO recommends that all pregnant women receive an ultrasound scan before 24 weeks' gestation to determine gestational age and to detect fetal anomalies and multiple pregnancies

(WHO, 2016). Contradictory to the proposal of multiple ultrasound measurements during pregnancy, the WHO does not recommend an ultrasound screening after 24 weeks' gestation should a scan have been done before 24 weeks. This recommendation is motivated mainly by the lack of evidence indicating whether antenatal ultrasounds have an improved population health outcome in low-resource settings (WHO, 2016).

Biometric measurements most commonly used in obstetrics to determine and evaluate fetal size include crown–rump length, BPD, HC, AC and FL (O'Gorman & Salomon, 2018). **Table 2-2** provides a brief explanation of each ultrasound measure (Papageorgiou *et al.*, 2009). The accuracy of these measurements is dependent upon the operator's skills, the technical characteristics of the ultrasound equipment, maternal body composition and the pathology present (Bertino *et al.*, 2018). These biometric measures are among those used to determine gestational age and EFW (Salomon *et al.*, 2019). Fetal HC and AC are also indicated in literature as serving as proxy measures for brain development (Koshy *et al.*, 2021; Volpe, 2018) and fetal weight (O'Gorman & Salomon, 2018), respectively. Femur length is likewise described as depicting bone development (Chang *et al.*, 2003) and linear growth (Prioreschi *et al.*, 2021). These biometric measures, as well as their interpretation, facilitate communication among the health care team, as well as aiding in the counselling of parents with regard to the expected birth weight, for example, (Kiserud *et al.*, 2017; Salomon *et al.*, 2019).

Table 2-2: Brief overview of fetal biometry measurements

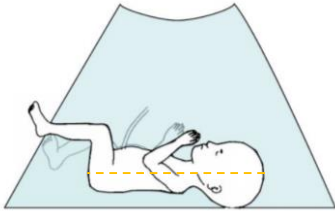
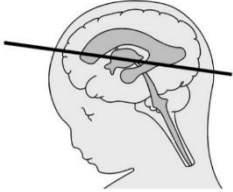
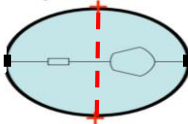
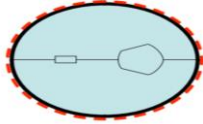
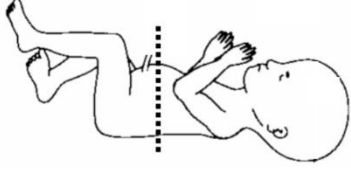
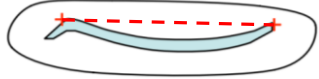
Measurement	Ultrasound examination
Crown–rump length	Fetus must be: - in a neutral position (not flexed or hyperextended), and - horizontal (to ensure a 90° to the angle of insonation). From the midsagittal plane, place the intersection of the calipers on the outer edges of the head and the rump¹. The ultrasound image should fill at least 30% of the monitor screen to ensure an accurate reading. 

Table 2-2: Brief overview of fetal biometry measurements (continued)

Measurement	Ultrasound examination
BPD	The BPD and the HC are determined from the same anatomical view, hence: obtain a cross-sectional view of the fetus's head at the level of the thalami; a symmetrical appearance of both hemispheres should be seen; the continuous midline echo must be centrally positioned, though the cerebellum is not seen; the view should be as close as possible to horizontal to ensure a 90° angle of insonation; the head must be oval and well magnified (at least 30% of the monitor screen should be filled by the image). For the BPD, the intersection of the calipers is to be placed on the outside edges¹ of the bones of the skull. The ellipse calipers should be used to determine the HC, and this should run along the border of the skull.    BPD HC
HC	
AC	The fetus' abdomen should be viewed as from the transverse section which is as close as possible to round. The short segment of the umbilical vein (at its anterior third) should be visible. The stomach bubble should be visible, though not the kidneys and bladder. As with the other measurements, the images should fill at least 30% of the monitor screen. As with HC, the ellipse calipers should be used to determine the AC. The measurement is taken at the external surface of the skin¹.  
FL	The measurements should be taken as close as possible to the horizontal plane, with the angle of insonation at about 90°. The bone closest to the probe must be measured, and the full length of this bone must be visualised. The bone should thus not be obscured by shadows of adjacent bony parts. The image should be magnified to ensure that the cross-section of the femur fills at least 30% of the monitor screen. The interception of the calipers is to be placed on the edges¹ of the femoral bone without including the trochanter in the measurement.  

BPD: biparietal diameter, HC: head circumference, AC: abdominal circumference, FL: femur length

¹ There are different methodologies as to where the interception of the ultrasound caliper should be placed (for example, "outer edge to inner edge", "outer edge to outer edge", or the "leading-edge" technique). It is recommended that the technique be used as indicated by the reference charts (Salomon *et al.*, 2011).

Source: Papageorghiou *et al.* (2009) and Salomon *et al.* (2011); Images from: Papageorghiou *et al.* (2009)

The accurate dating of a pregnancy is an important initial step as this guides the management of the pregnancy – especially when deciding upon the viability of preterm birth, management of an FGR fetus or the induction of a prolonged pregnancy (Butt *et al.*, 2014; O'Gorman & Salomon, 2018). Ideally, all women should receive a pregnancy-dating ultrasound during the first trimester. If not possible, an ultrasound during the second trimester is beneficial (Butt *et al.*, 2014). Crown–rump length is most accurate in determining gestational age during the first trimester once the embryo is visible (between 8 and 14 weeks' gestation) (Butt *et al.*, 2014; O'Gorman & Salomon, 2018). Should the crown–rump length during the first trimester be more than 84cm, HC should be used (O'Gorman & Salomon, 2018). If more than one ultrasound scan is performed during the first trimester, the earliest scan with a crown–rump length of more than 10mm should be used to date the pregnancy (Butt *et al.*, 2014). Head circumference is regarded as accurate in determining gestational age during the second trimester, with the use of multiple parameters (a combination of BPD, HC, AC and FL) recommended for later during the pregnancy (Butt *et al.*, 2014).

Estimated fetal weight is the most accurate method to monitor fetal growth and to determine fetal size (O'Gorman & Salomon, 2018). As for determining the gestational age, there are various formulae available to calculate the EFW (O'Gorman & Salomon, 2018). All formulae include AC because the AC, as mentioned, is a predictor of fetal weight (O'Gorman & Salomon, 2018). Irrespective of various efforts to develop new models for determining fetal weight, the formula (incorporating HC, AC and FL) published by Hadlock in 1985 (Hadlock *et al.*, 1985) remains the most accurate predictor of birth weight, even for fetuses suspected to be either too small or too large for gestational age (Hammami *et al.*, 2018).

The EFW indicator is not without shortcomings, however, as it is greatly operator-dependent and hence compromised by both intra- and inter-observer variability (Salomon *et al.*, 2019). Inaccuracies in estimating the fetal weight are thus common, especially in small-for-gestational-age and large-for-gestational-age fetuses (O'Gorman & Salomon, 2018; Salomon *et al.*, 2019). To limit the degree of error and possible false-positive detection of a fetal growth disorder, the International Society of Ultrasound in Obstetrics and Gynecology recommends ultrasound that scans should be at least three weeks apart, with some scans not used to determine the EFW (Salomon *et al.*, 2019).

Fetal growth can also be assessed using fetal growth charts (discussed below) and interval fetal growth. Interval fetal growth, or growth velocity, can be determined by the difference between two adequately separated biometric measures (for example AC) divided by the difference in gestational age. This can be calculated for any of the biometric measures. As with EFW, it is proposed that biometric measures used for determining interval fetal growth are at least three weeks apart, to account for intra- and inter-observer variability (O'Gorman & Salomon, 2018).

Monitoring fetal growth using fetal growth charts

Until recently, available fetal growth charts were based on data from mainly single populations in high- and upper-income countries (Kiserud *et al.*, 2018). Together with uncertainty with regard to the applicability of these charts to global populations, different cut-off points were used to identify abnormal fetal growth – this leading to diagnostic confusion and difficulty in comparing fetal growth outcomes (Papageorghiou *et al.*, 2014). In 2002, the WHO, after a review of literature on birthweight as a health outcome, was the first to identify the need for updated fetal growth charts based on multinational data. The WHO furthermore motivated this as part of its efforts to address the high rate of perinatal morbidity and mortality in low- and middle-income countries (Kiserud *et al.*, 2018; Kiserud *et al.*, 2017).

In recent years, two research groups have published fetal growth charts based on multinational data. Using a prospective approach similar to that of the WHO Multicenter Growth Reference Study from which the WHO child growth standards (0 – 60 months) were developed (de Onis *et al.*, 2004a), the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) published prescriptive growth standards in 2014 (Papageorghiou *et al.*, 2014) and 2017 (Stirnemann *et al.*, 2017) to complement the WHO child growth standards. In 2017, however, the WHO published its own set of fetal growth charts to accompany the child growth standards (Kiserud *et al.*, 2017). The INTERGROWTH-21st and WHO research groups included 4 321 pregnant women from eight countries (Brazil, Italy, Oman, United Kingdom, United States of America, China, India and Kenya) and 1362 pregnant women from 10 countries (Argentina, Brazil, the Democratic Republic of the Congo, Denmark, Egypt, France, Germany, India, Norway and Thailand). The inclusion and exclusion criteria used were similar in that both studies included singleton pregnant women between the ages of 18 and 35 years (the WHO included women up to the age of 40 years) with body mass index within normal ranges. The research participants also had no history of chronic illness or long-term medication usage, no history of previous pregnancy complications, and had no known environmental or socioeconomic constraints (Kiserud *et al.*, 2017; Papageorghiou *et al.*, 2014).

Although a similar approach was followed by the two research groups, when comparing the fetal growth charts, the 10th percentile of the INTERGROWTH-21st growth standards fall below that of the WHO growth references (Kiserud *et al.*, 2017). With growth standards and references being essentially the same (Cole, 2012), one needs to consider the underlying concepts followed to understand the difference in findings (Kiserud *et al.*, 2018). Whereas the WHO included data from pregnant women who developed relevant clinical conditions during the pregnancy (as this was found to have a limited effect on the overall outcome), the INTERGROWTH-21st group excluded data from these women from their overall data analysis (Kiserud *et al.*, 2018; Kiserud *et al.*, 2017; Papageorghiou *et al.*, 2018). The INTERGROWTH-21st group hence followed the theory that fetal

growth would be similar across various populations should the maternal conditions be optimal (Kiserud *et al.*, 2018). However, the research group from the WHO acknowledge that possible covariates (namely fetal sex, ethnicity, maternal age, height and weight, and parity) influence fetal growth, as their study also aimed to verify possible risk factors for poor birth outcomes (Kiserud *et al.*, 2018; Kiserud *et al.*, 2017).

Kiserud *et al.* (2018) conclude that should population-based references be available, these should be used to evaluate fetal growth. Should this, however, not be available, which is the case for most low- and middle-income countries, charts developed from multinational data should be used. Fetal growth charts published by the WHO and the INTERGROWTH-21st group include, among others, charts for HC, AC, BPD, FL and EFW (Kiserud *et al.*, 2017; Papageorgiou *et al.*, 2014; Stirnemann *et al.*, 2017).

Monitoring of fetal growth in the South African public health care setting

Fetal ultrasonography is regarded as an ordered examination for high-risk pregnancies in the South African public health care setting. According to the document “Guideline for Maternity Care in South Africa” (National Department of Health (South Africa), 2015), ultrasound screening does not form part of the routine services for pregnant women in primary health care clinics and community health care centres – generally the first point of entry for pregnant women into the health care system. Yet both these facilities are equipped to provide antenatal care to women with low- to intermediate-risk pregnancies, with the community health care centres having an obstetric unit where these women can give birth. This guideline document does, however, provide a comprehensive list of risk factors (similar to that indicated in **table 2-1**) authorising a pregnant woman to be referred to hospital for specialised care, which includes ultrasound screening (National Department of Health (South Africa), 2015).

Gestational age is determined at primary health care clinics and community health care centres by methods other than ultrasound screening. The method used should be noted as part of the pregnant woman’s maternity case record. The first estimated gestational age is to be used for the remainder of the pregnancy unless other information comes available. Methods used to determine gestational age include (National Department of Health (South Africa), 2015):

- Last menstrual history: the menstrual history is used should the women be sure of the date of the first day of her last menstrual period. Palpation of the uterus and the symphysis–fundal height must be compatible with the given dates;

- Symphysis–fundal height: this is a measurement from the mother’s pubic bone to the top of the womb. This is used when the estimated gestational age is more the 24 weeks, and the date of the last menstrual period is unknown or wrong;
- Clinical palpation: Palpation is used when the symphysis–fundal height is less than 20cm or more than 35cm. Bimanual and abdominal palpation is used during early pregnancy, and palpation of the fetal head towards the end of the pregnancy;
- Referral for an ultrasound is advised when the last menstrual period is unknown and the symphysis–fundal height is less than 24cm.

According to a Cochrane review published in 2015 (Robert *et al.*, 2015), there is not yet sufficient evidence available to conclude on the efficacy of the symphysis–fundal height and clinical palpation in determining fetal growth restriction. Although the WHO recommends that all pregnant women receive at least one ultrasound screen during pregnancy, they also recommend the continued use of symphysis–fundal height and clinical palptation in low-resource settings until further research is available to inform its use (WHO Reproductive Health Library, 2016).

2.4 Early childhood development: infant growth and development

2.4.1 Infant growth and development

Postnatal development, as with prenatal development, is a continuous and complex process (Berk, 2013). The development which occurs postnatally can be broadly categorised into three main domains. Although it is useful to distinguish between these domains, it is important to recognise that these domains are not distinct but in continuous interaction with one another as each domain influences and is influenced by another (Berk, 2013; Levine & Munsch, 2017). The three developmental domains are as follows (Berk, 2013; Levine & Munsch, 2017; Nyaradi *et al.*, 2013):

- Physical development refers to the biological changes that take place within the body and the brain. Physical development, therefore, includes changes in body size, proportions, appearance and functioning. This domain also comprises the development of fine and gross motor skills, and the integration of perceptual and motor capabilities;
- Cognitive development comprises the changes in how a child thinks, understands and reasons as it grows older. Cognition thus refers to a multifaceted set of higher mental functions and includes, amongst others, attention, memory, academic knowledge, learning, thinking, problem-solving, creativity and language;

- Social-emotional development refers to the changes that occur in how a child connects to another individual, as well as how he/ she understands and expresses emotions. Social-emotional development thus includes interpersonal skills, friendships, intimate relationships, emotional communication, self-understanding, and moral reasoning and behaviour.

The brain is imperative to the advancement of each of the developmental domains (Levine & Munsch, 2017). The first 24 months post-term are characterised by the further progression of primary brain circuits developed during the gestational period as synapse development peaks during this time (Georgieff *et al.*, 2018; Nyaradi *et al.*, 2013). Neural pathways are refined through the programmed elimination of cells and connections – allowing for a child to acquire motor, cognitive and social skills (Berk, 2013; Prado & Dewey, 2014). The refinement which takes place is reliant upon the child's environment and experiences (Prado & Dewey, 2014). Input from the surrounding environment ensures that synapses are strengthened and retained, forming an increasingly elaborated system to support complex abilities. Neurons not used or seldom stimulated lose their synapses by synaptic pruning and are either eliminated or return to an uncommitted state (Berk, 2013; Prado & Dewey, 2014). According to Prado and Dewey (2014), this is one of the primary mechanisms of brain plasticity as plasticity allows the brain to adjust to the environment and recover itself from injury. Georgieff *et al.* (2018) explain that the brain, as in the case of normal brain development, develops from a functionally nonspecific organ with high plasticity to a highly specific organ with low plasticity. Brain vulnerability during early life, however, often outweighs the plasticity, necessitating appropriate stimulation of a child's brain during peak synaptic formation periods (as indicated in figure 2) to ensure optimal development (Berk, 2013; Georgieff *et al.*, 2018). With neurodevelopment regarded as the most significant long-term health outcome of early development, an optimal environment for development is recommended rather than relying on catch-up growth (Georgieff *et al.*, 2018).

2.4.2 Developmental outcomes: factors influencing child development

The brain's development is affected by both biological and psychological factors (Black *et al.*, 2017; Walker *et al.*, 2011). Walker *et al.* (2007), Walker *et al.* (2011) and Britto *et al.* (2017) published reviews (in the latter three *Lancet* Series on early childhood development) on the modifiable biological and psychological risk and protective factors during early childhood development. Although there are similarities in the risk and protective factors experienced in high-, middle, and low-income countries, low-and middle-income countries are more likely to encounter a greater number of risk factors (often in co-occurrence) with fewer protective factors (Britto *et al.*, 2017).

The modifiable risk factors for poor child development, as portrayed by Walker *et al.* (2007) and Walker *et al.* (2011), are summarised in **table 2-3**. Based on the work by Walker *et al.* (2007) and Walker *et al.* (2011), Dawes *et al.* (2012) published a figure depicting how these risk factors interact to affect early childhood development (**figure 2-4**).

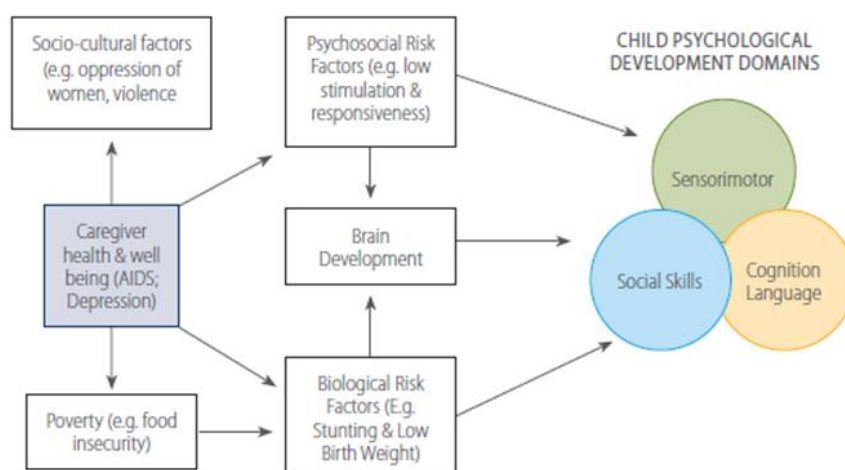
Table 2-3: Risk factors of early childhood development

Risk factors	Evidence
Biological risk factors	
<i>Nutrition</i>	
FGR (mainly due to poor maternal nutrition and/or infections)	Evidence is consistent in suggesting developmental deficits (e.g. lower cognitive scores and less active, vocal and cooperative) during early childhood; later deficits have been reported (behavioural problems during adolescence).
Chronic childhood undernutrition: stunting	Consistent evidence indicating that children who are stunted have poorer cognitive outcomes (deficits in intelligence and academic performance). Social-emotional problems were also reported.
Iodine deficiency (mild to severe deficiency)	Lower developmental levels consistently found in iodine-deficient children. Iodine deficiency <i>in utero</i> is also likely to cause congenital hyperthyroidism and poor development during childhood.
Iron-deficiency anaemia	Iron-deficiency anaemia during infancy is related to both short- and long-term deficits in development due to neurophysiological changes and neural mechanisms. Cognitive and behavioural effects reported.
<i>Infectious disease</i>	
Malaria	Severe malaria (specifically cerebral malaria) is associated with long-term neurological, behavioural and cognitive impairments in childhood survivors. Longitudinal studies suggest uncomplicated malaria attacks affect development and schooling, having a reduced ability at school entry as effect.
Human Immunodeficiency Virus infection	Substantial evidence indicates that infected children have delayed development. Cognitive deficits and mental health problems are also probable.
<i>Environmental exposures</i>	
Lead exposure	Consistent evidence indicates that low concentrations of prenatal exposure can have adverse effects on child development.

Table 2-3: Risk factors of early childhood development (continued)

Risk factors	Evidence
Psychological risk factors	
Cognitive stimulation or child learning opportunities	Consistent evidence from interventions studies indicates that providing increased cognitive stimulation or learning opportunities significantly increases a child's social-emotional and cognitive competencies.
Caregiver sensitivity and responsiveness	Increased maternal responsivity is associated with an increase in cognitive ability and decrease in behavioural problems in preschool children.
Maternal depression	Consistent evidence indicates that infants of mothers suffering from depression have lower cognitive and social-emotional competencies.
Exposure to violence	Exposure to violence has a detrimental effect on the cognitive and social-emotional development of a child.

FGR: fetal growth restriction

Source: Walker *et al.* (2007) and Walker *et al.* (2011)**Figure 2-4: Interaction of risk factors in influencing early childhood development**[Source: Dawes *et al.* (2012)]

Risk factors for poor childhood development are often grounded in poverty (Black *et al.*, 2017). Poverty is related to, among other factors, an inadequate household food supply, poor sanitation and hygiene, and an increase in infections. Poor maternal education, an increase in maternal stress and depression, and inadequate child stimulation at home are also common in impoverished households (Grantham-McGregor *et al.*, 2007). Inadequate nutrient supply to support rapid growth during early life and frequent infections are yet again the main causes of stunting in children (Dewey & Begum, 2011; Grantham-McGregor *et al.*, 2007). Stunting – defined as a length/height-for-age less than the -2 z-score of the WHO child growth standards (WHO,

2008) is regarded as the failure of a child to achieve its genetic potential for height (Dewey & Begum, 2011). Although a child is often classified as stunted only at the age of two to three years, stunting reflects a persistent and cumulative effect of a deficient environment, often due to poor nutrition (Dewey & Begum, 2011; Leroy & Frongillo, 2019). Occasionally, stunting, therefore, begins *in utero* as inadequate maternal nutritional intake and/or anaemia during pregnancy and restricts fetal growth as maternal nutrient intake is not sufficient to support rapid growth and development (Dewey & Begum, 2011).

To determine indicators for poor development, Grantham-McGregor *et al.* (2007) identified early childhood stunting and extreme poverty as global proxy measures for determining the number of children at risk of not attaining their developmental potential. These indicators are based on the findings that both stunting and poverty are closely associated with deficits in cognitive, motor and social-emotional development, educational performance and adult income (Grantham-McGregor *et al.*, 2007). These discrepancies in childhood development are probable as adversities during early life have been shown to alter a child's development by changing brain structure and function (Black *et al.*, 2017). Hair *et al.* (2015) published novel neuroscientific data on the associations between socioeconomic status and brain structure in 2015. Based on the 823 magnetic resonance imaging scans of 389 typically developing children from various backgrounds (aged four to 22 years and representative of the United States of America's demographics for income, race and ethnicity), Hair *et al.* (2015) found that children from low-income households had reduced grey matter in the frontal lobe, temporal lobe and hippocampus. Since these brain areas process, among others, complex thoughts, language comprehension, auditory information, memory and movement, these structural differences are likely to affect academic achievement negatively (Levine & Munsch, 2017). This was also supported by the finding that children from low socioeconomic households scored three to seven fewer points on a standardised test of achievement, with children from poorer households scoring notably fewer (Hair *et al.*, 2015).

Similar findings were reported by Noble *et al.* (2015). In a study including 1099 typically developing children between the ages of three and 20 years, parental education and family income were reported to be positively related to brain surface area. Family income was, in particular, found to be logarithmically associated with surface area. The brain surface areas mainly influenced included those areas supporting reading, language, executive function and spatial skills. Regardless, the mechanisms by which socioeconomic conditions influence brain development remain unclear (Noble *et al.*, 2015). Noble *et al.* (2015) indicate that, as poor socioeconomic status is a complex concept, adversities could stem from ongoing disparities starting during the prenatal period and continuing through to the postnatal period.

Britto *et al.* (2017) report on the interventions proven *effective* in promoting early childhood development. Focussing in particular on interventions concerning health, nutrition, education, child protection and social protection, they report that the following interventions during pregnancy improve development: the supplementation of folate, iron, multi-micronutrients, iodine and/ or energy-protein supplements before and during pregnancy; the provision of necessary treatment for women at risk for preterm birth; birth spacing and family planning; and psychological interventions for the management of maternal stress, depression and mental disorders (Britto *et al.*, 2017). This article by Britto *et al.* (2017) forms part of the 2017 Lancet series of early childhood development. This series was the first to describe the *nurturing care concept* which is now widely accepted as a framework for optimal childhood development (as discussed in section 2.2) (WHO *et al.*, 2018).

2.4.3 Monitoring postnatal growth and development

Monitoring the growth of infants

Anthropometry in infants serves as a non-invasive, economical, and universally acceptable measure to evaluate body size and proportion (WHO, 2021). Using the indicators weight-for-age, length-for-age, and weight-for-length, the global norm is to use the WHO Child Growth Standards published in 2006 as part of the Multicentre Growth Reference Study (WHO Multicentre Growth Reference Study Group, 2006; WHO & UNICEF, 2019). **Table 2-4** indicates, as per the WHO, the interpretation of these indicators based on the z-score (standard deviation scores), as well as the techniques for obtaining the anthropometric measures (WHO, 2008).

Weight-for-age is indicative of a child's body weight relative to chronological age and is used to assess underweight or overweight (WHO, 2020a). As this indicator, should the child's age be known, is generally easy to use, it is often the only indicator used to assess a child's growth (de Onis *et al.*, 2004c). This indicator is, however, not influenced by a child's length and can therefore not account for length-related deficits or excess in growth. It is therefore recommended that this indicator is interpreted together with the length-for-age and weight-for-length indicator (de Onis *et al.*, 2004c; WHO, 2008; WHO, 2020a). *Length-for-age* reflects the attained length of a child relative to chronological age, and is used mainly to identify stunting in children (WHO, 2008; WHO, 2020a). Stunting is regarded as a chronic form of malnutrition because it is, as mentioned above, due to a persistent and often cumulative effect of undernutrition (Dewey & Begum, 2011; Leroy & Frongillo, 2019; WHO, 2020b). *Weight-for-length* indicates a child's body weight in proportion to the attained growth in length (WHO, 2008). A low weight-for-length suggests that a child is wasted, which is indicative of an acute and severe weight loss usually caused by food

shortage and/or illness. Wasting is hence indicative of acute undernutrition. Conversely, a high weight-for-length signifies a child at risk of becoming overweight or being obese (WHO, 2008; WHO, 2020a).

Other than these indices, head and mid-upper arm circumference are also commonly used to assess infant growth. Whereas HC serves as an indicator of intracranial volume and brain growth (and is therefore also a proxy for neurodevelopment) (Georgieff *et al.*, 2018; Koshy *et al.*, 2021; Volpe, 2018), mid-upper arm circumference serves as an independent diagnostic criterion for the diagnosis of undernutrition in children between the age of six and 60 months. A mid-upper arm circumference of less than 115mm is indicative of severe wasting and hence severe acute malnutrition (WHO & UNICEF, 2009).

Table 2-4: Techniques for obtaining anthropometric measurements, and interpretation of growth indicators

Anthropometric measure	Interpretation of growth		
	Indicator	z-score	Interpretation of indicator
Weight Measured either using a calibrated, electronic infant scale or a calibrated electronic scale. Should an infant scale not be available, the mother's/ caregiver's weight will be subtracted from the weight of the mother/ caregiver and infant together. In the case of an infant scale, the infant will lie in the basin of the scale while the measurement is taken. In both cases the measurement is taken with minimal clothing (only a vest in the case of the infant) and preferably without a nappy.	Weight-for-age	<-3	Severe underweight
		<-2	Underweight
		>0	<i>Recommended to be interpreted together with weight-for-length</i>
	Length-for-age	<-3	Severely stunted
		<-2	Stunted
		>3	<i>Child is very tall. Although this is hardly ever a problem, it might be indicative of an endocrine disorder</i>
Recumbent length Generally measured using an infantometer; Child is placed with head against the head board (head pieces removed; vertical Frankfort plane) while legs are held together and straightened (nappy usually removed to allow for this). The foot board is pressed against the foot soles with the toes facing upwards. This measurement should preferably be taken by two individuals: one individual positioning the head and shoulders, with the other pressing the knees down gently while taking the measurement using the foot board.	Weight-for-length	<-3	Severe wasting
		<-2	Wasting
		>1	Possible risk of overweight
		>2	Overweight
		>3	Obese

Table 2-4: Techniques for obtaining anthropometric measurements, and interpretation of growth indicators (continued)

Anthropometric measure	Interpretation of growth		
	Indicator	z-score	Interpretation of indicator
HC Measured using a non-elastic measuring tape; Standing on the left-hand side of the child (sitting on mother's/ caregiver's lap), the measuring tapes is placed around the head (headpieces removed) and positioned above the eyebrows and over the protruding part of the skull at the back. When the measurement tape is in place it is pulled tight to compress the hair.	HC-for-age	<-2 -2 - +2 >+2	Microcephaly Normal head circumference Macrocephaly
Mid-upper arm circumference Also measured using a non-elastic measuring tape; Measured at the mid-arm (point halfway between the acromion process and the olecranon) of the left arm. The arm should be relaxed with the measuring tape placed around the arm at the marked mid-point. The tape should lie flat and not be pulled so tightly as to compress underlying tissue.		< 115mm: indicative of severe acute malnutrition 115 -125mm: indicative of moderate acute malnutrition >125mm: normal growth	

HC: head circumference

Source: WHO (2008) and de Onis *et al.* (2004b)

Monitoring infant development

As with growth, the acquisition of functional competencies and skills follows a set trajectory. This allows for the monitoring of a child's development to ensure prompt intervention when necessary (Sabanathan *et al.*, 2015). Early childhood development assessment tools (CDATs) are commonly used to assess and monitor cognitive, language, motor, executive functioning and social-emotional development (Fernald *et al.*, 2009; Sabanathan *et al.*, 2015). With assessment, a child's ability to perform a series of progressively complex activities thought to reflect the anticipated level of development at a particular age, is evaluated (Sabanathan *et al.*, 2015). As the developmental domains influence one another, the acquisition of skills occurs continually and in close succession (Fernald *et al.*, 2009; Sabanathan *et al.*, 2015). Development in one domain can thus lead to the development of another domain. Likewise, slow development in one domain can cause poor development of another (Fernald *et al.*, 2009).

A comprehensive assessment is recommended as development occurs rapidly in young children (Fernald *et al.*, 2009). **Table 2-5** illustrates the developmental competencies commonly evaluated

in children younger than the age of two years. It is important to note that the CDATs provide only a snapshot of the current developmental level of a child (Sabanathan *et al.*, 2015). So also, the developmental score obtained during infancy and up to the age of 3 years cannot be used to predict the future developmental trajectories as development is easily influenced by both risk factors and interventions to improve early childhood development. It is only between the age of three and five years that an assessment becomes predictive of later academic performance (e.g. during primary school) (Fernald *et al.*, 2009; Fernald *et al.*, 2017; Zhu *et al.*, 2019).

Table 2-5: Illustration of the functional competencies and skills assessed in children younger than the age of two years

Developmental Domain	Competencies and skills
Cognition The strategies and processes a child develops to interpret and respond to its environment and experiences (includes memory, attention, analytical skills and mental problem-solving).	Cognition in young children is evaluated as: • Problem-solving ability using objects, stacking or sorting objects. • Early mathematical skills by evaluating behaviours such as sorting objects or knowing what is meant when “one” or “two” of something is asked for. •
Language Includes receptive and expressive language: receptive language being the understanding of the spoken word and sentence structure, and expressive language the spoken vocabulary.	During infancy language development includes babbling, gesturing and pointing. The first words and use of sentences should emerge within the first two years. Assessment includes: • the repeating of vowels in a string (e.g. aa aa aa) or syllables in a string (e.g. ma ma ma); • using gestures or sounds instead of words to communicate; and • the number of words a child uses. •
Motor development Includes gross and fine motor development. Gross motor development includes the ability to walk, run, and coordinate complex physical activities. The capability to manipulate small objects are fine motor skills.	In children up to the age of two years, <u>gross motor development</u> is mainly assessed as the ability to walk and run. According to the six gross motor milestone published by the WHO as part of the Multicentre Growth Reference Study, gross development is assessed in the following order: • sitting without support, • standing with assistance, • hands-and-knees crawling, • walking with assistance, • standing alone, • walking alone. Each of these milestones has its period/window of achievement. A child aged 18 months should be able to walk alone. <u>Fine motor skills</u> are assessed as the ability to reach for, pick up, grasp and/or manipulate an object.

Table 2-5: Illustration of the functional competencies and skills assessed in children younger than the age of two years

Developmental Domain	Competencies and skills
Social-emotional Refers to the ability to understand one's feelings, as well as to comprehend the emotions of others. Also includes the ability to regulate one's behaviour.	During the first two years of life, much of a child's social-emotional development is centred around the caregiver. Infants and toddlers hence show preferential attachment to caregivers. They are, however, also eager to explore new objects and spaces and enjoy initiating and responding to social interaction. Social-emotional development is assessed based on: • Child's recognition of other people, • Responding to own name and vocalisation, • Ability to select a person to comfort him/her, • Interaction and play with others, • Taking care of others' needs, • Daily activities such as eating and going to bed, and • Dealing with, for example, disagreements, jealousy and the departure of parents.
Self-regulation and executive functioning This refers to the ability of a child to both cognitively and emotionally regulate emotional responses, behaviour and attention.	During the first years, a child develops an increasing intentional ability to control behaviour and cognition. This is influenced by both temperament (also referred to as "effortful control") and executive functioning (e.g the capability to maintain the attention and initiate an action). Self-regulation and executive functioning is assessed as: • Sustaining or switching attention required, and • Inhibition of a response provoked by a task or situation.

WHO: World Health Organisation

Source: Wijnhoven *et al.* (2004), Fernald *et al.* (2009), Sabanathan *et al.* (2015) and Fernald *et al.* (2017)

The assessment methods mainly used by CDATs are (1) direct assessment of a child by a trained assessor in a clinical environment, (2) verbal reporting or completion of a questionnaire by a parent, caregiver or teacher, and (3) an unstructured observation of a child in an environment familiar to the child by a trained assessor (Fernald *et al.*, 2009; Sabanathan *et al.*, 2015). These methods each have shortcomings, however, that can influence the test results. With direct testing in a clinical setting, for example, the child's engagement and participation might be restricted due to the unfamiliar environment and the assessor. Assessment based on the report from a parent or teacher may, however, be biased, whereas an unstructured observation might hinder the reproducibility and interpretation of the tool (Sabanathan *et al.*, 2015). The inclusion of aspects of all three methods within a CDAT is hence recommended to ensure a comprehensive assessment of a child's development (Sabanathan *et al.*, 2015).

Although there is a variety of tools available globally, only a few CDATs are currently available in low- and middle-income countries – the majority of which are used in research settings

(Sabanathan *et al.*, 2015). Generally, the tools used in low- and middle-income countries are either (1) a tool used in high-income countries applied without any adaptation, (2) a tool used in a high-income country adapted and/ or translated according to the local environment, (3) the inclusion of several items from tools used in high-income countries translated and adjusted for a low-income setting, or (4) a locally developed tool which is culturally specific (Sabanathan *et al.*, 2015). In the case of a test being adapted, when aptly adapted, the tool is regarded as a locally applicable tool equal to the original tool in measuring the underlying constructs (Fernald *et al.*, 2017). Based on a review by Sabanathan *et al.* (2015), CDATs developed for use in low- and middle-income countries suitable for children younger than the age of 2 years, include the Kilifi Developmental Checklist (Kenya), Kilifi Developmental Inventory (Kenya), the Developmental Milestone Checklist (Kenya), Guide to Monitoring Child Development (Turkey), the Rapid Neurodevelopmental Assessment (Bangladesh) and the Malawi Developmental Assessment Tool (Malawi).

A more recently developed tool that provides a comprehensive assessment of a child's psychomotor, language, and personal and social-emotional development is PCM-IT version. The PCM-IT is derived from infant assessment tools developed and standardised in Kenya. These assessment tools include the Kilifi Developmental Inventory (Abubakar *et al.*, 2008), the Developmental Milestone Checklist – Version 2 (Abubakar *et al.*, 2010; Prado *et al.*, 2014), and the Profile of Social-Emotional Development (Holding *et al.*, 2004). The Profile of Social-Emotional Development, which is in part based on the Brief Infant/Toddler Social Emotional Assessment (Briggs-Gowan *et al.*, 2002), assesses independence, maladaptive behaviour, emotional lability, social cognition and social-emotional competence (Holding *et al.*, 2004). Items included in the Developmental Milestone Checklist are derived from various published measures, including the Vineland Adaptive Behaviour Scale (Sparrow *et al.*, 1984) and the Griffiths Mental Developmental Scale for Infants (Griffiths, 1954).

The PCM-IT, conducted by a trained assessor, is based on a combination of parental report, assessor observation and direct assessment. Should the parent report, for example, that he/she has not yet observed the child performing a specific task, the assessor creates an opportunity for the child to perform the task (Pell *et al.*, 2016). Most of the items in this tool are scored according to four levels: a score of 0 indicates that the child was “not able” to complete the task; 1, that the child was “able to carry out the activity momentarily”; 2 that the child “could carry out the activity, but with limitations” and 3, that the child was “able to carry out the activity with little effort”. As for the emotional regulation items, a three-point Likert scale is used, with 0 indicating “never or rarely happens”. 1, “happens sometimes” and 2, “always happens or happens most of the time” (Pell *et al.*, 2016).

Fernald *et al.* (2017) indicate that an appropriate CDAT, depending on the purpose for which the tool is used (e.g. for research purposes, evaluation of a programme, or population monitoring), should be a tool that is easy to administer, has high reliability and validity, and is culturally appropriate. Culture, referring to the values, beliefs, attitudes and activities which guide how individuals live, is known to greatly influence how children develop as different cultures have different norms as to how and when skills should emerge. Abilities regarded as important in a specific culture and hence encouraged, are therefore likely to emerge earlier than abilities not encouraged. These culture-specific norms should ideally be considered when appraising the validity of a tool, and especially so when making comparisons between population groups and/or countries. To ensure the accuracy of the findings from a CDAT, Fernald *et al.* (2017) identify 10 ideal attributes of a tool. These attributes are:

- The test score should be a true representation of a child's ability;
- The test should serve as an appropriate and interpretable measure, with high validity and reliability, across different contexts and cultures;
- There should be variety in scores with age and ability;
- The test should be easily administered;
- Administration of the test should be of low cost and possible in a short period of time;
- The test should provide information on all developmental domains;
- The test score should be applicable for programme design and policy as it provides a score relevant to a child's practical functioning in everyday life;
- The test should serve as an indicator towards future success;
- The neuronal and brain systems fundamental to the performance of the test should be well known and understood; and
- The implications of health, nutrition and environmental factors on the test score must be known and clearly understood.

2.5 Maternal dietary patterns during pregnancy and associated outcomes

2.5.1 Overview of dietary patterns

Traditionally, nutrition research concentrated mainly on examining the association between the human diet and disease by focussing on single nutrients or specific foods (Agnoli *et al.*, 2019; Cespedes & Hu, 2015; Hu, 2002). Although studying single nutrients or foods is still valuable, nutrients are not consumed in isolation but as part of a diet which is comprised of different foods in different combinations (Hu, 2002). The combinations in which foods are eaten are normally complex with an interactive, synergistic and cumulative effect, making it difficult to examine the

distinct effect of a nutrient on health outcomes (Cespedes & Hu, 2015; Hu, 2002). Difficulty in scrutinising the effect of single nutrients is often due to a high level of inter-correlation among nutrients, a possibility of an effect size too small to detect, and the effect of a single nutrient often confounded by other dietary factors (Cespedes & Hu, 2015; Hu, 2002).

Dietary pattern analysis is thus regarded as an “alternative and complementary” method in examining the overall effect of the diet on the risk of poor health outcomes (Hu, 2002). It more closely resembles actual dietary intake as it accounts for overall eating behaviour – hence providing a more predictive approach towards disease risk. Dietary patterns are also considered to have an important public health implication as patterns are easier to translate into health messages and diets (Hu, 2002). Cespedes and Hu (2015) define the overall diet as “the foods, food groups, and nutrients included; their combination and variety; and the frequency with which and quantity in which they are habitually consumed”.

As dietary patterns cannot be measured directly, different statistical methods are used to characterise these patterns from dietary information collected through most dietary methodologies (e.g. 24-hour recall, food record and food frequency questionnaire) (Agnoli *et al.*, 2019; Hu, 2002). The approaches toward determining dietary patterns can broadly be grouped as *a priori* and *a posteriori* dietary pattern analysis (Cespedes & Hu, 2015; Hu, 2002). The following sections provide a short overview of each approach.

A priori dietary patterns

A priori dietary pattern analysis, also referred to as the hypothesis-oriented approach (Agnoli *et al.*, 2019), is regarded as a prominent method in assessing dietary patterns (Cespedes & Hu, 2015). Consisting of numerical *a priori* indices, this method measures adherence to a predefined dietary pattern (Cespedes & Hu, 2015). These predefined dietary patterns are based upon previous nutrition research and are thus constructed according to the current knowledge of what a healthy diet entails. *A priori* indices are consequently often constructed based on dietary recommendations considered important for health promotion (Burggraf *et al.*, 2018; Hu, 2002). As dietary recommendations frequently entail the dimensions of a high-quality diet, the components of the numerical *a priori* indices are quantified and aggregated to determine the overall dietary quality (Burggraf *et al.*, 2018). With “diet quality” referring to the overall nutrient adequacy or nutritional value of the dietary pattern, a higher *a priori* score indicates greater adherence to predefined dietary recommendations (Aljuraiban *et al.*, 2020; Burggraf *et al.*, 2018). Hu (2002) encapsulates the *a priori* dietary pattern by explaining that it is a diet quality index

which is a “summary score of the degree to which an individual’s diet conforms to a specific dietary recommendation”.

Other than being limited by the current knowledge of the diet–health relationship, the *a priori* method is also commonly limited by uncertainties regarding the construction of these indices (Burggraf *et al.*, 2018). An example of this is the method used to convert diet components into scores. The scores can either be calculated using absolute cut-off values (e.g. above or below a predefined level) or can be based on the relative distributions within the study population (e.g. based on quantiles of sex-specific intakes) (Aljuraiban *et al.*, 2020). As part of a critical appraisal on the application of *a priori* dietary quality scores to cardiovascular disease risk, Aljuraiban *et al.* (2020) indicate that the use of absolute cut-off values limits the overestimation of the score and allows for more useful comparison between studies. Limitations to comparison still exist, however, as there is variability in cultural practices, and hence the application of diet quality indices. Aljuraiban *et al.* (2020) therefore recommend that the foods, nutrients and/or other food components included in the scoring, as well as modifications, are clearly defined to allow for the replication of calculations in different population groups. Burggraf *et al.* (2018) published an article in 2018 in which the authors discuss, based upon relevant index construction criteria, the principles to consider when deciding upon an *a priori* index for studying a specific research question. **Table 2-6** provides a summary of the preferable features of a dietary quality index to determine *a priori* dietary patterns (Burggraf *et al.*, 2018).

Table 2-6: Preferable features of a dietary quality index to determine *a priori* dietary patterns

Category	Construction criteria	Recommendations ¹
Theoretical framework		
Index dimensions	Should be based upon the dimensions of diet quality, hence: • Adequacy (<i>adequate intake of nutrients/ foods</i>) • Moderation (<i>moderate intake of foods/ nutrients associated with chronic disease</i>) • Balance (<i>Overall balance of macronutrients and specific micronutrients</i>) • Variety (<i>variety in foods consumed</i>)	Adequacy, moderation and balance should be included. Variety, preferably within-food group variety, should be included only if it is not strongly correlated with adequacy and/or moderation or if the correlation is accounted for.
Index structure	• Unordered • Ordered • Nested	Nested structure (hence index with sub-indices) is preferred as this is likely to capture the different dimensions of diet quality – allowing the researcher or practitioner to determine the aspect of the diet which needs additional attention.

Table 2-6: Preferable features of a dietary quality index to determine *a priori* dietary patterns

Category	Construction criteria	Recommendations ¹
Indicator selection		
Component types	• Food-group indicators • Nutrient indicators • Combination of food-group and nutrient indicators	Food-group indicators recommended for when the application of the index is to communicate a health message to individuals. Nutrient indicators (used in combination with specific food-group indicators) are recommended when the index is used to assess the diet quality of a population.
Normalisation methods		
Scaling procedure	• Dichotomous • Ordinal • Metric	As diet quality is assessed, metric measures should be preferred to ordinal or dichotomous measures.
Cut-off values	• Normative • Percentile • Uniform • Group-specific	Preferably normative values which are based upon epidemiological data and/or dietary guidelines should be used.
Weighting and aggregation		
	• Unweighted linear • Weighted linear	Weighted aggregation is preferred as this accounts for component-specific health impacts and the correlation among the components.

¹ These recommendations are dependent upon the features of the dataset analysed.

Source: Burggraf *et al.* (2018)

There are various dietary quality indices presented in the literature to determine predefined *a priori* dietary patterns; examples include the Diet Quality Index, the Healthy Diet Indicator, the Healthy Eating Index and the Mediterranean Diet Score. Various updated, adjusted or revised versions of these indices are available (Agnoli *et al.*, 2019; Burggraf *et al.*, 2018; Cespedes & Hu, 2015). One index which meets most of the criteria given by Burggraf *et al.* (2018) is the Diet Quality Index–International (DQI-I) (Kim *et al.*, 2003). The DQI-I has a nested structure and describes all dimensions of a high-quality diet, namely adequacy, moderation, balance and variety (both overall variety and within-food group variety). This index is also very detailed in that a combination of nutrient and food-group indicators is included, the indicators are a mixture of metric and ordinal scales, and the cut-off values used for scoring are based upon epidemiological data and dietary guidelines (Burggraf *et al.*, 2018).

Published by Kim *et al.* (2003), the DQI-I is regarded as the most appropriate for international use as it aims to allow for cross-national comparison of diet quality between countries possibly at

different stages of nutrition transition. Other than focussing only on dietary concerns related to chronic disease, this index also allows for evaluating undernutrition – therefore also accounting for diet-related concerns in low- and middle-income countries (Burggraf *et al.*, 2018; Kim *et al.*, 2003). The DQI-I is hence viewed as a “global tool for monitoring healthfulness of a diet and for exploring aspects of diet quality related to the nutrition transition” (Kim *et al.*, 2003).

Broadly, the dietary guidelines upon which this index is based are (1) consumption of a variety of foods; (2) the adequate intake of essential foods and nutrients such as fruits, vegetables, complex carbohydrates and protein from a variety of sources; and (3) moderation in the intake of total fat, saturated fat, cholesterol, sugar and sodium (Kim *et al.*, 2003). Bearing in mind the guidelines presented by the WHO on what a healthy diet entails (as discussed in section 2.3), the guidelines upon which the DQI-I is based, are considered as the foundation for a healthy diet (Kim *et al.*, 2003; WHO, 2018). These guidelines form part of the main categories (variety, adequacy, moderation and balance) of the DQI-I index and the components of each. The DQI-I has an overall score of 100, with a score of 0 being the lowest and 100 the highest (Kim *et al.*, 2003). According to the criteria given by Kim *et al.* (2003), a score of less than 60 out of a possible 100 indicates a poor-quality diet. Addendum 12 provides the DQI-I index, an outline of the recommended dietary methodologies to use, and the scoring criteria (Kim *et al.*, 2003).

A posteriori dietary patterns

A posteriori dietary patterns are eating patterns derived from empirical dietary data using statistical modelling techniques (Hu, 2002; Moskal *et al.*, 2014). As empirical data are used, the patterns are indicative of foods that tend to be consumed together and hence do not always present optimal dietary patterns (Hu, 2002). Regardless of not presenting optimal dietary patterns, *a posteriori* dietary patterns are considered valuable in evaluating the biological interactions of the diet with health outcomes (Agnoli *et al.*, 2019).

Exploratory dimension reduction methods commonly used to derive empirical dietary patterns include factor and cluster analysis (Hu, 2002; Moskal *et al.*, 2014). Factor analysis, a generic term referring to both principal component analysis and simple factor analysis (Hu, 2002), aims to condense a large number of related variables into fewer independent components which explain most of the diet’s variability (Moskal *et al.*, 2014). These variables can be foods, food groups, nutrients or biomarkers (Moskal *et al.*, 2014). The independent components, referred to as the factors or patterns, indicate the degree to which food items correlate with one another (Hu, 2002). Cluster analysis, in contrast with factor analysis, entails the aggregation of individuals into homogeneous groups (clusters) based on a similar diet. Individuals can be clustered according

to “the percentage of energy contributed by each food or food group, the average grams of food intakes, standardised nutrient intakes, or a combination of dietary and biochemical measures” (Hu, 2002).

Although empirical dietary patterns are often derived for foods or food groups, Moskal *et al.* (2014) argue that nutrient patterns have several advantages. Granting that food patterns are more easily translated into public health messages, nutrients are universal and hence provide a simpler approach to comparing patterns between populations. Similarly, nutrient patterns have fewer non-consumers, which facilitates statistical analysis and interpretation - also easing cross-population comparison (Moskal *et al.*, 2014). Nutrient patterns, furthermore, better reflect the associations of a combination of nutrients within a complex biological mechanism with health outcomes, hence adhering to research recommending the use of nutritional biomarkers and metabolites in epidemiological research (Moskal *et al.*, 2014).

2.5.2 Associations between maternal dietary patterns and fetal growth

It is interesting to note that publications on the associations between maternal dietary patterns during pregnancy and fetal growth report mainly on the birth outcomes (e.g. birth weight and preterm birth), with only two articles (Bouwland-Both *et al.*, 2013; Wrottesley *et al.*, 2020), to the student’s knowledge, published on the associations between maternal dietary patterns during pregnancy and ultrasound-derived fetal growth. So also, *a posteriori* dietary patterns are mainly reported for foods or food groups, with seemingly no studies yet reporting on nutrient patterns. In the 2014 article published by Moskal *et al.* (2014), the authors make the statement that very limited research has been done on nutrient patterns. Pisa *et al.* (2015) confirmed this in 2015, indicating that, especially in Africa at that time, no studies had yet reported on nutrient patterns. Although various articles on this have been published since, no article reports on nutrient patterns during pregnancy.

In a systematic review and meta-analysis published by Chia *et al.* (2019) in 2019, articles reporting on *a priori* and/or *a posteriori* dietary patterns were included to determine the associations between maternal nutrition during pregnancy and birth outcomes. Considered one of the most up-to-date and comprehensive reviews on the topic, 36 articles, amounting to 167 507 participants, were included. Twenty-one studies reported on *a priori* or index-based dietary patterns, and 15 on *a posteriori* or data-driven patterns. The index-based and data-driven dietary patterns were grouped to identify two common dietary patterns (namely “healthy” and “unhealthy” dietary patterns) for the meta-analysis. The “healthy” dietary pattern was characterised by a high intake of fruit, vegetables, whole grains, low-fat milk and lean protein foods. A high intake of

refined carbohydrates, processed meat, and foods high in sugar and/or saturated fat described an “unhealthy” dietary pattern. Whereas a “healthy” dietary pattern during pregnancy was found to be associated with a lower risk of preterm birth, an “unhealthy” diet was associated with a higher risk of preterm birth and LBW. The “healthy” dietary pattern also showed a weak trend towards a lower risk of LBW infants. Interestingly, only a *posteriori* healthy dietary patterns were found to be associated with higher birth weight. This can be explained by the fact that a *posteriori* dietary patterns aim to explain the maximum variance of the food intake, whereas the associations of an *a priori* pattern can be weakened should all individuals not meet the dietary recommendations evaluated by the index (Chia *et al.*, 2019).

A recent systematic review published by Raghavan *et al.* (2019) and a systematic review and meta-analysis by Kibret *et al.* (2019) confirm the findings presented by Chia *et al.* (2019). Raghavan *et al.* (2019) conclude that “limited but consistent evidence” suggests that dietary patterns higher in vegetables, fruits, whole grains, nuts, legumes and seeds, and lower in red and processed meats and fried foods during pregnancy are associated with a lower risk of preterm birth. Kibret *et al.* (2019) also found a healthy dietary pattern to be associated with lower odds of preterm birth. Yet Raghavan *et al.* (2019) indicate that they could not determine the associations between dietary patterns and birth weight due to inconsistencies among the findings reported by the included studies, as well as variation in study design and methodologies. Both research groups, however, make the important observation that the majority of research on this topic was conducted in healthy Caucasian women with access to health care. Further research in low-income countries is hence advised to fully understand the impact of restricted resources on the maternal diet during pregnancy and birth outcomes (Kibret *et al.*, 2019; Raghavan *et al.*, 2019).

Reporting on fetal growth using biometric measures during pregnancy, Bouwland-Both *et al.* (2013) report, as part of the Generation R study conducted in the Netherlands between 2002 and 2006, on the associations between peri-conceptual dietary patterns and crown–rump length, EFW and birth weight. Using food groups obtained from a semi QFFQ reflecting dietary intake from the previous three months (obtained at enrolment, a median of 12 weeks’ gestation), “Mediterranean”, “energy-rich” and “Western” dietary patterns were derived using principal component factor analysis. The energy-rich pattern, comprising high intakes of nuts, margarine and bread, was the only one to be associated with crown–rump length: a higher adherence to this pattern resulted in a higher crown–rump length during the first trimester. This was attributed mainly to the energy-rich nourishment of the embryo *via* the endometrial glands during early pregnancy (Bouwland-Both *et al.*, 2013).

Wrottesley *et al.* (2020), found, furthermore, that a +1 standard deviation increase in the adherence to a “mixed, high-sugar” dietary pattern (high positive loadings for foods with added

sugar, as well as healthy foods such as wholewheat and brown bread, and dairy) was associated with an increased AC, HC, BPD and FL throughout pregnancy. These associations held after adjusting the linear mixed-effects models for body mass index and gestational weight gain. Regarded as novel evidence, these findings indicate that adherence to a diet high in sugar increases the risk of excessive fetal growth (Wrottesley *et al.*, 2020). Findings from both Bouwland-Both *et al.* (2013) and Wrottesley *et al.* (2020) are hence congruent in indicating that a diet high in energy might promote excessive fetal growth.

Crozier *et al.* (2009) are among the only authors to report on the change in dietary patterns before and during pregnancy. They conducted a study among women in Southampton in the United Kingdom (assessing the diets of 12 572 non-pregnant women; of the women who became pregnant, 2270 and 2649, respectively, provided complete dietary intake data at early and late pregnancy). Food intake was assessed at pre-pregnancy, during early pregnancy (about 11 weeks' gestation) and late pregnancy (34 weeks' gestation) using an interviewer-administrated food frequency questionnaire. An increase in the intake that included "white bread, breakfast cereals, cake and biscuits, processed meat, crisps, fruit and fruit juices, sweet spreads, confectionaries, milk, cheese, full-fat spread, cooking fat and salad oils, red meat and soft drinks" was noted during pregnancy. The intake of "rice and pasta, liver and kidney, vegetables, nuts, diet cola, tea and coffee, boiled potatoes and crackers", however, decreased. Using principal component analysis, two distinct dietary patterns (prudent and high-energy) were determined at each time point of data collection. Dietary pattern scores ("natural" score based on the dietary pattern defined at that time point, and an "applied" score based on the pattern defined before pregnancy) were used to assess the change in the patterns. The authors concluded that, regardless of the increase and decrease in the intake of certain foods, dietary patterns during pregnancy changed only slightly overall (Crozier *et al.*, 2009).

In a more recent publication by Crozier *et al.* (2017), nausea and vomiting during pregnancy were reported to only have a transient effect on the overall diet quality, as prudent diet scores decreased with more severe nausea and vomiting only during early pregnancy. Tielemans *et al.* (2015) investigated the associations between *a priori* and *a posteriori* dietary patterns during pregnancy and gestational weight gain as part of the Generation R Study (conducted in the Netherlands). Dietary patterns were determined using dietary data obtained via a QFFQ administered at a median gestational age of 13 weeks. As part of the study's limitations, the authors acknowledge that they used dietary data from only one time-point and thus could not account for a change in dietary intake, in particular with regard to nausea and vomiting during early pregnancy. After excluding from data analysis women who did experience nausea and vomiting during pregnancy, however, they did not find any change in their results (Tielemans *et al.*, 2015).

2.5.3 Associations between maternal dietary patterns and infant growth and development

As with the associations between maternal dietary patterns during pregnancy and fetal growth, research on the associations of dietary patterns during pregnancy with infant growth and development is limited. The studies reporting on these associations were all conducted in high-income countries, with no publications reporting on data from low- and middle-income countries. Although the importance of optimal nutrition during pregnancy for long-term offspring health is well publicised, the relationship between the maternal diet during pregnancy and child growth and development is less established (Borge *et al.*, 2017). With the maternal diet directly influencing the fetal nutrient exposures and, therefore, fetal programming, it is likely that the maternal diet will have a long-term effect on both child growth and development (Shapiro *et al.*, 2016; Tahir *et al.*, 2019). More research within this area is thus warranted.

Studies reporting on child growth investigate mainly the role of maternal dietary patterns during pregnancy in the risk of overweight and obesity in the offspring. The most recent publication on this was by Hu *et al.* (2020). Including 1257 mother-child pairs from Tennessee in the United Nations of America, Hu *et al.* (2020) described the associations between maternal dietary patterns during pregnancy and body mass index trajectories in the offspring from birth to the age of four years. Using the reduced-rank regression method, two dietary patterns, namely the fast-food pattern and the processed-food pattern, were identified (based upon dietary data obtained from a food frequency questionnaire during the second trimester). The fast-food pattern contained higher intakes of foods such as fried chicken and fish, fruit juices, mayonnaise, margarine/butter, and sugar-sweetened beverages. A higher intake of dairy, salad dressing, processed meats, breakfast cereal, canned fruit and French fries were described as the processed food pattern. Considering possible confounders, Hu *et al.* (2020) reported the fast-food pattern to be significantly associated with a greater risk of overweight and obesity in the offspring at the age of four years. No associations were found between the processed-food pattern during pregnancy and the outcomes evaluated.

Martin *et al.* (2016) published similar results as Hu *et al.* (2020). Exploring the associations of three *a posteriori* dietary patterns (based on dietary data obtained from a food-frequency questionnaire during the second trimester) with child body mass index between birth and the age of three years, Martin *et al.* (2016) also found a more unhealthy dietary pattern (characterised by high consumption of white bread, red and processed meat, fried chicken, French fries and vitamin C-rich drinks) during pregnancy to be associated with a higher risk of overweight and obesity in the offspring. Martin *et al.* (2016), interestingly, indicate that the more unhealthy dietary pattern is associated with a lower birth weight followed by a faster growth rate as compared with a healthier

dietary pattern (high consumption of vegetables, fruits, low-fat dairy, whole-wheat bread, baked chicken and water).

Tahir *et al.* (2019) and Shapiro *et al.* (2016) considered *a priori* dietary patterns in reporting on the association between the maternal diet during pregnancy and infant body fat percentage (including infants up to the age of six months and neonates, respectively). Both research groups found a higher diet quality to be associated with a lower body fat percentage. It is interesting to note, however, that Poon *et al.* (2013) found no relationship between *a priori* dietary patterns obtained during the third trimester and early infant growth.

Borge *et al.* (2017) published a meta-analysis in 2017 to review systematically whether the maternal diet during pregnancy influenced child neurodevelopment. Focussing on maternal diet quality, 18 articles reporting on *a priori* dietary indices during pregnancy were included. Publication bias and heterogeneity among the articles included, however, limited the findings of this review. Regardless, a small positive association was found between a higher maternal dietary quality and child neurodevelopment, especially in terms of the cognitive domain. The authors also highlight that the majority of studies did not control for the effect of the child's diet on neurodevelopment and that this should be considered in future studies (Borge *et al.*, 2017). No other studies have since, to the student's knowledge, been published on this topic. An article by Steenweg-de Graaff *et al.* (2014) is seemingly also the only study reporting on *a posteriori* maternal dietary patterns during pregnancy and offspring neurodevelopment. The "healthy" and "unhealthy" dietary patterns described by this study were included as *a priori* quality indices within the review by Borge *et al.* (2017).

2.6 Maternal nutrition and early childhood development in South Africa

2.6.1 South African policies, programmes and guidelines promoting maternal nutrition during pregnancy and early childhood development

In 2012 the South African government published the National Development Plan 2030 - a plan for the country collectively to reduce inequality and eliminate poverty by 2030 (National Planning Commission (South Africa), 2012). Adequate nutrition during pregnancy is promoted within this plan as one of the strategies for enhancing early childhood development. Early childhood development is promoted as essential to ensure that a child reaches its optimal development potential and hence as a measure to tackle the effect of poverty on millions of South Africans (National Planning Commission (South Africa), 2012).

To ensure health services for all pregnant women in South Africa, the updated “Guidelines for Maternity Care” was published by the National Department of Health in 2015 (National Department of Health (South Africa), 2015). This document serves as a manual for clinics, community health centres and district hospitals to improve the level of care provided to pregnant women making use of primary health care services. This guideline encourages regular attendance of pregnant women at antenatal care sessions (<12 weeks, 20 weeks, 26 – 28 weeks, 32 - 34 weeks, and 38 weeks) during which the pregnancy is to be monitored to ensure an optimal outcome (National Department of Health (South Africa), 2015). Although comprehensive with regard to guidelines on maternal care, this document is limited in dietary guidelines to ensure healthy eating during pregnancy. Nutrition-related care promoted by this document includes routine nutritional status screening using the mid-upper arm circumference and haemoglobin levels, as well as the daily micronutrient supplementation of ferrous sulphate (200mg per day), folic acid (5mg/ day) and calcium (1000mg per day) (National Department of Health (South Africa), 2015).

In the document “Roadmap for Nutrition in South Africa (2013 – 2017)” the South African food-based dietary guidelines are mentioned as a key nutrition intervention to ensure healthy eating habits and optimal weight gain during pregnancy (Department of Health (South Africa), 2013). Although the focus period of the Roadmap for Nutrition in South Africa has expired, an updated version has not yet been published. According to Vorster *et al.* (2013), the South African food-based dietary guidelines serve as “short, positive, science-based dietary recommendations” to inform members of the general public on making food and beverage choices that will ensure dietary adequacy and prudence. Following these recommendations will contribute towards optimal nutrition, health and well-being through every stage of the life-cycle (Vorster *et al.*, 2013). Considering the “healthy diet fact sheet” published by the WHO (as indicated in section 2.3) (WHO, 2018), the South African food-based dietary guidelines are in line with the guidelines promulgated by the WHO. The eleven South African food-based dietary guidelines are, in short, as follows (Vorster *et al.*, 2013):

- Enjoy a variety of foods;
- Be active!;
- Make starchy foods part of most meals;
- Eat plenty of vegetables and fruit every day;
- Eat dry beans, split peas, lentils and soya regularly;
- Have milk, maas or yoghurt every day;
- Fish, chicken, lean meat or eggs can be eaten daily;
- Drink lots of clean, safe water;
- Use fats sparingly. Choose vegetable oils rather than hard fats;

- Use sugar and foods and drinks high in sugar sparingly;
- Use salt and foods high in salt sparingly.

In 2003, following the outcome of the first National Food Consumption Survey which indicated deficiencies of various micronutrients (niacin, riboflavin, folate, vitamins B₆, A, C and E, iron, zinc and calcium) among children younger than the age of 9 years, fortification of commonly consumed staples became mandatory. These micronutrient deficiencies, which were also identified among adults, were attributed to commonly consumed foods among the South African population (e.g. bread, maize, sugar and tea) being deficient in these micronutrients (Steyn *et al.*, 2008). Legislation was therefore put in place in 2003 to promulgate the fortification of maize and wheat flour with thiamine, niacin, riboflavin, vitamin B₆, folic acid, vitamin A, zinc and iron (Department of Health (South Africa), 2003). As part of a secondary analysis, published only a few years after the mandatory fortification of foodstuff, Steyn *et al.* (2008) reported that the consumption of fortified foods to had had a positive outcome on micronutrient intakes among men. Iron intake was however, regardless of the fortification, below the recommended nutrient intake among women. Papathakis and Pearson (2012), conversely, found that breastfeeding women consumed iron above the estimated average requirement, but that the iron status remained unchanged from before fortification was implemented. A possible reason given for this was the low bioavailability of the electrolytic iron used for fortification (Papathakis & Pearson, 2012). There is also evidence pointing towards mills not adding sufficient amounts of nutrient premixes to their products (Yusufali *et al.*, 2012). Other than the iron intake, Papathakis and Pearson (2012) indicated that, regardless of fortification, more than 70% of their participants did not meet the requirements for vitamin A and B₆, riboflavin and zinc intake.

The South African Cabinet approved the National Integrated Early Childhood Development Policy in 2015. This policy, focussing on the period from preconception up to the year before a child enters formal schooling, is in adherence with the National Development Plan and calls for all children to be granted early learning opportunities to reach their full developmental potential. This policy also emphasises the importance of optimal nutrition (starting as early as preconception and during pregnancy) as imperative for early childhood development (Republic of South Africa, 2015).

As a part of the National Integrated Early Childhood Development Policy, the programme for the support of pregnant women, new mothers/fathers and children under the age of two years is managed by the National Department of Health (Republic of South Africa, 2015). The Department of Health, together with civil societies, academia and private foundations, launched the Side-by-Side campaign in 2018 (Side-by-Side, 2020). This campaign focuses on the health of children younger than the age of five years and aims to ensure that all children have access to nurturing

care, both in health care facilities and at household level. An updated and redesigned Road to Health Booklet is central to the campaign. Other than serving as a health record, this updated booklet contains valuable health promotion messages organised according to five “knowledge pillars” (nutrition, love, protection, health care and extra care) for caregivers (Slemming & Bamford, 2018). This booklet thus helps ensure that all mother–infant pairs receive the same broad range of care and services – hereby improving the quality of the postnatal care delivered (Hall *et al.*, 2019).

2.6.2 Nutritional status of pregnant women in South Africa

Studies reporting on the nutritional status of pregnant women in South Africa are sparse (Hall *et al.*, 2019; Symington *et al.*, 2018). Only four publications issued during the past decade report on the dietary intake of pregnant South African women. The scarcity of data is confirmed by a systematic review published by Harika *et al.* (2017). The systematic review evaluates the micronutrient status and dietary intake of iron, vitamin A, iodine, folate and zinc in women of reproductive age and pregnant women in Ethiopia, Kenya, Nigeria and South Africa. The authors indicate that the micronutrient status of pregnant women in South Africa could not be appraised as no studies met the inclusion criteria of being published between 2005 and 2015 (Harika *et al.*, 2017).

In a study published in 2018, Cormick *et al.* (2018) report on the nutritional status of pregnant women in South Africa and Zimbabwe as a sub-analysis to the Calcium and Pre-eclampsia trial - a multi-centre randomised, double-blind placebo-controlled clinical trial aimed at evaluating the effect of calcium supplementation on recurrent pre-eclampsia. Considering the nutritional status of South African women (224 women from Cape Town, East London and Johannesburg), Cormick *et al.* (2018) report that the majority of women enter pregnancy either overweight (27.7%) or obese (46%). Hardly any women were considered underweight (<1%). Although macronutrient intake, based on a 24 hour recall conducted at 20 weeks' gestation, was within the acceptable macronutrient distribution ranges, micronutrient intake (folate, calcium, iron and zinc) was reported to be inadequate in more than 90% of women. Considering the method used to analyse dietary intake (Food Finder III), it is unclear whether the research group accounted for food fortification. Folic acid supplementation was, however, reported by 62.9% of women, with 57.1% reporting iron supplementation. At 20 weeks' gestation, women stated that these supplements had been taken for a mean period of 2.1 to 2.7 months (Cormick *et al.*, 2018).

Krige *et al.* (2018) also report that the majority of study participants (239 pregnant women with gestational diabetes; ≥ 28 weeks' gestation) have an insufficient intake of folate (96.5%), iron

(91.3%) and vitamin D (87.4%) from dietary sources. As with Cormick *et al.* (2018), it is unclear whether Krige *et al.* (2018) accounted for fortification. Intake from macronutrients, based on a QFFQ, were also found to be within the acceptable macronutrient distribution ranges. Forty percent of participants, however, had a fat intake of more than 35% of total energy intake. The authors interestingly also inform on the overall fruit and vegetable intake among the study participants. Taking into consideration the recommendation of the WHO that ideally more than 400 grams of fruit and vegetables should be consumed per day (WHO, 2018), Krige *et al.* (2018) report that only a third of participants met this recommendation.

A very interesting work was published by Fahey *et al.* (2019) in 2019. Including 752 mother–infant pairs, they examined the seasonality of maternal dietary intake of women residing in the Vhembe District of the Limpopo province (considered as a rural area). Dietary data were collected at the time of delivery using a QFFQ asking about consumption during the previous month. As with the two previously mentioned studies, macronutrient intake in this study population was also found to be within the acceptable macronutrient distribution ranges. Seasonal variation had a significant effect on the composition of the maternal diet as carbohydrate intake declined during the harvest season (March to June), but increased during the time of vegetable gardening (July to October) and the “lean” season (November to February). The “lean” season coincides with high rainfall and labour-intensive preparation of fields and planting, contributing to extensive food insecurity during these months. Fat intake indicated an opposite trend to carbohydrate intake, with the fat intake being higher during the harvest seasons when food prices were generally lower (Fahey *et al.*, 2019).

The only study to date to report on maternal dietary patterns during pregnancy in South Africa was published by Wrottesley *et al.* (2017) as part of the Soweto First 1000-Day Study. The Soweto First 1000-Day Study was conducted in Johannesburg between 2013 and 2016, and aimed to understand the complex associations between maternal factors and fetal and infant outcomes. As a study nested within this larger study, Wrottesley *et al.* (2017) reported on the associations between the maternal dietary patterns during pregnancy and gestational weight gain. Using dietary data from 528 pregnant black women collected by means of a QFFQ, *a posteriori* dietary patterns were determined. Three distinct food patterns, namely a “western” pattern, “traditional” pattern and “mixed” pattern – renamed to a “mixed, high sugar” dietary pattern in a subsequent publication (Wrottesley *et al.*, 2020) – were observed. The western (energy-dense, processed foods) and mixed food patterns (containing both classically healthy foods and processed foods) were found to be associated with higher gestational weight gain. A lower weight gain was found to be associated with the traditional food pattern (high in whole grains, legumes, vegetables and traditional meats, and a decreased intake of processed foods) (Wrottesley *et al.*, 2017).

Irrespective of the limited information available on the maternal diet, it is well established that the high levels of poverty and unemployment [32.5% during the fourth quarter of 2020 after lockdown measures throughout the year due to the COVID-19 pandemic (Stats SA (Statistics South Africa), 2021)] in South Africa affected the access to adequate food (Hall *et al.*, 2019). This lack of access to adequate nutrition often leads to hunger, undernutrition and micronutrient deficiencies within a household – frequently also affecting pregnant women (Hall *et al.*, 2019). As a qualitative study, Scorgie *et al.* (2015) report on the experiences of poverty among pregnant women (n=22) within an urban healthcare setting in Johannesburg. With regard to nutrition, food intake during pregnancy was largely found to be influenced by what is available within the household, due to financial constraints. However, the women expressed their concern as to whether they were meeting the additional dietary requirements, as well as a desire to follow a healthy, diversified diet (Scorgie *et al.*, 2015).

It is important, furthermore, to note that South Africa is undergoing a nutrition transition with a shift from a traditional diet to a more Westernised diet due to urbanisation and economic and social development, and adapting to new cultures (Bourne *et al.*, 2002; Vorster *et al.*, 2011; Wentzel-Viljoen *et al.*, 2018). The traditional South African diet is characterised by a high intake of fibre and low intake of fat from mainly starchy foods and foods rich in plant protein (legumes). This diet is associated with a low prevalence of degenerative diseases. Conversely, the Westernised diet is known to increase the risk of obesity and non-communicable disease as it is described by a higher intake of animal products, as well as processed foods high in sodium and fat (Bourne *et al.*, 2002). With the shift from a traditional to a more Westernised diet, Vorster *et al.* (2011) describe that the dietary patterns change to a more appetising and attractive diet comprising convenience and fast food, more snack foods, meat and also fruit. This has the effect of an increase in the total energy intake (including total carbohydrate and fat intake) which increases the risk of weight gain, and therefore overweight and obesity. A change in the type of fat consumed, and an increase in dietary fibre intake, protein from animal sources and micronutrients were also noted. Regardless of higher micronutrient intake, iron, zinc, calcium and the intake of some vitamins remains suboptimal to micronutrient recommendation in participants following a Westernised diet (Vorster *et al.*, 2011).

2.6.3 Early childhood development in South Africa

In response to the objectives set out in the National Development Plan and the National Integrated Early Childhood Development Policy, the annual South African Early Childhood Review provides data on the components regarded as essential for early childhood development in South Africa

(Hall *et al.*, 2019). Focused on the period from conception up to the age of six years, the domains informed on by this review include (1) primary level maternal and child health care, (2) social services and income support, (3) nutritional support, (4) support for the primary caregivers and (5) stimulation for early learning (Hall *et al.*, 2019). These five components are aligned with the Nurturing Care Framework published by the WHO, UNICEF and the World Bank Group (WHO *et al.*, 2018). Regardless of monitoring systems put in place during the latter years, information on child development in South Africa remains sparse. Based on available data, the picture portrayed by the 2019 review is bleak – this even though progress has been made since 2012 (Hall *et al.*, 2019). **Figure 2-5** provides an overview of child development in South Africa based on the key indicators as provided by the Early Childhood Review of 2019 (Hall *et al.*, 2019).

Primary level maternal and child health

- 31% of pregnant women are HIV positive
- 96% of all births occur in health facilities under the care of trained personnel
- 77% of children younger than the age of 1 years completed the primary immunisation course
- Infant mortality rate: 23 in 1000 live births
- Under-5 years mortality rate: 32 in 1000 live births

Stimulation for early learning

- 21% of children aged 0-2 years attend early childhood development programmes
- 69% of children aged 3-5 years attend early childhood development programmes
- More than 1 million children between 3 and 5 years do not have access to early childhood development programmes
- 78% of grade 4 children are not able to reach the lowest benchmark reading score



Nutritional support

- 33% of women of reproductive age have an iron deficiency, and 13% a vitamin A deficiency
- 15% of infants are born with a low birth weight
- 32% of children under the age of 6 months are exclusively breastfed
- In children younger than 5 years:
 - 27% are stunted
 - 6% are underweight
 - 13% are overweight
 - 61% has a form of anaemia
- 12% of children younger than 6 years live in households which experience hunger

Support for primary caregivers

- 47% of pregnant women suffer from antenatal depression, with up to 35% suffering from post-natal depression
- 67% of women attend antenatal care before 20 weeks pregnancy
- 76% of women had at least 4 antenatal care visits during their pregnancy

Social services and income support

- 81% of eligible children younger than the age of 6 years receive a child support grant
- One in three children experience sexual abuse or physical violence before the age of 18 years

Figure 2-5: Key indicators for early childhood development in South Africa

(Compiled from Hall *et al.*, 2019)

The majority of South African children are born in environments not conducive to optimal development (Hall *et al.*, 2019). Based on data published by the latest General Household Survey, two-thirds (65%) of children younger than the age of six years are living in households with a per capita income of less than the upper poverty line (Stats SA, 2018). The upper poverty line refers to the amount of money needed to cover nutritional and other basic needs (for example, clothing) of the household (Hall *et al.*, 2019). Of these, 2.5 million children younger than the age of six

years live below the food poverty line, and hence in households that do not have sufficient income to meet the basic nutritional needs. In 2017, just under a third (29%) of children were living in households in which no members were working (Stats SA, 2018). Poverty also contributes to caregivers not engaging in activities such as reading, storytelling and playing which are likely to support brain development. This is often due to a lack of time and/ or resources (for example, toys and books) to participate in these activities (Hall *et al.*, 2019).

Considering the components regarded as essential for early childhood development in South Africa, Hall *et al.* (2019) indicate that healthcare is the only component that delivers a decent level of service. As a result, South African “children are surviving but not thriving”. Although the South African government regards early childhood development as critical in addressing the inequalities in the country, much more needs to be done to realise the ambitious goals set out within the National Development Plan for 2030 (Hall *et al.*, 2019).

2.7 Conclusion

Maternal nutrition during pregnancy is regarded as an important and modifiable factor for fetal growth and early childhood development, and therefore also for the long-term health and well-being of the offspring. Most of the evidence informing this relationship is based on research focused on single nutrients. Lately, some studies have explored this relationship focusing on the diet as a whole through dietary pattern analysis. The majority of these studies were, however, conducted in high-income countries with data from low- and middle-income countries still being limited. Further exploration of the associations between the maternal diet as a whole during pregnancy using dietary patterns analysis is thus necessary, particularly in low- and middle-income countries.

Data on the adequacy and prudence of the maternal diet among pregnant South African women are also sparse. With South Africa being a highly unequal society and the majority of South African children being born into circumstances not conducive to optimal development, exploring maternal nutrition during pregnancy in relation to fetal growth and early childhood development can make a significant contribution towards the development of local strategies and hence the achievement of goals set out in the National Development Plan 2030.

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CHAPTER 3 ARTICLE 1

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A Priori and a Posteriori Dietary Patterns among Pregnant Women in Johannesburg, South Africa: The NuPED Study

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Abstract: Dietary pattern analyses allow assessment of the diet as a whole. Limited studies include both a priori and a posteriori dietary pattern analyses. This study aimed to explore the diet of pregnant women in urban South Africa through both a priori and a posteriori dietary pattern analyses and associated maternal and household factors. Dietary data were collected during early pregnancy using a quantified food frequency questionnaire from 250 pregnant women enrolled in the Nutrition During Pregnancy and Early Development (NuPED) cohort. A priori dietary patterns were determined using the Diet Quality Index-International (DQI-I), and a posteriori nutrient patterns using exploratory factor analysis. Based on the DQI-I, the study population followed a borderline low-quality diet. Three a posteriori nutrient patterns were identified: Pattern 1 “plant protein, iron, thiamine, and folic acid”; pattern 2 “animal protein, copper, vitamin A, and vitamin B₁₂”; pattern 3 “fatty acids and sodium”. Pattern 1 was associated with higher dietary quality ($p < 0.001$), lower maternal educational level ($p = 0.03$) and socioeconomic status ($p < 0.001$). Pattern 3 was significantly associated with lower dietary quality. The low dietary quality among pregnant women residing in urban South Africa should be addressed to ensure optimal maternal and offspring health outcomes.

Keywords: dietary patterns; a priori-defined dietary patterns; a posteriori-derived nutrient patterns; nutrition; pregnancy

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1. Introduction

Maternal nutrition during pregnancy is building the foundation for offspring growth, development, and health [1]. With fetal growth being greatly determined by nutrient supply from the mother [2,3], poor maternal diet and lifestyle choices can have a negative effect on pregnancy outcomes and the health of the offspring [4]. Literature reports both maternal under- and overnutrition to influence an offspring’s growth and development [5–7], with a poor maternal nutritional status during pregnancy affecting growth, neurodevelopment, and pulmonary, cardiometabolic, and immune function [6]. Long-term effects of maternal malnutrition include an increased risk for chronic illness later in life, and a decreased birth weight within the subsequent generation [6,8]. Pregnancy is thus regarded as a unique period in life during which the health and well-being of the next generation can be influenced [9].

Data on dietary intake among pregnant South African women are, however, sparse [10], with only four articles [11-14] having been published during the past decade. It is therefore yet unknown as to how the maternal diet affects health outcomes among the South African population. Although both Cormick et al. [11] and Krige et al. [13] found pregnant women to consume diets within the acceptable macronutrient distribution ranges but deficient in key micronutrients, they did not evaluate the overall quality of the diet.

Hu et al. [15] propose the use of dietary pattern analyses as a complementary method in assessing dietary intake. With nutrients not consumed in isolation but as part of a diet comprising of different foods, dietary pattern analyses account for the cumulative and interactive components of the diet to reflect the complexity of the human diet [15,16]. Dietary pattern analyses, therefore, provide a more predictive approach towards studying health outcomes [15] and is thus an imperative methodology in studying the role of the diet during pregnancy in maternal- and offspring health. However, it is only recently that dietary pattern analyses are being used to study the maternal diet during pregnancy. Most data available are from high-income countries with Raghavan et al. [17], indicating that the majority of research available is from healthy Caucasian women with access to medical care. Kibret et al. [18] concluded that research in low-income countries is needed to comprehend the impact of restricted resources on maternal dietary intake.

Dietary patterns can be derived either using the a priori or a posteriori method. The a priori method, also referred to as the hypothesis-oriented approach, entails the use of a dietary quality index to determine adherence to a predefined dietary pattern or dietary recommendation [15,19]. Conversely, the a posteriori method is a data-driven approach whereby dietary patterns are derived through statistical modeling techniques from empirical data [15,20]. A posteriori dietary patterns, therefore, provide insight into dietary behaviors as they reflect on actual food or nutrient intake [21]. Although these two methods are regarded to provide complementary information with regard to the overall diet [21], only a few studies [22-24] have used both methods to explore the maternal diet during pregnancy. Furthermore, to our knowledge, all studies reporting on a posteriori dietary patterns during pregnancy used foods or food groups as variables to determine patterns. Moskal et al. [20] though advocated for the use of nutrients as variables to determine empirical dietary patterns, as nutrients are universal in consumption, and allow for easier comparison between populations.

Only one study to date reported on maternal dietary patterns among pregnant South African women. Wrottesley et al. [14] found three distinct food patterns followed by their study population, namely, a “western”, “mixed”, and “traditional” food pattern. To address the sparsity of research, the purpose of this study was to explore the maternal diet of pregnant women residing in urban Johannesburg, South Africa, through both a priori and a posteriori dietary pattern analyses. Maternal- and household factors associated with these patterns are also determined.

2. Materials and Methods

2.1. Study Design and Participants

This study was embedded within the Nutrition During Pregnancy and Early Development (NuPED) cohort, a prospective study conducted in Johannesburg, South Africa. The details of the NuPED study have previously been described [25]. Data collection took place at early pregnancy (<18 weeks’ gestation), mid-pregnancy (± 22 weeks), late pregnancy (± 36 weeks), birth, as well as postnatally (6 weeks, 6 months, 7.5 months, and 12 months’ postnatal age). The current analysis reports on data collected at baseline (early pregnancy).

In brief, the recruitment of generally healthy urban pregnant women from primary health care clinics in Johannesburg took place between March 2016 and November 2017. Based on the South African socioeconomic profile, it is mainly the poorer proportion of the population that makes use of medical care provided by primary health care facilities

[26]. Women were regarded as eligible for inclusion if they were 18 to 39 years old, less than 18 weeks of gestation with a singleton pregnancy, born within South Africa or in a neighboring country (Lesotho, Swaziland, Zimbabwe, Botswana, or Namibia), and able to effectively communicate in the local languages (English, Afrikaans, Sotho, Zulu or Xhosa). Women born in a neighboring country had to have been living in South Africa for at least 12 months. Pregnant women diagnosed with a non-communicable disease (namely, hypertension, hypercholesterolemia, diabetes, and renal disease), infectious disease (namely, tuberculosis and hepatitis), or serious illness (namely, lupus, cancer, and psychosis) were excluded. Women were also excluded if they used illicit drugs (self-reported) and/or smoked (currently or in the past year). As South Africa has a high prevalence of human immunodeficiency virus (HIV) infections (22.7% of women of reproductive age [27]), HIV status was not considered exclusion criteria for enrolment.

Five-hundred and ninety-five pregnant women were invited to take part in the NuPED study of which 313 (53%) women volunteered. A further 63 women were excluded for not meeting the inclusion and exclusion criteria. In total, 250 pregnant women provided informed consent and were enrolled. Participants were followed-up at a tertiary hospital (Rahima Moosa Mother and Child Hospital) where data collection took place alongside routine maternal care. All 250 pregnant women completed data collection at baseline (<18 weeks' gestation).

2.2. Ethical Considerations

All women eligible and willing to partake in the study were provided with an informed consent form during recruitment. Written informed consent was obtained during the first study visit before any data were collected. The study was conducted according to the guidelines set out by the World Medical Association Declaration of Helsinki. Ethical approval was obtained from both the Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1) and the University of the Witwatersrand, Johannesburg (M 150968). The City of Johannesburg District Research Committee (Gauteng Department of Health) and the clinical manager at Rahima Moosa Mother and Child hospital provided permission for the study to take place in the relevant clinical setting.

2.3. Dietary Intake Assessment

Dietary intake was assessed during early pregnancy using an interviewer-administered quantified food-frequency questionnaire (QFFQ). The 140-item QFFQ was validated previously for energy and nutrient intake in an African population in South Africa [28], and its reproducibility was established [29,30]. Trained fieldworkers used standard probing questions [31] to inquire in as much detail as possible about the type/brand, cooking method, frequency, and amount of all foods and drinks consumed over the past four weeks. Household utensils, together with "dish-up and measure", food packaging material, and two- and three-dimensional food models, were used to quantify the portion sizes reported. Portion sizes were converted to grams by three registered dietitians/nutritionists using the South African Medical Research Council (SAMRC) Food Quantities Manual [32]. All foods and drinks were coded according to the South African Food Composition Database [33]. Daily energy, macro-, and micronutrient intake were calculated by the SAMRC by linking the coded and quantified dietary intake data to the most recent food composition database available at the time.

The daily dietary intake data are reflective of nutrient intake from food, excluding any micronutrient supplementation used. Maize meal and wheat flour are subject to mandatory micronutrient fortification as per South African legislation [34], and these fortified micronutrients (vitamin A, thiamine, riboflavin, niacin, pyridoxine, folic acid, iron, and zinc) were considered in the nutrient analysis. All participants provided complete dietary intake information.

2.3.1. A Priori Defined Dietary Patterns

The a priori dietary patterns were defined using the Diet Quality Index-International (DQI-I) [35]. Validated for international use and cross-national comparison of dietary quality [36,37], the DQI-I is regarded as a valuable tool for exploring diet quality related to nutrition transition as it accounts for both dietary concerns contributing to chronic disease and undernutrition. South Africa is known to be undergoing a rapid nutrition transition alongside urbanization [38], contributing to a growing burden of malnutrition within the country [39]. In addition, being sensitive towards various dietary practices and allowing for the use of country-specific recommendations in the evaluation of the diet, the DQI-I serves as a good set of guidelines according to which dietary quality of populations can be evaluated [35].

The DQI-I describes all dimensions of a high-quality diet, namely variety, adequacy, moderation, and overall balance. Each of these categories contains components (including both nutrient and food-group indicators) according to which the diet is assessed, allowing for users to determine the aspect(s) of the diet which most likely needs improvement [40]. The four categories of the DQI-I amount to an overall score of 100, with a higher score indicating greater adherence to a higher quality diet. According to the criteria given by Kim et al. [35], a score of less than 60 out of a possible 100 is indicative of a poor quality diet.

The daily dietary intake for the study participants, based on the QFFQ, was scored as specified by Kim et al. [35]. Adjustments to the DQI-I criteria were made as follows: (1) serving sizes were determined both according to the guidelines provided by the South African Food-Based Dietary Guidelines [41] and the United States' Food Guide Pyramid serving size definitions [42]; (2) adequacy of micronutrient intake (iron, calcium, and vitamin C) was based on the Dietary Reference Intakes for pregnant women [43]; (3) the cut-off values for sodium were adjusted as the QFFQ used does not report on discretionary salt intake. According to a paper by Wentzel-Viljoen et al. [44], it is estimated that about 60% of the total salt intake among the South African population is from processed foods, with the remainder (40%) being the discretionary use of salt during food preparation and meals. Based on this observation, the sodium cut-off values were adjusted as follows: ≤ 1440 mg (6 points), >1440 – 2040 mg (3 points) and >2040 mg (0 points). The DQI-I scoring criteria, together with how the study participants scored, are indicated in Table 1.

Table 1. Participant scores according to the Diet Quality Index-International (DQI-I) scoring criteria ($n = 250$) [35].

Category and Component		Scoring Criteria	n (%) ¹
Variety 0–20 points			
Overall food group variety (meat/poultry/fish/eggs; dairy beans; grain; fruit; vegetables)	0–15 points	>1 serving from each food group/d = 15	92 (37)
		Any 1 food group missing/d = 12	97 (39)
		Any 2 food groups missing/d = 9	38 (15)
		Any 3 food groups missing/d = 6	21 (8)
		>4 food groups missing/d = 3	2 (1)
		None from any food groups = 0	0
Within-group variety for protein source (meat; poultry; fish; dairy/beans; eggs)	0–5 points	>3 different sources/d = 5	137 (55)
		2 different sources/d = 3	72 (29)
		From 1 source/d = 1	31 (12)
		None = 0	10 (4)

Table 1. Participant scores according to the Diet Quality Index-International (DQI-I) scoring criteria (*n* = 250) [35]
(continued).

Category and Component		Scoring Criteria	n (%) ¹
Adequacy 0–40 points			
Vegetable group ^{2,3}	0–5 points	>3–5 servings/d = 5, 0 servings/d = 0	
		>100%	14 (6)
		50–100%	78 (31)
Fruit group ^{2,3}	0–5 points	<50%	158 (63)
		>2–4 servings/d = 5, 0 servings/d = 0	
		>100%	93 (37)
Grain group ^{2,3}	0–5 points	50–100%	97 (39)
		<50%	60 (24)
Fiber ^{2,3}	0–5 points	>6–11 servings/d = 5, 0 servings/d = 0	
		>100%	71 (28)
		50–100%	153 (61)
Protein	0–5 points	<50%	26 (10)
		>20–30 g/d = 5, 0 g/d = 0	
		>100%	149 (60)
Iron	0–5 points	50–100%	97 (39)
		<50%	4 (2)
Calcium	0–5 points	>10% of energy/d = 5, 0% of energy/d = 0	
		>100%	241 (96)
		50–100%	9 (4)
Vitamin C	0–5 points	<50%	0
		>100% RDA/d = 5, 0% RDA/d = 0	
		>100%	28 (11)
Sodium ⁴	0–6 points	50–100%	162 (65)
		<50%	60 (24)
		>100% AI/d = 5, 0% AI/d = 0	
Total fat	0–6 points	>100%	50 (20)
		50–100%	125 (50)
		<50%	75 (30)
Saturated fat	0–6 points	>100% RDA/d = 5, 0% RDA/d = 0	
		>100%	162 (65)
		50–100%	67 (27)
Cholesterol	0–6 points	<50%	21 (8)
		<20% of total energy/d = 6	15 (6)
		>20–30% of total energy/d = 3	88 (35)
Sodium ⁴	0–6 points	>30% of total energy/d = 0	147 (59)
		<7% of total energy/d = 6	39 (16)
		>7–10% of total energy/d = 3	111 (44)
Total fat	0–6 points	>10% of total energy/d = 0	100 (40)
		<300 mg/d = 6	102 (41)
		>300–400 mg/d = 3	46 (18)
Saturated fat	0–6 points	>400 mg/d = 0	102 (41)
		<2400 mg/d = 6	44 (18)
		>2400–3400 mg/d = 3	53 (21)
Cholesterol	0–6 points	>3400 mg/d = 0	153 (61)

Table 1. Participant scores according to the Diet Quality Index-International (DQI-I) scoring criteria ($n = 250$) [35]
(continued).

Category and Component		Scoring Criteria	n (%) ¹
Empty calories	0–6 points	<3% of total energy/d = 6	47 (19)
		>3–10% of total energy/d = 3	131 (52)
		>10% of total energy/d = 0	72 (29)
Overall balance 0–10 points			
Macronutrient ratio ⁵ (carbohydrate:protein:fat)	0–6 points	55~65:10~15:15~25 = 6	10 (4)
		52~68:9~16:13~27 = 4	26 (10)
		50~70:8~17:12~30 = 2	43 (17)
		Otherwise = 0	171 (68)
Fatty acid ratio (PUFA:MUFA:SFA)	0–4 points	P/S = 1~1.5 and M/S=1~1.5 = 4	54 (22)
		Else if P/S = 0.8~1.7 and M/S = 0.8~1.7 = 2	84 (34)
		Otherwise = 0	112 (45)

RDA: recommended dietary allowance; AI: adequate intakes; MUFA: monounsaturated fatty acids; SFA, saturated fatty acids; PUFA: polyunsaturated fatty acids; P/S, ratio of PUFA to SFA intake; M/S, ratio of MUFA to SFA intake. ¹ $n = 250$. ² Used as a continuous variable. ³ Based on 1700 kcal (7118 kJ)/2200 kcal (9211 kJ)/2700 kcal (11,304 kJ) diet; 1 kcal = 4.1868 kJ. ⁴ Based on sodium from food sources, excluding the discretionary use of table salt. ⁵ Ratio of energy from carbohydrate to protein to fat.

2.3.2. A Posteriori-Derived Nutrient Patterns

Nutrient patterns were determined from 22 nutrients by exploratory factor analysis [45]. Using the dietary intake data obtained from the QFFQ, total protein was divided into animal- and plant protein, and total fat into saturated-, monounsaturated- and polyunsaturated fatty acids. Carbohydrate intake was reported as total carbohydrate- and total sugar intake. The correlation structure of the nutrient intake data was explored for stability using the Spearman and Pearson correlation coefficients. The difference between the coefficients was minimal (less than 0.1) and, therefore, raw nutrient data were used for the analysis. Nutrient data were energy-adjusted according to the nutrient density model proposed by Willet et al. [46]. The principal factor method was applied with the correlation matrix, and the reliability of the factor analysis verified using the Kaiser–Meyer–Olkin measure of sampling adequacy and Bartlett’s test of sphericity. A Kaiser–Meyer–Olkin value of more than 0.5 and significance ($p < 0.05$) on Bartlett’s test were regarded as adequate. Factors were retained and interpreted for further analysis according to the eigenvalues (more than 1.00), scree plot inspection, the proportion of the total variance explained, and the natural interpretability of the factors. Retained factors (patterns) were rotated by Varimax (orthogonal) rotation for a simpler structure and to improve interpretation. Patterns were named and interpreted according to nutrients with an absolute factor loading of equal or greater than 0.40. A positive factor loading indicates a nutrient to be positively associated with the nutrient pattern and a negative loading that a nutrient is negatively associated with the pattern. Factor scores were calculated for each participant to indicate the degree towards which a participant’s nutrient intake conforms to the identified patterns. Factor scores were computed by weighting the standardized intakes of each nutrient with their factor loadings and then summing the nutrients within the respective patterns [47].

2.4. Assessment of Maternal and Household Factors

Several maternal and household factors were considered as possible determinants for dietary patterns during pregnancy. Interviewer-administered questionnaires were used to obtain sociodemographic and socioeconomic information, information on household-level food insecurity, medical history, and risk for prenatal depression and fatigue.

Sociodemographic and socioeconomic information obtained included maternal age, ethnicity, country of birth, marital status, educational level, employment status, and household beneficiaries of social support grants. Living standard data were also obtained to allow for classification of the socioeconomic status according to the Living Standard Measure in South Africa [48]. Food insecurity was assessed using the Community Childhood Hunger Identification Project (CCHIP) index [49,50]. This index investigates food insecurity as reflected by access to food on three levels, namely, the household-, adult/individual- and the child level. The extent of household food insecurity (CCHIP index total score) could not be determined as a great proportion of participants (n = 113; missing data n = 9) were not the parent or caretaker of a child in that household. We therefore only report on the three questions assessing household-level food insecurity, namely: (1) “does your household ever run out of money to buy food”; (2) “do you ever rely on a limited number of foods to feed your family because you are running out of money to buy food for a meal”; (3) “do you ever cut the size of meals or skip meals because there is not enough money for food” [49]. Households were regarded as “at risk for food insecurity” if the participant answered “yes” to one or more of the three questions; “no risk” was considered when the participant answered “no” to all three questions.

Medical history considered in this study included parity, pregnancy symptoms (nausea and/or vomiting experienced), and HIV status (routinely tested as part of antenatal care). Participants recorded pregnancy symptoms (nausea and/or vomiting) during the seven days after enrolment using a pictorial morbidity calendar. Gestational age was confirmed using fetal ultrasonography during early pregnancy. Prenatal fatigue and depression were assessed using the Multidimensional Assessment of Fatigue (MAF) scale [51] and the Edinburgh Postnatal Depression Score (EPDS) [52,53], respectively. MAF measures the severity of fatigue, distress, and the degree to which it influences daily activities. The global fatigue index (GFI) was calculated with higher scores indicating higher levels of fatigue, and a cut-off of 28 out of a possible 50 was used to define women with prenatal fatigue [54]. A cut-off value of ≥ 9 out of a possible 30 was used for the EPDS to indicate the risk for depressive symptoms [53].

Maternal anthropometric measures were also assessed although not considered as possible determinants for the dietary patterns in this analysis. The exclusion of maternal weight as a determinant is based on the observation by Doyle et al. [55] that the relationship between maternal weight and dietary patterns is more difficult to interpret as maternal weight can serve both as an outcome and a determinant of dietary patterns. Maternal height, weight, and mid-upper arm circumference (MUAC) were assessed during early pregnancy using the standardized methods indicated by the International Society for the Advancement of Kinanthropometry [56]. All measurements were taken twice and recorded to the nearest 0.05 kg for weight and 0.1 cm for height and MUAC. A calibrated scale was used for weight measurements (Seca 813, Hamburg, Germany), a mobile stadiometer for height (Seca 213, Hamburg, Germany), and a non-stretchable metal tape for the MUAC. As weight gain and edema during pregnancy decrease the reliability of the body mass index (BMI) [57], maternal weight at enrolment was adjusted (assuming that 2.5 kg was gained during the first 14 weeks of gestation) according to the gestational weight gain guidelines provided by the Institute of Medicine [58] to calculate an approximate pre-pregnancy BMI. The MUAC cut-offs for underweight and obesity as indicated by the South African Maternity Care guidelines [59] were also considered to evaluate maternal nutritional status, i.e., ≤ 23 cm considered as underweight and ≥ 33 cm as obese.

2.5. Statistical Analysis

The sample size was set as 250 participants; calculations of the sample size have been previously published [25]. IBM SPSS version 26 (SPSS Inc., Chicago, IL, USA) was used for data processing and statistical analysis. Dietary data were captured in Microsoft Excel, with all other raw data captured in Microsoft Access (Microsoft Corporation, Washington,

DC, USA). All dietary data were double-checked to ensure accuracy of food codes used and amounts captured. Twenty percent of all other raw data were randomly checked for correctness.

Data were tested for normality using histograms, q-q plots, and the Shapiro–Wilk test. For normally distributed data, continued variables are reported as mean and standard deviation, and for non-normally distributed data as the median and interquartile range (IQR). Categorical data are reported as frequencies and percentages. Both the DQI-I total scores and nutrient pattern factor scores were divided into tertiles for further analysis. To determine food groups associated with each nutrient pattern, analysis of variance (ANOVA) was used to determine the difference between each food group and the nutrient pattern tertiles. The 140-items of the QFFQ were aggregated into 39 food groups expressed as a percentage of the total energy intake (Supplementary Tables S1–S3). ANOVA was also used to determine differences between DQI-I scores and the nutrient pattern tertiles. In both instances, post-hoc comparisons for unequal variance were carried out using the Games–Howell test.

Hierarchical multiple linear regression models were applied to test for associations between the dietary patterns and maternal- and household factors. Hierarchical steps were based on the conceptual framework for multiple determinants of diet during pregnancy as proposed by Doyle et al. [55] and were as follows: step 1 investigates all sociodemographic factors (maternal age, level of education, and marital status), step 2 the sociodemographic and socioeconomic factors (employment, social grants received by the household, household-level food insecurity, and living standard measure), step 3 the sociodemographic-, socioeconomic-, pregnancy-related factors (parity, nausea- and/or vomiting experienced) and HIV status, and step 4 the sociodemographic-, socioeconomic-, pregnancy-related factors, HIV status and psychological factors. Significance was defined as $p < 0.05$.

3. Results

3.1. Characteristics of Study Participants

Characteristics of the study participants at early pregnancy are shown in Table 2. The median (IQR) age was 27 (24–32) years and the median length of gestation at enrolment 14 (12–16) weeks. Most enrolled women were of black-African descent (88%), followed by women of mixed ancestry (11%). The distribution with regard to the number of previous pregnancies was equal as the same proportion of women (35%) were primiparous and multiparous, respectively. A quarter of the women (26%) had a positive HIV status, and almost half of the women reported experiencing nausea (52%) and vomiting (48%) within seven days after enrolment. Based on the calculated pre-pregnancy BMI, half of the women (52%) entered pregnancy either being overweight or obese. This was confirmed by the MUAC categories which indicated, when compared to the BMI categories, near similar proportions of the study participants to be underweight (4%) and obese (26%). A quarter of the study participants presented with a more severe level of prenatal fatigue (26%) and risk for prenatal depression (26%), respectively.

A quarter of women (23%) reported having tertiary education, with 73% having some form of secondary schooling. Half of the participants (49%) were unemployed at the time of the study, with two-thirds (67%) indicating that no social grants were received by the household. Almost half of all households (47%) were though at risk for food insecurity. Most women (59%) were categorized as have a medium living standard.

Table 2. Characteristics of study participants ($n = 250$) at early pregnancy (<18 weeks' gestation).

Subject Characteristics	Total Sample ¹
	Median (IQR) or n (%)
Age (years)	27 (24–32)
Gestational age (weeks)	14 (12–16)
Parity	
Nulliparous	74 (30)
Primiparous	88 (35)
Multiparous	88 (35)
Calculated pre-pregnancy BMI (kg/m²) ²	25 (22–30)
Underweight (<18.5 kg/m ²)	14 (6)
Normal weight (18.5–24.99 kg/m ²)	105 (42)
Overweight (25–29.99 kg/m ²)	73 (29)
Obese (≥ 30 kg/m ²)	57 (23)
MUAC (cm)	30 (27–33)
Underweight or chronic wasting (≤ 23 cm)	10 (4)
Normal weight and overweight (23.1–32.9 cm)	176 (70)
Obese (≥ 33 cm)	64 (26)
HIV status	
Positive	64 (26)
Negative	186 (74)
Vomiting ³	
Experienced vomiting	111 (48)
Number of days	2 (1–4)
Nausea ³	
Experienced nausea	122 (52)
Number of days	2 (1–4)
Ethnicity	
Black African	219 (88)
Mixed ancestry	28 (11)
Indian	1 (<1)
White	1 (<1)
Country of birth	
South Africa	172 (72)
Zimbabwe	60 (25)
Lesotho	4 (2)
Swaziland	3 (1)
Highest level of education	
Primary/None	9 (4)
Grade 8–10	37 (15)
Grade 11–12	145 (58)
Tertiary	58 (23)
Employment	
Unemployed	123 (49)
Self-employed	11 (4)
Wage-earner	111 (45)
Other	4 (2)

Table 2. Characteristics of study participants ($n = 250$) at early pregnancy (<18 weeks' gestation) (continued).

Subject Characteristics	Total Sample ¹ Median (IQR) or n (%)
Marital status	
Unmarried	100 (40)
Married	68 (27)
Living together	57 (23)
Traditional marriage ⁴	22 (9)
Divorced/Separated	2 (1)
Social grant(s) received by household	
None	162 (67)
Child support	69 (29)
Social relief	3 (1)
Disability	2 (1)
Old-age pension	6 (3)
Living standard measure (LSM)	
Low (LSM 1–4)	17 (7)
Medium (LSM 5–7)	148 (59)
High (LSM 8–10)	85 (34)
Household-level food insecurity ⁵	
No risk for household food insecurity	130 (53)
At risk for household food insecurity	114 (47)
Risk for prenatal depression ⁶	5 (2–9)
No/low risk for prenatal depression	183 (74)
At risk for prenatal depression	63 (26)
Risk for prenatal fatigue ⁷	19 (1–28)
No/low severity for prenatal fatigue (GFI < 27.9)	179 (74)
More severe level of prenatal fatigue (GFI score ≥ 28)	62 (26)

IQR: interquartile range; BMI: body mass index; MUAC: mid-upper arm circumference; HIV: human immunodeficiency virus; LSM: living standard measure; CCHIP: Community Childhood Hunger Identification Project; EPDS: Edinburgh Postnatal Depression Score; GFI: Global Fatigue Index. Data presented as n (%) for categorical variables and median (IQR) for continuous variables.

¹Missing data: approximate pre-pregnancy BMI ($n = 1$); vomiting and nausea ($n = 17$); ethnicity ($n = 1$); country of birth ($n = 11$); level of education ($n = 1$); employment ($n = 1$); marital status ($n = 1$); social grants received by household ($n = 8$); household-level food security ($n = 6$); risk for prenatal depression ($n = 4$); risk for prenatal fatigue ($n = 9$). ²Maternal weight was adjusted according to the Institute of Medicine's guidelines [58] for gestational weight gain to determine an approximate pre-pregnancy BMI. ³Nausea and vomiting experienced within 7 days after enrolment. ⁴A traditional marriage does not require approval from an officer of validation but is rather entered between parties based on tradition. Recognized under customary law in South Africa, traditional marriage also allows for polygamous marriage. ⁵Determined using the CCHIP index's questions on household-level food insecurity. ⁶Determined using the Edinburgh Postnatal Depression Score [52,53]; a score of 9 or more out of a possible 30 is indicative of a risk for depressive symptoms. ⁷Determined using the Multidimensional Assessment of Fatigue scale from which the Global Fatigue Index was calculated [51]; a cut-off value of 28 out of a possible 50 was used [54], with a higher score indicating greater severity of fatigue.

3.2. Dietary Pattern Analysis

3.2.1. A Priori Defined Dietary Patterns

The median total DQI-I score was 60 (54–66) out of a possible 100 (Table 3). The “variety” category had the highest achieved score, followed by the “adequacy” and “moderation” categories. The “overall balance” category was the weakest component of the diet, with a median score of 2 (0–4) out of a possible 10.

About one-third (37%) of participants included at least one serving of each of the five food groups considered for overall food-group variety (meat/poultry/fish/eggs; dairy/beans; grain; fruit and vegetables), with 55% consuming protein from more than three different protein sources per day (Table 1). Vegetable intake was poorer than fruit intake; 63% of the women consumed less than half of the recommended amount of vegetables per day, while 24% consumed less than half of the recommended amount of fruit. A larger percentage of the participants had an intake of more than 50% of the recommendation for grain, fiber, protein, iron, calcium, and vitamin C. Only 11% and 20% achieved the Dietary Reference Intakes for pregnant women for iron and calcium, respectively, from food sources. With regard to the “moderation” category, most participants scored poorly for total fat, saturated fat, and sodium intakes. More than half (59%) of the women had a total fat intake of more than 30% of the total energy intake, with 40% of participants having a daily saturated fat intake of more than 10% of the total energy intake. Almost two-thirds of participants (61%) consumed foods with high sodium content. The high intake of total fat was reflected in the “overall balance” category as a high percentage of participants had a macronutrient (68%) and fatty acid (45%) intake outside of the ratios considered for optimal health.

Table 3. Median (IQR) scores for DQI-I components ($n = 250$).

Category and Component	Score Range (Points)	Median (IQR)
Total DQI score	0–100 points	60 (54–66)
Variety	0–20 points	17 (14–20)
Overall food group variety	0–15 points	12 (12–15)
Within-group variety for protein sources	0–5 points	5 (3–5)
Adequacy	0–40 points	31 (28–33)
Vegetable group	0–5 points	2 (1–3)
Fruit group	0–5 points	4 (3–5)
Grain group	0–5 points	4 (3–5)
Fiber	0–5 points	5 (4–5)
Protein	0–5 points	5 (5–5)
Iron	0–5 points	3 (3–4)
Calcium	0–5 points	3 (2–5)
Vitamin C	0–5 points	5 (4–5)
Moderation	0–30 points	9 (6–15)
Total fat	0–6 points	0 (0–3)
Saturated fat	0–6 points	3 (0–3)
Cholesterol	0–6 points	3 (0–6)
Sodium ¹	0–6 points	0 (0–3)
Empty calories	0–6 points	3 (0–3)
Overall balance	0–10 points	2 (0–4)
Macronutrient ratio	0–6 points	0 (0–2)
Fatty acid ratio	0–4 points	2 (0–2)

IQR: interquartile range; DQI-I: Diet Quality Index-International. ¹ Based on sodium from food sources, excluding the discretionary use of table salt.

3.2.2. A Posteriori-Derived Nutrient Patterns

Three nutrient patterns were retained by exploratory factor analysis, explaining 57% of the total variance in nutrient intake (eigenvalue > 2.5). Both the Kaiser–Meyer–Olkin measure (0.7) and Bartlett’s test ($p < 0.001$) indicated the analysis to be appropriate for the study sample. Patterns were named according to the dominant nutrients (higher factor loadings) within each factor. The factor loadings and names assigned to each nutrient pattern are indicated in Table 4. The three nutrient patterns were further explored by determining associations between nutrient pattern tertiles and the consumption of food groups based on the percentage of total energy intake.

Pattern 1, named “plant protein, iron, thiamine, and folic acid”, had high positive loadings for plant protein, carbohydrates, fiber, iron, zinc, thiamine, niacin, vitamin B₆ and folic acid. Animal protein, saturated- and monounsaturated fatty acids, and calcium were negatively associated with this pattern. All micronutrients used for fortification according to South African legislation [34], except for vitamin A and riboflavin, reflected high positive loadings on this factor matrix. Pattern 1 explained 27% of the total variance in nutrient intakes. Based on the associations of this nutrient pattern with the food groups, intake of maize, whole wheat- and brown bread, and legumes were positively associated with nutrient pattern 1 (Supplementary Table S1) as intake of these food groups was significantly higher across the nutrient pattern tertiles (higher tertile indicating that women are having a dietary intake closer to the respective nutrient pattern (higher factor scores)). Intake of maize increased the most from tertile 1 to tertile 3. Conversely, the intake of cakes, biscuits and pudding, cheese, dairy, fatty foods, fruit juice, processed- and red meat, rice and pasta, salad oils, salad vegetables, sugar-sweetened dairy and -drinks, and sweets and chocolates were significantly lower across the nutrient pattern tertiles. Nutrient pattern 1 is therefore reflective of a “fortified grain and legume” dietary pattern.

Pattern 2, named “animal protein, copper, vitamin A, and vitamin B₁₂”, had high positive loadings for animal protein, cholesterol, zinc, copper, vitamin A, riboflavin, and vitamin B₁₂, and explained 18% of the total variance. Cheese, chicken, eggs, fish and seafood, nuts and nut spreads, and organ meat and offal were positively associated with nutrient pattern 2 as the intake of these foods was higher across the nutrient pattern tertiles (Supplementary Table S2). Intake of fatty foods, roast potatoes and chips, sugar, and white bread was, though, significantly lower across the tertiles of nutrient pattern 2. Nutrient pattern 2 is, therefore, reflective of an “animal products” dietary pattern.

Pattern 3, named “fatty acids and sodium”, explained 12% of the variance and had high positive loadings for saturated-, monounsaturated- and polyunsaturated fatty acids, sodium, and vitamin E. Intake of cheese, fatty foods, nuts and nut spreads, processed- and red meat, salad oils, and sugar-sweetened drinks was positively associated with the nutrient pattern 3 (Supplementary Table S3), with the intake of fatty foods increasing the most across the tertiles. Intake of dairy, fresh and dried fruit, maize, and other cooked porridges, and sugar was significantly lower across pattern 3 tertiles. Nutrient pattern 3 is, therefore, representative of a “fatty- and processed foods” dietary pattern.

3.2.3. Associations between the a Priori and a Posteriori Dietary Patterns

Table 5 indicates the median DQI-I scores for each of the nutrient patterns. One-way ANOVA with post-hoc comparisons indicated the DQI-I total scores (higher scores indicative of higher dietary quality) to significantly increase across the tertiles (tertile 3 presenting higher factor loadings) of nutrient pattern 1 (plant protein, iron, thiamine, and folic acid (fortified grain and legume)), but significantly decrease across nutrient pattern 3 (fatty acids and sodium (fatty- and processed foods)). The category scores “moderation” and “overall balance” were significantly higher across nutrient pattern 1, but significantly lower across the tertiles of nutrient pattern 2 (animal protein, copper, vitamin A, and vitamin B₁₂ (animal products)) and nutrient pattern 3. Conversely, the scores for the “variety” category were higher across the tertiles of nutrient pattern 2 ($p < 0.001$) and nutrient pattern 3 ($p < 0.001$), but significantly lower across nutrient pattern 1.

Table 4. Nutrient patterns and factor loadings extracted using factor analysis during early pregnancy ($n = 250$).

Nutrients and Variance Explained	Factors (Nutrient Patterns) ¹		
	Factor 1	Factor 2	Factor 3
	(Plant Protein, Iron, Thiamine, and Folic Acid)	(Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂)	(Fatty Acids and Sodium)
Animal protein	-0.46	0.53	0.32
Plant protein	0.86	-0.09	-0.00
Saturated fat	-0.68	0.08	0.44
Monounsaturated fat	-0.51	0.08	0.67
Polyunsaturated fat	-0.15	-0.08	0.57
Cholesterol	-0.09	0.58	0.32
Carbohydrates	0.61	-0.21	-0.70
Total sugars	-0.23	0.05	-0.68
Total fiber	0.70	0.10	-0.24
Calcium	-0.44	0.20	-0.34
Iron	0.76	0.35	0.02
Sodium	0.04	0.01	0.64
Zinc	0.45	0.44	0.30
Copper	0.25	0.79	-0.08
Vitamin A	0.12	0.81	-0.07
Thiamine	0.77	0.10	-0.05
Riboflavin	0.01	0.63	-0.14
Niacin	0.54	0.39	0.31
Vitamin B ₆	0.67	0.03	0.26
Folic acid	0.73	0.36	-0.07
Vitamin B ₁₂	0.10	0.86	-0.03
Vitamin E	0.04	0.03	0.41
% of variance			
Total variance: 57%	27%	18%	12%

¹ Factor analysis performed on 22 nutrients; estimates presented after rotation. Nutrients considered to have a strong association with the nutrient patterns (factor loading ≤ 0.4 and ≥ 0.4) are indicated in bold.

Table 5. DQI-I total and category scores by tertiles of nutrient pattern scores ($n = 250$).

DQI-I Categories	Nutrient Pattern 1 Scores				Nutrient Pattern 2 Scores				Nutrient Pattern 3 Scores			
	(Plant Protein, Iron, Thiamine, and Folic Acid)				(Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂)				(Fatty Acids and Sodium)			
	Tertile 1	Tertile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3	
	Median (IQR)	Median (IQR)	Median (IQR)	<i>p</i> -Value	Median (IQR)	Median (IQR)	Median (IQR)	<i>p</i> -Value	Median (IQR)	Median (IQR)	Median (IQR)	<i>p</i> -Value
Total score	56.0 ^c (52.2–60.4)	60.4 ^b (55.3–64.9)	65.2 ^a (58.3–71.3)	<0.001	60.4 (52.7–65.8)	60.4 (54.7–65.2)	59.5 (54.0–66.2)	0.889	65.8 ^a (58.0–73.1)	59.8 ^b (54.8–64.1)	56.4 ^c (49.9–60.5)	<0.001
Variety	17.0 ^a (15.0–20.0)	17.0 ^a (14.0–20.0)	15.0 ^b (10.0–17.0)	<0.001	15.0 ^b (11.0–18.0)	17.0 ^a (14.0–20.0)	17.0 ^a (15.0–20.0)	<0.001	15.0 ^b (10.0–18.0)	17.0 ^a (15.0–20.0)	17.0 ^a (14.0–20.0)	<0.001
Adequacy	30.3 (27.8–33.9)	30.8 (27.6–35.1)	31.4 (29.0–32.7)	0.980	29.8 ^b (27.3–32.5)	31.0 ^{a,b} (28.2–33.2)	31.7 ^a (29.0–35.1)	0.040	30.3 (27.4–32.5)	31.3 (28.4–34.6)	31.8 (28.0–34.2)	0.168
Moderation	6.0 ^c (3.0–9.0)	9.0 ^b (6.0–15.0)	15.0 ^a (9.0–21.0)	<0.001	12.0 ^a (6.0–18.0)	9.0 ^b (6.0–15.0)	9.0 ^b (3.0–15.0)	0.009	18.0 ^a (12.0–24.0)	9.0 ^b (6.0–12.0)	6.0 ^c (3.0–9.0)	<0.001
Overall balance	0.0 ^c (0.0–2.0)	2.0 ^b (2.0–4.0)	4.0 ^a (2.0–6.0)	<0.001	2.0 (2.0–4.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)	0.045	4.0 ^a (2.0–6.0)	2.0 ^b (0.0–4.0)	1.0 ^c (0.0–2.0)	<0.001

IQR: interquartile range. Significant difference between the median of the tertiles indicated in bold ($p < 0.05$) (according to Welsh test). Medians with a different letter in their superscript are significantly different at the 0.05 level according to the Games–Howell test.

3.3. Factors Associated with Dietary Patterns

Table 6 shows the multiple regression coefficients of the dietary patterns retained for the maternal and household factors. When considering the sociodemographic-, socioeconomic-, pregnancy-related factors and HIV status (steps 1 to 3), having a maternal age equal to and older than 27 years (step 3: $\beta = -1.9$, $SE = 0.9$, $p = 0.046$), a lower level of education (<Grade 10) (step 3: $\beta = 2.0$, $SE = 1.0$, $p = 0.034$) and a lower level of living standard (step 3: $\beta = 2.0$, $SE = 1.0$, $p = 0.049$) were significantly associated with higher scores for nutrient pattern 1 (plant protein, iron, thiamine and folic acid (fortified grain and legume)). However, the association with maternal age did not hold when all maternal and household factors were included in the model (step 4), resulting in women of a lower education ($\beta = 2.1$, $SE = 1.0$, $p = 0.032$) and living standard measure ($\beta = 2.0$, $SE = 1.0$, $p = 0.049$) to have higher scores for nutrient pattern 1. For nutrient pattern 3 (fatty acids and sodium (fatty- and processed foods)), only step 1 (sociodemographic factors) had a significant model fit, but none of these factors were significantly associated with nutrient pattern 3 scores.

A maternal age equal to and older than 27 years was also significantly associated with the DQI-I. This association was retained throughout model steps 1 to 3 (step 4 had a non-significant model fit), indicating women equal and older than 27 years of age among our study population to have greater adherence to a diet with a higher dietary quality (step 3: $\beta = -5.8$, $SE = 1.6$, $p = 0.001$). No other maternal and household factors were significantly associated with the dietary patterns among our study population.

Table 6. Associations of maternal and household factors with nutrient patterns and DQI-I ¹.

	Nutrient Pattern 1 Plant protein, iron, thiamine, and folic acid			Nutrient Pattern 2 Animal protein, copper, vitamin A, and vitamin B ₁₂			Nutrient Pattern 3 Fatty acids and sodium			DQI-I		
	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value
Step 1 ²												
Maternal age												
<27 years vs. ≥27 years (RC)	-2.5	0.8	0.002	0.0	0.5	1.000	0.8	0.4	0.060	-5.0	1.3	<0.001
Education												
≤ Grade 10	2.4	1.0	0.012	-0.4	0.6	0.496	-0.8	0.5	0.128	-0.7	1.6	0.678
Grade 11–12 (RC)												
Tertiary	-0.9	0.8	0.291	-0.2	0.5	0.695	0.6	0.5	0.168	-1.3	1.4	0.359
Marital status												
Married/cohabitating vs. Single (RC)	0.7	0.7	0.321	-1.0	0.5	0.042	-0.6	0.4	0.157	-0.5	1.2	0.699
Step 2 ²												
Maternal age												
<27 years vs. ≥27 years (RC)	-2.1	0.8	0.009	-0.2	0.5	0.749	0.7	0.4	0.103	-4.8	1.4	0.001
Education												
≤ Grade 10	1.9	1.0	0.051	-0.3	0.6	0.593	-0.8	0.5	0.149	-0.2	1.6	0.483
Grade 11–12 (RC)												
Tertiary	-0.4	0.9	0.687	-0.4	0.6	0.518	0.6	0.5	0.186	-0.8	1.5	0.616
Marital status												
Married/cohabitating vs. Single (RC)	0.7	0.8	0.336	-0.9	0.5	0.067	-0.6	0.4	0.154	-0.5	1.3	0.678
Employment												
Unemployed vs. Employed (RC)	-0.8	0.7	0.256	0.6	0.5	0.209	0.4	0.4	0.290	-0.5	1.2	0.707
Grants received by the household												
Not received vs. Received (RC)	-0.9	0.8	0.279	-0.2	0.5	0.728	0.0	0.4	0.934	-1.0	1.4	0.451

Table 6. Associations of maternal and household factors with nutrient patterns and DQI-I ¹ (continued).

	Nutrient Pattern 1 Plant protein, iron, thiamine, and folic acid			Nutrient Pattern 2 Animal protein, copper, vitamin A, and vitamin B ₁₂			Nutrient Pattern 3 Fatty acids and sodium			DQI-I		
	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value
Household-level food insecurity												
No risk vs. At risk (RC)	-0.8	0.7	0.282	-0.1	0.5	0.823	-0.2	0.4	0.687	-1.8	1.3	0.170
Living standard measure												
Low living standard measure (1–5)												
vs.												
High living standard measure (6–10) (RC)	2.1	1.0	0.030	-0.9	0.6	0.159	-0.3	0.5	0.618	0.8	1.7	0.639
Step 3 ²												
Maternal age												
<27 years vs. ≥27 years (RC)	-1.9	0.9	0.046	0.1	0.6	0.918	0.6	0.5	0.249	-5.8	1.6	0.001
Education												
≤ Grade 10	2.0	1.0	0.034	-0.3	0.6	0.620	-0.8	0.5	0.129	-0.9	1.7	0.593
Grade 11–12 (RC)												
Tertiary	-0.1	0.9	0.889	-0.2	0.6	0.701	0.6	0.5	0.257	-1.1	1.6	0.501
Marital status												
Married/cohabitating vs. Single (RC)	1.2	0.8	0.128	-0.7	0.5	0.161	-0.7	0.4	0.084	-0.5	1.3	0.699
Employment												
Unemployed vs. Employed (RC)	-0.8	0.7	0.278	0.5	0.5	0.262	0.4	0.4	0.316	-0.1	1.3	0.920
Grants received by the household												
Not received vs. Received (RC)	-1.0	0.8	0.219	-0.3	0.5	0.587	0.1	0.4	0.849	-0.7	1.4	0.611
Household-level food insecurity												
No risk vs. At risk (RC)	-0.8	0.7	0.278	-0.1	0.5	0.880	-0.2	0.4	0.710	-1.9	1.3	0.139

Table 6. Associations of maternal and household factors with nutrient patterns and DQI-I ¹ (continued).

	Nutrient Pattern 1 Plant protein, iron, thiamine, and folic acid			Nutrient Pattern 2 Animal protein, copper, vitamin A, and vitamin B ₁₂			Nutrient Pattern 3 Fatty acids and sodium			DQI-I		
	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value
Living standard measure												
Low living standard measure (1–5) vs. High living standard measure (6– 10) (RC)	2.0	1.0	0.049	–1.1	0.6	0.101	–0.3	0.5	0.593	1.0	1.7	0.572
Parity												
Nulliparous vs. Primi- and multiparous (RC)	–1.1	1.0	0.253	–0.6	0.6	0.341	0.5	0.5	0.385	1.3	1.7	0.455
Nausea experienced ³												
Yes vs. No (RC)	–1.0	0.7	0.185	–0.3	0.5	0.591	0.3	0.4	0.414	–0.7	1.3	0.558
Vomiting experienced ³												
Yes vs. No (RC)	0.6	0.7	0.793	0.5	0.5	0.263	0.1	0.4	0.765	–0.2	1.3	0.862
HIV status												
Negative vs. Positive (RC)	1.6	0.8	0.055	0.3	0.5	0.602	–0.6	0.5	0.205	1.9	1.4	0.180
Step 4 ²												
Maternal age												
<27 years vs. ≥27 years (RC)	–1.9	0.9	0.050	0.1	0.6	0.862	0.6	0.5	0.253	–5.7	1.6	0.001
Education												
≤ Grade 10	2.1	1.0	0.032	–0.3	0.6	0.685	–0.8	0.5	0.131	–0.8	1.7	0.612
Grade 11–12 (RC)												
Tertiary	–0.1	0.9	0.914	–0.2	0.6	0.744	0.6	0.5	0.262	–1.0	1.6	0.513
Marital status												
Married/cohabitating vs. Single (RC)	1.2	0.8	0.120	–0.7	0.5	0.153	–0.7	0.4	0.083	–0.5	1.4	0.699
Employment												
Unemployed vs. Employed (RC)	–0.8	0.7	0.297	0.5	0.5	0.269	0.4	0.4	0.331	–0.1	1.3	0.914

Table 6. Associations of maternal and household factors with nutrient patterns and DQI-I ¹ (continued).

	Nutrient Pattern 1 Plant protein, iron, thiamine, and folic acid			Nutrient Pattern 2 Animal protein, copper, vitamin A, and vitamin B ₁₂			Nutrient Pattern 3 Fatty acids and sodium			DQI-I		
	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value
Grants received by the household												
Not received vs. Received (RC)	-1.0	0.8	0.206	-0.3	0.5	0.501	0.1	0.4	0.849	-0.8	1.4	0.590
Household-level food insecurity												
No risk vs. At risk (RC)	-0.8	0.7	0.292	0.0	0.5	0.953	-0.2	0.4	0.712	-1.9	1.3	0.147
Living standard measure												
Low living standard measure (1–5) vs.	2.0	1.0	0.049	-1.2	0.6	0.068	-0.3	0.5	0.577	0.9	1.7	0.605
High living standard measure (6– 10) (RC)												
Parity												
Nulliparous vs. Primi- and multiparous (RC)	-1.1	1.0	0.238	-0.6	0.6	0.314	0.5	0.5	0.379	1.2	1.7	0.464
Nausea experienced ³												
Yes vs. No (RC)	-0.9	0.7	0.239	-0.1	0.5	0.789	0.3	0.4	0.436	-0.6	1.3	0.612
Vomiting experienced ³												
Yes vs. No (RC)	0.6	0.7	0.454	0.5	0.5	0.258	0.1	0.4	0.751	-0.2	1.3	0.862
HIV status												
Negative vs. Positive (RC)	1.5	0.8	0.073	0.3	0.5	0.617	-0.6	0.5	0.230	1.9	1.5	0.188
Risk for prenatal depression												
At risk vs. No risk (RC)	0.8	1.5	0.598	2.6	1.0	0.008	0.1	0.8	0.891	1.8	2.6	0.485
Risk for prenatal fatigue												
Global Fatigue Index (continues)	0.6	0.8	0.445	0.1	0.5	0.873	-0.2	0.4	0.716	0.1	1.4	0.961

β : unstandardized coefficients; SE: standard errors; RC: reference category after categorical coding in regression analysis (dummy variables); HIV: human immunodeficiency virus. ¹Grey sections indicates regression coefficients of models which did not have a significant model fit. ²Step 1: sociodemographic factors; step 2: sociodemographic and socioeconomic factors; step 3: sociodemographic-, socioeconomic-, and pregnancy-related factors and HIV status; step 4: sociodemographic-, socioeconomic-, and pregnancy-related factors, HIV status and psychological factors. ³Nausea and vomiting experienced within 7 days after enrolment. Significance ($p < 0.05$) indicated in bold.

4. Discussion

We explored the diet of pregnant women living in an urban South African setting during early pregnancy using both a priori and a posteriori dietary pattern analyses. Three distinct dietary patterns were identified, namely, pattern 1 “plant protein, iron, thiamine, and folic acid”; pattern 2 animal protein, copper, vitamin A, and vitamin B₁₂”; pattern 3 “fatty acids and sodium”. These nutrient patterns, based on their associations with food groups, represent a “fortified grain and legume”, “animal products”, and “fatty- and processed foods” dietary pattern, respectively. Based on the a priori index, our study population had a borderline low-quality diet (DQI-I total score of 60). Nutrient pattern 1 was positively associated and nutrient pattern 3 negatively associated with dietary quality indicated by the a priori index. Possible determinants for the dietary patterns were found to be maternal age, level of education, and socioeconomic status.

The borderline low-quality diet observed in this study population can be attributed to low scores on the “moderation” and “overall balance” categories of the DQI-I as most participants consumed a diet high in total- and saturated fat, and foods high in sodium. Poor scorings on the total- and saturated fat categories could be due to the use of the stringent cut-off values proposed by Kim et al. [35]. However, these cut-off values are in line with that advocated by the South African Food-Based Dietary Guidelines and were chosen to emphasize the importance of moderate fat intake. A high intake of total fat among pregnant urban South African women was also reported by Krige et al. [13] with two-thirds of their study population consuming more than 30% of their total energy intake from fat. Jordaan [60] indicated similar findings when evaluating the dietary intake among two ethnic groups (including males and females between the ages of 20 and 30 years) of varying socioeconomic backgrounds residing in urban areas. A fat intake of more than 30% of the total energy intake among the urban South African population was indicated by Vorster et al. [38] as an adverse effect of the nutrition transition occurring due to urbanization. A high sodium intake among the South African population is also well described [61,62], hence the implementation of the mandatory legislation in 2016 to reduce the sodium content of certain foodstuffs [63].

In a recent publication, the World Health Organization recommended the intake of total fat to not exceed 30% of total energy as a higher fat intake is often a contributing factor towards unhealthy weight gain in adults [64]. Total fat intake was, however, found to only have a weak positive association with weight gain in the Nurses’ Health Study, with saturated-, trans-, and polyunsaturated fat having stronger positive relationships with bodyweight [65]. Rosqvist et al. [66] found in an overfeeding trial participants to gain similar amounts of weight regardless of consuming a diet high in saturated- or polyunsaturated fat. A diet high in saturated fat though resulted in more visceral adipose fat and liver fat being gained, whereas high intakes of polyunsaturated fat were found to increase lean body tissue [66]. It is, hence, important to consider the quality and type of dietary fat when evaluating health and disease risk [67]. The consensus is that saturated fat should rather be replaced with naturally occurring unsaturated fat, with the intake of industrially produced trans-fat excluded from the diet [64,67]. It should also be considered that often when people follow a diet high in saturated- and trans-fat, other unhealthy lifestyle factors such as a high intake of fast foods and sugar-sweetened beverages, which can contribute to poor health outcomes, are often followed [65].

Nutrient pattern 1 (plant protein, iron, thiamine, and folic acid), which is reflective of a “fortified grain and legume” pattern, represents a more traditional South African diet. The traditional South African diet, which is associated with a lower prevalence of degenerative diseases [68], is characterized by a high fiber and low fat intake as a result of a high plant protein (particularly legumes) and starchy food consumption [29,69]. The representation of nutrient pattern 1 of the traditional diet is supported by a high positive loading for total fiber and high negative loadings for saturated- and monounsaturated fat on the factor matrix, as well as the higher consumption of legumes and lower

consumption of products of animal origin and processed foods. Upon determining the associations between the a posteriori-derived nutrient patterns and a priori dietary patterns, nutrient pattern 1 was found to be associated with higher dietary quality. This higher dietary quality is attributed to more favorable scores in the “moderation” and “overall balance” categories of the DQI-I, which is also supported by the loadings of the factor matrix and the lower intake of products of animal origin and processed foods. Dietary variety was negatively associated with this pattern since traditional diets are typically more monotonous [70].

Nutrient pattern 2 (animal protein, copper, vitamin A, and vitamin B₁₂) and 3 (fatty acids and sodium) are, conversely, reflective of the nutrition transition. The nutrition transition is described as the increase in the intake of foods of animal origin and processed foods high in fat and sodium as populations adapt to a more modern lifestyle often due to urbanization and economic- and social development [38,71]. These changes in dietary intake are well documented and have been associated with the increasing prevalence of obesity and non-communicable diseases [38]. Although the food groups associated with nutrient pattern 2 were mainly animal products, nutrient pattern 2 was not found to be associated with dietary quality. Nutrient pattern 3, reflecting a “fatty- and processed foods” pattern, was found to be associated with a lower dietary quality, which was mainly driven by poor scorings in the “moderation” and “overall balance” categories. This is supported by high positive loadings on fat (saturated-, monounsaturated- and polyunsaturated fatty acids) and sodium on the factor matrix, together with the higher consumption of fatty foods, processed- and red meat, cheese, nuts and nut spreads, and sugar-sweetened beverages.

Nutrient pattern 1 was found to be adhered to by women with a lower level of education and a poorer socioeconomic status. Considering the positive association between nutrient pattern 1 scores and dietary quality, maternal age (≥ 27 years) can also be regarded as a determinant for this pattern. In a systematic review on determinants of dietary patterns and dietary quality during pregnancy, Doyle et al. [55] described a social gradient whereby women of older age, a higher education, a higher income, and/or other markers indicating affluence are more likely to follow a healthier dietary pattern [55]. Although our findings were similar with regard to maternal age, a higher quality diet was followed by less affluent women among our study population. This higher dietary quality can be explained by the higher intake of whole wheat- and brown bread, legumes, and maize, which are generally more affordable when compared to fatty foods and processed animal products. Bourne et al. [68] found that individuals within nutrition transition who were more traditionally orientated to frequently be under-employed and therefore have time available to prepare the lower costing maize meal and legume-based dishes, which have relatively long cooking times. Equally, employed city dwellers tend to more frequently choose unhealthy fast foods and convenience foods, which are generally refined and higher in fat due to long commuting times to and from work [68]. Nevertheless, it is important to note that the finding by Doyle et al. [55], in which women of a higher social gradient followed a diet of higher quality, was based on data mainly from high-income countries. This disparity in findings with regard to determinants for dietary patterns between high-income and middle-income countries was also reported by López-Olmedo et al. [72] who indicated individuals from a lower socioeconomic status in Mexico to follow a higher quality diet than individuals from higher socioeconomic status.

In a recently published review, Chia et al. [73] grouped both a priori and a posteriori dietary patterns to identify “healthy” and “unhealthy” patterns to conduct a meta-analysis on the associations between maternal dietary patterns during pregnancy and birth outcomes. A healthier dietary pattern was reported to be associated with a lower risk for preterm birth, with an unhealthy dietary pattern associated with a higher risk for preterm birth and low-birth weight. Considering the associations between the nutrient patterns and dietary quality identified by our study, nutrient pattern 1 reflects a more “healthy” dietary pattern, with nutrient pattern 3 reflecting an “unhealthy” dietary pattern. Based on the findings by Chia et al. [73], it is likely that women with higher

adherence to nutrient pattern 3 have an increased risk for adverse pregnancy outcomes. A possible rationale for this is that nutrient pattern 3, which is reflective of a “fatty and processed food” pattern and nutrition transition, increases the risk for overweight, obesity, and non-communicable disease [38]. In one of the only studies to evaluate the change in dietary patterns from before pregnancy and during pregnancy, Crozier et al. [74] found that, although there was a slight difference in the food products consumed, the dietary patterns remain mainly unchanged from before pregnancy. Women following an unhealthy dietary pattern during pregnancy are, therefore, likely to have followed an unhealthy pattern before conception too. Overweight, obesity, and non-communicable diseases both before and during pregnancy are well described to increase the risk for morbidity (gestational diabetes, preeclampsia, and macrosomia) and mortality during pregnancy [7,75-77].

A limitation to our study is that the dietary data used to score the a priori dietary patterns were obtained using a QFFQ. As the QFFQ reports on a range of foods or food groups consumed over a long period [78], it is likely that when converting the dietary data to intake per day, a greater variety of foods was reported, which could have led to an overestimation of the “variety” and “adequacy” scorings of the DQI-I. In addition, the QFFQ is not always accurate with regard to the estimated portion sizes consumed as this questionnaire relies heavily on memory [78]. However, the scoring of the DQI-I was performed stringently according to the guidelines given by Kim et al. [35], and we are confident that the results represent an accurate overview of the maternal dietary quality. Furthermore, the associations investigated between the maternal and household factors and the dietary patterns were likely to have been influenced by the relatively small sample size (multiple testing correction was not applied) of our study, as well as our study population being mainly from an urban setting.

5. Conclusions

We present a comprehensive analysis of the diet of pregnant women residing in an urban South African setting by including both a priori and a posteriori dietary pattern analyses. Although three distinct a posteriori dietary patterns were followed by participants in our study population, the overall dietary quality was poor. Considering possible poor maternal outcomes associated with lower dietary quality, the poor dietary quality among pregnant South African women, especially women of younger age, should be addressed through nutritional education. It is also advised that further research be carried out to truly understand the impact of the maternal diet on health outcomes among the South African population. Our study also confirms that the a priori and a posteriori methods, based on their methodological construction, evaluate the diet by different means and, therefore, provide complementary and useful information in exploring the diet as a whole. Determining associations between the a priori and a posteriori dietary patterns is also worthwhile as this aids in the better understanding of the a posteriori patterns that are representative of the actual dietary intake.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Table S1: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 1 ($n = 250$), Table S2: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 2 ($n = 250$), Table S3: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 3 ($n = 250$).

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by both the Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1) and the University of the Witwatersrand, Johannesburg (M 150968). The City of Johannesburg District Research Committee (Gauteng Department of Health) and the clinical manager at Rahima Moosa Mother and Child hospital provided permission for the study to take place in the relevant clinical setting.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: As required by the Human Research Ethics Committee of the North-West University, South Africa, the researcher signed confidentiality agreements in which they agreed "not to disclose confidential information to anyone other than North West University unless required to do so by law or by court order". Participant consent forms were also clear for the purposes of data usage. Permission to obtain the data can be obtained from the North-West University Health Research Ethics Committee, Prof. Wayne Towers: wayne.towers@nwu.ac.za.

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Table S1: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 1 (n = 250).

	Nutrient pattern 1						
	<i>Plant protein, iron, thiamine and folic acid</i>						
	<u>Tertile 1</u>		<u>Tertile 2</u>		<u>Tertile 3</u>		p-value
	Median	IQR	Median	IQR	Median	IQR	
Breakfast cereals	1.44	(0.00 – 3.00)	0.82	(0.00 – 3.21)	0.72	(0.00 – 3.67)	0.203
Cakes, biscuits and pudding	3.62 ^a	(0.97 – 7.37)	3.14 ^a	(0.60 – 6.22)	1.23 ^b	(0.00 – 3.21)	<0.001
Cheese	0.50 ^a	(0.00 – 1.51)	0.13 ^{a,b}	(0.00 – 0.81)	0.00 ^b	(0.00 – 0.52)	0.021
Chicken	3.41	(1.55 – 6.21)	3.37	(1.68 – 5.40)	2.37	(0.83 – 5.42)	0.411
Crackers	0.00	(0.00 – 0.00)	0.00	(0.00 – 0.00)	0.00	(0.00 – 0.00)	0.423
Dairy ¹	5.33 ^a	(3.12 – 7.19)	5.15 ^{a,b}	(2.24 – 7.99)	2.87 ^b	(1.11 – 6.30)	0.019
Decaffeinated tea	0.00	(0.00 – 0.04)	0.01	(0.00 – 0.05)	0.01	(0.00 – 0.06)	0.170
Eggs	2.14	(0.47 – 3.76)	1.77	(0.00 – 3.99)	1.38	(0.34 – 4.31)	0.825
Fatty foods ²	4.47 ^a	(2.07 – 7.27)	2.93 ^{a,b}	(1.33 – 5.68)	1.99 ^b	(0.00 – 5.81)	0.005
Fish and seafood	1.08	(0.28 – 2.57)	0.87	(0.28 – 2.01)	0.62	(0.06 – 1.84)	0.204
Fresh and dried fruit	7.35	(4.62 – 10.84)	7.28	(4.76 – 9.60)	8.61	(5.10 – 11.68)	0.282
Fruit juice	2.38 ^a	(0.68 – 4.36)	0.79 ^{a,b}	(0.00 – 3.02)	0.29 ^b	(0.00 – 2.38)	0.001
Leafy vegetables	0.34	(0.08 – 1.08)	0.73	(0.21 – 1.96)	0.85	(0.27 – 1.90)	0.184
Legumes	1.01 ^b	(0.06 – 1.95)	1.01 ^{a,b}	(0.04 – 2.23)	1.18 ^a	(0.00 – 3.20)	0.011
Maize	4.68 ^c	(1.88 – 8.12)	11.03 ^{a,b,c}	(5.42 – 15.53)	15.23 ^a	(8.34 – 22.63)	<0.001
Margarine	0.28	(0.00 – 0.80)	0.14	(0.00 – 0.94)	0.00	(0.00 – 0.87)	0.144
Miscellaneous ³	0.61	(0.11 – 1.77)	0.53	(0.07 – 1.41)	0.30	(0.00 – 1.24)	0.379
Nuts and nut spreads	0.53	(0.00 – 1.39)	0.42	(0.00 – 1.85)	0.67	(0.00 – 3.12)	0.373
Organ meat and offal	0.41	(0.00 – 1.45)	0.70	(0.00 – 2.39)	0.60	(0.00 – 2.20)	0.062
Cooked porridge ⁴	0.25	(0.00 – 1.80)	0.53	(0.00 – 3.84)	0.35	(0.00 – 3.96)	0.454
Other vegetables ⁵	0.99	(0.48 – 1.69)	1.07	(0.33 – 2.62)	1.30	(0.46 – 3.00)	0.043
Potatoes and sweet potatoes	0.88	(0.34 – 2.34)	1.30	(0.34 – 2.54)	0.83	(0.17 – 2.98)	0.416
Processed meat	4.16 ^a	(1.74 – 6.69)	2.36 ^{b,c}	(0.77 – 4.23)	1.62 ^c	(0.14 – 4.20)	<0.001
Red meat	5.75 ^a	(2.39 – 10.09)	2.74 ^{a,b,c}	(0.32 – 6.52)	1.42 ^c	(0.10 – 3.74)	<0.000
Relish	0.15	(0.00 – 0.73)	0.35	(0.00 – 1.47)	0.00	(0.00 – 0.62)	0.065
Rice and Pasta	4.56	(2.54 – 7.30)	3.95	(2.21 – 6.26)	2.70	(1.10 – 5.41)	<0.049
Roast potatoes and chips	1.61	(0.25 – 5.06)	1.50	(0.00 – 4.70)	1.34	(0.00 – 4.19)	0.655
Salad oils	0.86 ^a	(0.08 – 3.29)	0.58 ^{a,b}	(0.00 – 1.88)	0.02 ^b	(0.00 – 1.23)	0.001
Salad vegetables	0.33 ^{a,b}	(0.13 – 0.63)	0.34 ^a	(0.05 – 0.72)	0.22 ^b	(0.00 – 0.40)	0.026
Savoury snacks	3.10	(0.87 – 6.67)	2.17	(0.75 – 5.51)	2.37	(0.56 – 6.19)	0.276
Sugar	2.40	(0.59 – 4.01)	2.13	(1.05 – 4.23)	2.22	(0.61 – 4.68)	0.591
Sugar-sweetened drinks	1.63 ^a	(0.33 – 3.20)	1.81 ^a	(0.75 – 3.10)	0.67 ^b	(0.00 – 2.07)	0.015
Sugar-sweetened dairy ⁶	0.98 ^a	(0.00 – 2.89)	0.62 ^a	(0.00 – 2.17)	0.00 ^b	(0.00 – 0.83)	<0.001
Sweet spreads and jam	0.00	(0.00 – 0.41)	0.00	(0.00 – 0.00)	0.00	(0.00 – 0.00)	0.120
Sweets and chocolates	1.59 ^a	(0.00 – 5.07)	0.54 ^{b,c}	(0.00 – 1.49)	0.00 ^c	(0.00 – 1.68)	0.002
Tea and coffee	0.01	(0.00 – 0.08)	0.00	(0.00 – 0.08)	0.00	(0.00 – 0.07)	0.470
Vitamin A rich vegetables	0.50	(0.19 – 0.96)	0.42	(0.09 – 0.85)	0.34	(0.00 – 0.76)	0.374
White bread	2.39	(0.00 – 4.67)	1.10	(0.00 – 6.54)	0.00	(0.00 – 6.18)	0.502
Whole wheat and brown bread	0.00 ^c	(0.00 – 2.60)	2.51 ^{a,b,c}	(0.00 – 6.18)	4.86 ^a	(0.00 – 12.86)	<0.001

IQR: interquartile range

¹Including both full fat and skim dairy products.

²Pies, 'vetkoek', pizza, hamburgers and pizza.

³Soup powders, sauces (chutney, tomato, mushroom and white), and meat and vegetable extract bread spreads.

⁴Oats and sorghum porridges.

⁵Including amongst others beetroot, broccoli, cauliflower, mealies, tomatoes, cabbage, green beans and sweet peppers.

⁶Ice cream, milk shake and malted milk beverages.

Significant difference between the median of the tertiles indicated in **bold** ($p < 0.05$) (according to Welsh test)

Medians with a different letter in their superscript are significantly different at the 0.05 level according to a Games-Howell test.

Table S2: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 2 (n = 250).

	Nutrient pattern 2						
	<i>Animal protein, copper, vitamin A and vitamin B₁₂</i>						
	Tertile 1		Tertile 2		Tertile 3		p-value
	Median	IQR	Median	IQR	Median	IQR	
Breakfast cereals	0.74	(0.00 - 2.79)	1.74	(0.00 - 3.78)	0.72	(0.00 - 3.27)	0.105
Cakes, biscuits and pudding	2.87	(0.67 - 7.13)	2.92	(0.73 - 5.61)	1.56	(0.00 - 4.29)	0.183
Cheese	0.12 ^b	(0.00 - 0.66)	0.21 ^{a,b}	(0.00 - 0.72)	0.36 ^a	(0.00 - 1.57)	0.022
Chicken	2.18 ^c	(0.82 - 4.70)	3.83 ^{a,b}	(2.10 - 5.52)	2.86 ^b	(1.46 - 6.85)	0.006
Crackers	0.00	(0.00 - 0.00)	0.00	(0.00 - 0.00)	0.00	(0.00 - 0.00)	0.974
Dairy ¹	3.90	(2.35 - 6.79)	4.97	(2.27 - 7.86)	4.71	(1.73 - 7.47)	0.504
Decaffeinated tea	0.01	(0.00 - 0.05)	0.01	(0.00 - 0.05)	0.01	(0.00 - 0.06)	0.317
Eggs	1.09 ^b	(0.00 - 2.72)	1.97 ^{b,c}	(0.31 - 3.75)	3.16 ^a	(0.96 - 5.53)	<0.001
Fatty foods ²	4.47 ^a	(1.25 - 7.66)	2.77 ^{a,b}	(1.15 - 6.10)	2.40 ^b	(0.78 - 4.85)	0.009
Fish and seafood	0.72 ^b	(0.16 - 1.64)	1.10 ^{a,b}	(0.20 - 2.30)	0.80 ^a	(0.28 - 2.63)	0.036
Fresh and dried fruit	7.09	(4.76 - 10.04)	7.62	(4.61 - 10.31)	8.35	(5.42 - 11.40)	0.251
Fruit juice	1.17	(0.00 - 4.29)	1.20	(0.00 - 3.19)	0.91	(0.00 - 2.74)	0.265
Leafy vegetables	0.48	(0.11 - 1.15)	0.65	(0.18 - 1.63)	0.75	(0.29 - 2.00)	0.155
Legumes	1.31	(0.15 - 2.20)	0.84	(0.00 - 2.75)	0.98	(0.00 - 2.23)	0.836
Maize	12.44	(4.38 - 19.77)	9.37	(4.60 - 14.71)	8.12	(3.94 - 14.16)	0.066
Margarine	0.21	(0.00 - 0.96)	0.33	(0.00 - 0.84)	0.00	(0.00 - 0.66)	0.070
Miscellaneous ³	0.36	(0.08 - 1.10)	0.65	(0.09 - 1.85)	0.49	(0.00 - 1.27)	0.294
Nuts and nut spreads	0.63	(0.00 - 1.82)	0.43	(0.00 - 2.76)	0.69	(0.00 - 3.07)	0.044
Organ meat and offal	0.18 ^b	(0.00 - 0.69)	0.44 ^{b,c}	(0.00 - 1.26)	1.53 ^a	(0.36 - 3.49)	<0.001
Cooked porridge ⁴	0.06	(0.00 - 3.38)	0.56	(0.00 - 2.24)	0.60	(0.00 - 2.93)	0.432
Other vegetables ⁵	0.68 ^b	(0.20 - 1.76)	1.10 ^{a,b}	(0.50 - 2.63)	1.30 ^a	(0.55 - 2.53)	0.030
Potatoes and sweet potatoes	1.10	(0.24 - 2.28)	0.85	(0.25 - 2.33)	1.31	(0.25 - 2.71)	0.694
Processed meat	2.22	(0.79 - 5.30)	2.99	(1.31 - 4.75)	2.73	(0.59 - 4.92)	0.584
Red meat	1.58	(0.00 - 5.75)	3.75	(0.78 - 6.90)	3.38	(1.30 - 7.30)	0.087
Relish	0.12	(0.00 - 1.06)	0.20	(0.00 - 0.87)	0.12	(0.00 - 0.95)	0.460
Rice and Pasta	3.15	(1.54 - 6.13)	3.91	(2.08 - 6.23)	4.18	(2.01 - 6.73)	0.922
Roast potatoes and chips	3.01 ^a	(0.19 - 6.88)	1.84 ^{b,c}	(0.00 - 4.23)	0.51 ^c	(0.00 - 2.52)	0.002
Salad oils	0.43	(0.00 - 1.73)	0.67	(0.00 - 1.97)	0.22	(0.00 - 2.22)	0.632
Salad vegetables	0.28	(0.03 - 0.48)	0.28	(0.08 - 0.56)	0.31	(0.05 - 0.69)	0.311
Savoury snacks	2.38	(0.85 - 6.15)	3.34	(1.07 - 6.80)	1.86	(0.22 - 5.37)	0.795
Sugar	2.99 ^a	(1.41 - 4.87)	2.67 ^a	(1.07 - 4.80)	1.61 ^b	(0.44 - 3.21)	<0.001
Sugar-sweetened drinks	1.16	(0.13 - 3.04)	1.67	(0.44 - 3.09)	1.11	(0.15 - 2.20)	0.124
Sugar-sweetened dairy ⁶	0.59	(0.00 - 1.74)	0.67	(0.00 - 1.97)	0.43	(0.00 - 1.46)	0.733
Sweet spreads and jam	0.00	(0.00 - 0.19)	0.00	(0.00 - 0.06)	0.00	(0.00 - 0.00)	0.204
Sweets and chocolates	0.55	(0.00 - 3.16)	0.54	(0.00 - 2.53)	0.33	(0.00 - 2.16)	0.939
Tea and coffee	0.01	(0.00 - 0.09)	0.00	(0.00 - 0.08)	0.00	(0.00 - 0.06)	0.244
Vitamin A rich vegetables	0.38	(0.04 - 0.75)	0.34	(0.00 - 0.80)	0.53	(0.18 - 1.28)	0.052
White bread	2.60 ^a	(0.00 - 8.81)	0.71 ^{a,b}	(0.00 - 5.87)	0.34 ^b	(0.00 - 4.13)	0.032
Whole wheat and brown bread	0.00	(0.00 - 5.43)	3.19	(0.00 - 7.42)	2.01	(0.00 - 7.53)	0.320

IQR: interquartile range

¹Including both full fat and skim dairy products.

²Pies, 'vetkoek', pizza, hamburgers and pizza.

³Soup powders, sauces (chutney, tomato, mushroom and white), and meat and vegetable extract bread spreads.

⁴Oats and sorghum porridges.

⁵Including amongst others beetroot, broccoli, cauliflower, mealies, tomatoes, cabbage, green beans and sweet peppers.

⁶Ice cream, milk shake and malted milk beverages.

Significant difference between the median of the tertiles indicated in **bold** ($p < 0.05$) (according to Welsh test)

Medians with a different letter in their superscript are significantly different at the 0.05 level according to a Games-Howell test.

Table S3: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 3 (n = 250).

Nutrient pattern 3							
<i>Fatty acids and sodium</i>							
	Tertile 1		Tertile 2		Tertile 3		p-value
	Median	IQR	Median	IQR	Median	IQR	
Breakfast cereals	0.72	(0.00 - 4.10)	0.85	(0.00 - 2.55)	1.73	(0.00 - 3.31)	0.081
Cakes, biscuits and pudding	1.57	(0.09 - 4.35)	3.10	(1.21 - 5.99)	2.87	(0.17 - 6.75)	0.078
Cheese	0.00 ^b	(0.00 - 0.41)	0.18 ^{a,b}	(0.00 - 0.76)	0.50 ^a	(0.00 - 1.69)	0.014
Chicken	2.16	(0.81 - 5.39)	3.37	(1.78 - 6.54)	3.37	(1.81 - 5.62)	0.167
Crackers	0.00	(0.00 - 0.00)	0.00	(0.00 - 0.00)	0.00	(0.00 - 0.00)	0.680
Dairy ¹	5.86 ^a	(218 - 10.43)	4.37 ^{b,c}	(2.27 - 7.13)	3.39 ^c	(1.98 - 6.39)	0.006
Decaffeinated tea	0.01	(0.00 - 0.06)	0.01	(0.00 - 0.06)	0.00	(0.00 - 0.03)	0.085
Eggs	0.65	(0.00 - 3.25)	2.14	(0.74 - 4.24)	2.34	(0.80 - 3.88)	0.135
Fatty foods ²	1.57 ^c	(0.31 - 4.00)	3.12 ^{a,b,c}	(1.62 - 6.19)	4.47 ^a	(2.34 - 8.20)	<0.001
Fish and seafood	0.64	(0.07 - 1.96)	1.07	(0.22 - 2.45)	0.92	(0.24 - 2.22)	0.285
Fresh and dried fruit	8.89 ^a	(6.12 - 12.34)	7.07 ^{a,b}	(4.59 - 10.83)	6.65 ^b	(3.68 - 9.33)	0.001
Fruit juice	0.85	(0.00 - 3.26)	1.51	(0.30 - 3.63)	0.86	(0.00 - 3.16)	0.439
Leafy vegetables	0.85	(0.20 - 1.63)	0.49	(0.12 - 1.48)	0.62	(0.14 - 2.19)	0.208
Legumes	1.29	(0.00 - 3.20)	0.73	(0.00 - 1.89)	0.78	(0.06 - 2.19)	0.104
Maize	14.16 ^a	(6.89 - 22.58)	10.22 ^{a,b,c}	(5.13 - 15.67)	6.01 ^c	(1.99 - 10.54)	<0.001
Margarine	0.14	(0.00 - 0.62)	0.13	(0.00 - 0.96)	0.30	(0.00 - 0.87)	0.691
Miscellaneous ³	0.28	(0.00 - 0.73)	0.58	(0.07 - 1.60)	0.77	(0.22 - 1.70)	0.229
Nuts and nut spreads	0.20 ^b	(0.00 - 1.32)	0.69 ^{a,b}	(0.00 - 2.18)	0.85 ^a	(0.00 - 3.62)	0.026
Organ meat and offal	0.24	(0.00 - 1.27)	1.01	(0.00 - 2.48)	0.54	(0.00 - 2.11)	0.259
Cooked porridge ⁴	0.68 ^a	(0.00 - 5.81)	0.37 ^{a,b}	(0.00 - 2.52)	0.14 ^b	(0.00 - 1.80)	0.004
Other vegetables ⁵	1.10	(0.44 - 2.89)	0.99	(0.34 - 2.06)	1.27	(0.38 - 2.30)	0.867
Potatoes and sweet potatoes	0.88	(0.20 - 2.03)	0.84	(0.22 - 2.34)	1.29	(0.54 - 3.06)	0.262
Processed meat	1.29 ^c	(0.12 - 3.03)	2.92 ^{a,b,c}	(1.37 - 4.89)	4.28 ^a	(1.70 - 7.19)	<0.001
Red meat	1.01 ^c	(0.00 - 3.84)	2.88 ^{a,b}	(0.67 - 6.65)	4.95 ^a	(2.34 - 9.10)	<0.001
Relish	0.10	(0.00 - 0.90)	0.08	(0.00 - 1.11)	0.18	(0.00 - 0.95)	0.997
Rice and Pasta	3.66	(1.28 - 6.67)	4.01	(2.22 - 6.24)	3.83	(2.16 - 5.86)	0.835
Roast potatoes and chips	1.14	(0.00 - 4.99)	2.09	(0.35 - 4.45)	1.26	(0.00 - 4.29)	0.613
Salad oils	0.02 ^c	(0.00 - 0.84)	0.71 ^{a,b}	(0.00 - 2.30)	0.90 ^a	(0.00 - 2.98)	<0.001
Salad vegetables	0.15	(0.00 - 0.44)	0.31	(0.09 - 0.63)	0.38	(0.13 - 0.63)	0.208
Savoury snacks	1.61	(0.47 - 5.63)	2.80	(0.66 - 5.27)	3.10	(0.99 - 7.91)	0.219
Sugar	2.86 ^a	(0.71 - 6.07)	2.38 ^{a,b,c}	(1.11 - 4.16)	1.82 ^c	(0.49 - 3.27)	<0.001
Sugar-sweetened drinks	0.96 ^{a,b}	(0.00 - 3.04)	1.81 ^a	(0.64 - 3.24)	1.11 ^b	(0.23 - 2.39)	0.036
Sugar-sweetened dairy ⁶	0.00	(0.00 - 1.06)	0.74	(0.00 - 1.85)	0.71	(0.00 - 1.98)	0.089
Sweet spreads and jam	0.00	(0.00 - 0.00)	0.00	(0.00 - 0.18)	0.00	(0.00 - 0.07)	0.613
Sweets and chocolates	0.10	(0.00 - 1.70)	0.74	(0.00 - 2.27)	0.64	(0.00 - 3.66)	0.164
Tea and coffee	0.00	(0.00 - 0.04)	0.00	(0.00 - 0.09)	0.03	(0.00 - 0.09)	0.790
Vitamin A rich vegetables	0.34	(0.00 - 0.86)	0.41	(0.17 - 0.87)	0.46	(0.13 - 0.92)	0.971
White bread	0.50	(0.00 - 4.04)	1.78	(0.00 - 7.77)	1.42	(0.00 - 5.93)	0.125
Whole wheat and brown bread	2.00	(0.00 - 7.54)	1.15	(0.00 - 8.00)	2.35	(0.00 - 5.48)	0.485

IQR: interquartile range

¹Including both full fat and skim dairy products.

²Pies, 'vetkoek', pizza, hamburgers and pizza.

³Soup powders, sauces (chutney, tomato, mushroom and white), and meat and vegetable extract bread spreads.

⁴Oats and sorghum porridges.

⁵Including amongst others beetroot, broccoli, cauliflower, mealies, tomatoes, cabbage, green beans and sweet peppers.

⁶Ice cream, milk shake and malted milk beverages.

Significant difference between the median of the tertiles indicated in **bold** ($p < 0.05$) (according to Welsh test)

Medians with a different letter in their superscript are significantly different at the 0.05 level according to a Games-Howell test.

CHAPTER 4 ARTICLE 2

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Maternal nutrient patterns are associated with fetal head circumference and femur length

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Ethical statement

Ethical approval was obtained from both the Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1) and the University of the Witwatersrand, Johannesburg (M 150968). Permission was also obtained from the City of Johannesburg's District Research Committee (Gauteng Department of Health) and the Rahima Moosa Mother and Child Hospital's clinical manager. The study was conducted as per the guidelines set by the World Medical Association Declaration of Helsinki. Written informed consent was obtained from all eligible women before data collection took place.

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Contributor statement

C.M.S., J.B., L.M., E.A.S., and M.F. designed and conducted the research study; C.C. and C.M.S. conceptualisation of article; C.C. conducted the data analysis; C.C. wrote original draft of the article; C.M.S., J.B., M.F. reviewed and edited the article; funding for the study was obtained by E.A.S. and C.M.S.

Conflict of interest

None of the authors has any conflict of interest to report.

Maternal nutrient patterns are associated with fetal head circumference and femur length

Abstract

Evaluating fetal growth during pregnancy is one of the fundamental components of antenatal care. Although birth weight is indicative of fetal growth during pregnancy, it does not account for possible growth variation during the fetal period. Regardless of maternal nutrition during pregnancy being an important external stimulus to fetal growth, research on the associations between maternal dietary patterns during pregnancy and longitudinal ultrasound-derived fetal growth is limited. The aim of this study was hence to investigate these associations in 250 pregnant women enrolled in the Nutrition during Pregnancy and Early Development (NuPED) cohort in Johannesburg, South Africa. Maternal dietary intake was described as *a posteriori* nutrient patterns at <18 weeks' gestation. Dietary intake data were obtained using a quantified food frequency questionnaire. Ultrasound-derived fetal growth was described using ultrasound scans at mid ($n = 418$) and late ($n = 226$) pregnancy in terms of biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC), estimated fetal weight (EFW), as well as interval fetal growth. A 'plant protein, iron, thiamine and folic acid' pattern was found to have a small positive correlation with HC interval growth between mid- and late pregnancy ($r = 0.18$, $p = 0.041$). A 'fatty acids and sodium' pattern was conversely negatively correlated with FL at mid-pregnancy ($r = -0.16$, $p = 0.028$). With head circumference being a proxy for brain growth and femur length for linear growth, these results indicate that dietary patterns during pregnancy contribute to fetal development, which could influence neurodevelopmental outcomes later in life.

Keywords: pregnancy, dietary intake, *a posteriori* dietary patterns, fetal growth, ultrasounds, fetal interval growth, neurodevelopment

Key message:

- A maternal diet of higher quality providing essential nutrients contributes positively to fetal development and, therefore, to offspring health outcomes.
- A diet of poor quality and deficient in nutrients might, conversely, negatively influence fetal growth.
- Using nutrient pattern analysis is advisable as it provides better insight into the association of a combination of nutrients with health outcomes.

- Ultrasound-derived fetal growth should be assessed as a means of evaluating fetal growth, as this provides greater insight into the role maternal nutrition plays in offspring health outcomes.

INTRODUCTION

Evaluating fetal growth for abnormalities during pregnancy is one of the key components of antenatal care (Lees et al., 2020). Even though birth weight is an indicator for fetal growth (Kiserud et al., 2018), Bloomfield et al. (2006) describe birth weight as a 'single, cross-sectional summative measurement' that does not reflect fetal growth trajectories during pregnancy. Birth weight within normal ranges hence does not exclude the possibility of fetal adaptation and growth variation (Bloomfield et al., 2006). Monitoring fetal growth by at least two ultrasound scans separated in time during pregnancy is therefore recommended (Salomon et al., 2019).

Fetal growth is influenced by various factors, of which maternal nutrition is regarded as one of the most important external stimuli (Lees et al., 2020; Timmermans et al., 2012). The growth of the fetus is greatly dependent upon the maternal nutrient supply and transportation of these nutrients (water, glucose, amino acids, fatty acids and micronutrients) across the placenta into fetal circulation (Brett et al., 2014). As nutrients are not consumed in isolation but as part of a diet comprising different foods (Hu, 2002), dietary pattern analysis is a decisive methodology for studying the role of maternal dietary intake in fetal growth. Most articles published on the associations between dietary patterns during pregnancy and fetal growth, however, report on birth outcomes (birth weight and preterm birth) rather than using ultrasound-determined fetal growth.

In one of the few studies that reported on the associations between maternal dietary patterns and longitudinal ultrasound-determined fetal growth, Bouwland-Both et al. (2013) showed, as part of the Generation R study conducted in the Netherlands, that an 'energy-rich' dietary pattern (high positive loadings for bread, margarine and nuts) is positively associated with crown-rump length during the first trimester. No associations were found with estimated fetal weight (EFW) during the second and third trimester. Wrottesley et al. (2020) indicated that adherence to a 'mixed, high-sugar' dietary pattern was positively associated with fetal growth among black women in Soweto, South Africa. With high positive loading for food products containing added sugar, among others, the 'mixed, high-sugar' dietary pattern was associated with higher abdominal circumference (AC), head circumference (HC), biparietal diameter (BPD) and femur length (FL) across pregnancy.

As fetal adaptations due to maternal dietary intake might have life-long health consequences for the offspring (Gluckman et al., 2010; Timmermans et al., 2012), as well as because research on the associations between maternal dietary patterns and fetal growth is sparse, this study aims to add to this body of knowledge by presenting associations between maternal dietary patterns during pregnancy and fetal growth.

METHODOLOGY

Study design, setting and participants

This study forms part of the Nutrition during Pregnancy and Early Development (NuPED) cohort, a prospective study conducted in Johannesburg, South Africa, between March 2016 and November 2017. The protocol has previously been published (Symington et al., 2018).

In short, this study recruited healthy pregnant women aged 18 to 39 years from primary health care clinics in the city of Johannesburg. It is mainly the poorer proportion of the population that makes use of the health care services provided by primary health care centres in South Africa (Harris et al., 2011). Data were collected at three time points, namely early pregnancy (<18 weeks' gestation), mid-pregnancy (22 weeks' gestation, ± 12 days) and late pregnancy (36 weeks' gestation, ± 12 days). Pregnant women were regarded as eligible for enrolment if they were at <18 weeks' gestation with a singleton pregnancy and born in South Africa or a neighbouring country (Namibia, Botswana, Zimbabwe, Swaziland and Lesotho; residing in South Africa for at least 12 months) and could effectively communicate in a local language (Afrikaans, English, Zulu, Sotho or Xhosa). Women were excluded from the study based on a diagnosis of non-communicable disease (diabetes mellitus, hypertension, hypercholesterolaemia, and/ or renal disease), infectious disease (hepatitis and tuberculosis), or a serious illness (cancer, lupus and psychosis). Women were also excluded if they smoked (during the past year or currently) or used illicit drugs (self-reported). Human immunodeficiency virus (HIV) status was, however, not used as a criterion for exclusion owing to the high prevalence of HIV among the South African population (22.7% of women of child-bearing age) (Stats SA, 2019). Data collection took place at a tertiary hospital (Rahima Moosa Mother and Child Hospital) in Johannesburg, as a part of routine maternal care.

The sample size was calculated using the G*Power 3.1.9.2 statistical program. The calculation entailed multiple linear regression analysis (fixed-model, single-regression coefficient), a small effect size F^2 of 0.05, probability of error (alpha) of 5%, power of 80%, and ten predictors having birth weight as an outcome. This amounted to a required 196 participants. Taking into account that participants might opt out of the study (at 25% rate), it was calculated that a minimum of 245 participants should be recruited. The sample size was set at 250 participants.

Written informed consent was obtained from all eligible women willing to participate in the study. The NuPED cohort was approved by both the Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1) and the University of the Witwatersrand, Johannesburg (M 150968). Permission was also obtained from the City of Johannesburg's District Research Committee (Gauteng Department of Health) and the

Rahima Moosa Mother and Child Hospital's clinical manager. The study was conducted as per the guidelines set by the World Medical Association Declaration of Helsinki.

Maternal and household characteristics

Socio-demographic and socioeconomic information (including maternal age, country of birth, ethnicity, marital status, employment status, the highest level of education and household social grant beneficiaries) and micronutrient supplement usage (iron, folate and omega-3 fatty acids) were obtained using interviewer-administered questionnaires. Household socioeconomic status was determined using the South African Audience Research Foundation Living Standard Measure (Haupt, 2006). Parity and HIV status (routine antenatal care) were noted as part of the medical history obtained from medical records.

Maternal height, recorded to the nearest 0.1 cm, was measured at baseline (early pregnancy) using a mobile stadiometer (Seca 213, Hamburg, Germany). Weight was measured at each data collection time point using a calibrated scale (Seca 813, Hamburg, Germany) and recorded to the nearest 0.05 kg. All anthropometric measurements were conducted according to the International Society of the Advancement of Kinanthropometry standards (Marfell-Jones M et al., 2012), and were taken twice. With oedema and weight gain during pregnancy decreasing the reliability of the body mass index (BMI), maternal weight at enrolment was adjusted (assuming that an average of 2.5 kg was gained up to the point of enrolment) according to the gestational weight gain (GWG) guidelines of the Institute of Medicine (IoM) (Institute of Medicine & National Research Council, 2009) to determine an approximate pre-pregnancy BMI. Gestational weight gain, reported as gram/week, was calculated as [(late pregnancy maternal weight – mid-pregnancy maternal weight) / (period between late- and mid-pregnancy)]. Gestational weight gain was categorised as per the IoM guidelines, namely inadequate, adequate and excessive weight gain (Institute of Medicine & National Research Council, 2009).

Fetal sex, birth weight and gestational age at birth were recorded at delivery.

Outcome measures: Fetal ultrasonography

Fetal ultrasonography examination took place at each of the three data collection time points to confirm gestation (early pregnancy), determine gestational age (early pregnancy), determine the number of fetuses (early pregnancy) and confirm fetal movement (at each visit). Pregnancy dating for participants in their first trimester of pregnancy was done using crown–

rump length, with a combination of biometric measurements (BPD, HC, FL and AC) used for participants in their second trimester (Butt et al., 2014). The gestational age determined at baseline was used to determine gestational age at subsequent data collection time points.

Owing to a large variation in gestational age [median (interquartile range (IQR): 14 (12-16) weeks, min: 6 weeks; max: 18 weeks] among participants at enrolment, there was a large number of missing data as mainly crown–rump length was measured for fetuses <14 weeks' gestational age. For this reason, we described fetal growth using only data from mid- (± 22 weeks) and late pregnancy (± 36 weeks). According to Salomon et al. (2019), two ultrasound scans separated in time (preferably more than three weeks apart) are sufficient to monitor fetal growth. Fetal growth was described using the biometric measurements BPD, HC, FL and AC at each time point. Estimated fetal weight, calculated using HC, AC and FL according to Hadlock et al. (1985), was also determined. Growth trajectories could, however, not be determined since data were available from only two time points. We therefore determined interval fetal growth calculated as the difference between a biometric measure at two time points divided by the difference in gestational age (e.g. [(late-pregnancy AC – mid-pregnancy AC) / (late-pregnancy gestational age – mid-pregnancy gestational age)] (O'Gorman & Salomon, 2018).

All fetal ultrasonography measurements were taken by an obstetrician using a Medison (models used: MNT-17 X8 and SonoAce X8; Medison Co, LTD, Seoul, Korea;) ultrasound machine.

Exposure measures: Dietary patterns

Dietary intake at early pregnancy were described using a *posteriori* dietary pattern analysis. A detailed description of how these patterns were derived is given in Conradie et al. (2021). Dietary patterns were described at only one time point during pregnancy as, although there is a slight variation in the intake of food products, dietary patterns from before and during pregnancy remain largely unchanged (Crozier et al., 2009). With nutrients regarded as more universal and allowing for easier comparison across population groups (Moskal et al., 2014), nutrients rather than foods or foods groups were used as variables in the pattern analysis.

Habitual dietary intake was assessed using an interviewer-administered 140-item quantified food frequency questionnaire (QFFQ). The QFFQ was previously validated for a South African population group (MacIntyre et al., 2001) and its reproducibility has been proven (MacIntyre et al., 2002; Wentzel-Viljoen et al., 2011). Standard probing questions (Shim et al., 2014) were

used by trained fieldworkers to determine, as comprehensively as possible, the foods and drinks consumed during the previous four weeks. Foods and drinks were described according to type/brand, cooking methods used, frequency and portion size (determined using two- and three-dimensional food models, food packaging material, 'dish-up and measure', and household food utensils). Three registered dietitians/nutritionists converted the portion sizes to grams and coded foods and drinks using, respectively, the South African Medical Research Council (SAMRC) Food Quantities Manual (SAFOODS, 2018) and South African Food Composition Tables (SAFOODS, 2017). The coded and quantified dataset was linked by the SAMRC to the most recent food composition database to determine daily energy and nutrient intake. Nutrient intake was reflective of nutrients consumed as part of the diet, excluding nutrients from supplements. Complete dietary intake data were obtained from all participants.

Exploratory factor analysis with correlation matrix and Varimax rotation was applied to 22 nutrients to determine nutrient patterns (Field, 2012). The reliability of the method was verified using the Kaiser-Meyer-Olkin measure of sampling adequacy and Bartlett's test of sphericity. An eigenvalue of >1 , scree plot inspection, total variance explained, and the natural interpretability of the factors were used to retain factors. Retained factors (nutrient patterns) were named and interpreted based on nutrients with an absolute factor loading of ≥ 0.40 . Factor scores were calculated for each participant to indicate the degree to which the participant's nutrient intake matched the identified nutrient patterns.

Covariates

The World Health Organization indicates that fetal sex, country, maternal age, maternal height and weight, and parity influence fetal growth percentiles (Kiserud et al., 2017). Lewandowska (2021) indicated that an excessive pre-pregnancy BMI and a GWG above recommendations to play a bigger role in, specifically, macrosomia than other maternal factors. Also, we have previously found in the NuPED study that maternal iron and omega-3 intake and status are associated with birth outcomes (Symington, 2019; Symington et al., 2019). Considering these publications, the covariates for this study were set as follows: maternal age, fetal sex, parity, maternal height, pre-pregnancy BMI, GWG, and maternal iron supplementation. Compliance to folate supplementation was also considered as a covariate owing to its role in fetal development and birth outcomes (Scholl & Johnson, 2000), and because, together with iron supplementation, it forms part of routine primary health antenatal care in South Africa (National Department of Health (South Africa), 2015). Omega-3 supplementation was excluded from analysis as only a few women ($n=11$, 4%) used daily omega-3 supplementation.

Statistical analysis

All data, except for the dietary data, were captured in Microsoft Access and 20% were randomly checked for accuracy. Dietary data, captured in Microsoft Excel (Microsoft Corporation, Washington, DC, USA), were entirely double-checked to ensure the correctness of dietary codes and quantities used. Data processing and statistical analysis was done using IBM SPSS version 27 (SPSS Inc., Chicago, IL, USA).

Normality was checked using q-q plots, histograms and the Shapiro-Wilk test. Parametric data are reported as means and standard deviation and non-parametric median and IQR. Frequencies and percentage describe categorical data. The study population is described according to birth outcomes (preterm birth and birth weight) using univariate analysis (Mann-Whitney U test for continuous data and Pearson Chi-square for categorical data). Fetal growth (individual biometric measures and EFW) is graphically presented according to gender. The difference between nutrient pattern adherence (tertiles) and fetal growth parameters was described using analysis of covariance (ANCOVA) with Bonferroni correction. Spearman's Rho correlations (Supplementary table 2), followed by partial correlations adjusting for associated covariates, were used to determine associations between maternal nutrient patterns (continuous factor scores) and fetal growth parameters at both data collection time points, as well as for interval fetal growth. Significance was set at $p < 0.05$.

RESULTS

Participant characteristics

Of 595 pregnant women recruited to take part in the study, 250 women were eligible (Figure 1). In total, 232 women completed data collection up to the point of delivery: 7 women experienced a miscarriage/ intrauterine death during this time, and 11 women were lost to follow-up. Birth data from a further 29 participants were not available as these women opted to deliver their babies elsewhere.

The characteristics of the study population at enrolment, according to birth outcomes, are indicated in Supplementary Table 1. The majority (88%) of participants were of Black African descent, with a median age of 27 (24 – 32) years. Unmarried women made up 40% of the population, with 59% indicating that they lived with their partner (either married, in a traditional marriage, or living together without being married). An equal number of women (49%) indicated that they were employed and unemployed, respectively. Almost 60% of participants had a medium household socioeconomic status and congruently two-thirds of participant

households (67%) reported not receiving a monthly social support grant. Whereas the majority of women used daily folate (94%) and iron supplementation (84%), only 11 (4%) participants reported taking daily omega-3 supplementation. Most participants (74%) had a negative HIV status.

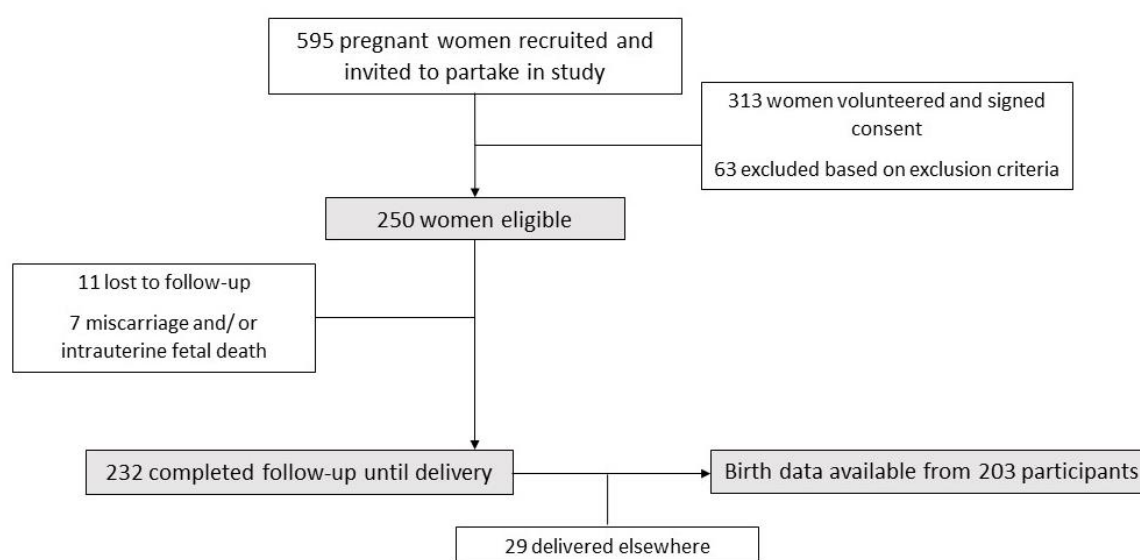


Figure 1: Flow-chart of participants in the NuPED study

About half (52%) of enrolled women, based on the calculated pre-pregnancy BMI, entered pregnancy either overweight or obese. A high percentage of participants (41%) also gained an excessive amount of weight between mid- (± 22 weeks' gestation) and late pregnancy (± 36 weeks' gestation). With a tendency towards significance ($p = 0.051$), women who delivered babies with macrosomia, though, had a lower GWG rate than women who delivered low birthweight infants. A significant relationship between BMI categories and infant birth-weight categories was also found: whereas overweight women were more likely to give birth to infants with macrosomia (50%), a greater percentage of normal (45%) and underweight (19%) women gave birth to low-birth-weight infants. Slightly more male (54%) fetuses were born to the study participants. The median birth weight was 3050 (2790 – 3380) grams among all infants.

Dietary patterns

Three distinct nutrient patterns were identified, namely a 'plant protein, iron, thiamine and folic acid' pattern, an 'animal protein, copper, vitamin A and vitamin B₁₂' pattern and a 'fatty acids

and sodium' pattern (Table 1). These patterns explain 57% of the total variance in nutrient intake (Conradie et al., 2021).

Table 1: Factor loadings of nutrient patterns at early pregnancy (n = 250)

Nutrients and variance explained	Factors (nutrient patterns) ¹		
	Nutrient pattern 1 (Plant protein, iron, thiamine, and folic acid)	Nutrient pattern 2 (Animal protein, copper, vitamin A, and vitamin B ₁₂)	Nutrient pattern 3 (Fatty acids and sodium)
Animal protein	-0.46	0.53	0.32
Plant protein	0.86	-0.09	-0.00
Saturated fat	-0.68	0.08	0.44
Monounsaturated fat	-0.51	0.08	0.67
Polyunsaturated fat	-0.15	-0.08	0.57
Cholesterol	-0.09	0.58	0.32
Carbohydrates	0.61	-0.21	-0.70
Total sugars	-0.23	0.05	-0.68
Total fibre	0.70	0.10	-0.24
Calcium	-0.44	0.20	-0.34
Iron	0.76	0.35	0.02
Sodium	0.04	0.01	0.64
Zinc	0.45	0.44	0.30
Copper	0.25	0.79	-0.08
Vitamin A	0.12	0.81	-0.07
Thiamine	0.77	0.10	-0.05
Riboflavin	0.01	0.63	-0.14
Niacin	0.54	0.39	0.31
Vitamin B ₆	0.67	0.03	0.26
Folic acid	0.73	0.36	-0.07
Vitamin B ₁₂	0.10	0.86	-0.03
Vitamin E	0.04	0.03	0.41
% of variance	27%	18%	11.5%
Total variance: 56.5%			

Reprinted with permission from Conradie et al. (2021). ¹Factor analysis performed on 22 nutrients; estimates presented after rotation. Nutrients considered as having a strong association with the nutrient patterns (factor loading ≤ -0.4 and ≥ 0.4) are indicated in **bold**.

Fetal growth

Enrolled women received an ultrasound scan at each data collection time point. Because of the large variation in gestational age at early pregnancy, this article describes only the fetal growth at mid- [median (IQR): 22 [22 – 23) weeks] and late pregnancy [median (IQR): 35 (34 – 36) weeks]. We report on data from 418 ultrasound scans: 226 scans at mid-pregnancy and 192 at late pregnancy. Supplementary Figure 1 depicts fetal growth in terms of AC, HC, BDM, FL and EFW per gender. None of these biometric measurements differed significantly between male and female fetuses at mid- or late pregnancy.

Considering the analysis of covariance, a higher adherence, compared with moderate and low adherence, to a ‘plant protein, iron, thiamine and folic acid’ pattern was associated with a greater HC ($p = 0.002$) and BPD ($p = 0.005$) growth rate between mid- and late pregnancy (Table 2). This pattern, based on Spearman’s Rho correlation, also had a small positive correlation with HC interval growth ($r = 0.23$, $p = 0.008$) (Supplementary Table 2). When adjusting for maternal age and compliance to folate supplementation (Table 3), this correlation weakens yet still holds ($r = 0.18$, $p = 0.041$).

The ‘fatty acids and sodium’ pattern was conversely found to be negatively correlated with both HC ($r = -0.14$, $p = 0.035$) and FL ($r = -0.15$, $p = 0.022$) at mid-pregnancy (Supplementary Table 2). Although also small in effect size, only the correlation with FL held after accounting for fetal sex, iron and compliance to folate supplementation ($r = -0.16$, $p = 0.028$) (Table 3). This correlation was, however, not supported by the analysis of covariance (Table 2).

Table 2: Fetal growth parameters per nutrient pattern adherence (n = 232)

	‘Plant protein, iron, thiamine and folic acid’ pattern				‘Animal protein, copper, vitamin A and vitamin B ₁₂ ’ pattern				‘Fatty acids and sodium’ pattern			
	Low adherence	Moderate adherence	High adherence	p-value	Low adherence	Moderate adherence	High adherence	p-value	Low adherence	Moderate adherence	High adherence	p-value
	Terile 1	Terile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3	
	Median (IQR)	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	Median (IQR)	
Mid-pregnancy												
AC (mm)	175.0 (167.0 - 179.0)	175.0 (165.0 - 180.0)	171.8 (167.0 - 178.0)	0.091	175.0 (167.0 - 179.3)	171.0 (166.0 - 178.0)	175.0 (167.0 - 178.0)	0.875	175.0 (167.8 - 179.0)	173.5 (167.0 - 180.0)	172.0 (166.3 - 177.0)	0.209
BPD (mm)	54.0 ^a (53.0 - 56.0)	54.0 (53.0 - 55.0)	54.0 ^b (52.0 - 55.0)	0.018	54.0 (52.0 - 56.0)	54.0 (52.0 - 55.3)	54.5 (53.0 - 56.0)	0.460	54.0 (53.0 - 56.0)	54.0 (53.0 - 56.0)	54.0 (52.0 - 55.0)	0.875
HC (mm)	200.0 (194.5 - 206.8)	201.0 (197.8 - 206.3)	200.0 (192.0 - 203.0)	0.075	200.0 (193.0 - 206.0)	199.5 (192.8 - 205.0)	201.0 (198.0 - 205.3)	0.892	202.0 (194.0 - 207.0)	201.0 (195.0 - 207.3)	199.0 (193.0 - 203.0)	0.501
FL (mm)	39.0 (38.0 - 40.5)	39.0 (37.0 - 40.0)	38.0 (37.0 - 40.0)	0.165	39.0 (37.5 - 40.0)	38.0 (37.0 - 40.0)	39.0 (38.0 - 40.0)	0.719	39.0 (38.0 - 40.0)	39.0 (38.0 - 40.0)	38.0 (37.0 - 40.0)	0.277
EFW (mm)	500.2 (452.5 - 537.7)	500.2 (447.6 - 535.8)	489.9 (454.7 - 514.1)	0.237	498.6 (447.9 - 536.3)	488.7 (454.7 - 522.3)	495.9 (456.8 - 530.3)	0.213	492.8 (457.6 - 524.7)	496.2 (450.1 - 541.0)	495.6 (444.0 - 523.3)	0.278
Late-pregnancy												
AC (mm)	315.0 (303.7 - 323.4)	313.6 (304.0 - 322.8)	310.9 (296.9 - 319.9)	0.272	317.9 (303.8 - 323.6)	313.1 (302.7 - 320.5)	311.6 (299.5 - 320.0)	0.704	315.5 (303.1 - 323.4)	313.2 (300.0 - 321.5)	311.7 (298.6 - 320.9)	0.514
BPD (mm)	88.1 (85.3 - 91.3)	88.0 (85.5 - 90.4)	88.1 (85.4 - 90.6)	0.966	87.7 (85.3 - 90.7)	88.1 (85.6 - 89.6)	88.1 (85.3 - 91.2)	0.575	88.2 (85.3 - 91.0)	87.4 (85.5 - 89.6)	87.9 (85.3 - 91.5)	0.066
HC (mm)	314.5 (305.3 - 321.3)	316.8 (308.9 - 321.8)	316.5 (308.5 - 322.7)	0.880	315.4 (307.5 - 321.5)	316.9 (310.9 - 321.8)	316.3 (306.7 - 322.8)	0.856	316.9 (308.6 - 323.4)	316.2 (306.9 - 321.6)	315.4 (307.7 - 321.6)	0.469
FL (mm)	68.7 (67.1 - 71.0)	68.6 (66.6 - 70.5)	68.5 (67.0 - 71.1)	0.345	68.8 (66.8 - 71.0)	68.4 (67.0 - 70.5)	68.7 (67.1 - 71.0)	0.950	69.0 (67.2 - 70.8)	68.3 (67.1 - 70.6)	68.5 (66.7 - 70.9)	0.343
EFW (mm)	2646.5 (2415.8 - 2811.1)	2670.5 (2408.1 - 2861.7)	2630.9 (2333.5 - 2795.7)	0.438	2689.4 (2463.7 - 2888.4)	2606.1 (2326.4 - 2798.1)	2581.2 (2353.8 - 2759.3)	0.582	2670.2 (2450.9 - 2856.8)	2606.1 (2315.5 - 2835.0)	2606.7 (2356.3 - 2752.3)	0.993

Table 2: Fetal growth parameters per nutrient pattern adherence (n = 232), continued

	‘Plant protein, iron, thiamine and folic acid’ pattern				‘Animal protein, copper, vitamin A and vitamin B ₁₂ ’ pattern				‘Fatty acids and sodium’ pattern			
	Low adherence	Moderate adherence	High adherence	p-value	Low adherence	Moderate adherence	High adherence	p-value	Low adherence	Moderate adherence	High adherence	p-value
	Terile 1	Terile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3	
	Median (IQR)	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	Median (IQR)	
Interval fetal growth												
AC	10.3 (9.7 - 10.8)	10.3 (9.8 - 10.8)	10.1 (9.57 - 10.9)	0.480	10.2 (9.8 - 10.7)	10.3 (9.7 - 10.8)	10.2 (9.6 - 11.2)	0.130	10.2 (9.6 - 10.6)	10.3 (9.8 - 10.9)	10.4 (9.6 - 11.1)	0.780
BPD	2.4 ^b (2.3 - 2.7)	2.5 ^b (2.3 - 2.7)	2.6 ^a (2.4 - 2.8)	0.005	2.5 (2.2 - 2.8)	2.5 (2.3 - 2.7)	2.5 (2.4 - 2.8)	0.422	2.5 (2.3 - 2.7)	2.6 (2.3 - 2.8)	2.5 (2.4 - 2.8)	0.882
HC	8.3 ^b (7.4 - 9.2)	8.2 ^b (7.6 - 9.2) ^a	9.0 ^a (8.2 - 9.8) ^b	0.002	8.7 (7.5 - 9.6)	8.7 (8.0 - 9.5)	8.4 (7.7 - 9.3)	0.885	8.5 (7.5 - 9.4)	8.7 (7.9 - 9.6)	8.8 (7.7 - 9.2)	0.742
FL	2.2 (2.0 - 2.4)	2.1 (1.9 - 2.3) ^a	2.3 (2.0 - 2.6) ^b	0.104	2.2 (2.0 - 2.5)	2.2 (2.0 - 2.5)	2.2 (2.0 - 2.5)	0.859	2.1 (1.9 - 2.5)	2.3 (2.0 - 2.5)	2.2 (2.1 - 2.4)	0.327

IQR: interquartile range; AC: abdominal circumference; BPD: biparietal diameter; HC: head circumference; FL: femur length; EFW: estimated fetal weight.

Missing data: *mid-pregnancy*: AC and EFW (n = 8), BPD, HC, and FL (n = 7); *late-pregnancy*: AC, BPD, HC, FL (n = 40) and EFW (n = 41); *interval growth*: AC (n = 48), BPD and HC (n = 96), and FL (n = 97).

Covariates included in ANCOVA: maternal age, fetal sex, parity, maternal height, pre-pregnancy BMI, GWG, and compliance to iron and folate supplementation

Significant difference between adherence (median of tertiles) indicated in **bold** ($p < 0.05$). Different letters in superscript indicate medians to be significantly different according to Bonferroni correction ($p < 0.05$).

Table 3: Crude and adjusted correlation coefficients of nutrient patterns associated with fetal growth parameters

	Correlation coefficients				
	Mid-pregnancy HC		Mid-pregnancy FL		Interval fetal growth HC
	n = 225				n = 136
	<i>r</i>	<i>p</i> -value	<i>r</i>	<i>p</i> -value	<i>r</i> <i>p</i> -value
'Plant protein, iron, thiamine and folic acid' pattern					
Crude					0.23 0.008
Adjusted ¹					0.18 0.041
'Fatty acids and sodium' pattern					
Crude	-0.14	0.035	-0.15	0.022	
Adjusted ²	-0.09	0.186	-0.16	0.028	

HC: head circumference, FL: femur length, *r*: correlation coefficient. ¹adjusted for maternal age and folate supplementation; ²adjusted for fetal sex iron and folate supplementation; *p* < 0.05

DISCUSSION

With this study, we add to the limited knowledge base on the associations between maternal dietary patterns during pregnancy and ultrasound-derived fetal growth. While only a few studies report on these associations, the current study is, to our knowledge, the only one to present on fetal interval growth. After adjusting for covariates, a ‘plant protein, iron, thiamine and folic acid’ pattern was found to be positively associated with HC interval growth between mid- and late pregnancy, although small in effect size. The ‘fatty acids and sodium’ pattern was conversely found to correlate negatively with FL at mid-pregnancy.

Head circumference during early life is reflective of intracranial volume and brain growth and hence serves as a proxy for neurodevelopment in children (Georgieff et al., 2018; Koshy et al., 2021; Volpe, 2018). Neurodevelopment is considered one of the most lasting health outcomes of the early life environment (Georgieff et al., 2018). From findings reported by Gale et al. (2006) and Sammallahti et al. (2014), prenatal and HC growth during infancy are associated with neurocognitive outcomes in childhood and early adulthood, respectively. Sammallahti et al. (2014) looked at the rate of HC growth from birth to term in prematurely born infants and found prenatal growth rather than growth after term to be associated with cognition, visual memory and executive functioning. Prenatal brain development is therefore crucial as this forms the foundation for later brain development and neurodevelopmental outcomes. Nutrition, in particular, is an important modifiable factor for early life brain development, with the effect of postnatal nutrition on brain development being subject to prenatal nutritional status (Georgieff et al., 2018).

Among our study population, we found adherence to a ‘plant protein, iron, thiamine and folic acid’ pattern to have a more positive association with HC growth between mid- and late pregnancy. This is probable because, with high positive loadings for plant protein, carbohydrates, iron, zinc, thiamine, niacin, vitamin B₆ and folate, this pattern provides nutrients essential for brain growth and neurodevelopmental processes (Dewey & Begum, 2011; Georgieff et al., 2018). These nutrients, among others, are involved in the closure of the neural tube (folate), energy production (carbohydrates and iron), growth factors (protein, zinc), brain and neuronal structure (protein, folate), myelination (iron), the efficacy of synapses (zinc) and in neurotransmitters (protein) (Georgieff et al., 2018; Nyaradi et al., 2013).

The ‘plant protein, iron, thiamine and folic acid’ pattern, as depicted in Conradie et al. (2021), is, based on its associations with food groups reflective of a ‘fortified grain and legume’ pattern, which represents a more traditional South African diet. The traditional South African diet is characterised by the intake of starchy foods and foods rich in plant proteins (e.g. legumes), resulting in a low-fat, high-fibre intake (MacIntyre et al., 2002; Wentzel-Viljoen et al., 2018). The

starchy foods consumed as part of this pattern were mainly maize and bread (Conradie et al., 2021) – products fortified as per South African legislation (Department of Health, 2003). The nutrients reflected in this pattern are congruent with the nutrients used for fortification, namely thiamine, riboflavin, niacin, pyridoxine, folate, iron, zinc and vitamin A. This may indicate that the South African food fortification programme plays a valuable role in maternal nutrition status, and probably in fetal and offspring neurodevelopment. This pattern was also found to have a higher dietary quality, based on its association with the Diet Quality Index-International, (Conradie et al., 2021).

In contrast, the ‘fatty acids and sodium’ pattern was negatively correlated with FL. Chang et al. (2003) report that a higher dairy intake among a thousand pregnant African American adolescents was associated with a higher femur length and hence improved fetal bone development. This was attributed mainly to calcium of which dairy products are a good source. A possible explanation for the ‘fatty acids and sodium’ pattern being negatively associated with FL in our study population might be that calcium was negatively loaded on the factor matrix of this pattern as dairy intake was significantly lower with an increased adherence to this pattern (Conradie et al., 2021).

Femur length is also described in the literature as being indicative of linear growth (Prioreshi et al., 2021). Linear growth retardation, which can already commence *in utero* (Dewey & Begum, 2011), is indicated by Leroy and Frongillo (2019) as being provoked by a deficient environment. Maternal malnutrition and anaemia, often due to a diet poor in quality, might deprive the fetus of nutrients required to support rapid growth and development (Dewey & Begum, 2011). We have previously indicated that the ‘fatty acids and sodium’ pattern has low dietary quality and accordingly, a great number of nutrients was negatively associated with this pattern (Conradie et al., 2021). It is hence likely that this pattern, reflective of a ‘fatty acids and processed foods’ pattern, deprives the fetus of key nutrients for fetal development. Since linear growth retardation can have a long-term effect on child development (Dewey & Begum, 2011; Leroy & Frongillo, 2019), the consequences of following such a pattern might be long lasting.

A strength of this study is that nutrient patterns rather than single nutrients were used to determine associations with fetal growth. Hu (2002) describes dietary patterns as being more predictive in determining risk factors for health outcomes. So also, fetal growth was investigated using fetal ultrasounds rather than only birth outcomes. A limitation of this study was however, the small sample size and high numbers of missing ultrasound data. Also, with fetal biometry being available from only two time points, fetal growth trajectories accounting for covariates could not be determined using statistical modelling techniques. Interval growth rate has been criticised in the literature as being susceptible to inaccuracies owing to intra- and inter-observer inconsistency and hence it is recommended that ultrasound scans for interval growth are at least three weeks

apart (O'Gorman & Salomon, 2018). We reported on data that were 12 weeks apart and therefore we believe the interval growth presented to be an accurate indication of the growth that occurred.

We can conclude that a higher quality diet providing essential nutrients to contribute positively to fetal development and could influence neurodevelopmental outcomes later in life. Efforts should be made to educate pregnant women on healthy food choices to ensure optimal dietary intake. Future research considering more fetal biometric data, as well as offspring development, is recommended.

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Supplementary table 1: Characteristics of the NuPED study participants at enrolment according to birth outcomes (n = 250)

Subject characteristics	Total sample ¹ (n = 250) Median (IQR) or n (%)	Gestational age ²			Birth weight ²			
		Preterm birth n=26 (11%)	Term n=205 (89%)	p-value ³	LBW n =31 (15%)	Normal birth weight n =162 (80%)	Macrosomia n=10 (5%)	p-value ³
Maternal age (years)	27 (24 - 32)	28 (22 - 33)	27 (24 - 32)	0.833	28 (23 - 32)	27 (24 - 32)	32 (29 - 33)	0.288
Ethnicity								
Black African	219 (88)	22 (88)	180 (88)	0.940	25 (81)	143 (88)	8 (80)	0.159
Mixed ancestry	28 (11)	3 (12)	24 (12)		5 (16)	19 (12)	2 (20)	
White	1 (<1)	0	0		0	0	0	
Indian	1 (<1)	0	1 (<1)		1 (3)	0	0	
Marital status								
Unmarried	100 (40)	14 (56)	78 (38)	0.364	19 (61)	61 (38)	4 (40)	0.212
Married	68 (27)	4 (16)	59 (29)		5 (16)	43 (27)	3 (30)	
Living together	57 (23)	4 (16)	49 (24)		4 (13)	42 (26)	1 (10)	
Traditional marriage ⁴	22 (9)	3 (12)	17 (8)		2 (7)	15 (9)	2 (20)	
Divorced/ Separated	2 (1)	0	2 (1)		1 (3)	1 (<1)	0	
Highest level of education								
Primary/ None	9 (4)	0	9 (4)	0.288	1 (3)	4 (3)	0	0.819
Grade 8 -10	37 (15)	6 (24)	27 (13)		4 (13)	23 (14)	0	
Grade 11 - 12	145 (58)	12 (48)	123 (60)		17 (55)	96 (59)	8 (80)	
Tertiary	58 (23)	7 (28)	46 (22)		9 (29)	39 (24)	2 (20)	
Employment								
Unemployed	123 (49)	16 (64)	108 (53)	0.556	21 (68)	81 (50)	5 (50)	0.637
Self-employed	11 (4)	0	1 (<1)		0	1 (<1)	0	
Wage-earner	111 (45)	9 (36)	92 (45)		10 (32)	76 (47)	5 (50)	
Other	4 (2)	0	4 (2)		0	4 (3)	0	
Household social grants								
None	162 (67)	15 (60)	133 (67)	0.666	17 (55)	106 (68)	5 (50)	0.054
Child support	69 (29)	10 (40)	57 (29)		14 (45)	43 (27)	3 (30)	
Social relief	3 (1)	0	3 (2)		0	3 (2)	0	
Disability	2 (1)	0	1 (<1)		0	1 (<1)	0	
Old-age pension	6 (3)	0	6 (3)		0	4 (3)	2 (20)	
Living standard measure								
Low (LSM 1 - 4)	17 (7)	1 (4)	14 (7)	0.844	2 (7)	10 (6)	0	0.771
Medium (LSM 5 - 7)	148 (59)	16 (62)	123 (60)		17 (55)	98 (61)	5 (50)	
High (LSM 8 -10)	85 (34)	9 (35)	68 (33)		12 (39)	54 (33)	5 (50)	

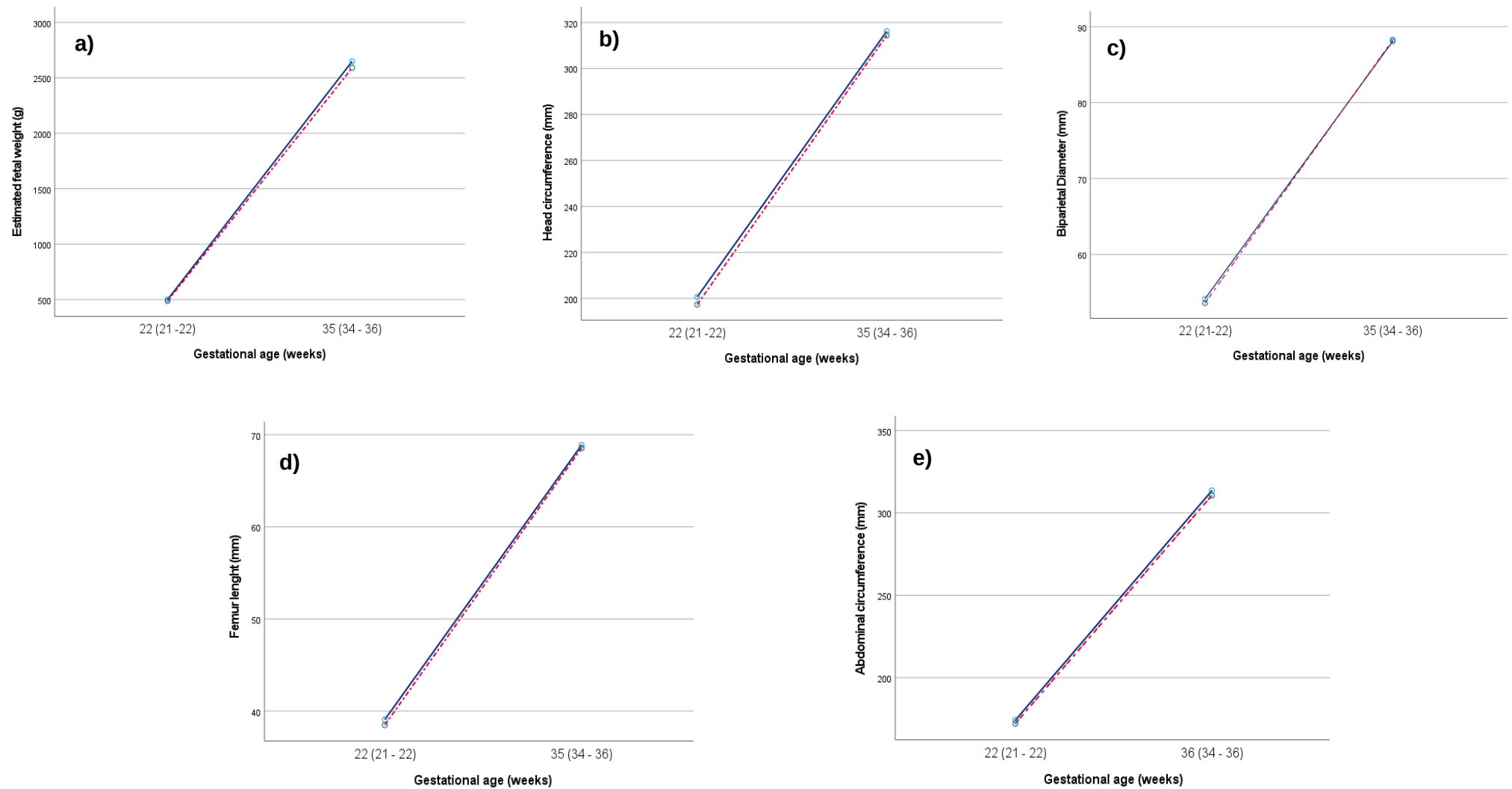
Supplementary table 1: Characteristics of the NuPED study population according to birth outcomes (n = 250)

Subject characteristics	Total sample (n = 250) Median (IQR) or n(%)	Gestational age at birth			Birth weight			p-value ³
		Preterm birth n=26 (11%)	Term n=205 (89%)	p-value ³	LBW n =31 (15%)	Normal birth weight n =162 (80%)	Macrosomia n=10 (5%)	
HIV status								
Positive	64 (26)	5 (19)	55 (27)	0.405	5 (16)	48 (30)	2 (20)	0.263
Negative	186 (74)	21 (81)	150 (73)		26 (84)	114 (70)	8 (80)	
Parity								
Nulliparous	74 (30)	6 (23)	65 (32)	0.430	9 (29)	49 (30)	2 (20)	0.446
Primiparous	88 (35)	12 (46)	69 (34)		14 (45)	51 (32)	5 (50)	
Multiparous	88 (35)	8 (31)	71 (35)		8 (26)	62 (38)	3 (30)	
Height (cm)	159 (155 - 162)	158 (153 - 161)	160 (155 - 162)	0.173	159 (155 - 162)	159 (155 - 162)	159 (152 - 162)	0.926
Pre-pregnancy BMI (kg/m²)⁵	25 (22 - 30)	24 (20 - 32)	25 (22 - 29)	0.797	25 (21 - 31)	25 (22 - 30)	27 (25 - 29)	0.610
Underweight	14 (6)	3 (12)	10 (5)	0.248	6 (19)	6 (4)	0	0.007
Normal weight	105 (42)	14 (54)	86 (42)		14 (45)	70 (43)	2 (20)	
Overweight	73 (29)	5 (19)	62 (30)		6 (19)	50 (31)	3 (30)	
Obese	57 (23)	4 (15)	47 (23)		5 (16)	36 (22)	5 (50)	
Gestational weight gain (g/week)⁶	0.4 (0.2 - 0.5)	0.4 (0.3 - 0.5)	0.4 (0.2 - 0.5)	0.407	0.5 (0.4 - 0.6)	0.4 (0.2 - 0.5)	0.3 (0.2 - 0.4)	0.051
Inadequate	46 (30)	5 (31)	38 (30)	0.643	4 (21)	28 (29)	3 (43)	0.649
Adequate	44 (29)	3 (19)	37 (29)		5 (26)	31 (32)	1 (14)	
Excessive	63 (41)	8 (50)	51 (41)		10 (53)	37 (39)	3 (43)	
Iron supplementation								
Yes	201 (84)	19 (73)	168 (86)	0.970	7 (23)	130 (84)	8 (80)	0.616
No	39 (16)	7 (27)	28 (14)		24 (77)	24 (16)	2 (20)	
Folate supplementation								
Yes	223 (93)	22 (15)	184 (94)	0.086	28 (90)	143 (93)	10 (100)	0.587
No	17 (7)	4 (85)	12 (6)		3 (10)	11 (7)	0	
Omega 3 supplementation								
Yes	11 (4)	2 (8)	8 (4)	0.371	1 (3)	7 (4)	0	0.773
No	239 (96)	24 (92)	197 (96)		30 (97)	155 (96)	10 (100)	
Fetal sex								
Male	119 (54)	12 (48)	107 (55)	0.516	13 (42)	92 (58)	6 (60)	0.267
Female	102 (46)	13 (52)	88 (45)		18 (58)	68 (43)	4 (40)	
Birth weight (g)	3050 (2790 - 3380)	2080 (1700 - 2533)	3132 (2898 - 3403)	0.000	2255 (1810 - 2350)	3120 (2904 - 3380)	4383 (4085 - 5088)	0.000

LBW: Low birth weight; HIV: Human Immunodeficiency virus; LSM: Living Standard Measure; BMI: body mass index. Continuous data presented as median (IQR) and categorical data as n (%).

¹ Missing data: gestational age at birth (n=19), birth weight (n=47), ethnicity, marital status, highest level of education, employment and approximate pre-pregnancy BMI (n=1); household social grants (n=8); gestational weight gain (n=97); iron and folate supplementation (n=10), fetal sex (n=29). ² Preterm birth: <37 weeks' gestation, and term birth: ≥37 weeks' gestation; LBW: ≤2500g, normal birth weight: 2500 – 4000g, and macrosomia: ≥4000g. ³ Chi-square test for categorical- and Mann-Whitney U test for continuous data. ⁴ Recognised under the customary law of South Africa, traditional marriage is entered into

by parties according to tradition and do not require approval of an officer for validation. Allows for polygamous marriages. ⁵ An approximate pre-pregnancy BMI was calculated by adjusting maternal weight at enrolment according to the IoM guidelines for GWG (Institute of Medicine & National Research Council, 2009). ⁶ Categories as per the IoM GWG recommendations: inadequate GWG, underweight: ≤ 0.51 , normal weight ≤ 0.42 , overweight ≤ 0.28 , obese ≤ 0.22 ; adequate GWG, underweight 0.44 – 0.58, normal weight 0.35 - 0.50, overweight 0.23 – 0.33, and obese 0.17 – 0.27; excessive GWG, underweight ≥ 0.58 , normal weight ≥ 0.50 , overweight ≥ 0.33 and obese ≥ 0.27 .



Supplemenatry figure 1: Fetal growth parameters [(a) estimated fetal weight (EFW), (b) head circumference (HC), (c) biparietal diameter (BPD), (d) femur length (FL) and (e) abdominal circumference (AC)] presented per gender

Blue solid line: males (EFW and AC: n=95; HC and BPD: n=93; FL: n=92); Red dotted line: female (EFW: n=82; HC, BPD and FL: n=67; AC: n=83)

Supplementary Table 2: Spearman's Rho correlation coefficients for nutrient patterns, fetal growth parameters and possible covariates

	Correlation coefficients																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1) Nutrient pattern 1	1.00	-0.02	-0.50**	-0.03	-0.10	-0.04	-0.10	-0.04	-0.11	0.03	0.11	-0.01	-0.05	-0.06	0.23**	0.15	0.13	-0.08	-0.12	0.15*	0.11	0.00	-0.04	-0.06	-0.08
2) Nutrient pattern 2		1.00	0.25**	0.03	0.09	0.06	0.05	0.05	-0.12	0.02	0.04	-0.02	-0.14	-0.01	0.02	0.10	0.08	-0.06	0.06	0.05	0.04	-0.07	-0.03	-0.03	0.03
3) Nutrient pattern 3			1.00	-0.04	-0.06	-0.14*	-0.15*	-0.02	-0.04	0.00	-0.04	-0.07	-0.10	0.13	0.08	0.12	0.16	0.09	0.03	-0.10	-0.07	-0.01	-0.07	.163*	.139*
Mid-pregnancy																									
4) AC				1.00	-0.02	-0.04	-0.10	0.90**	0.27**	0.10	0.18*	-0.03	0.28**	-0.32**	0.10	0.07	-0.04	-0.12	-0.03	0.11	-0.04	.154*	-0.08	-0.11	0.04
5) BPD					1.00	0.76**	0.55**	-0.06	0.09	0.25**	0.18*	0.14	0.07	0.00	-0.25**	-0.32**	-0.18*	-0.11	-0.04	-0.09	0.03	-0.01	-0.07	-0.04	-0.06
6) HC						1.00	0.63**	-0.04	0.08	0.13	0.21**	0.12	0.10	-0.02	-0.35**	-0.30**	-0.25**	-0.11	0.02	-0.07	0.09	-0.01	0.01	-0.03	-0.09
7) FL							1.00	-0.05	-0.11	0.06	0.09	0.24**	-0.06	-0.08	-0.21*	-0.15	-0.32**	-0.17*	0.05	-0.01	0.06	-0.08	0.08	-0.10	-0.01
8) EFW								1.00	0.20**	0.04	0.15*	-0.10	0.24**	-0.30**	0.07	0.04	-0.10	-0.13	-0.03	0.09	-0.03	.168*	-0.11	-0.04	0.09
Late pregnancy																									
9) AC								1.00	0.05	0.04	-0.03	0.91**	0.40**	-0.28**	-0.29**	-0.29**	-0.06	-0.09	-0.10	-0.13	-0.05	-0.09	-0.08	0.07	
10) BPD									1.00	0.64**	0.28**	0.02	-0.06	0.33**	0.59**	0.13	0.00	-0.04	-0.02	-0.07	-0.06	0.09	-0.10	0.04	
11) HC										1.00	0.31**	0.03	-0.03	0.57**	0.46**	0.25**	-0.12	0.03	-0.04	-0.02	0.00	0.10	-0.05	0.01	
12) FL											1.00	-0.05	0.00	0.13	0.12	0.58**	-0.02	0.01	0.13	0.02	0.01	0.07	-.167*	-0.07	
13) EFW												1.00	0.24**	-0.37**	-0.37**	-0.38**	-0.03	-0.11	0.00	-0.10	-0.08	-0.19	-0.06	0.11	
Interval fetal growth																									
14) AC														1.00	0.16	0.17*	0.25**	-0.05	-0.04	-0.13	-0.12	-.151*	0.09	0.09	-0.02
15) HC															1.00	0.83**	0.67**	0.00	0.00	0.01	-0.14	0.13	0.17	-0.03	-.227**
16) BPD																1.00	0.60**	0.06	0.02	0.04	-0.16	0.07	0.17	0.00	-0.15
17) FL																	1.00	-0.02	-0.01	0.10	-0.06	0.14	0.11	-0.02	-.250**
Covariates																									
18) Fetal sex																		1.00	-0.09	0.03	-0.01	-0.06	-0.02	0.02	-0.02
19) Parity																			1.00	0.14*	-0.08	-0.03	0.01	-0.04	0.04
20) Mother age																				1.00	-0.08	-0.09	-0.04	0.05	0.04
21)Mother height																					1.00	0.01	0.04	-0.05	-0.07

Supplementary Table 2: Spearman correlation coefficients for nutrient patterns, fetal growth parameters and possible covariates

Correlation coefficients																								
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
22) Pre-pregnancy BMI																					1.00	-0.26**	-0.11	-0.10
23) GWG (g/week)																						1.00	-0.07	-0.05
24) Iron supplementation																							1.00	0.10
25) Folate supplementation																								1.00

AC: abdominal circumference, BPD: biparietal diameter, HC: head circumference, FL: femur length, EFW: estimated fetal weight

* $p < 0.05$, ** $p < 0.01$

CHAPTER 5 ARTICLE 3

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Associations between maternal nutrient patterns during pregnancy and offspring growth and neurodevelopment – the NuPED study

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ABSTRACT

Postnatal development is a continuous and complex process, with neurodevelopment being imperative hereto. Nutrition is known to be an important controllable factor for both child growth and neurodevelopment. Research investigating associations between maternal dietary patterns during pregnancy and offspring growth and development is though limited, especially in low- and middle-income countries. With this study, we aimed to investigate these associations among 250 pregnant women and their offspring enrolled in the Nutrition during Pregnancy and Early Development (NuPED) cohort. Maternal *a posteriori* nutrient patterns were derived using exploratory factor analysis from nutrient data obtained by means of a quantified food frequency questionnaire conducted at <18 weeks' gestation. Infant growth was described by anthropometric indices and neurodevelopment using the Protocol for Child Monitoring – Infant-Toddler (PMC-IT) version. Assessments to evaluate infant growth and neurodevelopment were conducted at 6 and 12 months postpartum. The 'plant protein, iron, thiamine, and folic acid' nutrient pattern was found to be negatively correlated with adaptive skills at 6 months postpartum after adjusting for covariates ($r = -0.339$, $p = 0.009$). Moderate to higher adherence, compared to a lower maternal adherence, to the 'animal protein, copper, vitamin A, and vitamin B₁₂' pattern and the 'fatty acids and sodium' pattern, respectively, was associated with lower social-emotional development scores ($p = 0.015$) at 12 months, and lower WAZ ($p = 0.005$ and $p = 0.007$) and LAZ ($p = 0.016$ and $p = 0.012$) at 6 and 12 months postpartum. Providing an optimal environment for prenatal development by ensuring optimal maternal dietary intake is advised rather than relying on later catch-up growth and development.

Keyword: *a posteriori* nutrient patterns, pregnancy, infant growth, infant neurodevelopment

Short running title: Associations nutrient patterns and offspring outcomes

INTRODUCTION

Postnatal development, broadly categorised as physical, cognitive and social-emotional development, is a complex and continuous process¹. Neurodevelopment is imperative for the advancement of these developmental domains² and, therefore, one of the most important life-long health outcomes of early life development³. Brain development commences soon after conception, and the developing brain increase in capacity throughout the fetal period to allow for fundamental behavioural functions (such as taste, hearing, touch, pain sensation, and, to a lesser extent, vision) to be present at birth^{3,4}. With synapses development peaking between 34 weeks' gestation and the age of 2 years^{5,6}, the neural circuits formed prenatally establish the foundation upon which postnatal neurodevelopment occurs³. Neural pathways refine during the first 24 months postnatally through the retainment and strengthening of synapses *via* input from the environment and experiences, as well as synaptic pruning of synapses seldom used or stimulated⁴. During this time, the brain develops from a non-specific organ with high plasticity, into a highly specific organ with low plasticity³.

With nutrients involved in neurodevelopmental processes, nutrition is regarded as a prominent and modifiable environmental factor in brain development^{3,4}. Georgieff *et al.* indicate, however, that the effect of postnatal nutrition on brain development is greatly dependent on the prenatal fetal nutritional status³, and hence maternal dietary intake which directs fetal nutrient exposures^{7,8}. Nutrition is also known to be a key determinant of a child's growth, with fetal growth retardation and linear growth known to be a risk factor for poor childhood developmental outcomes^{9,10}. As nutrients, consumed as a combination of foods, are in interaction and synergy with each other^{11,12}, Hu *et al.* propose dietary pattern analysis as a complementary method for better understanding the effect of the diet as a whole on health outcomes¹². Moskal *et al.* encourage the use of nutrients rather than foods or food groups for dietary pattern analysis as nutrients, compared to foods, have fewer non-consumers, which aids in statistical analysis and interpretation, and allows for easier comparison between population groups¹³.

Research on the associations between maternal dietary patterns during pregnancy and offspring growth and development is though limited. Most studies focus on the maternal diet as a possible risk factor for offspring overweight and obesity, with evidence indicating that a maternal dietary pattern of low quality during pregnancy is associated with offspring adiposity^{7,8,14,15}. In one of the few studies including *a posteriori* dietary patterns and child behavioural outcomes, Steenweg-de Graaff *et al.* reported that low adherence to the Mediterranean diet and high adherence to a traditional Dutch diet were associated with child externalising problems, such as aggression and inattention, up to the age of 6 years¹⁶. Borge *et al.*, as part of a meta-analysis, considered the associations between maternal dietary quality during

pregnancy and offspring neurodevelopment. Regardless of disparities between the publications included, a small positive association was found between a higher maternal dietary quality and child neurodevelopment, particularly with regard to cognition ¹⁷. It is important to note that these studies were all conducted in high-income countries.

We previously found among urban black South African women that a 'plant protein, iron, thiamine and folic acid' nutrient pattern was positively associated with fetal head circumference growth between mid- and late pregnancy ¹⁸. With head circumference serving as a proxy for brain development during early life ¹⁹, it is probable that this pattern, which was also found to be of higher dietary quality ²⁰, has a more positive outcome on brain development. Conversely, a 'fatty acid and sodium' pattern (which had a lower dietary quality ²⁰) was negatively associated with femur length ¹⁸, which can be indicative of fetal linear growth ²¹. In this study, we determined the associations of the maternal dietary patterns with offspring growth and development, and aims to add to the limited body of knowledge available on this in low- and middle-income countries.

METHODS

Study design and research participants

The *Nutrition during Pregnancy and Early Development* (NuPED) study (conducted between March 2016 and June 2019 in Johannesburg, South Africa) aimed to assess maternal dietary intake and nutritional status during pregnancy and to determine associations with maternal health, birth outcomes and offspring development. Pregnant urban women were enrolled at early pregnancy (<18 weeks' gestation) and followed up throughout pregnancy, at birth, and, together with their offspring, up to the age of 12 months. The protocol for this prospective cohort study has previously been described ²². This article reports on data collected at enrolment (< 18 weeks' gestation), at birth, and at 6 and 12 months postnatally.

Healthy pregnant women residing in Johannesburg were recruited from primary health care clinics within the catchment area of Rahima Moosa Mother and Child Hospital (RMMCH), a provincial hospital delivering paediatric and maternal health care. Based on the socio-economic profile, primary health care clinics in South Africa provide health care services mainly to the poorer proportion of the South African population ²³. The inclusion criteria for this study were as follows: planned delivery at RMMCH; maternal age between 18 and 39 years; gestational age of <18 weeks; pregnant with a single fetus; country of birth [South Africa or a neighbouring country (Namibia, Botswana, Zimbabwe, Swaziland and Lesotho); must have resided in South Africa for at least one year]; and fluency in a local language (Afrikaans, English, Xhosa, Zulu and/ or Sotho). Women were excluded from the study if they used illicit

drugs (self-reported), smoked (during the past year and/or currently), or were previously diagnosed with a non-communicable disease (high cholesterol, hypertension, renal disease and/ or diabetes mellitus), infectious disease (hepatitis and/ or tuberculosis) and/or a serious illness (psychosis, cancer and/or lupus). Human immunodeficiency virus (HIV) was, however, not regarded as an exclusion criterion owing to the prevalence of HIV among women of reproductive age in South Africa (2 out of every 10 women ²⁴). Offspring of all enrolled pregnant women were regarded as eligible for inclusion.

Data collection took place at RMMCH: prenatal data were collected at the prenatal clinic as part of routine maternal care; birth data were collected at the relevant hospital wards; and postnatal data were collected at Empilweni Services and Research Unit situated at RMMCH. The sample size was calculated at 250 participants; the calculations on how this sample size was derived are published in Symington *et al* ²².

Ethical Considerations

An informed-consent form was provided to all women eligible and willing to participate in the study during recruitment. Informed consent was obtained during the first study visit after an opportunity to ask questions. Initial consent was given for both the pregnancy and postnatal follow-up of the study; written informed consent was again obtained, however, before the postnatal infant assessments. Participants were assured throughout that participation was voluntary and that non-participation would not affect maternal care received.

Ethical approval was granted by the Human Research Ethics Committee of the North-West University, Potchefstroom (NWU-00186-15-A1; NWU-00049-16-A1) and the University of the Witwatersrand, Johannesburg (M161045; M161045). Permission to perform the study at RMMCH was also obtained from the Gauteng Department of Health, City of Johannesburg District Research Committee and the RMMCH hospital manager. The study was conducted as per the guidelines of the World Health Association's Declaration of Helsinki.

Outcome variable: infant growth and neurodevelopment

Infant anthropometry

Infant growth was reported in terms of infant anthropometry, namely weight, length and head circumference. Anthropometric measurements were taken by trained fieldworkers at birth, and at 6 months and 12 months postpartum. All measurements were taken twice and were based on the guidelines provided by the World Health Organization (WHO) ^{25, 26}. If the weight varied by more than 50 grams and length by more than 0.2 centimetres, a third measurement was taken.

Birth measurements were taken within 12 hours after birth; if the fieldworker was not able to take the measurements within this period, data were recorded from the medical file (same equipment and techniques used). For newborn weight, the infant was minimally clothed (without a nappy) and weighed using a calibrated digital infant scale (Seca 334, Hamburg, Germany). The crown–heel length was determined by placing the infant in a supine position with arms and legs extended on a non-elastic measuring tape (Seca 201, Hamburg, Germany) on a flat surface. The measurement was taken from the vertex to the heel of the foot with the foot in a horizontal position to the leg. Weight was recorded to the nearest 10 grams, and head circumference and crown–heel length to the nearest 0.5 centimetres. All measurements were taken using a non-metallic measuring tape to prevent possible lesions.

Before anthropometric measurements were taken at 6 and 12 months of age, the child was assessed for oedema (none of the infants however presented with oedema at either 6 or 12 months of age). Weight was taken to the nearest 5 grams using a calibrated digital infant scale with the infant dressed in minimal clothing and without a nappy. Length and head circumference were measured to the nearest 0.1 centimetre using an infantometer (Seca 416, Hamburg, Germany) and non-elastic measuring tape, respectively.

Growth indicators for weight, length and head circumference were calculated using WHO Anthro Survey Analyser (version 3.2.2) ²⁷. Underweight, stunting and wasting were defined as a weight-for-age (WAZ), length-for-age (LAZ) and weight-for-length (WLZ) below the -2 z-score of the WHO child growth standard, respectively, with a WLZ of more than +2 indicative of a risk of overweight and obesity ²⁵. A head circumference between the -2 and +2 z-score was regarded as normal growth ²⁸.

Protocol for Child Monitoring – Infant-Toddler version

Infant neurodevelopment was described at 6 and 12 months using a comprehensive child development assessment tool, namely the Protocol for Child Monitoring – Infant-Toddler version (PCM-IT). The PCM-IT evaluates child psychomotor, language and social-emotional development and is comprised of assessment tools previously developed and standardised in Kenya which has been used in various African settings, namely the Kilifi Developmental Inventory ²⁹, Developmental Milestone Checklist – version 2 ^{30, 31}, and the Profile for Social-Emotional Development ³². Supplementary Table 1 illustrates the developmental domains assessed by the PCM-IT, the tests used up to the age of 12 months, as well as the assessment tool from which the items were derived.

The PCM-IT was conducted by medical doctors at Empilweni Services and Research Unit. The assessors received training on the administration of the PCM-IT by one of the researchers

involved in the compilation of the PCM-IT. All assessments took place in a standardised manner, using the same assessment equipment, and in a private area without any distractions and with space for movement. The PCM-IT is based on a combination of interviewer observations, parental report and direct assessment – if the parent mentioned that a specific task had not been observed, the assessor created an opportunity for the child to perform the task. The task was demonstrated to the child before it was expected to attempt the task. If needed, support was given to assist the child in completing the task, whereafter the child was granted an opportunity to try on its own. Items evaluated were grouped progressively from skills acquired earlier to more advanced skills. Should a more advanced skill have been observed, less advanced skills were scored without administration. The majority of the items were scored on four levels, with '0' denoting a child not able to complete the task to '3' indicating that the child was able to complete the task independently. All items assessing emotional development were scored on a three-point Likert scale: '0' indicating 'never or rarely happens'; '1' 'happens sometimes; and '2' 'always happens or most of the time'. The absolute scores per developmental domain are also indicated in Supplementary Table 1. No cut-off values or expected performance ranges per age have yet been determined for the PCM-IT.

Exposure variable: maternal dietary patterns

Maternal dietary patterns during pregnancy have been described elsewhere ²⁰. In brief, a *posteriori* nutrient patterns were determined from 22 nutrients, using exploratory factor analysis ³³. The nutrient intake was derived from maternal dietary intake data obtained from a quantified food frequency questionnaire (QFFQ) at early pregnancy (<18 weeks' gestation). Maternal dietary patterns were determined at only one time point during pregnancy as Crozier *et al.* have indicated that, regardless of variation in the types of foods consumed, maternal dietary patterns change only slightly before and during pregnancy ³⁴. Steenweg-de Graaff *et al.* also determined maternal dietary patterns only at early pregnancy (median 13.5 weeks) to investigate associations with offspring behaviour ¹⁶. The Kaiser-Meyer Olkin measure of sampling adequacy and Bartlett's test of sphericity was used to determine the reliability of the exploratory factor analysis with a correlation matrix. Factors (patterns) were retained based on an eigenvalue of more than one, the scree plot, total variance of the factors, and the natural interpretability of the factors. Varimax rotation was applied to the retained factors, after which the factors were named and interpreted according to nutrients with a factor loading of more than 0.40. A factor score for each participant was calculated to indicate the degree to which each participant's nutrient intake conformed to the identified patterns.

The QFFQ used for the collection of dietary intake data was previously validated ³⁵ and the reproducibility proven ^{36, 37} for a South African population. The 140-item questionnaire, administered by trained fieldworkers, inquired in as much detail as possible about the type/brand of foods and drinks consumed during the previous four weeks. Using standard probing questions ³⁸, fieldworkers also inquired on the frequency and amount of each type of food consumed, as well as the cooking methods used. Portion sizes were determined using 'dish-up and measure', household utensils, two- and three-dimensional food models, and food packaging. The portion sizes reported were converted to grams as per the Food Quantities Manual of the South African Medical Research Council (SAMRC) ³⁹. All foods and drinks were coded according to the SAMRC Food Composition Tables ⁴⁰ whereafter it was linked by a statistician at the SAMRC to the latest version of the food composition database to determine daily energy, macronutrient and micronutrient intake. The nutrients included for the nutrient pattern analysis were representative of nutrients obtained from foods only and did not account for micronutrient supplementation. Dietary data were obtained from all women (n = 250) at enrolment.

Covariates

Walker *et al.* ^{9, 41} and Britto *et al.* ⁴² published, as part of the Lancet series on early childhood development, possible risk and protective factors for early childhood development. Considering neurodevelopmental outcomes more specifically, Abubakar *et al.* indicated that stunting, underweight, poor child health, high gravidity and low levels of maternal schooling were possible predictors of poor child development in an African population ⁴³. Engebretsen *et al.* ⁴⁴ and Arifeen *et al.* ⁴⁵ have, however, indicated that gender, poor feeding practices after birth, length of exclusive breastfeeding (3 to 5 months have a positive outcome on child growth), and socioeconomic status are determinants of infant growth in Eastern Uganda and Bangladesh, respectively. Tahir *et al.* ⁸ also considered gestational weight gain and maternal pre-pregnancy body mass index (BMI) as possible covariates in the association between maternal dietary patterns during pregnancy and infant body fat percentage and fat mass. Considering these publications, the covariates for child development were divided into covariates for (1) child growth (anthropometry) and (2) child neurodevelopment. Covariates for child growth included gender, socioeconomic status, maternal pre-pregnancy BMI, gestational weight gain (GWG) during pregnancy, and infant feeding practices. Possible covariates for child neurodevelopment were determined as length-for-age (indicator for stunting/ chronic undernutrition), weight-for-length (indicator for wasting/ acute undernutrition), parity, maternal level of education, and maternal psychological wellbeing. Although Borge *et al.* ¹⁷ recommend that future studies control for infant feeding practices when determining

associations between maternal dietary patterns and offspring neurodevelopment, we did not account for this as poor feeding practices are likely to reflect in anthropometric indices. Parity was also considered rather than gravidity, as parity provides a better indication of other children the mother is likely to care for. In both cases, we also controlled for maternal compliance to micronutrient supplementation during pregnancy (iron and folate form part of routine maternal care at primary health care clinics in South Africa), as well as infant gestational age and birth weight. Methodology on how the data of the covariates were collected are indicated in Symington *et al.*²² and Conradie *et al.*^{18, 20}.

Statistical analysis

The raw dietary data were captured in Microsoft Excel; all data were double-checked to ensure that the foods/drinks were correctly quantified and that the correct codes were used. All other raw data were captured in Microsoft Access. Apart from the PCM-IT data, twenty percent of the data were randomly checked to ensure accuracy. PCM-IT data were checked on a case-by-case basis and missing variables were imputed as follows: for more progressive developmental tasks a '0' was given assuming that the administrator did not observe the task and hence the child could not perform the task; and for skills generally acquired before the observed task, a '3' was given on the assumption the child could successfully perform the task.

The distribution of the data was checked using the Shapiro-Wilks test, q-q plots and histograms. Normally distributed data are reported as mean and standard deviation, and non-normally distributed as the median and interquartile range (IQR). Categorical data are presented as frequencies and percentages. Difference between growth (n = 80) and neurodevelopmental (n = 55) parameters between the two data collection time points were determined using paired univariate analysis (Friedman's test for categorical data and Wilcoxon Signed Rank test for continuous data). The population was furthermore described according to the anthropometric indices per covariates at age 6 and 12 months [Supplementary Table 2 - 3, (similar analysis could not be performed for neurodevelopmental outcomes owing to a large number of missing data)]. Repeated-measure linear modelling could not be applied to determine associations between maternal dietary patterns and infant growth and development over time because of the small sample size and large number of missing data. Spearman-rho correlation (data not shown), followed by partial correlation, was hence used to determine the relationship between the maternal dietary patterns during pregnancy and infant growth and neurodevelopment including the covariates. Analysis of covariance (ANCOVA) with Bonferroni correction was used to determine the difference between dietary pattern adherence (nutrient

pattern tertiles) and infant growth and neurodevelopmental outcomes at each data collection time point. Significance was set at $p < 0.05$.

RESULTS

Characteristics of the study population

A total of 595 pregnant women were recruited to take part in the study: 313 volunteered and provided informed consent; of these 63 women did not meet the inclusion criteria. This resulted in 250 women being enrolled in the study. Birth data from 203 women were available as 7 women experienced intrauterine fetal death, 11 were lost to follow-up, and a further 29 opted to deliver their infants elsewhere. A high number of mother–infant pairs were, however, lost to follow-up postnatally, resulting in data from 98 mother–infant pairs being available at 6 months of age and from 100 at 12 months (Figure 1).

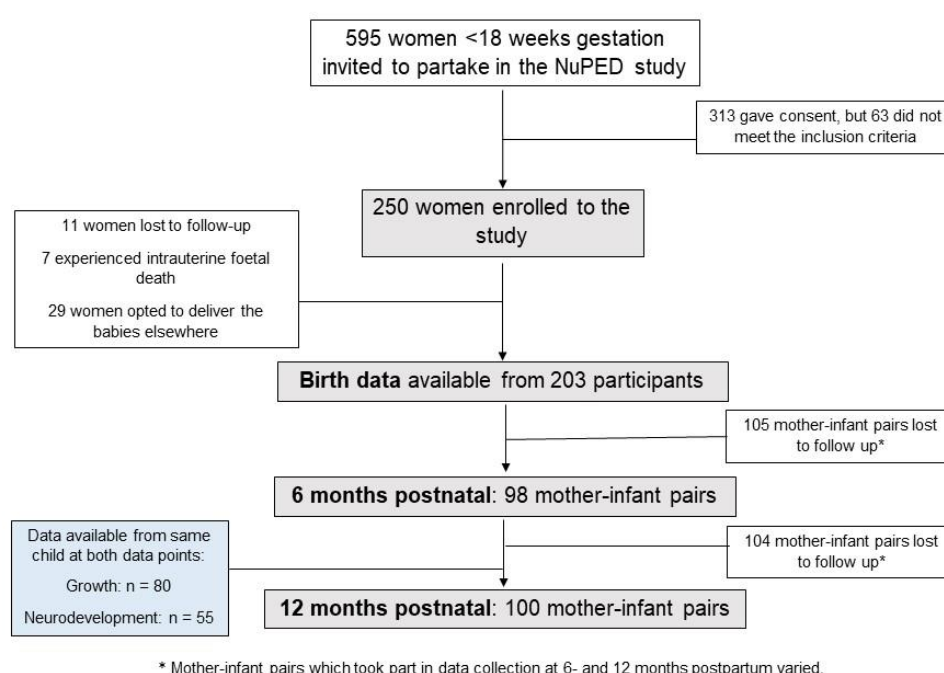


Figure 1: Flow diagram of mother–infant pairs enrolled to the NuPED study

A detailed description of the characteristics of the enrolled pregnant women and the infant birth outcomes is given in Conradie *et al.*^{20, 18} and Symington *et al.*⁴⁶, respectively. The study participants had a median (IQR) age of 27 (24 – 32) years and were predominantly of black African ethnicity (88%). Almost two-thirds (59%) of the enrolled women had a medium

socioeconomic status with an equal number of the participants (49%) reported being employed and unemployed, respectively. Half (52%) of the enrolled women entered their pregnancy either overweight or obese, with 41% gaining an excessive amount of weight between mid- and late pregnancy. Twenty-six percent of the participants were HIV positive.

Table 1 shows a description of the infants enrolled in the NuPED study at baseline (6 months of age), with Supplementary Table 2 – 3 describing the infants at 6 and 12 months of age according to anthropometrical indices and covariates. Both these tables provide data on the entire sample available at the respective time points (cross-sectional). At age 6 months, the infant study population comprised of more males (59%) than females (41%). The majority of infants were born at term (87%) with a birth weight within normal ranges ($n = 77\%$). A quarter (24%) of the infants were mix fed (receiving both breast- and breastmilk substitutes) by the age of 6 months, with complementary foods introduced before the age of 4 months in almost half of the infants (49%). Based on maternal parity, it is likely that most infants (75%) were raised in households including other children. Most mothers to the infants lived with their partners [either married (30%) or living together (30%)] and had a high school education (72%). Twenty-one percent and 16% of the mothers though had symptoms indicative of depression and fatigue, respectively.

Among our study population, more females were underweight ($p < 0.001$; $p < 0.001$), stunted ($p < 0.001$; $p < 0.001$) and had a small head circumference ($p = 0.002$; $p = 0.004$) at 6 and 12 months of age. At 12 months, females were also more likely to be wasted ($p = 0.042$). This is contrarily to the results found by Nyati *et al.* in a similar urban population. Nyati *et al.* reported black-African males rather than females to suffer from undernutrition⁴⁷. Infants born with a low birth weight were also more likely to have lower anthropometrical indices at both 6 and 12 months of age than infants born with a birth weight within normal ranges (Supplementary Table 2 – 3).

Table 2 provides, however, longitudinal data on the difference in growth and neurodevelopmental parameters between 6 and 12 months (paired analysis). There was no significant difference in the anthropometric indices between age 6 and 12 months. However, there was a significant improvement in all neurodevelopmental domains between the two data points.

Table 1: Description of infants from mothers enrolled in the NuPED study at 6 months of age; n = 98)

Subject characteristics	Total sample Median (IQR) or n (%)
Infant characteristics	
Gender	
Male	57 (59)
Female	39 (41)
Gestational age at birth ¹	
Preterm	12 (13)
Term	84 (87)
Birth weight ²	
LBW	14 (16)
Normal	68 (77)
Macrosomia	6 (7)
Feeding practices ³	
Mixed feeding	22 (24)
Only breastmilk/ breastmilk substitutes	68 (76)
Age at which complementary foods were introduced	
<4 months	32 (49)
4 – 6 months	18 (28)
≥6 months	15 (23)
Household characteristics	
Socio-economic status ⁴	
Low (LSM 1 – 4)	2 (2)
Medium (LSM 5 – 7)	61 (64)
High (LSM 8 – 10)	33 (34)
Maternal characteristics	
Parity	
Nulliparous	24 (25)
Primiparous	33 (34)
Multiparous	39 (41)
Level of education	
Primary/ None	3 (3)
Grade 8–10	15 (16)
Grade 11–12	53 (56)
Tertiary	24 (25)
Marital status	
Unmarried	31 (33)
Married	29 (30)
Living together ⁵	28 (30)
Traditional marriage	6 (6)
Divorced/ separated	1 (1)
Pre-pregnancy BMI ⁶	
Underweight	3 (3)
Normal weight	43 (45)
Overweight	29 (30)
Obese	21 (22)
Risk for postnatal depression ⁷	
No/ Low risk	69 (79)
At risk	18 (21)
Risk for postnatal fatigue ⁸	
No/ Low risk	77 (84)
At risk	15 (16)

IQR: Interquartile range; LBW: low birth weight; LSM: living standard measure;

Missing data: Gender, gestational age at birth, socio-economic status, parity and pre-pregnancy BMI (n = 2), birth weight (n = 10), mixed feeding (n = 8), age when complementary foods were introduced (n = 33), level of education and marital status (n = 3)

¹ Preterm birth defined a birth before 37 weeks' gestation, and term birth a birth ≥37 weeks' gestation; ² LBW defined as birth weight less than 2500g and macrosomia as a birth weight more than 4000g; ³ Mixed feeding was defined if the mother indicated

that both breast- and breastmilk substitutes were given before 6 months of age; ⁴ Determined using the South African Audience Research Foundation Living Standard Measure ⁴⁸; ⁵ Entered between parties based on tradition and hence does not need approval from an officer of validation. It is though recognised under South African customary law. Allows for polygamous marriage; ⁶ BMI classifications: underweight (<18.5 kg/m²), normal weight (18.5 – 24.9 kg/m²), overweight (25 – 29.9 kg/m²) and obese (>30 kg/m²); ⁷ Determined using the Edinburgh Postnatal Depression Score ^{49, 50}; a score of 9 or more out of possible 30 was regarded as a high risk for postnatal depression; ⁸ Determined using the Global Fatigue Index calculated from the Multidimensional Assessment Fatigue scale ⁵¹; a cut-off of 28 out of a possible 50 was indicative as a risk for fatigue ⁵².

Table 2: Difference in infant growth and neurodevelopmental parameters between age 6 and 12 months (n = 80 for growth- and n = 55 for neurodevelopmental parameter)

	Data collection time points		
	6 months post-partum ¹	12 months post-partum ¹	p-value ²
	n (%) or median (IQR)		
Infant growth: Anthropometric indices ³			
WAZ			
<-2	10 (11)	11 (11)	0.257 ⁴
-2 to +2	80 (85)	81 (82)	
>2	4 (4)	7 (7)	
LAZ			
<-2	15 (16)	19 (19)	0.655
>-2	80 (84)	80 (81)	
WLZ			
<-2	3 (3)	5 (5)	0.763
-2 to +2	88 (93)	86 (86)	
>2	4 (4)	9 (9)	
HCZ			
<-2	4 (4)	5 (5)	0.527 ⁴
-2 to +2	74 (78)	77 (79)	
>2	17 (18)	15 (16)	
Infant neurodevelopment: PCM-IT ^{3, 5}			
Psychomotor development scores (72)	22 (18 – 26)	62 (56 - 67)	<0.001
Gross motor (45)	16 (12 – 19)	37 (34 – 40)	<0.001
Fine motor (12)	6 (4 – 9)	19 (16 – 21)	<0.001
Cognition (15)	0 ⁶	7 (4 – 8)	<0.001
Language development scores (33)	3 (2 – 5)	10 (9 – 13)	<0.001
Social-emotional development scores (69)	30 (28 – 32)	34 (32 – 36)	<0.001
Social interaction (18)	9 (8 – 11)	12 (11 – 13)	<0.001
Emotional development (24)	12 (11 – 13)	10 (9 – 12)	<0.001
Adaptive skills (27)	9 (8 – 10)	11 (10 – 12)	<0.001

IQR: Interquartile range; WAZ: weight-for-age z-score, LAZ: length-for-age z-score, WLZ: weight-for-length z-score, HCZ: head-circumference-for-age z-score; PCM-IT: Protocol for Child Monitoring – Infant-Toddler version.

¹ Median (IQR) age at 6 months: 5.7 (5.6 – 6.0) months, and at 12 months 12.1 (12 – 12.4) months; ² Friedman's Test for categorical data, and Wilcoxon Signed Rank Test for continuous data; ³ Anthropometric indices: 6 months' postpartum n = 95 and 12 months' postpartum n = 100; Infant neurodevelopment: 6 months' postpartum n = 66 and 12 months' postpartum n = 99 (1 case excluded for being an extreme low value; the child was indicated to be ill during the assessment); Missing data: 6 months' postpartum WAZ (n = 1); 12 months' postpartum HAZ and WAZ (n = 1) and HCZ (n = 3); ⁴ Difference between parameters determined for WAZ on a sample of a sample n = 79 and HCZ n = 78; ⁵ Absolute maximum scores indicated in brackets next to each category. All categories have a minimum possible score of 0; ⁶ All infants scored 0 on cognition at age 6 months.

Significance (p < 0.05) indicated in **bold**.

***A posteriori* nutrient patterns**

The *a posteriori* nutrient patterns have been previously described ²⁰. The three nutrient patterns explained a total of 57% of the total variance in nutrient intake and were as follows: a 'plant protein, iron, thiamine, and folic acid'-, an 'animal protein, copper, vitamin A, and vitamin B₁₂'- and a 'fatty acids and sodium' nutrient pattern (Table 3).

Table 3: Maternal nutrient patterns at early pregnancy (n = 250)

Nutrients and variance explained	Factors (nutrient patterns) ¹		
	Nutrient pattern 1 (Plant protein, iron, thiamine, and folic acid)	Nutrient pattern 2 (Animal protein, copper, vitamin A, and vitamin B ₁₂)	Nutrient pattern 3 (Fatty acids and sodium)
Animal protein	-0.46	0.53	0.32
Plant protein	0.86	-0.09	-0.00
Saturated fat	-0.68	0.08	0.44
Monounsaturated fat	-0.51	0.08	0.67
Polyunsaturated fat	-0.15	-0.08	0.57
Cholesterol	-0.09	0.58	0.32
Carbohydrates	0.61	-0.21	-0.70
Total sugars	-0.23	0.05	-0.68
Total fibre	0.70	0.10	-0.24
Calcium	-0.44	0.20	-0.34
Iron	0.76	0.35	0.02
Sodium	0.04	0.01	0.64
Zinc	0.45	0.44	0.30
Copper	0.25	0.79	-0.08
Vitamin A	0.12	0.81	-0.07
Thiamine	0.77	0.10	-0.05
Riboflavin	0.01	0.63	-0.14
Niacin	0.54	0.39	0.31
Vitamin B ₆	0.67	0.03	0.26
Folic acid	0.73	0.36	-0.07
Vitamin B ₁₂	0.10	0.86	-0.03
Vitamin E	0.04	0.03	0.41
% of variance	27%	18%	11.5%
Total variance: 56.5%			

Reprinted with permission from Conradie *et al.* ²⁰. ¹ Factor analysis performed on 22 nutrients; estimates presented after rotation. Nutrients considered to have a strong association with the nutrient patterns (factor loading ≤ -0.4 and ≥ 0.4) are indicated in bold.

Associations between maternal nutrient patterns and infant growth and development

Table 4 presents the correlation coefficients [presenting both crude and adjusted data (partial correlation coefficients)] of the maternal nutrient patterns with the offspring neurodevelopmental outcomes. No correlations were found for infant growth outcomes. Table 5 and 6, respectively, indicates the difference in the growth and neurodevelopmental parameters based on adherence to the nutrient patterns.

The 'plant protein, iron, thiamine, and folic acid' nutrient pattern was found to have a negative correlation with infant adaptive skills ($r = -0.339$, $p = 0.009$), a sub-category of social-emotional development, at 6 months postpartum after adjusting for the maternal level of education and fatigue (Table 4). This correlation was though not found to be associated with the adherence to this nutrient pattern (Table 6). A moderate to higher adherence, compared to a lower adherence, to the 'animal protein, copper, vitamin A and vitamin B₁₂' pattern resulted in lower social-emotional development scores ($p = 0.015$) at 12 months of age. These lower social-emotional scores were probably driven by the trend towards significance seen with the lower scores on social-interaction ($p = 0.080$) and emotional development ($p = 0.058$) with higher adherence to the 'animal protein, copper, vitamin A and Vitamin B₁₂' pattern. With regards to growth, although also not seen in the correlation analysis, a moderate to higher compared to a lower maternal adherence to the 'fatty acids and sodium' pattern resulted in lower WAZ ($p = 0.005$ and $p = 0.007$) and LAZ ($p = 0.016$ and $p = 0.012$) at both 6 and 12 months postpartum (Table 3).

Table 4: Crude and adjusted correlation coefficients of maternal nutrient patterns during early pregnancy with infant neurodevelopmental outcomes

	Correlation coefficients	
	Infant neurodevelopment at 6 months (n = 65)	
	Self-help	
	<i>r</i>	<i>p</i> -value
'Plant protein, iron, thiamine and folic acid' pattern		
Crude	-0.324	0.009
Adjusted ¹	-0.339	0.009

r: correlation coefficient.

¹ Adjusted for maternal level of education and the Global Fatigue Index at 6 months postpartum (n = 60). Significant ($p < 0.05$) indicated in **bold**.

Table 5: Infant growth per nutrient pattern adherence at 6 (n = 98) and 12 months of age n = 100)

	‘Plant protein, iron, thiamine and folic acid’ pattern				‘Animal protein, copper, vitamin A and vitamin B ₁₂ ’ pattern				‘Fatty acids and sodium’ pattern			
	Low adherence	Moderate adherence	High adherence	p-value	Low adherence	Moderate adherence	High adherence	p-value	Low adherence	Moderate adherence	High adherence	p-value
	Tertile 1	Tertile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3		Tertile 1	Tertile 2	Tertile 3	
	Mean ± SD	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	Mean ± SD	
Infant growth: 6 months postpartum												
WAZ	-0.2 ± 1.6	-0.5 ± 1.2	-0.1 ± 1.2	0.754	-0.6 ± 1.4	-0.2 ± 1.3	-0.1 ± 1.3	0.718	-0.1 ± 1.3 ^a	-0.4 ± 1.3 ^b	-0.3 ± 1.4 ^b	0.005
LAZ	-0.4 ± 1.3	-0.5 ± 1.6	-0.3 ± 1.5	0.707	-0.2 ± 1.5	-0.7 ± 1.5	-0.4 ± 1.4	0.402	-0.2 ± 1.4 ^a	-0.7 ± 1.6 ^b	-0.5 ± 1.3 ^b	0.016
WLZ	0.1 ± 1.6	-0.1 ± 1.0	0.3 ± 1.0	0.975	-0.5 ± 1.3	0.4 ± 1.0	0.4 ± 1.2	0.227	0.1 ± 1.2	0.1 ± 1.2	0.0 ± 1.4	0.413
HCZ	0.9 ± 1.4	0.5 ± 1.6	0.6 ± 1.6	0.478	0.5 ± 1.5	0.7 ± 1.5	0.8 ± 1.5	0.191	0.7 ± 1.5	0.6 ± 1.8	0.8 ± 1.2	0.910
Infant growth: 12 months postpartum												
WAZ	-0.1 ± 1.4	-0.5 ± 1.3	-0.2 ± 1.4	0.670	-0.4 ± 1.4	-0.4 ± 1.3	-0.1 ± 1.4	0.379	-0.1 ± 1.3 ^a	-0.5 ± 1.3 ^b	-0.2 ± 1.4	0.007
LAZ	-0.6 ± 1.0	-1.0 ± 1.5	-0.7 ± 1.5	0.413	-0.8 ± 1.6	-0.9 ± 1.4	-0.6 ± 1.1	0.330	-0.6 ± 1.6 ^a	-0.9 ± 1.3 ^b	-0.8 ± 1.1	0.012
WLZ	0.2 ± 1.5	0.0 ± 1.2	0.2 ± 1.3	0.943	0.9 ± 1.4	0.1 ± 1.2	0.3 ± 1.4	0.619	0.3 ± 1.3	0.0 ± 1.3	0.2 ± 1.4	0.086
HCZ	0.8 ± 1.3	0.7 ± 2.5	0.8 ± 1.3	0.576	0.6 ± 1.4	0.9 ± 2.4	0.8 ± 1.4	0.427	1.1 ± 2.5	0.7 ± 1.4	0.6 ± 1.1	0.719

SD: standard deviation; WAZ: weight-for-age z-score, LAZ: length-for-age z-score, WLZ: weight-for-length z-score, HCZ: head-circumference-for-age z-score

Covariates included in the ANCOVA: gender, socioeconomic status, maternal pre-pregnancy BMI, GWG during pregnancy, infant feeding practices, maternal micronutrient supplementation (iron and folate), birth weight and gestational age.

Missing data: 6 months: WAZ (n = 1); 12 months: WAZ, LAZ (n = 1), HCZ (n = 3). Significant difference in the adherence to nutrient patterns (mean of tertiles) indicated in **bold** ($p < 0.05$).

Different letters in superscript indicate means to be significantly different according to Bonferroni correction ($p < 0.05$).

Table 6: Infant neurodevelopment per nutrient pattern adherence at 6 (n = 65) and 12 months of age (n = 100) ¹

	‘Plant protein, iron, thiamine and folic acid’ pattern				‘Animal protein, copper, vitamin A and vitamin B ₁₂ ’ pattern				‘Fatty acids and sodium’ pattern			
	Low adherence	Moderate adherence	High adherence	<i>p</i> -value	Low adherence	Moderate adherence	High adherence	<i>p</i> -value	Low adherence	Moderate adherence	High adherence	<i>p</i> -value
	<i>Tertile 1</i> Median (IQR)	<i>Tertile 2</i> Median (IQR)	<i>Tertile 3</i> Median (IQR)		<i>Tertile 1</i> Median (IQR)	<i>Tertile 2</i> Median (IQR)	<i>Tertile 3</i> Median (IQR)		<i>Tertile 1</i> Median (IQR)	<i>Tertile 2</i> Median (IQR)	<i>Tertile 3</i> Median (IQR)	
Infant neurodevelopment: 6 months postpartum												
Psychomotor development	24 (18 – 27)	22 (15 – 30)	21 (19 – 25)	0.772	24 (16 – 26)	23 (19 – 27)	21 (17 – 25)	0.178	21 (17 – 27)	23 (17 – 24)	23 (18 – 27)	0.808
Gross motor	18 (13 – 19)	14 (11 – 20)	16 (11 – 18)	0.310	18 (10 – 19)	16 (13 – 20)	16 (12 – 19)	0.246	16 (11 – 19)	16 (12 – 19)	17 (12 – 19)	0.805
Fine motor	6 (4 – 8)	6 (4 – 10)	6 (4 – 9)	0.724	6 (3 – 10)	7 (5 – 10)	6 (3 – 8)	0.419	6 (5 – 10)	5 (3 – 8)	6 (4 – 9)	0.590
Cognition	0	0	0		0	0	0		0	0	0	
Language development	4 (23 – 5)	3 (2 – 5)	3 (1 – 4)	0.226	4 (2 – 4)	3 (3 – 5)	3 (1 – 5)	0.833	3 (1 – 4)	4 (3 – 5)	3 (2 – 4)	0.994
Social-emotional development	30 (28 – 33)	30 (29 – 32)	30 (27 – 32)	0.927	32 (29 – 33)	30 (29 – 32)	29 (26 – 32)	0.257	30 (29 – 32)	29 (27 – 32)	31 (27 – 33)	0.853
Social interaction	9 (8 – 11)	10 (9 – 11)	9 (7 – 12)	0.666	11 (8 – 12)	9 (8 – 11)	9 (7 – 11)	0.475	9 (8 – 11)	9 (8 – 11)	10 (8 – 11)	0.949
Emotional development	12 (10 – 13)	12 (11 – 13)	13 (12 – 13)	0.701	12 (10 – 13)	13 (11 – 13)	12 (11 – 13)	0.461	13 (11 – 13)	12 (11 – 13)	12 (11 – 13)	0.559
Adaptive skills	9 (8 – 10)	9 (8 – 10)	8 (7 – 9)	0.212	9 (8 – 10)	9 (8 – 10)	9 (7 – 9)	0.131	9 (8 – 10)	9 (8 – 9)	9 (8 – 10)	0.790
Infant neurodevelopment: 12 months postpartum												
Psychomotor development	61 (57 – 71)	62 (55 – 67)	61 (56 – 68)	0.576	61 (55 – 67)	62 (47 – 67)	62 (58 – 70)	0.538	61 (55 – 65)	63 (56 – 68)	63 (57 – 71)	0.699
Gross motor	36 (34 – 41)	36 (33 – 40)	38 (35 – 40)	0.161	36 (34 – 40)	36 (33 – 40)	37 (36 – 41)	0.858	36 (34 – 39)	37 (33 – 41)	38 (34 – 40)	0.627
Fine motor	20 (15 – 22)	18 (16 – 21)	18 (17 – 22)	0.948	18 (16 – 22)	19 (14 – 21)	19 (16 – 21)	0.299	18 (16 – 20)	20 (17 – 21)	20 (15 – 23)	0.588
Cognition	7 (5 – 9)	5 (4 – 8)	6 (4 – 8)	0.958	6 (4 – 8)	7 (4 – 8)	7 (5 – 8)	0.756	5 (4 – 8)	7 (5 – 9)	7 (5 – 8)	0.934
Language development	10 (9 – 13)	10 (9 – 13)	10 (9 – 14)	0.905	10 (8 – 14)	10 (9 – 12)	10 (9 – 14)	0.748	10 (8 – 14)	11 (9 – 14)	9 (9 – 11)	0.829
Social-emotional development	34 (32 – 36)	34 (32 – 36)	34 (33 – 36)	0.362	35 (33 – 37) ^a	34 (32 – 36) ^b	34 (32 – 36) ^b	0.015	34 (33 – 36)	34 (32 – 36)	34 (32 – 37)	0.946
Social interaction	12 (11 – 13)	13 (11 – 14)	12 (11 – 13)	0.482	13 (12 – 14)	12 (11 – 13)	12 (11 – 13)	0.080	13 (12 – 13)	12 (12 – 13)	13 (11 – 14)	0.304
Emotional development	10 (9 – 13)	11 (9 – 12)	10 (9 – 12)	0.718	11 (9 – 12)	10 (9 – 12)	10 (9 – 13)	0.058	10 (9 – 12)	11 (10 – 12)	10 (9 – 12)	0.619
Adaptive skills	11 (10 – 12)	11 (10 – 12)	11 (10 – 12)	0.774	11 (10 – 12)	11 (10 – 12)	11 (10 – 13)	0.831	11 (10 – 12)	11 (10 – 12)	11 (11 – 13)	0.239

IQR: interquartile range

Covariates included in ANCOVA: length-for-age, weight-for-length, parity, maternal level of education, and maternal psychological wellbeing

¹Neurodevelopmental data collected from only 65 of the 98 infants enrolled at 6 months (missing data n = 33). Data from all 100 enrolled infants at age 12 months were collected; one case though excluded for being an extreme low value (n = 99).

Significant difference in the adherence to nutrient patterns (median of tertiles) indicated in **bold** (*p* < 0.05). Different letters in superscript indicate means to be significantly different according to Bonferroni correction (*p* < 0.05).

DISCUSSION

Research on the associations between maternal dietary patterns during pregnancy and infant growth and neurodevelopment is limited, especially in low- and middle-income countries. With this study, we aimed to add to this body of knowledge by investigating associations between the dietary patterns consumed by pregnant South African women in an urban setting and their offspring's growth and neurodevelopmental outcomes up to the age of 12 months. Amongst our study population, a 'plant protein, iron, thiamine, and folic acid' nutrient pattern was found to be negatively correlated with adaptive skills, a sub-category to social-emotional development, at 6 months postpartum after adjusting for covariates. Higher adherence to the 'animal protein, copper, vitamin A and vitamin B₁₂' and 'fatty acids and sodium' patterns, respectively, resulted to lower social-emotional development scores at 12 months, and lower WAZ and LAZ at both 6 and 12 months postpartum.

Social-emotional development is referred to as a child's ability to regulate social interactions and emotional responses and includes both self-regulation skills and temperament⁵³. Adaptive skills, also referred to as adaptive behaviour, denote conceptual, practical and social skills required to function in daily life, such as dressing self, feeding self, bladder control and interacting with others^{53, 54}. Altered social-emotional behaviour may influence how a child reacts to an environment and consequently how a caregiver responds to the child. This affects how a child experiences a physical and social environment and often, especially when accompanied with nutritional deficits (for example undernutrition or iron deficiency anaemia), has to effect that a child does not benefit from a developmentally supportive experience⁵⁵.

Research on the associations between nutrition and social-emotional development is restricted, with, to our knowledge, no studies as yet considering the associations with dietary patterns, nevertheless associations with maternal dietary patterns during pregnancy. Considering studies reporting on single nutrients, Chang *et al.* found Chinese children with iron deficiency anaemia before the age of 2 years to have poorer social-emotional skills at the age of 4 years compared with children without anaemia⁵⁶. Lozhoff *et al.* reported similar findings among healthy full-term Chilean infants during the first year of life with infants not receiving iron supplementation responding less positively to the physical and social environment by the age of 12 months⁵⁷. In a long-term follow-up, the infants who received iron supplementation between six and 12 months of age showed more adaptive behaviour at the age of 10 years compared to those children who did not receive iron supplementation during infancy⁵⁵. Metwally *et al.* furthermore reported low serum zinc levels in Egyptian infants between 6 and 24 months of age to be a possible predictor of social-emotional development⁵⁸.

The 'plant protein, iron, thiamine, and folic acid' nutrient pattern has previously been described as being reflective of a traditional South African diet based on its associations with food groups²⁰. Consumption of bread and maize, products fortified per South African legislation⁵⁹, were significantly positively associated with higher adherence to the 'plant protein, iron, thiamine, and folic acid' pattern²⁰. The factor matrix of this nutrient pattern is therefore congruent with the nutrients (iron, zinc, vitamin A, thiamine, riboflavin, pyridoxine, niacin and folate) used for fortification²⁰. The 'animal protein, copper, vitamin A, and vitamin B₁₂' pattern was yet again associated with a higher intake of animal products²⁰. This is reflected in the factor matrix as nutrients of which animal products are good sources of. This pattern, as previously described²⁰, is reflective of a nutrition transition from a traditional to a westernised diet, which is characterised by an increased intake of foods of animal origin^{60, 61}.

Although iron and zinc, as well as other nutrients important for brain development and functioning (including protein, copper and B vitamins)^{3, 4}, loaded positively on the matrix of both the 'plant protein, iron, thiamine, and folic acid' and 'animal protein, copper, vitamin A, and vitamin B₁₂' patterns, both patterns were associated with aspects of poorer social-emotional development. Other than reported low bioavailability, insufficient dosage and poor absorption of the electrolytic iron used for fortification which could possibly negatively influence maternal iron status of mother adhering to the 'plant protein, iron, thiamine, and folic acid' nutrient pattern⁶², polyunsaturated fatty acids were negatively loaded on the matrix of both these nutrient patterns. Polyunsaturated fatty acids, particularly eicosapentaenoic- (EPA) and docosahexaenoic acid (DHA), are well described in the literature to be integral for neurodevelopment as it is involved in key processes (including neuron proliferation, myelination and neurotransmission) of brain development^{3, 4}. With brain development commencing soon after conception with the most rapid development occurring between 34 weeks' gestation and the age of two years, the brain is vulnerable towards nutrient deficiencies³. The long-chain fatty acids EPA and DHA are though mainly found in fatty fish and their oils⁶³. Considering the foods related with each pattern²⁰, the 'plant protein, iron, thiamine, and folic acid' pattern was not associated with fish and seafood intake, whereas, although associated, fish and seafood provided about one percent of the total energy intake in participants adhering to the 'animal protein, copper, vitamin A, and vitamin B₁₂' pattern. Further investigation is though needed to clarify the possible reasons for these findings.

A higher adherence to the 'fatty acids and sodium' pattern was furthermore associated with lower WAZ and LAZ postnatally. With this pattern being of low dietary quality²⁰, these findings are congruent to that previously reported by Sharipo *et al.* and Tahir *et al.* in that maternal dietary quality during pregnancy are inversely associated with infant weight and adiposity at birth and 6 months, respectively^{7, 8}. This finding also supports data previously reported by this research group showing the 'fatty acids and sodium' nutrient pattern to negatively correlate with fetal femur

length¹⁸. With fetal femur length indicative of infant linear growth²¹, it is probable that linear growth retardation of infants born to mothers adhering to this dietary pattern commenced *in utero* already. Leroy and Frongillo (2019) describes linear growth retardation to be provoked by a deficient environment. With the 'fatty acids and sodium' pattern being of low quality, as well as a number of nutrients loaded negatively to the factor matrix of this pattern, it is probably that the maternal adherence to this pattern could be contributory towards an *in utero* environment not optimal for infant growth. It should also be acknowledged that linear growth retardation is associated with poor child neurodevelopment^{9,10}.

A great strength of this work is that maternal dietary patterns rather than single nutrients were assessed. Dietary patterns consider the diet as a whole and are regarded as a more predictive approach in determining risk factors for health outcomes¹². Our results were, however, limited by the small sample size and the large number of missing data, particularly the PCM-IT data at 6 months. Regardless, our findings confirm maternal nutrition during pregnancy, as indicated as part of the Developmental Origins of Health and Disease theory^{64,65}, to be of utmost importance and to likely have a lasting outcome on offspring growth and neurodevelopment. Pregnancy presents an environment in which fetal nutrient exposure can be greatly controlled⁶⁵. Providing optimal nutrition, rather than relying on catch-up growth during the postnatal period when various factors are known to influence growth and development, is recommended^{3,9,10,66}. Nutritional education programmes should hence be put in place to educate pregnant women on optimal dietary intake and its importance. Future studies including a larger study sample, as well as a longer follow-up period, are recommended.

Ethical statement

Ethical approval was granted by the Human Research Ethics Committee of the North-West University, Potchefstroom (NWU-00186-15-A1; NWU-00049-16-A1) and the University of the Witwatersrand, Johannesburg (M161045; M161045). Permission to perform the study at RMMCH was also obtained from the Gauteng Department of Health, City of Johannesburg District Research Committee and the RMMCH hospital manager. The study was conducted as per the guidelines of the World Health Association's Declaration of Helsinki.

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Contributor statement

C.M.S., J.B., L.M., E.A.S., and M.F. designed and conducted the research study; C.C and C.M.S conceptualisation of article; C.C. conducted the data analysis; C.C. wrote original draft of the article; C.M.S., J.B., M.F. reviewed and edited the article; funding for the study was obtained by E.A.S and C.M.S.

Conflict of interest

None of the authors has any conflict of interest to report.

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Supplementary Table 1: Description of the Protocol for Child Monitoring – Infant-Toddler version (PCM-IT) used for the assessment of infants enrolled in the NuPED study up to the age of 12 months

Developmental Domain	Tests/ Items	Absolute scores (min, max)	Assessment tool from which items are obtained
Psychomotor development		0, 96	Kilifi Developmental Inventory & Developmental Milestone Checklist II
Gross motor	<i>Lying prone:</i> upper body control, lifting of the upper body, rolls over and sitting with support <i>Sitting to standing:</i> Sits without support, reaches and returns to sitting position, moving/ crawling, moves from lying to sitting, and static balance <i>Standing to sitting:</i> Stands without support, moves from sitting to standing, and can sit down steadily from standing position <i>Walking:</i> Walks with support, walks without support and walks backwards	0, 45	
Fine motor	<i>Holding of objects:</i> Reaches for moving object, manipulates object, picks up an object, and retains one object	0, 36	
Cognition	Holds pen purposefully, draws shapes with pen, removes cubes from container, places cubes into a container, puts the lid back on the container	0, 15	
General language development		0, 33	Developmental Milestone Checklist II
	Repeats vowels in strings, repeats syllables in strings, understands gestures to request something, uses gestures to communicate, uses sounds instead of words, demonstrates by words or gestures that he/ she understands when told 'no', number of words child uses, identifies familiar objects, identifies body parts, uses 3 words in combination, can sing a song		
Social-emotional development		0, 69	Developmental Milestone Checklist II & Profile for Social-Emotional Development
Social development	Feeding, going to bed, can select a person to comfort him/ her, recognition of other people, reacts to own name, plays with others	0, 18	
Emotional development	Jealousy, reaction to parent's departure, independence of daily tasks, anger management, hits/ bites/ kicks parents, tantrums, solving disputes, overall mood	0, 24	
Adaptive skills	Following moving person with eyes, responds to vocalisation, drinks from a cup, feeds self, bladder control, control of bowel movement, indicates when nappy is wet/dirty, overall activity	0, 27	

Supplementary Table 2: Description of infants enrolled in the NuPED study per anthropometric indices and covariates at 6 months of age (n = 98)

Growth indicators ^{1,2}															
	WAZ ²				LAZ ⁴			WLZ ⁵				HCZ ⁶			
	<-2 (n = 10)	-2 to +2 (n = 80)	>2 (n = 4)	p-value ⁷	<-2 (n = 15)	>-2 (n = 80)	p-value ⁷	<-2 (n = 3)	-2 to +2 (n = 88)	>2 (n = 4)	p-value ⁷	<-2 (n = 4)	-2 to +2 (n = 74)	>2 (n = 17)	p-value ⁷
Total sample	10 (11)	80 (85)	4 (4)	0.085	15 (16)	80 (84)	0.195	3 (3)	88 (93)	4 (4)	0.174	4 (4)	74 (78)	17 (18)	0.654
Gender															
Male	0	52 (65)	4 (100)	<0.001	1 (7)	56 (70)	<0.001	1 (33)	51 (58)	4 (100)	0.183	0	42 (57)	15 (88)	0.002
Female	10 (100)	28 (35)	0		14 (93)	24 (30)		2 (67)	37 (42)	0		4 (100)	32 (43)	2 (12)	
Gestational age															
Preterm ⁸	3 (30)	9 (11)	0	0.186	4 (28)	8 (10)	0.093	1 (33)	11 (13)	0	0.390	1 (25)	9 (12)	2 (12)	0.554
Term	7 (70)	71 (89)	4 (100)		11 (73)	72 (90)		2 (67)	77 (87)	4 (100)		3 (75)	65 (88)	15 (88)	
Birth weight															
LBW ⁹	6 (67)	8 (10)	0	0.001	9 (64)	5 (7)	<0.001	1 (33)	13 (16)	0	0.374	4 (100)	10 (15)	0	0.001
Normal birth weight	3 (33)	62 (83)	2 (67)		5 (36)	62 (85)		2 (67)	63 (78)	3 (75)		0	53 (79)	14 (88)	
Macrosomia ⁹	0	5 (7)	1 (33)		0	6 (8)		0	5 (6)	1 (25)		0	4 (6)	2 (12)	
Feeding practices															
Mixed feeding ¹⁰	4 (40)	18 (25)	0	0.464	6 (43)	16 (22)	0.178	0	22 (28)	0	0.458	4 (100)	14 (21)	4 (27)	0.006
Only breast- or breastmilk substitutes	6 (60)	53 (75)	3 (100)		8 (57)	55 (78)		3 (100)	57 (72)	3 (100)		0	52 (79)	11 (73)	
Complementary feeding															
<4 months	0	29 (54)	0	<0.001	3 (33)	27 (51)	0.584	0	29 (51)	1 (50)	0.120	0	23 (47)	7 (64)	0.406
4 – 6 months	1 (20)	17 (32)	0		3 (33)	15 (28)		1 (33)	17 (30)	0		1 (50)	14 (29)	3 (27)	
≥6 months	4 (80)	8 (15)	2 (100)		3 (33)	11 (21)		2 (67)	11 (19)	1 (50)		1 (50)	12 (25)	1 (9)	
SES ¹¹															
Low (LSM 1 – 4)	1 (10)	1 (1)	0	0.328	1 (7)	1 (1)	0.389	0	2 (2)	0	0.555	0	2 (3)	0	0.507
Medium (LSM 5 – 7)	6 (60)	53 (66)	2 (50)		9 (60)	52 (65)		3 (100)	56 (64)	2 (50)		2 (50)	50 (67)	9 (53)	
High (LSM 8 – 10)	3 (30)	26 (33)	2 (50)		5 (33)	27 (34)		0	30 (34)	2 (50)		2 (50)	22 (30)	8 (47)	
Maternal pre-pregnancy BMI ¹²															
	21 (20 – 26)	26 (23 – 30)	25 (21 – 26)	0.020	24 (20 – 30)	25 (22 – 29)	0.257	23 (21 – 24)	26 (22 – 30)	26 (22 – 26)	0.182	21 (19 – 24)	26 (22 – 30)	25 (22 – 28)	0.049
Underweight	1 (10)	2 (3)	0		2 (13)	1 (1)		0	3 (3)	0		2 (50)	1 (1)	0	
Normal weight	6 (60)	34 (43)	1 (25)	0.515	7 (47)	35 (44)	0.077	1 (33)	40 (46)	1 (25)	0.735	2 (50)	32 (43)	8 (47)	0.032
Overweight	2 (20)	25 (31)	2 (50)		5 (33)	24 (30)		1 (33)	27 (31)	1 (25)		0	25 (34)	4 (24)	
Obese	1 (10)	19 (24)	1 (25)		1 (7)	20 (25)		1 (33)	18 (21)	2 (50)		0	16 (22)	5 (29)	

Supplementary Table 2: Description of infants enrolled in the NuPED study per anthropometric indices and covariates at 6 months of age (n = 98)
(continued)

Growth indicators ^{1, 2}															
	WAZ ²				LAZ ⁴			WLZ ⁵				HCZ ⁶			
	<-2 (n = 10)	-2 to +2 (n = 80)	>2 (n = 4)	p- value ⁷	<-2 (n = 15)	>-2 (n = 80)	p- value ⁷	<-2 (n = 3)	-2 to +2 (n = 88)	>2 (n = 4)	p- value ⁷	<-2 (n = 4)	-2 to +2 (n = 74)	>2 (n = 17)	p-value ⁷
Maternal GWG (g/ week) ¹³															
Inadequate	0	11 (23)	0	0.205	0	12 (26)	0.103	0	11 (22)	0	0.144	0	12 (29)	0	0.017
Adequate	3 (75)	14 (30)	0		5 (56)	12 (26)		2 (100)	16 (32)	3 (100)		2 (67)	14 (33)	1 (10)	
Excessive	1 (25)	22 (47)	3 (100)		4 (44)	22 (48)		0	23 (46)	0		1 (33)	16 (38)	9 (90)	
Iron supplementation ¹⁴															
Yes	7 (70)	59 (79)	3 (75)	0.757	11 (73)	59 (79)	0.735	2 (67)	65 (79)	2 (50)	0.230	4 (100)	54 (77)	12 (75)	0.788
No	3 (30)	16 (21)	1 (25)		4 (27)	16 (21)		1 (33)	17 (21)	2 (50)		0	16 (23)	4 (25)	
Folate supplementation ¹⁴															
Yes	10 (100)	72 (96)	4 (100)	1.000	15 (100)	72 (96)	1.000	2 (67)	80 (98)	4 (100)	0.103	4 (100)	67 (96)	16 (100)	1.000
No	0	3 (4)	0		0	3 (4)		1 (33)	2 (2)	0		0	3 (4)	0	

WAZ: weight-for-age z-score; LAZ: length-for-age z-score; WLZ: weight-for-length z-score; HCZ: head-circumference-for-age z-score; LBW: low birth weight; SES: socioeconomic status; LSM: living standard measure; BMI: body mass index; GWG: gestational weight gain.

¹ n (%) for categorical data and median (interquartile range) for continuous data; ² Missing data: WAZ (n = 4), LAZ (n = 3), WLZ (n = 3), HCZ (n = 3), birth weight (WAZ and WLZ: n = 7, LAZ and HCZ: n = 8), mixed feeding (WAZ: n = 14, LAZ, WLZ and HCZ: n = 10), complementary feeding (n = 33), GWG (n = 40), iron – and folate supplementation (WAZ, LAZ and HCZ: n = 5, WLZ: n = 6); ³ WAZ: <-2 indicative of underweight and >+2 possible risk for overweight (to be interpreted together with the WLZ); ⁴ LAZ: <-2 indicative of stunting, ≥-2 indicates normal growth; ⁵ WLZ: <-2 indicative of wasting and >+2 of overweight and/ or obesity; ⁶ HCZ: <-2 and >+2 regarded abnormal development – micro- and macrocephaly, respectively; ⁷ Categorical data: Fisher Exact/ Fisher-Freemant-Halton Exact test, and Continuous data: Mann-Whitney U test; significance indicated bold ($p < 0.05$); ⁸ Preterm birth defined a birth before 37 weeks' gestation and term birth as birth ≥37 weeks' gestation; ⁹ LBW defined as birth weight less than 2500g and macrosomia as a birth weight more than 4000g; ¹⁰ Mixed feeding was defined if the mother indicated that both breast- and breastmilk substitutes were given before 6 months of age; ¹¹ Determined using the South African Audience Research Foundation Living Standard Measure ⁴⁴; ¹² BMI classifications: underweight (<18.5 kg/m²), normal weight (18.5 – 24.9 kg/m²), overweight (25 – 29.9 kg/m²) and obese (>30 kg/m²); ¹³ Gestational weight gain categories as per the Institute of Medicine GWG recommendations ⁴⁹: inadequate GWG, underweight: ≤0.51, normal weight ≤0.42, overweight ≤0.28, obese ≤0.22; adequate GWG, underweight 0.44 – 0.58, normal weight 0.35 - 0.50, overweight 0.23 – 0.33, and obese 0.17 – 0.27; excessive GWG, underweight ≥0.58, normal weight ≥0.50, overweight ≥0.33 and obese ≥0.27; ¹⁴ Reflective of micronutrient supplementation during pregnancy.

Supplementary Table 3: Description of infants enrolled in the NuPED study per anthropometric indices and covariates at 12 months of age (n = 99)

Growth indicators ^{1, 2}															
	WAZ ²				LAZ ⁴			WLZ ⁵				HCZ ⁶			
	<-2 (n = 10)	-2 to +2 (n = 81)	>2 (n = 7)	p-value ⁷	<-2 (n = 18)	>-2 (n = 80)	p-value ⁷	<-2 (n = 5)	-2 to +2 (n = 85)	>2 (n = 9)	p-value ⁷	<-2 (n = 5)	-2 to +2 (n = 76)	>2 (n = 15)	p-value ⁷
Total sample	10 (10)	81 (83)	7 (7)	0.238	18 (18)	80 (82)	0.219	5 (5)	85 (86)	9 (9)	0.311	5 (5)	76 (79)	15 (16)	0.842
Gender															
Male	0	48 (59)	5 (71)	<0.001	0	53 (66)	<0.001	0	47 (55)	6 (67)	0.042	0	41 (54)	12 (80)	0.004
Female	10 (100)	33 (41)	2 (29)		18 (100)	27 (34)		5 (100)	38 (47)	3 (33)		5 (100)	35 (46)	3 (20)	
Gestational age															
Preterm ⁸	2 (20)	10 (12)	0	0.584	3 (17)	9 (11)	0.690	1 (20)	10 (12)	1 (11)	0.792	1 (20)	9 (12)	1 (7)	0.668
Term	8 (80)	71 (88)	7 (100)		15 (83)	71 (89)		4 (80)	75 (88)	8 (89)		4 (80)	67 (88)	14 (93)	
Birth weight															
LBW ⁹	5 (56)	12 (16)	0	0.001	8 (50)	9 (12)	0.003	3 (60)	13 (17)	1 (11)	0.008	3 (60)	11 (16)	2 (13)	0.020
Normal birth weight	4 (44)	61 (80)	3 (50)		8 (50)	60 (80)		2 (40)	62 (79)	5 (56)		2 (40)	56 (81)	10 (67)	
Macrosomia ⁹	0	3 (4)	3 (50)		0	6 (8)		0	3 (4)	3 (33)		0	2 (3)	3 (20)	
Feeding practices															
Mixed feeding ¹⁰	3 (43)	15 (24)	1 (20)	0.565	6 (46)	13 (21)	0.083	1 (20)	17 (27)	1 (17)	1.000	3 (75)	12 (21)	3 (27)	0.071
Only breast- or breastmilk substitutes	4 (57)	47 (76)	4 (80)		7 (54)	48 (79)		4 (80)	47 (73)	5 (83)		1 (25)	45 (79)	8 (73)	
Complementary feeding <4 months	0	25 (53)	0		2 (25)	23 (51)		1 (33)	25 (52)	0		1 (50)	20 (46)	3 (43)	
4 – 6 months	1 (33)	13(28)	1 (33)		2 (25)	13 (29)		1 (33)	12 (25)	2 (67)		0	12 (28)	3 (43)	
≥6 months	2 (67)	9 (19)	2 (67)	0.027	4 (50)	9 (20)	0.195	1 (33)	11 (23)	1 (33)		1 (50)	11 (26)	1 (14)	0.830
SES ¹¹															
Low (LSM 1 – 4)	1 (10)	4 (5)	0	0.439	2 (11)	3 (4)	0.432	1 (20)	3 (4)	1 (12)	0.057	0	5 (7)	0	0.812
Medium (LSM 5 – 7)	7 (70)	52 (64)	3 (43)		11 (61)	51 (64)		1 (20)	57 (67)	4 (44)		4 (80)	48 (63)	9 (60)	
High (LSM 8 – 10)	2 (20)	25 (31)	4 (57)		5 (28)	26 (32)		3 (60)	25 (29)	4 (44)		1 (20)	23 (30)	6 (40)	
Maternal pre-pregnancy BMI ¹²															
	23 (20 – 33)	25 (22 – 30)	26 (23 – 29)	0.292	25 (20 – 36)	25 (22 – 29)	0.854	23 (21 – 32)	25 (22 – 30)	29 (26 – 31)	0.616	23 19 – 28)	25 (22 – 30)	26 (22 – 29)	0.213
Underweight	2 (20)	5 (6)	0	0.205	3 (17)	4 (5)	0.217	1 (20)	6 (7)	0	0.248	1 (20)	5 (7)	1 (7)	0.163
Normal weight	5 (50)	31 (38)	1 (14)		8 (44)	29 (36)		2 (40)	33 (39)	3 (33)		4 (80)	25 (33)	6 (40)	
Overweight	2 (20)	27 (33)	2 (29)		5 (28)	26 (33)		1 (20)	29 (34)	1 (11)		0	28 (37)	3 (20)	
Obese	1 (10)	18 (22)	4 (57)		2 (11)	21 (26)		1 (20)	17 (20)	5 (56)		0	18 (23)	5 (33)	

Supplementary Table 3: Description of infants enrolled in the NuPED study per anthropometric indices and covariates at 12 months of age (n = 99)
(continued)

Growth indicators ^{1, 2}															
	WAZ ²				LAZ ⁴			WLZ ⁵				HCZ ⁶			
	<-2 (n = 10)	-2 to +2 (n = 81)	>2 (n = 7)	p-value ⁷	<-2 (n = 18)	>-2 (n = 80)	p-value ⁷	<-2 (n = 5)	-2 to +2 (n = 85)	>2 (n = 9)	p-value ⁷	<-2 (n = 5)	-2 to +2 (n = 76)	>2 (n = 15)	p-value ⁷
Maternal GWG (g/ week) ¹³															
Inadequate	1 (25)	9 (19)	0	0.150	1 (11)	9 (19)	0.124	0	10 (20)	0	0.150	0	9 (20)	1 (12)	0.681
Adequate	2 (50)	18 (38)	0		6 (67)	14 (30)		0	21 (40)	0		3 (75)	14 (32)	3 (28)	
Excessive	1 (25)	20 (43)	5 (100)		2 (22)	24 (51)		1 (100)	21 (40)	4 (100)		1 (25)	21 (48)	4 (50)	
Iron supplementation ¹⁴															
Yes	9 (90)	59 (78)	6 (86)	0.788	15 (83)	59 (79)	0.757	3 (60)	63 (80)	8 (89)	0.475	5 (100)	58 (81)	10 (71)	0.530
No	1 (10)	17 (22)	1 (14)		3 (17)	16 (21)		2 (40)	16 (20)	1 (11)		0	14 (19)	4 (29)	
Folate supplementation ¹⁴															
Yes	9 (90)	72 (95)	7 (100)	0.645	16 (89)	72 (96)	0.247	5 (100)	76 (96)	7 (89)	0.093	5 (100)	69 (96)	12 (86)	0.389
No	1 (10)	4 (5)	0		2 (11)	3 (4)		0	3 (4)	2 (11)		0	3 (4)	2 (14)	

WAZ: weight-for-age z-score; LAZ: length-for-age z-score; WLZ: weight-for-length z-score; HCZ: head-circumference-for-age z-score; LBW: low birth weight; SES: socioeconomic status; LSM: living standard measure; BMI: body mass index; GWG: gestational weight gain.

¹ n (%) for categorical data and median (interquartile range) for continuous data; ² Missing data: WAZ (n = 1), LAZ (n = 1), HCZ (n = 3), birth weight (n = 7), mixed feeding (n = 24), complementary feeding (WAZ, LAZ, WHZ: n = 45; HCZ: n = 44), GWG (WAZ, LAZ, WLZ: n = 42, HCZ: n = 40), iron – and folate supplementation (WAZ, LAZ and HCZ: n = 5, WLZ: n = 6); ³ WAZ: <-2 indicative of underweight and >+2 possible risk for overweight (to be interpreted together with the WLZ); ⁴ LAZ: <-2 indicative of stunting, ≥-2 indicates normal growth; ⁵ WLZ: <-2 indicative of wasting and >+2 of overweight and/ or obesity; ⁶ HCZ: <-2 and >+2 regarded abnormal development – micro- and macrocephaly, respectively; ⁷ Categorical data: Fisher Exact/ Fisher-Freemant-Halton Exact test, and Continuous data: Mann-Whitney U test; significance indicated bold (p < 0.05); ⁸ Preterm birth defined a birth before 37 weeks' gestation and term birth as birth ≥37 weeks' gestation; ⁹ LBW defined as birth weight less than 2500g and macrosomia as a birth weight more than 4000g; ¹⁰ Mixed feeding were defined if the mother indicated that both breast- and breastmilk substitutes were given before 6 months of age; ¹¹ Determined using the South African Audience Research Foundation Living Standard Measure ⁴⁴; ¹² BMI classifications: underweight (<18.5 kg/m²), normal weight (18.5 – 24.9 kg/m²), overweight (25 – 29.9 kg/m²) and obese (>30 kg/m²); ¹³ Gestational weight gain categories as per the Institute of Medicine GWG recommendations ⁴⁹: inadequate GWG, underweight: ≤0.51, normal weight ≤0.42, overweight ≤0.28, obese ≤0.22; adequate GWG, underweight 0.44 – 0.58, normal weight 0.35 - 0.50, overweight 0.23 – 0.33, and obese 0.17 – 0.27; excessive GWG, underweight ≥0.58, normal weight ≥0.50, overweight ≥0.33 and obese ≥0.27; ¹⁴ Reflective of micronutrient supplementation during pregnancy.

CHAPTER 6: SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

6.1 Background to and rationale for the study

Pregnancy presents a unique opportunity for determining the health and well-being of offspring (Cetin & Laoreti, 2015). Maternal nutrition is regarded as an important controllable environmental factor that influences fetal growth and development (Georgieff *et al.*, 2018; Prado & Dewey, 2014). Growth and development, including brain development, is a complex and continuous process that commences soon after conception (Berk, 2013; Moore *et al.*, 2015). As nutrients play an important role in neurodevelopmental processes, nutrition is regarded as a key factor for optimal brain development (Georgieff *et al.*, 2018; Prado & Dewey, 2014). Georgieff *et al.*, however, indicate that the influence of postnatal nutrition on offspring brain development is greatly dependent on the fetal nutritional status (Georgieff *et al.*, 2018), which, to a large extent, is determined by the maternal nutrient intake (Shapiro *et al.*, 2016; Tahir *et al.*, 2019). Neurodevelopment is also imperative to the advancement of all postnatal developmental domains (physical, cognition, and social-emotional development) (Berk, 2013; Levine & Munsch, 2017). Fetal growth- and linear growth retardation, often as a result of suboptimal nutrient intakes, are, however, known to be risk factors for poor early childhood development (Walker *et al.*, 2011; Walker *et al.*, 2007).

Nutrients are not consumed in isolation but as part of a diet consisting of different foods. Hu (2002), therefore, introduced dietary pattern analysis as a complementary method of evaluating dietary intake. Accounting for the diet as a whole, dietary pattern analysis is regarded as an imperative method in studying dietary risk factors for health outcomes. Moskal *et al.* (2014) encourage the use of nutrients rather than foods or food groups as variables in dietary pattern analysis, as nutrients are more universal with fewer non-consumers. This aids in statistical analysis and allows for easier comparison between studies. Research on the associations between maternal dietary patterns during pregnancy and offspring growth and development are limited, however, with most available studies conducted in high-income countries. To our knowledge, no studies on maternal dietary patterns and offspring outcomes have to date included nutrient pattern analysis. Furthermore, information on the dietary intake among pregnant South African women is limited. Only one study to date has conducted dietary pattern analysis using food groups on a South African group of pregnant women, reporting on the associations with gestational weight gain (Wrottesley *et al.*, 2017) and fetal growth (Wrottesley *et al.*, 2020).

With this in mind, the aim of this study was to assess the associations of maternal dietary patterns (based on nutrients) during pregnancy with fetal and infant growth and development up to the age of 12 months in Johannesburg, South Africa. The results found by this study are summarised in the following sections.

6.2 Summary of the findings

Dietary patterns adhered to by pregnant South African women in an urban setting

Maternal dietary intake during pregnancy was described using both *a priori* and *a posteriori* dietary pattern analysis. An in-depth description of these methods is given in chapter 3. Figure 6-1 illustrates the main findings.

As per the *a priori* method, the DQI-I was used to determine the overall maternal dietary quality. The DQI-I is regarded as comprehensive in assessing dietary quality as it reports on variety, adequacy, moderation and overall balance (Kim *et al.*, 2003). Our study population followed an overall borderline low-quality diet which was attributed mainly to high intakes in total and saturated fat, as well as sodium. Both high fat and high sodium intakes have previously been reported among the South African population (Eksteen & Mungal-Singh, 2015; Krige *et al.*, 2018; Swanepoel *et al.*, 2016; Vorster *et al.*, 2011) and can be ascribed to a nutrition transition due to urbanisation (Vorster *et al.*, 2011). With a higher fat intake often contributing to weight gain (Field *et al.*, 2007; World Health Organization, 2019), this could be a possible reason for half of our study population entering pregnancy either overweight or obese. Furthermore, high fat and sodium intakes are often accompanied by additional unhealthy lifestyle factors (Field *et al.*, 2007).

Exploratory factor analysis was applied to determine *a posteriori* patterns. Three distinct nutrient patterns explaining 57% variance in nutrient intake were derived, namely a “plant protein, iron, thiamine, and folic acid”, an “animal protein, copper, vitamin A, and vitamin B₁₂” and a “fatty acids and sodium” nutrient pattern. Based on the patterns’ associations with food groups, these patterns, respectively, presented a “fortified grain and legume”, an “animal products”, and a “fatty and processed foods” dietary pattern.

The “plant protein, iron, thiamine, and folic acid” nutrient pattern was, based on its association with the *a priori* patterns of higher dietary quality. This pattern was also reflective of a traditional South African diet owing to the higher maize, wholemeal bread and legume intake associated with higher adherence to this pattern (MacIntyre *et al.*, 2002; Wentzel-Viljoen *et al.*, 2018). The factor matrix of this pattern was also congruent with the micronutrients used for the fortification of maize and bread flour as per South African legislation (Department of Health, 2003). Among our study population, it was mainly women of older age, with poorer socioeconomic circumstances and a lower level of education that adhered to this pattern. As opposed to Doyle *et al.* (2017), who report a social gradient whereby women of older age, higher socioeconomic status and higher educational levels follow a healthier dietary pattern, the higher dietary quality among the poorer

proportion of our population can be ascribed to the foods associated with this dietary pattern being more affordable than processed and fatty foods.

The “animal protein, copper, vitamin A, and vitamin B₁₂” and “fatty acids and sodium” nutrient patterns were conversely indicative of a nutrition transition that is characterised by a higher intake of animal products and processed foods as persons adapt to more modern lifestyles as a result of urbanisation (Popkin, 2002; Vorster *et al.*, 2011). Dietary intake accompanying a nutrition transition is well documented as being associated with obesity and lifestyle diseases (Vorster *et al.*, 2011) as the more advanced the stage of transition, the poorer the dietary quality (Steyn & McHiza, 2014). Although associated mainly with the intake of animal products, the “animal protein, copper, vitamin A, and vitamin B₁₂” pattern was not found to be associated with dietary quality. Based on the associations with the *a priori* index, the “fatty acids and sodium” nutrient pattern was considered to be of lower dietary quality.

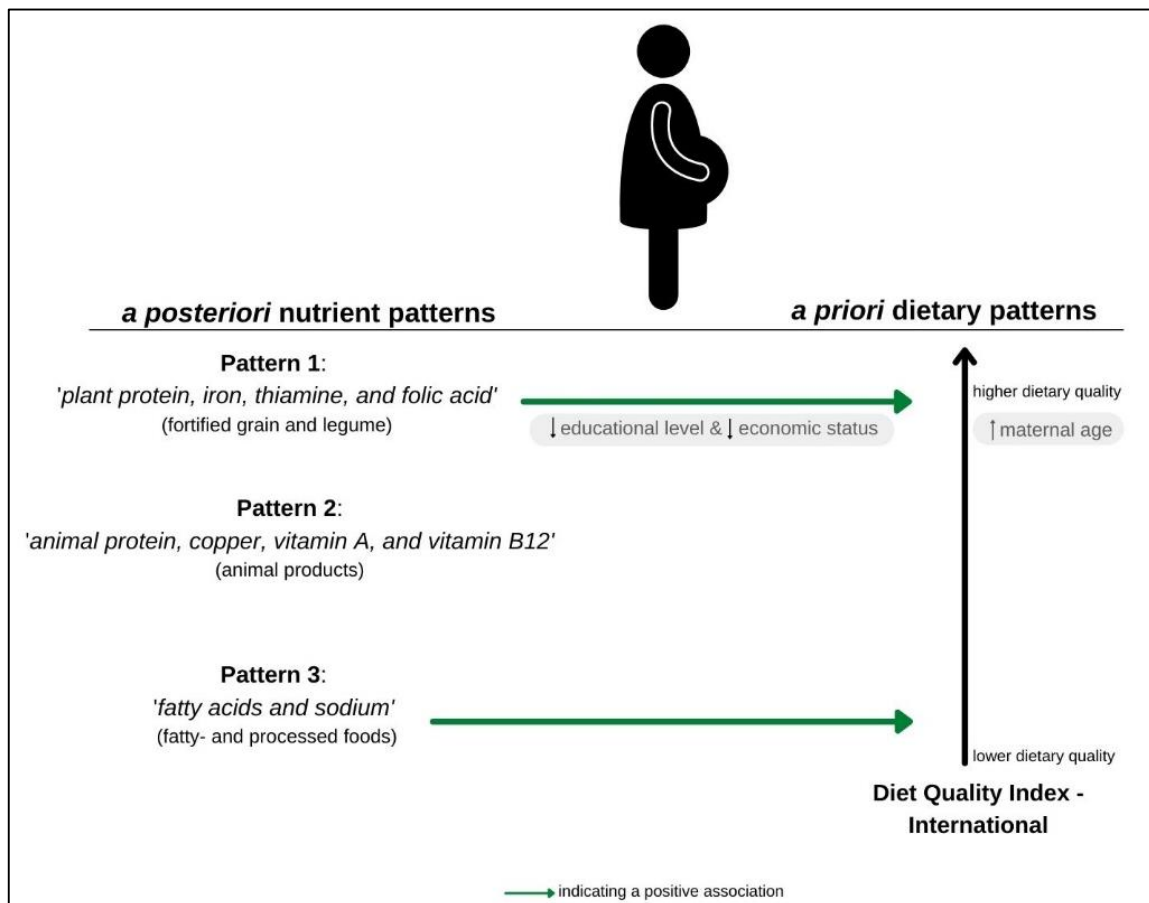


Figure 6-1: Illustration of dietary patterns adhered to by pregnant women in an urban setting in South Africa

Associations of maternal dietary patterns during pregnancy with ultrasound-derived fetal growth

Chapter 4 reports on the associations between maternal dietary patterns and fetal growth. We found the “plant protein, iron, thiamine, and folic acid” pattern to have a small positive correlation ($r = 0.18$, $p = 0.041$) with HC growth rate between mid- and late pregnancy after accounting for maternal age and folate supplementation as covariates. Higher maternal adherence to this pattern were also associated with great HC interval growth ($p = 0.002$). Head circumference is reported in the literature to serve as a proxy for intracranial volume and brain development during early life (Georgieff *et al.*, 2018; Koshy *et al.*, 2021; Volpe, 2018). A possible explanation for the association found could be that the nutrients important for brain development (Georgieff *et al.*, 2018) loaded positively on the pattern factor matrix, such as plant protein, carbohydrates, iron, zinc, thiamine, niacin, vitamin B₆ and folate. The micronutrients associated with this pattern are largely provided by the fortified staple foods related to this pattern. It is, therefore, probable that nutrients provided through a large-scale food fortification programme could play a valuable role in fetal growth and development.

The “fatty acids and sodium” pattern was negatively correlated with FL at mid-pregnancy ($r = -0.15$, $p = 0.027$) after accounting for fetal sex, iron and folate supplementation. Fetal femur length serves as a proxy for both bone development (Chang *et al.*, 2003) and linear growth (Prioreshi *et al.*, 2021). In terms of bone development, calcium, a nutrient important for bone accretion during the fetal period (Chang *et al.*, 2003), was negatively loaded with this pattern. The “fatty acids and sodium” pattern, as evident by its low quality, was poor in various micronutrients needed for optimal growth and development. This deficient intake of nutrients by the mother could have contributed towards a deficient environment for fetal growth by depriving the fetus of essential nutrients (Dewey & Begum, 2011; Leroy and Frongillo, 2019).

Associations between maternal dietary patterns during pregnancy and infant growth and development up to the age of 12 months

Chapter 5 presents the associations between maternal dietary patterns during pregnancy and infant growth and development. The “plant protein, iron, thiamine, and folic acid” nutrient pattern was found to be inversely correlated with adaptive skills, a sub-category of social-emotional development, at 6 months postpartum after adjusting for covariates ($r = -0.339$, $p = 0.009$). Moderate to higher adherence, compared to a lower maternal adherence, to the “animal protein, copper, vitamin A, and vitamin B₁₂” pattern was also found to be associated with lower social-emotional development scores ($p = 0.015$) at 12 months. These findings were seen regardless to nutrients loaded positively to the factor matrix of both these nutrient patterns being reflective of

that regarded important for fetal and infant brain development (including protein, copper and B vitamins) (Georgieff *et al.*, 2018). Other than reports indicating the electrolytic iron used in fortification not to positively influence maternal iron status (Papathakis & Pearson, 2012), polyunsaturated fatty acids were negatively loaded on the matrix of both these nutrient patterns. The long-chain polyunsaturated fatty acids eicosapentaenoic- (EPA) and docosahexaenoic acid (DHA) (mainly found in fatty fish and their oils) are in particular well described in the literature to be imperative for optimal brain development (Georgieff *et al.*, 2018; Prado & Dewey, 2014). The consumption of fish and seafood was though not associated with the “plant protein, iron, thiamine, and folic acid” nutrient pattern, whereas fish and seafood only provided about one percent of the total energy intake of participants adhering to the “animal protein, copper, vitamin A, and vitamin B₁₂” nutrient pattern.

We also found the “fatty acids and sodium” nutrient pattern to be associated with lower weight-for-age and length-for-age z-scores at both 6 and 12 months postpartum, even after accounting for gender, socioeconomic status, maternal pre-pregnancy body mass index, gestational weight gain during pregnancy, maternal micronutrient supplementation (iron and folate) during pregnancy, birth outcomes and infant feeding practices. Other than these findings being congruent to Shapiro *et al.* (2016) and Tahir *et al.* (2019) indicating maternal dietary quality to be inversely associated with infant weight and adiposity at birth and 6 months, these findings support the findings of this pattern also being associated with lower fetal femur length during pregnancy. Considering the deficient environment for fetal development contributed towards by the “fatty acids and sodium” nutrient pattern as various nutrients were negatively loaded on the pattern matrix, it is likely that these children experienced linear growth restriction *in utero* already. With linear growth restriction well described to be associated with poor early childhood development (Walker *et al.*, 2011; Walker *et al.*, 2007), it is likely that these children might later also present with poor neurodevelopment. It is also important to consider that as the quality of the maternal diet influences an infant’s dietary intake (Robinson *et al.*, 2007), mothers who adhered to either of these nutrient patterns raised their infants on similar foods associated with patterns.

6.3 Conclusion to the study findings

The findings of this study can be summarised in that a dietary pattern of a higher quality (the “plant protein, iron, thiamine, and folic acid” pattern) contributed more positively towards fetal and infant (neuro)development, whereas a pattern of lower quality (“fatty acids and sodium” pattern) had a more negative effect on development. The “plant protein, iron, thiamine, and folic acid” pattern was reflective of a traditional South African diet (Conradie *et al.*, 2021). Although not a

diverse diet (MacIntyre *et al.*, 2002), the micronutrient adequacy of the traditional diet has improved due to the national food fortification programme (Department of Health, 2003). The higher quality attributed to the “plant protein, iron, thiamine, and folic acid” pattern was though driven by its “moderation” in the intake of nutrients related to chronic diseases, as well as the “overall balance” (Conradie *et al.*, 2021) – making this pattern a healthier pattern to follow than a more Westernised diet. This pattern and its positive associations with fetal and infant development therefore supports the current drive towards more plant-based diet (Willett *et al.*, 2019). The associations found with poorer social-emotional development are though worrisome; however, advocating for higher fish consumption by women adhering to this pattern might address these findings.

Regardless of the associations between the maternal dietary patterns and offspring growth and development being limited and of small effect size, the role of the maternal diet remains imperative. Not all factors influencing pregnancy outcomes can be controlled; maternal dietary intake and nutritional status are, however, seen as a modifiable factor in pregnancy outcomes (Georgieff *et al.*, 2018; Harding, 2001). So also, post-natal factors that influence growth and development are known to be vast (Walker *et al.*, 2011; Walker *et al.*, 2007). In a comprehensive review and meta-analysis of the associations between maternal dietary patterns and birth outcomes, Chia *et al.* (2019) indicate that a more healthy dietary pattern during pregnancy is associated with a decreased risk of preterm birth, whereas an unhealthy dietary pattern contributes to an increased risk of preterm birth and LBW. Low birth weight has yet again been reported to be associated with poorer neurodevelopmental outcomes (Bell *et al.*, 2018; Donald *et al.*, 2019; Rocha *et al.*, 2021). Therefore, although the observed associations between maternal dietary patterns and offspring growth and developmental outcomes is small, the influence of maternal nutrition by way of birth outcomes can be long lasting. It is hence probable that, as per the Developmental Origins of Health and Disease theory (Harding, 2001; Hsu & Tain, 2019), maternal nutrition during pregnancy not only influences offspring health outcomes, but also growth and neurodevelopmental outcomes. Providing an environment in which the fetus can develop optimally rather than relying on later catch-up growth and development is, therefore, recommended.

Furthermore, with maternal nutritional status at conception being important for fetal development (Stephenson *et al.*, 2018), the focus should be not only on an optimal dietary intake during pregnancy but also on consuming a diet of high quality before conception. Stephenson *et al.* (2018) indicate that an improvement of the maternal diet during pregnancy did not affect maternal and newborn health outcomes. Following and maintaining a healthy dietary pattern as long as three years before pregnancy, was, however, found to be associated with a decreased risk of preterm birth and pregnancy complications. Based on the work of Crozier *et al.* (2009), it is likely

that women continue following a similar dietary pattern during pregnancy as they did before pregnancy. Furthermore, the quality of the maternal dietary pattern likely to influence the diet on which an infant is raised (Robinson *et al.*, 2007).

A greater effort should hence be made to ensure that women of childbearing age are equipped to follow a high-quality diet providing adequate nutrients. Considering the South African setting, the South African government is committed to reducing poverty in the country by methods that, among others, ensure optimal nutrition during pregnancy for improved early childhood developmental outcomes (National Planning Commission (South Africa), 2012). The public healthcare “Guidelines for Maternity Care in South Africa” are limited, however, with regard to nutrition-related care, focussing mainly on the daily supplementation of iron, folate and calcium (National Department of Health (South Africa), 2015). Nutrition programmes educating South African women on a high-quality diet are hence necessary and should form a crucial part of prenatal nutritional care. With the South African food-based dietary guidelines being science-based recommendations to ensure dietary adequacy and prudence (Vorster *et al.*, 2013), there is no need for new guidelines to be formulated. Rather, the South African food-based dietary guidelines should be implemented and promulgated to a larger extent.

6.4 Recommendations

Recommendations for future research

- Dietary pattern analysis, specifically the use of nutrients as variables, should be considered as a supplemental method in describing the dietary intake of a population.
- The research at hand is believed to be of relevance, and hence studies considering larger sample sizes and longer follow-up periods are recommended to further explore the associations between the maternal diet and offspring health and developmental outcomes.
- Research in low- and mid-income countries is limited. More research in such settings is urged to truly understand the impact of restricted environments on the maternal diet, and hence on offspring health and developmental outcomes.

Public health-related recommendations

- Programmes should be put in place to educate women of childbearing age and equip them to follow a diet of high quality providing adequate nutrients.
- In South Africa, programmes promulgating the South African food-based dietary guidelines as a means of ensuring that a higher quality diet is followed are recommended.

- With food fortification indicated as possibly having a positive effect on offspring growth and development, food fortification programmes should be well managed to ensure that they contribute towards a better nutritional status within population groups.

6.5 Strengths and limitations to the study

A great strength of this study is that dietary patterns, specifically nutrient patterns, were considered within the analysis. Dietary patterns provide a more predictive approach in determining nutrition-related risk factors for health outcomes. So also, considering ultrasound-derived fetal growth provides a better look at fetal development as birth weight is only a cross-sectional measure that does not account for variation in fetal growth. The NuPED study also collected prospective data with multiple data collection points during the prenatal and postnatal phases of this study. Extensive data were collected at the different data collection timepoints, allowing for covariates to be included in the analysis. One should be aware, however, that it was not possible to assess and include all confounding factors. To account for this, the inclusion and exclusion criteria of the study were set so as to enrol only generally healthy pregnant women residing within the Johannesburg area.

The study was limited, however, by various factors, of which the small sample size and a large number of missing data restricted the findings. Also, with data collected as part of an observational study, no definite conclusion can be drawn on causality of the observed relationships. Collecting dietary data using a QFFQ was also a limiting factor to this study. The QFFQ reported on 140 items consumed over a four-week period. Completion of a QFFQ relies heavily on memory and does not always provide accurate dietary intake information. The QFFQ was previously, however, validated for a South African population, and was administrated by a train fieldworker. It was, furthermore, likely that when converting the QFFQ data to intake per day, a greater variety of foods were reported. This could have led to an overestimation in the 'variety' and 'adequacy' categories of the DQI-I. The DQI-I was, however, stringently scored as per the guidelines set out by Kim *et al.* (2003). Considering, we are confident that the dietary data presents an accurate overview of the habitual dietary intake of the study population.

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ADDENDUM 1
Publication of the NuPED study protocol

<https://bmcpregnancychildbirth.biomedcentral.com/track/pdf/10.1186/s12884-018-1943-6.pdf>



STUDY PROTOCOL

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Nutrition during pregnancy and early development (NuPED) in urban South Africa: a study protocol for a prospective cohort

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Abstract

Background: Adequate nutrition during pregnancy is important to ensure optimal birth outcomes, maternal health and offspring development. However, little is known about the dietary intake and nutritional status of pregnant women residing in urban South Africa. Therefore, the Nutrition during Pregnancy and Early Development (NuPED) cohort study was initiated to assess early nutrition-related exposures predictive of early childhood development in urban South Africa.

Methods: The aims of this prospective cohort study are: 1) to assess dietary intake and nutritional status of urban pregnant women in Johannesburg, South Africa, and 2) to determine associations with birth outcomes, measures of maternal health, as well as measures of offspring health and development. Pregnant women (< 18 weeks' gestation) ($n = 250$) are being recruited from primary healthcare clinics in Johannesburg and are followed-up at a provincial hospital. Participants' dietary intake and nutrient status (focus on micronutrients and fatty acids) are assessed at < 18, 22 and 36 weeks' gestation. Additional assessments during pregnancy include anthropometric and blood pressure measurements, obstetric ultrasound screens, and assessments of food security, maternal fatigue, prenatal depression, allergy, immune function, morbidity and gestational diabetes. At birth, maternal and neonatal health is assessed and an umbilical cord blood sample collected. Maternal and offspring health is followed-up at 6 weeks, as well as at 6, ≈ 7.5 and 12 months after birth. Follow-up assessments of mothers include anthropometric measures, diet history, nutrient status, blood pressure, breast milk composition, and measures of postnatal depression and fatigue. Follow-up assessments of the offspring include feeding practices, nutrient status, measures of growth, psychomotor, socio-emotional and immune development, morbidity, allergy, as well as analysis of the gut microbiome and the epigenome.

Discussion: Ensuring adequate nutrition during pregnancy is one of the key actions endorsed by the South African Government to promote optimal early childhood development in an effort to eradicate poverty. The results from this study may serve as a basis for the development of context-specific nutritional interventions which can improve birth outcomes and long-term quality of life of the mother and her offspring.

Keywords: Maternal health, Maternal diet, Nutrition, Pregnancy, Birth outcomes, Early development, DOHaD

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Background

Recent estimates indicate that 250 million children in low- and middle income countries are at risk of not reaching their developmental potential [1]. This is worrisome as suboptimal childhood development is associated with poorer adult health, well-being and productivity – leading to an intergenerational cycle of poverty. As the trajectories of physical and mental health later in life are determined fundamentally during the first 1000 days of life, both the World Health Assembly Nutrition Targets and the Sustainable Developmental Goals call for action to, among others, improve maternal, infant and young child nutrition in an effort to ensure sustainable social and economic progress.

Maternal health and nutrition gained heightened attention three decades ago with the publication of the developmental origins of health and disease (DOHaD) hypothesis. Barker and Osmond [2] proposed that the cardiovascular disease they observed in an adult population from England and Wales was at least partly associated with poor early nutrition, and specifically undernutrition in utero [3]. Undernourishment in utero can stress the foetus in ways that permanently affect physiological growth and development, and can be described as a reprogramming of the foetus's developing phenotype [4]. Apart from the long-term health consequences, severe growth-restricted foetuses are at increased risk of stillbirth, and the live births have an increased risk of neonatal death, morbidity and permanent deficits in growth and neurocognitive development [5, 6].

Several maternal nutritional factors have been investigated in relation to adverse pregnancy outcomes, as well as offspring health and development [7–9]. The nutrients most studied during pregnancy include B-vitamins (particularly folic acid), vitamin D, iron, long-chain polyunsaturated fatty acids (particularly n-3 fatty acids) and iodine [8, 10]. However, adequate maternal intakes of zinc and vitamin A may also be important for optimal pregnancy outcomes, as well as for maternal and offspring health [11–13]. Furthermore, better overall diet quality has been associated with a lower risk for maternal perinatal depression and gestational weight gain, which in turn are risk factors for suboptimal offspring development [14–16].

The health of the adult South African population is a concern. South Africa has large economic disparities and 20% of the population are living in extreme poverty, indicating they cannot afford the minimum required food intake [17]. During a national survey in 2012, approximately 40% of the population were reported to have a monotonous diet based mainly on starches [18]. The country is undergoing a rapid nutrition transition characterised by changes in dietary patterns and nutrient intake alongside urbanisation [19, 20], which has resulted in a growing double-burden of under- and over-nutrition [20, 21].

Hence, not surprisingly, 31% and 13% of South African women of reproductive age are anaemic [22] and vitamin A deficient [18], respectively, while 68% of women are overweight or obese, and 46% hypertensive [22]. The effects are also seen in children, with 27% of under-fives being stunted [22]. Both stunting and poverty are known risk factors for poor child development [23]. Maternal short stature is, in turn, a risk factor for birth complications [24] – illustrating the intergenerational effect of poor nutrition.

Ensuring adequate nutrition during pregnancy is one of the key actions endorsed by the South African Government to promote optimal early childhood development in an effort to eradicate poverty [25]. The *Guidelines for maternity care in South Africa* [26] therefore recommend routine nutritional assessment – such as measuring mid-upper arm circumference and haemoglobin levels – and daily supplementation of 200 mg ferrous sulphate, 1000 mg calcium and 5 mg folic acid. However, studies show that the majority of South African women only seek or get access to public antenatal care in their second trimester of pregnancy [27–30], which might be too late for the routine supplementation programme or other interventions to be effective.

Very little is known about the diet and nutritional status of pregnant women in South Africa, specifically residing in urban areas. Furthermore, understanding the associations of maternal diet and nutritional status during pregnancy with birth outcomes, as well as offspring health and development in the South African population will form the basis for the development of context-specific nutrition interventions that may improve birth outcomes and long-term quality of life of the mother and her offspring. Consequently, the *Nutrition during Pregnancy and Early Development (NuPED)* cohort study was initiated to investigate nutritional status during pregnancy and assess early nutrition-related exposures predictive of early childhood development in urban South Africa.

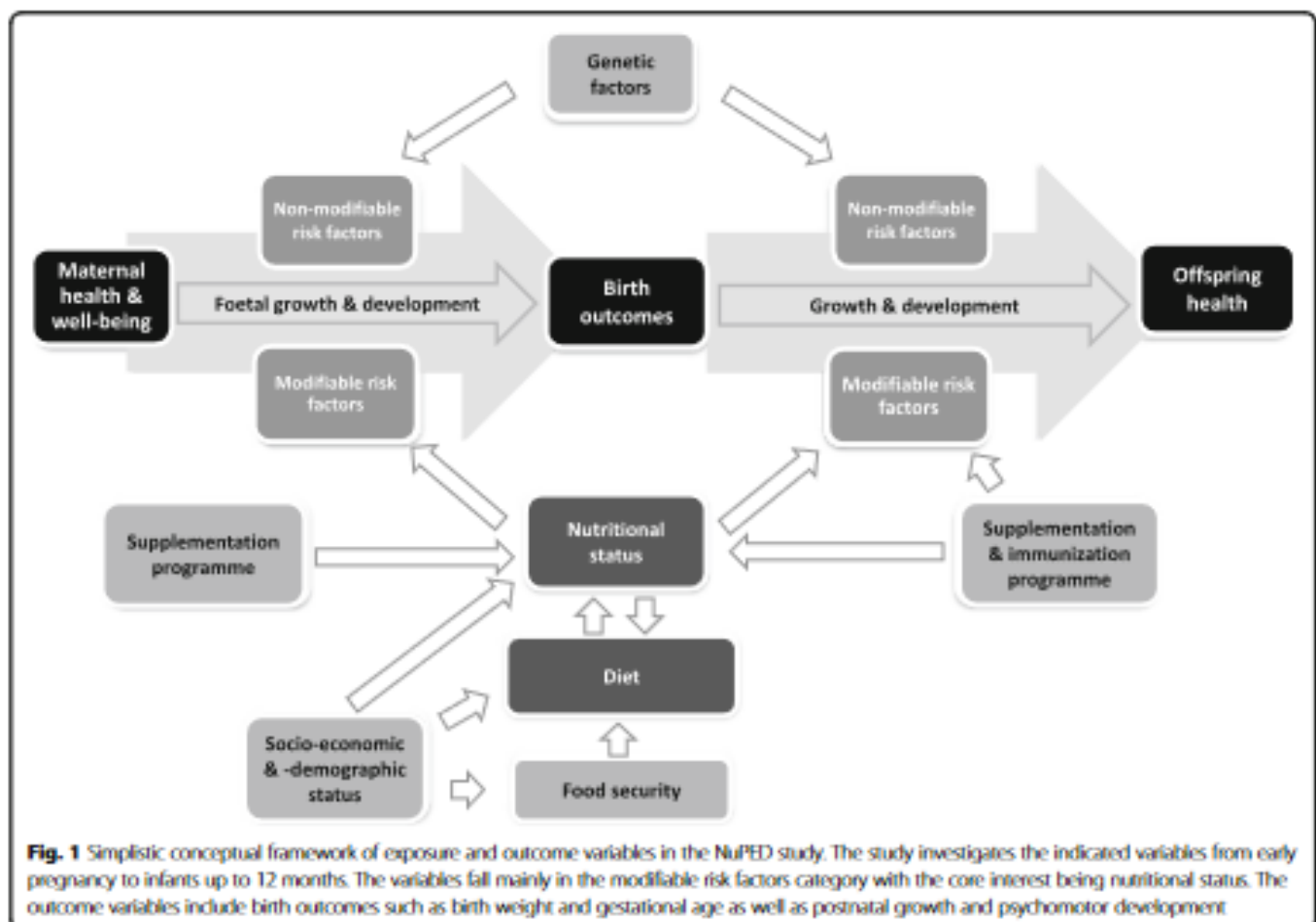
Aims of the study

The aims of the NuPED study are 1) to assess dietary intake and nutritional status of urban pregnant women in Johannesburg, South Africa, and 2) to determine associations with birth outcomes, measures of maternal health, as well as measures of offspring health and development. A simplistic conceptual framework showing the modifiable and non-modifiable exposure variables, as well as the outcome variables that will be determined to achieve the aims, is shown in Fig. 1.

Methods/design

Study design

This prospective cohort study follows 250 women throughout pregnancy to birth, and their infants up to



12 months of age. Briefly, data are collected early pregnancy, mid-pregnancy, late pregnancy and at birth. Postnatal assessments focus mainly on offspring health and development at 6 weeks, 6 months, 7.5 months (6 months + 6 weeks) and 12 months' postnatal age.

Recruitment of participants started on 7 March 2016 and completion of data collection is expected in June 2019.

Setting

The study is situated in Johannesburg, the largest city in South Africa. Recruitment of study participants takes place in two of the seven municipal regions of the city from which four primary health care clinics were identified. These clinics fall in the catchment area of Rahima Moosa Mother and Child Hospital (RMMCH). RMMCH is a provincial hospital focusing on maternal and paediatric healthcare, delivering more than 10,000 babies annually. Pregnancy data are collected at the antenatal care (ANC) clinic of RMMCH in addition to routine care. Birth data are collected in the relevant wards at RMMCH. Postnatal data are collected at the Empilweni Services and Research Unit (ESRU) at RMMCH. The execution of the

study is coordinated by the Centre of Excellence for Nutrition of the North-West University.

Study population

The study population is urban pregnant women attending ANC at either one of four selected primary health care clinics or at the ANC clinic of the hospital. Women interested to partake in the study are screened according to inclusion and exclusion criteria, and referred to RMMCH ANC clinic for signing informed consent and data collection if eligible.

The inclusion criteria applied during recruitment screening are: 1) Confirmed pregnancy and planning to deliver her baby at RMMCH; 2) < 18 weeks' gestational age; 3) Born in South Africa, Lesotho, Swaziland, Zimbabwe, Botswana or Namibia and has been living in South Africa for at least 12 months; 4) Able to communicate effectively in one of the following languages: English, Afrikaans, Sotho, Zulu or Xhosa.

The exclusion criteria are 1) < 18 and > 39 years; 2) Multiple pregnancy; 3) Using illicit drugs (self-confessed); 4) Smoking (current and/or in past year); 5) Known non-communicable disease (NCD) namely diabetes, renal disease, high cholesterol, and hypertension; 6)

Known infectious disease namely tuberculosis and hepatitis; 7) Known serious illness namely cancer, lupus or psychosis.

Even though women with infectious disease are excluded, women who are HIV positive are still included. Due to the high prevalence of HIV in the country (36% of women aged 30–34 years [31]), their inclusion will make generalisation to the wider South African population a possibility.

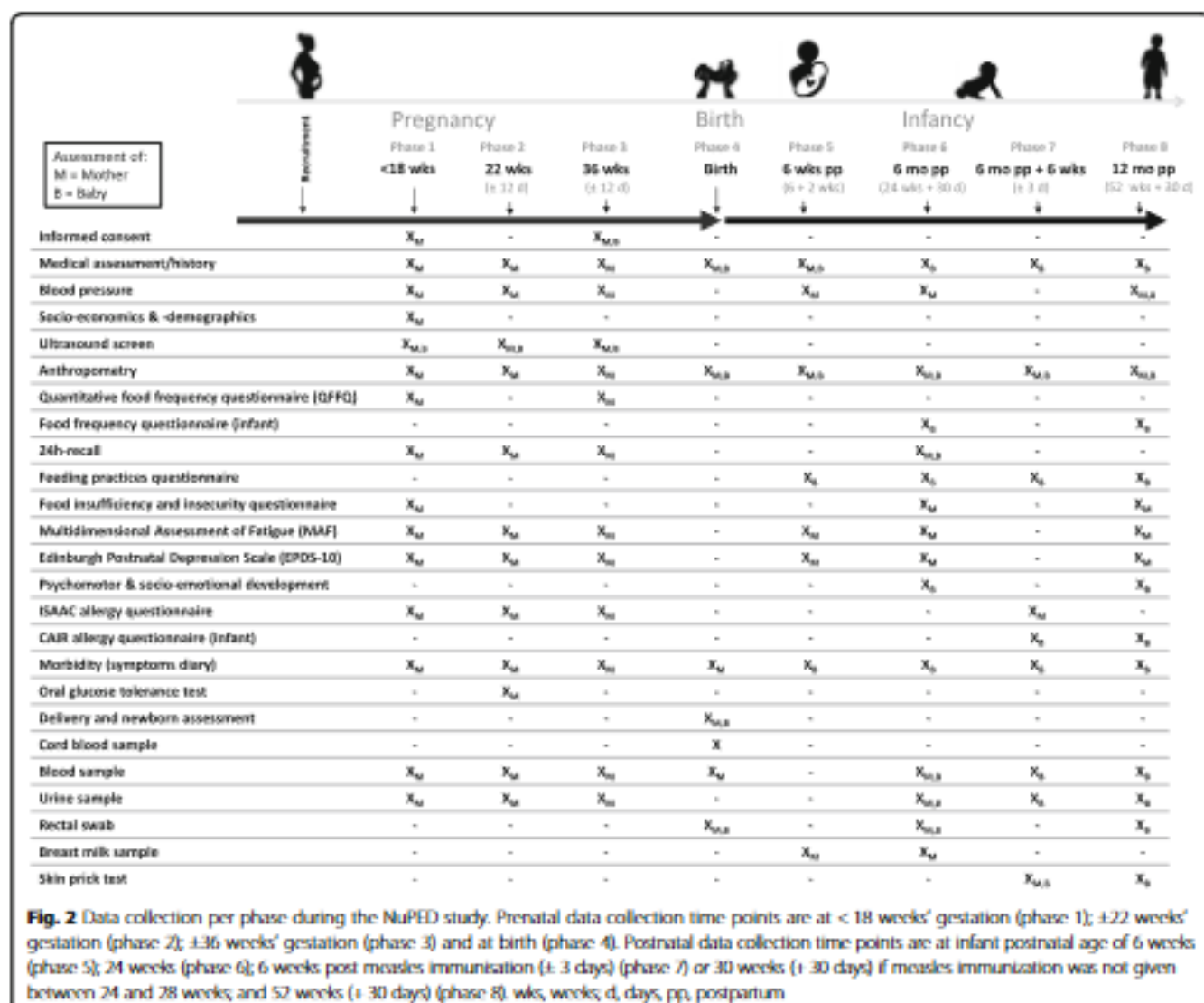
Recruitment and consent procedures

Consecutive sampling is applied, thus, all accessible pregnant women at the recruitment sites may form part of the sample, if they meet the inclusion and exclusion criteria, arrive at study site on their booked date and sign informed consent. All pregnant women in the waiting areas of the ANC clinics are informed about the study. Those interested, receive a study information leaflet and are screened for eligibility individually in a private space upon which a booking date is supplied if eligible. The informed consent

form is given to the participant to read, consider and discuss with her partner and/or family. Upon arrival at RMMCII on the booked date, the trained fieldworkers explain the informed consent form in local languages and all are given the opportunity to ask questions. All are assured that participation is voluntary and that participation or non-participation in the study will not affect their clinical care. All research participants provide written informed consent before data collection. Written informed consent is again obtained before infant assessments at 6 weeks postnatally.

Data collection

Figure 2 summarises the measurements and time points of data collection throughout the project. There are eight data collection time points (here forth referred to as phases). All data are collected either by health professionals on site or by trained fieldworkers. Phase 1 data are collected at < 18 weeks' gestation (as confirmed by



obstetric ultrasound). These data will supply information on the nutritional status of women early in their pregnancy. It is important to note that in Johannesburg only 45% of women access ANC before 20 weeks gestation and only 23% in their first trimester (as reported from other urban areas) [30]. Thus, for practical purposes, the *early pregnancy window* was set at < 18 weeks' gestation. Phase 2 data are collected at 22 weeks' gestation (window ± 12 days) when anomaly ultrasounds are typically scheduled. Phase 3 data are collected at 36 weeks' gestation (window ± 12 days). Study midwives and/or fieldworkers collect birth data (phase 4) within a window of 12 h. Postnatal data are collected at 6 weeks (+ 14 days) (phase 5); 24 weeks (+ 30 days) (phase 6); 6 weeks post measles immunisation (± 3 days) (phase 7) or 30 weeks (+ 30 days) if measles immunization was not given between 24 and 28 weeks; and 52 weeks (+ 30 days) (phase 8) postnatal age. The purpose of the phase 7 data collection point specifically is to assess measles immunoglobulin G (IgG) as marker of response to immunisation at 6 months and immune function.

Maternal socio-economics and -demographics

Socio-economic and -demographic data are collected at phase 1 by means of a structured interview. Data include date and country of birth, marital status, educational level, home language, employment status, household income, number of members in the household, and beneficiaries of social grants. Lastly, living standards data are obtained to allow classification according to the Living Standards Measure (LSM) developed by the South African Audience Reference Foundation (SAARF) [32]. This measure is widely used in South Africa to describe the socio-economic status of the population [33].

Maternal household food insufficiency and insecurity

The level of the participating women's household food insufficiency and insecurity is assessed at phase 1 in pregnancy and again at phases 6 and 8 postnatally. In a structured interview, women are asked questions on food insecurity and child hunger using the Community Childhood Hunger Identification Project (CCHIP) index [34] that was also used to determine the status of food security in previous national surveys in South Africa [35]. Furthermore, women were asked a validated, single-item question on food insufficiency – "How many days in the past week have you gone hungry? By this I mean days when you felt you didn't have enough to eat." – that was previously used to determine food insufficiency in pregnant women in South Africa [36].

Maternal dietary intake

Maternal dietary intake data are obtained by means of two dietary assessment methods, namely the 24-h recall

(24-HR) and a quantified food frequency questionnaire (QFFQ). Both methods are interviewer administered by using standardised probing questions [37]. Standard measuring equipment, common size containers (e.g. cups, bowls and glasses) as well as two- and three-dimensional food models are being used to assist in quantifying portion sizes.

A single 24-HR, which obtains details about nutritional supplement use as well, is administered at phases 1, 2 and 3 in pregnancy, as well as at 6 months postnatally (phase 6). Each participant is requested to recall all foods and drinks consumed the previous day from when she woke up until the next day the same time. The recall is done chronologically unless the participant wishes to recall randomly. The purpose of the single 24-HR is to describe the average intake of the group [38]. All supplement use, as well as food cravings and aversions, are additionally recorded daily by participants on a calendar.

The second dietary assessment method, the QFFQ, is completed at phases 1 and 3. It was validated for the population in the Transition and Health during Urbanisation of South Africans (THUSA) study [39] and its reproducibility was proven [40, 41]. It was also used previously to assess individual and total omega-3 and omega-6 fatty acid intake in a rural and urban South-African population [42]. This QFFQ includes a list of typically consumed foods and minor changes were made to the questionnaire according to vernacular used by the study population in that particular area. Participants are asked according to the ~140 food items listed in the QFFQ, the type/brand, cooking methods, frequency and the amount of all food and drink consumed in the past 4 weeks.

For the QFFQ data, portion sizes are converted to grams per week per food item, by two registered dietitians/nutritionists. For the 24-HR all portion sizes are converted to grams per day per food item. The resources to assist with this include the Condensed Food Composition Tables for South Africa [43] and the South African Medical Research Council (SAMRC) Food Quantities Manual [44].

Maternal anthropometric measurements

Maternal weight and mid-upperarm circumference (MUAC) are obtained at each phase (1 to 8), and height only at phase 1 and 5. All measurements are done twice and recorded to the nearest 0.05 kg for weight, 0.1 cm for MUAC and height. Standardised methods of the International Society for the Advancement of Kinanthropometry [45] are used with a calibrated digital scale for weight, a mobile stadiometer for height; and non-stretchable metal measuring tape for MUAC.

Maternal medical assessment and history

Medical history is obtained at each prenatal visit (phases 1 to 3) by means of participant responses and inspection

of medical files. Information includes medication use (including vaccines), HIV status, obstetric history, hospital admission during pregnancy, use of alcohol, and exposure to passive smoking. At the first postnatal visit (phase 6) a follow-up is made on the maternal medical history at birth. Blood pressure is measured at each prenatal visit (phases 1 to 3) as well as postnatally (phases 5, 6 and 8) according to international guidelines [46] using calibrated equipment. Appropriate sized cuffs are used for obese participants.

Standard procedures are used for a 2-h 75 g oral glucose tolerance test (OGTT) between 24 and 28 weeks gestation to determine development of gestational diabetes mellitus [47].

Maternal morbidity

Maternal morbidity symptoms are assessed from enrolment to birth using a daily calendar. Mothers are instructed on how to complete the calendar and to return completed calendars at each visit. The infectious morbidity symptoms assessed are fever, headache, diarrhoea, nasal discharge and coughing. Other possible pregnancy-related symptoms included are constipation, nausea, vomiting, extreme tiredness and heartburn. Any medication and supplementation use is also recorded daily.

Maternal allergy assessment

The International Study for Asthma and Allergies in Childhood (ISAAC) questionnaire [48] is used to assess allergy symptoms in maternal participants at phases 1 to 3 during pregnancy, and 7 postnatally. Additionally, skin prick tests for common allergens are used at phase 7 postnatally to assess sensitisation [49]. The questionnaire is designed to assess rhinitis, asthma and eczema in children and has been used successfully in an older black population in South Africa [50]. A positive score on any of these three symptoms indicates an allergic phenotype.

Maternal skin prick tests are performed by a medical doctor according to the procedure described in the Allergy Society of South Africa's position statement on skin prick testing [49]. In mothers, sensitisation to a house dust mite mixture including *Dermatophagoides farinae*, as well as German cockroach, mould mixture, cat and dog dander, maize pollen, Bermuda grass and *Quercus robur* (English oak), Eucalyptus, *Cypripedium arizonica* (Arizona cypress), *Platanus hybrida* (London plane) and Acacia trees are measured. A diagnosis of 1) sensitised with clinical symptoms, 2) sensitised and clinically tolerant, 3) sensitised and unknown clinical reactivity, 4) not sensitised with clinical symptoms, 5) unknown sensitization with clinical symptoms or 6) not sensitized with no clinical symptoms is made. The mother is given medical advice and referred if necessary.

Maternal depression and fatigue

Perinatal depression is assessed at phases 1 to 3 during pregnancy and at phases 5, 6 and 8 postnatally using the Edinburgh Postnatal Depression Scale (EPDS). The EPDS is a 10-item scale assessing depressive symptoms experienced in the past 7 days [51], which has been validated for assessing perinatal depression in African settings, including South Africa [52]. Maternal fatigue is assessed at the same time points using the Multidimensional Assessment of Fatigue (MAF) scale, which was shown to be a reliable and valid measure of fatigue in pregnant and postpartum women [53]. Both questionnaires are interviewer administered.

Foetal ultrasonography: Gestational age and foetal growth

Foetal ultrasonography examination is carried out by an obstetrician at the first data collection time point to confirm gestation. Estimation of foetal crown rump length and/or biparietal diameter or femur length between 6 and 18 weeks' gestation indicates an accuracy within 5–7 days [54]. Foetal crown-rump length is used to determine gestational age of participants in their first trimester [55]. For participants in their second trimester, a combination of multiple biometric parameters (biparietal diameter, head circumference, abdominal circumference, and femur length) are used to determine gestational age [55]. Ultrasound is also used to determine the number of foetuses and confirm foetal movement, as well as foetal growth at 22 and 36 weeks' gestation (phases 2 and 3).

Birth and neonatal assessments

Maternal data collected at birth (phase 4) are obtained from maternal medical files and include hospital admission and discharge dates and times, mode of delivery, induction/augmentation of delivery, type of anaesthetic or pain relief if any, rapid plasma reagin (RPR) status (indicative of syphilis infection), HIV status, rhesus negative status and presence of maternal diabetes mellitus. If the delivery is induced or caesarean section conducted, the reason for this intervention is obtained. The study nurses obtain maternal weight before birth with a calibrated digital scale.

Neonatal data collected at birth from the medical file include date and time of birth, gender, Apgar score (at 1 and 5 min) [56], vital signs, medical interventions required, foetal distress and presence of meconium stained liquor. Four identically trained study nurses obtain newborn anthropometry (weight, midarm circumference (MAC), crown-heel length (CHL), head circumference (HC) and thoracic circumference (TC)) within 12 h of birth [57]. If the measurements cannot be taken by the study nurses, hospital records are used to obtain anthropometrical data (using the same calibrated infant scale).

Newborn weight is measured with a calibrated digital infant scale to the nearest 10 g. In order to minimize intra-observer variability all circumferences and CHL are measured with an inelastic tape to the nearest 0.5 cm (metal measuring tape not used to prevent possible lacerations). CHL is measured by placing the newborn in supine position on the tape measure on a flat surface with all limbs extended and measurement taken from vertex to heel of foot, with foot held in a perpendicular position to the leg.

Infant dietary intake and feeding practices

Data on infant feeding practices are collected at each postnatal phase (5 to 8). Mothers are asked how soon after birth the infant was breastfed, if the infant is currently being breastfed and if not, the duration of breastfeeding. All mothers are asked details about any other food or drink (including infant formula, medicine and supplements) given to the infant.

An unquantified food frequency questionnaire for the infant is administered at phases 6 and 8 for qualitative assessment (types and frequency) of milk and complementary feeding at 6 and 12 months postnatally. An adapted questionnaire previously used in the South African context is used [58]. Frequency of the type of food eaten during the past month can be reported by the mother as *every day*, *most days* (not every day, but at least 4 times per week); *once a week* (less than 4 times per week, but at least once per week) or *never*.

A single 24-HR for the infant is administered at phase 6 for quantitative assessment (macro- and micronutrient intakes) of intakes at 6 months postnatally. Similar methods and aids are used as described for maternal dietary intake. However, smaller bowls and different sizes of small spoons are used for infant dietary intake to ease realistic reporting for the mother. Also, emphasis is placed on dished food not eaten and the amount left in the bowl to ensure actual intake is reported.

Infant anthropometric measurements

Infant growth is assessed at each postnatal visit. Before measurements are taken, the infant is assessed for presence of oedema. The infant is weighed on a calibrated scale with minimum of clothing, namely only a vest, and without a nappy; and recorded to the nearest 5 g.

Recumbent length of the infants is taken by means of an infantometer to the nearest 0.1 cm. All foot and headwear is removed before measurements are taken. The measurement is taken with the infant lying on his/her back on the infantometer, legs extended with the head and foot board making contact with the infant.

Infant medical assessments

A medical doctor performs a general and physical medical assessment of infants at each postnatal visit. The infant

assessment includes HIV status history and a general, ear, nose and throat, respiratory, cardiovascular, abdominal and neurological examination as well as any current complaints. It also includes a medical plan for the infant.

Infant morbidity

Infant morbidity assessment is performed at each postnatal visit by a medical doctor with a structured questionnaire. A morbidity calendar, kept daily by the mother/caregiver, is used as reference. The calendar and symptoms are explained to the mother at birth and each postnatal visit up to phase 7, whereby each new section of the calendar is handed to the mother for return at the next visit. Symptoms assessed are fever, diarrhoea, vomiting, nasal discharge, coughing, diaper and other rash. Any unscheduled visits to a medical facility and medicine given to the infant are also recorded. The medical doctor diagnoses and determines the duration of each morbidity event using the structured questionnaire with reference to the morbidity calendar.

Infant allergy assessment

A medical doctor assesses the allergy phenotype and sensitisation of infants with the Childhood Allergy and Immunology Research (CAIR) questionnaire and skin prick tests at phases 7 and 8 postnatally. The CAIR questionnaire was developed by the School of Paediatrics and Child Health of the University of Western Australia and is designed to assess asthma, rhinitis and eczema in infants.

Infant skin prick tests are performed at phases 7 and 8 by a medical doctor according to the procedure described in the Allergy Society of South Africa's position statement on skin prick testing [49]. Skin prick tests to determine sensitisation to common allergens are common medical practice in infants older than 4 months [59, 60]. In infants, sensitization to a house dust mite mixture including *Dermatophagoides farinae*, German cockroach, mould mixture, cat and dog dander, maize pollen, Bermuda grass, chicken egg, cow's milk, cod fish, peanuts, wheat and soy bean flour and potato are measured. A diagnosis of 1) sensitised with clinical symptoms, 2) sensitised and clinically tolerant, 3) sensitised and unknown clinical reactivity, 4) not sensitised with clinical symptoms, 5) unknown sensitization with clinical symptoms or 6) not sensitized with no clinical symptoms is made. The infant's medical plan is managed accordingly.

Infant immune response

The infant's IgG response to measles immunisation is assessed at phase 7, which is 6 weeks after measles immunisation was administered at the study site. The measles immunisation in South Africa forms part of the National Expanded Programme for Immunisation and permission to administer it at the study site has been

granted by the Department of Health of Gauteng Province and the City of Johannesburg. Response to an immunisation is regarded as a good marker to measure immune function *in vivo* [61] and the response will be in the log phase 6 weeks after immunisation, which is the most sensitive stage to measure differences in response among infants.

Infant psychomotor and socio-emotional development

Psychomotor and socio-emotional development of the offspring is being assessed using the Protocol for Child Monitoring –Infant version (PCM-I), which combines both parental report and direct observation by trained assessors to provide a comprehensive evaluation of a child's motor skills, cognition, language, personal and socio-emotional development [62]. The PCM-I consists of items derived from: 1) the Kilifi Developmental Inventory (KDI) [63], previously used by the investigators to determine psychomotor development in an infant population in South Africa [64], 2) the Developmental Milestone Checklist (DMC-II) [65, 66], and 3) the Profile of Social-Emotional Development (PSED), which is based in part on the Brief Infant/Toddler Social Emotional Assessment [67].

Biological sample collection

Venous blood (42 ml) is drawn from the participating women into labelled EDTA-coated, serum and trace element free evacuated tubes at phases 1–4 during pregnancy and at phase 6 postnatally. At birth (phase 4), umbilical cord blood samples are taken immediately after the separation of the newborn from the umbilical cord and before placental delivery into labelled EDTA-coated, serum and trace element free evacuated tubes. Venous blood from the infant (3 ml) is drawn at phases 6, 7 and 8. Dry blood spots are collected on filter paper cards (Whatman, Inc) immediately after blood collection (maternal, cord and infant). The filter paper cards are allowed to dry at room temperature for 24 h, placed in ziplock bags with desiccants, and stored at -20°C until analysis. In case venous blood cannot be obtained from the infants, capillary blood is being collected by foot venepuncture.

Venous blood is processed within 1 h after blood draw; plasma/serum separated and red blood cells washed twice with normal saline. Buffy coats are stored in 1:1 vol: vol RNA later (Ambion).

Midstream spot urine samples (5 ml) are collected from the participating women at phases 1, 2 and 3 during pregnancy and at phase 6 postnatally into a urine collection cup. From the infants, a 2–5 ml urine sample is collected at phases 6, 7 and 8 using adhesive paediatric urine collection bags. Urine samples are transferred

into labelled microtubes and stored at -20°C within 4 h.

Breast milk samples (fore-milk) are collected from lactating mothers at phases 5 and 6 as described previously [68].

Rectal swabs (FLOQSwab, COPAN) are collected from both the mother and the baby at phases 4 and 6 of data collection. The mucosal microbe sample is taken approximately ± 3 cm into the anal canal, beyond the anal verge. After collection the cotton bud end of the swab with the collected sample is immediately preserved in RNAlater (Ambion) and stored at -20°C .

Biological samples are processed on site and stored at -20°C for a maximum of 14 days. Thereafter, frozen samples are transported to the North-West University for storage at -80°C until analysis. Storage temperature is monitored and logged for the entire duration of the study.

Biochemical analyses

Haemoglobin is determined on site in whole blood (20 μL) using HemoCue (Hb 201+, Ängelholm, Sweden). The iron status indices, ferritin and transferrin receptor, as well as the vitamin A status indicator retinol binding protein will be determined using the Q-Plex[™] Human Micronutrient Array (7-plex, Quansys Bioscience, Logan, UT, USA) [69]. This multiplex immune-assay also includes the acute phase proteins C-reactive protein (CRP) and alpha1-acid glycoprotein (AGP), as well as the malaria marker HRP2 and thyroglobulin, which is a marker of iodine status. Urinary iodine concentrations are determined in spot urine samples using a modification of the Sandell-Kolthoff reaction with spectrophotometric detection [70]. Vitamin A and E status will be determined using high pressure liquid chromatography (HPLC) and ultraviolet light detection [71]. Vitamin D status will be determined by measuring total 25-Hydroxyvitamin D [25(OH)D] concentrations in serum using liquid chromatography tandem mass spectrometry (LCMSMS) [72]. Fatty acids in red blood cell total phospholipids are determined using gas chromatography tandem mass spectrometry (GCMSMS) [73]. Zinc concentrations are determined in serum using atomic absorption spectrometry [74].

Thyroid hormones (thyroid stimulating hormone, thyroglobulin, total thyroxine) will be determined in whole blood spots by using electrochemiluminescence immunoassays. Lipid-derived immune modulators will be determined with LCMSMS [75]. Cytokines and hepcidin will be determined using ELISA.

Kynurenine pathway metabolites (mediates interactions between immunological and neurological function) will be determined using LCMSMS [76]. Brain-derived neurotrophic factor (BDNF) as a potential marker of neuronal growth and differentiation will be determined using ELISA [77].

Gut microbiome profiling will be done by isolating microbial DNA from the collected rectal swabs using Qiagen Stool minikit and analysing the 16S rRNA genes DNA sequences on the Ion Torrent 16S metagenomics solution offered by ThermoFisher Scientific.

Targeted epigenetic marks, specifically DNA methylation signatures, will also be assessed in the context of the primary and secondary outcomes of this study. Gene specific DNA methylation will be assessed using the Qiagen EpiTect system. Both, the EpiTect Methyl II Signature and EpiTect Methyl II Complete PCR Arrays (Qiagen) will be considered.

Targeted genotyping of genes of interest in the context of fatty acid, lipid and micronutrient metabolism will also be investigated following the Ion AmpliSeq Targeted Sequencing approach using the Ion Chef™ and Ion S5™ Systems (ThermoFisher).

Data management and analysis

Sample size calculation

The number of participants to sample has been calculated using the G*Power 3.1.9.2 statistical programme [78]. The statistical calculation involved is the linear multiple regression: fixed model, single regression coefficient. The calculation was based on a small effect size F^2 of 0.05; probability of error (alpha) of 5%; a power of 80% and ten predictors on the birth outcome "low birth weight". The result was that 196 participants will be required. Taking into consideration that participants may opt out of the project (at 25% rate), it is calculated that a minimum of 245 participants should be recruited. We intended to recruit a minimum of 250 participants. However, should the researchers be able to obtain additional funding, additional participants may be included.

Data management

Data are managed by two dedicated data managers. Raw data are captured and saved in password protected Microsoft Access documents with passwords known only to the operator responsible for data imputing and the principal investigators. A second person checks 20% of all the captured data randomly and notes and corrects any errors. If there are more than 5% errors, respective data are re-captured. The final version of the database will be stored under protected zipped files. Data are collected on dual core electronic archives with automatic backup. Information of the single datasets are stored using anonymous IDs. The document linking anonymous IDs to participants will be collected and stored separately.

Dietary data are captured in Microsoft Excel (Microsoft Corporation, Washington, USA) and all electronic entries are double checked by a registered dietitian for the correct food code and a reasonable amount reported. Analyses will be done by the SAMRC by linking data to the most

recent food composition database. Data will then be screened by means of range checks and for outliers in total energy, protein, fat, vitamin A and vitamin C intake.

Data analysis

Overall, data processing and statistical analysis are performed using the SAS statistical package (SAS, Cary, NC, USA). Analysis of baseline (phase 1) data will be conducted to describe the nutritional status and basic socio-economic characteristics of the pregnant women. Data will be tested for outliers and normality by means of Q-Q plots and histogram visual inspection. Test for normality will be performed by the Shapiro-Wilk test. Normally distributed data will be expressed as means $\pm$ SD; non-normally distributed data will be expressed as medians (25th percentile, 75th percentile).

Data will be analysed cross-sectionally to determine associations between variables at each time point by using appropriate statistical methods (e.g. multiple linear regression analysis, ANCOVA, logistic regression analysis), adjusting for potential covariates.

Data will be analysed prospectively to determine associations between variables at different time points (longitudinally) by using appropriate statistical methods (e.g. linear mixed effects models), adjusting for potential time-dependent and static covariates.

Data will also be analysed retrospectively in matched-control sub-studies by determining associations between observed outcomes and variables collected at previous time points.

The level of significance will be set at $P < 0.05$.

Discussion

The importance of perinatal nutrition and its role in offspring health, is recognised [79]. Nutrition during pregnancy is an important factor associated with both maternal and infant health outcomes [80]. To date, however, South African public health nutrition interventions for pregnant women are limited to folic-iron and calcium supplementation, while it is highly likely that the diet of pregnant women living in South Africa is lacking vital micronutrients and essential fatty acids beyond those supplied, or is even containing excessive amounts of specific micro- and macro-nutrients. In order to advocate evidence-based healthcare policy and practice, the identification of nutrient deficiencies and poor eating patterns of pregnant women in South Africa, which are associated with adverse neonatal outcomes and delayed early offspring development, is imperative.

Little is known about the dietary behaviour and nutritional status of pregnant women living in South Africa. To the best of our knowledge, this is the first South African study focusing on the assessment of both maternal

dietary intake and nutritional status in women pre- and postnatally and to investigate associations with outcomes of maternal and infant health. This study is novel due to the comprehensive set of nutrition related data and indicators of maternal and infant health being obtained in a South African setting. Therefore, this explorative project will contribute to identifying factors that may be targeted in future pre- and/or post-conception maternal interventions for optimal offspring development and possibly reduction in adult NCD risk.

This study also has its challenges. The inclusion and exclusion criteria for participants were designed as such to obtain a sample of generally healthy women, who are able to speak the local language and who could be followed-up from early pregnancy until the infants are 12 months old. South African statistics show that only 52% of women attend antenatal care before 20 weeks' gestation [30], thus access to women early in pregnancy is restricted and limits enrolment into the study. Furthermore, many healthcare facilities in Johannesburg serve a predominantly migrant population [81] posing a challenge for longitudinal data collection. Additionally, these women may choose to eat traditional foods [82] that do not form part of the South African Food Database for nutritional analysis; and may not be able to speak a local language [83] hampering detailed reporting during dietary assessments. Thus, migrating women or those unable to speak local languages could not be included in the study.

A limitation of the study is that women who fit the inclusion criteria are invited to join the study by visiting the data collection site at an agreed date. Having this option of attending may contribute to self-selection bias. Our recruitment data to date indicate that of those invited to take part in the study; only approximately 50% arrive at the data collection site on the booked date.

Even so, this study will provide a comprehensive and unique database from an urban South African setting which will allow for cross-sectional, prospective and retrospective analyses to describe the nutritional status and dietary intake of pregnant women, and to determine associations with health outcome measures. These results will supply context to intervention studies with the aim to improve maternal as well as offspring health in South Africa.

Abbreviations

24-HR: 24-h recall; AGP: Alpha1-acid glycoprotein; ANC: Antenatal care; BDNF: Brain-derived neurotrophic factor; CHL: Crown-heel length; CRP: C-reactive protein; DOHaD: Developmental Origins of Health and Disease; ELISA: Enzyme-linked immunosorbent assay; ESRU: Empilweni Services and Research Unit; GC-MS/MS: Gas chromatography-mass spectrometry; HC: Head circumference; HPLC: High-performance liquid chromatography; HRP2: Histidine-rich protein 2; MAC: Mid-arm circumference; MUAC: Mid-upper arm circumference; NCD: Non-communicable disease; NUPED study: Nutrition during pregnancy and early development study; OGTT: Oral glucose tolerance test; QFFQ: Quantified food frequency questionnaire; RMMCH: Rahima Moosa Mother and Child Hospital; RPR: Rapid plasma reagin; SD: Standard deviation; TC: Thoracic circumference

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed for the purposes of this protocol article.

Authors' contributions

EAS, JB, LM, LZ and CMS conceptualised and designed the study. EAS, JB, LM and LZ are implementing the research. LM and LZ are responsible for laboratory analyses. JB, LM and RC are responsible for data capturing and analyses. EAS drafted the paper with equal contributions from JB, LM, LZ and CMS. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1 and NWU-00049-16-A1) and the University of Witwatersrand, Johannesburg (M150968 and M161045) provided ethical approval for the study. Permission to conduct the research in the relevant clinical setting was obtained from the Gauteng Health Department, City of Johannesburg District Research Committee and the Clinical Manager of Rahima Moosa Mother and Child Hospital. All participants sign written informed consent before data collection.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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<https://doi.org/10.1111/apa.12540>

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ADDENDUM 2

**Ethical approval from the Human Research Ethics Committee, North
West University**





NORTH-WEST UNIVERSITY
YUNIBESITHI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT

Private Bag X8001, Potchefstroom
South Africa 2520

Tel: (018) 299-4900
Faks: (018) 299-4910
Web: <http://www.nwu.ac.za>

Institutional Research Ethics Regulatory Committee

Tel +27 18 299 4849
Email Ethics@nwu.ac.za

ETHICS APPROVAL CERTIFICATE OF PROJECT

Based on approval by Health Research Ethics Committee (HREC), the North-West University Institutional Research Ethics Regulatory Committee (NWU-IRERC) hereby approves your project as indicated below. This implies that the NWU-IRERC grants its permission that, provided the special conditions specified below are met and pending any other authorisation that may be necessary, the project may be initiated, using the ethics number below.

Project title: Nutrition in Pregnancy and Early Development: The NuPED study																															
Project Leader: Prof CM Smuts																															
Ethics number:	<table border="1"> <tr> <td>N</td><td>W</td><td>U</td><td>-</td><td>0</td><td>0</td><td>1</td><td>8</td><td>6</td><td>-</td><td>1</td><td>5</td><td>-</td><td>A</td><td>1</td> </tr> <tr> <td colspan="3">Institution</td> <td colspan="6">Project Number</td> <td colspan="2">Year</td> <td colspan="4">Status</td> </tr> </table> Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation	N	W	U	-	0	0	1	8	6	-	1	5	-	A	1	Institution			Project Number						Year		Status			
N	W	U	-	0	0	1	8	6	-	1	5	-	A	1																	
Institution			Project Number						Year		Status																				
Approval date: 2015-11-18	Expiry date: 2017-12-30																														
Risk	Minimal																														

Special conditions of the approval (if any): None

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:

- The project leader (principle investigator) must report in the prescribed format to the NWU-IRERC:
 - annually (or as otherwise requested) on the progress of the project,
 - without any delay in case of any adverse event (or any matter that interrupts sound ethical principles) during the course of the project.
- The approval applies strictly to the protocol as stipulated in the application form. Would any changes to the protocol be deemed necessary during the course of the project, the project leader must apply for approval of these changes at the NWU-IRERC. Would there be deviation from the project protocol without the necessary approval of such changes, the ethics approval is immediately and automatically forfeited.
- The date of approval indicates the first date that the project may be started. Would the project have to continue after the expiry date, a new application must be made to the NWU-IRERC and new approval received before or on the expiry date.
- In the interest of ethical responsibility the NWU-IRERC retains the right to:
 - request access to any information or data at any time during the course or after completion of the project;
 - withdraw or postpone approval if:
 - any unethical principles or practices of the project are revealed or suspected,
 - it becomes apparent that any relevant information was withheld from the NWU-IRERC or that information has been false or misrepresented,
 - the required annual report and reporting of adverse events was not done timely and accurately,
 - new institutional rules, national legislation or international conventions deem it necessary.

The IRERC would like to remain at your service as scientist and researcher, and wishes you well with your project. Please do not hesitate to contact the IRERC for any further enquiries or requests for assistance.

Yours sincerely

Linda du
Plessis

Digitally signed by Linda du Plessis
DN: cn=Linda du Plessis, o=NWU,
ou=West Triangle Campus,
email=Linda.duplessis@nwu.ac.za,
c=ZA
Date: 2015.11.20 21:38:38 +0200

Prof Linda du Plessis

Chair NWU Institutional Research Ethics Regulatory Committee (IRERC)



ETHICS APPROVAL CERTIFICATE OF STUDY

Based on approval by Health Research Ethics Committee (HREC) on 17/11/2016 after being reviewed at the meeting held on 11/05/2016, the North-West University Institutional Research Ethics Regulatory Committee (NWU-IRERC) hereby approves your study as indicated below. This implies that the NWU-IRERC grants its permission that provided the special conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: Nutrition during Pregnancy and Early Development: the NuPED postnatal study.

Study Leader/Supervisor: Prof CM Smuts

Ethics number:

N	W	U	-	0	0	0	4	9	-	1	6	-	A	1
Institution				Study Number						Year			Status	

Status: S = Submission; R = Re-Submission; P = Provisional Authorisation; A = Authorisation

Application Type: Larger study

Risk: Medium – Mothers

Category 2: Greater than minimal with direct benefit - Babies

Commencement date: 2016-11-17

Continuation of the study is dependent on receipt of the annual (or as otherwise stipulated) monitoring report and the concomitant issuing of a letter of continuation up to a maximum period of three years.

Special conditions of the approval (if applicable):

- Translation of the informed consent document to the languages applicable to the study participants should be submitted to the HREC (if applicable).
- Any research at governmental or private institutions, permission must still be obtained from relevant authorities and provided to the HREC. Ethics approval is required BEFORE approval can be obtained from these authorities.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, please note the following:

- The study leader (principal investigator) must report in the prescribed format to the NWU-IRERC via HREC:
 - annually (or as otherwise requested) on the monitoring of the study, and upon completion of the study
 - without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.
- Annually a number of studies may be randomly selected for an external audit.
- The approval applies strictly to the proposal as stipulated in the application form. Would any changes to the proposal be deemed necessary during the course of the study, the study leader must apply for approval of these amendments at the HREC, prior to implementation. Would there be deviation from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.
- The date of approval indicates the first date that the study may be started.
- In the interest of ethical responsibility the NWU-IRERC and HREC retains the right to:
 - request access to any information or data at any time during the course or after completion of the study;
 - to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process;
 - withdraw or postpone approval if:
 - any unethical principles or practices of the study are revealed or suspected,
 - it becomes apparent that any relevant information was withheld from the HREC or that information has been false or misrepresented,
 - the required amendments, annual (or otherwise stipulated) report and reporting of adverse events or incidents was not done in a timely manner and accurately,
 - new institutional rules, national legislation or international conventions deem it necessary.
- HREC can be contacted for further information or any report templates via Ethics-HRECAppl@nwu.ac.za or 018 299 1206.

The IRERC would like to remain at your service as scientist and researcher, and wishes you well with your study. Please do not hesitate to contact the IRERC or HREC for any further enquiries or requests for assistance.

Yours sincerely

Prof Linda du Plessis

Chair NWU Institutional Research Ethics Regulatory Committee (IRERC)

07 November 2019

ETHICS APPROVAL LETTER OF STUDY

Based on approval by the North-West University Health Research Ethics Committee (NWU-HREC) on 07/11/2019, the NWU-HREC hereby approves your study as indicated below. This implies that the NWU-HREC grants its permission that, provided the general conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: Associations between maternal dietary patterns during pregnancy and early childhood development in Johannesburg, South Africa

Principal Investigator/Study Supervisor/Researcher: Prof CM Smuts

Student: C Conradie-25872283

Ethics number:

N	W	U	-	0	0	1	8	6	-	1	5	-	A	1	-	0	5
Institution			Study Number				Year			Status			Sub-study				

Status: S = Submission; R = Re-Submission; P = Provisional Authorisation;
A = Authorisation

Application Type: Sub-study

Commencement date: 07/11/2019

Expiry date: 30/11/2020

Risk:

Minimal

Approval of the study is provided for a year, after which continuation of the study is dependent on receipt and review of an annual monitoring report and the concomitant issuing of a letter of continuation. A monitoring report is due at the end of November annually until completion.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, the following general terms and conditions will apply:

- *The principal investigator/study supervisor/researcher must report in the prescribed format to the NWU-HREC:*
 - *Annually on the monitoring of the study, whereby a letter of continuation will be provided annually, and upon completion of the study; and*
 - *without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.*
- *The approval applies strictly to the proposal as stipulated in the application form. Should any amendments to the proposal be deemed necessary during the course of the study, the principal investigator/study supervisor/researcher must apply for approval of these amendments at the NWU-HREC, prior to implementation. Should there be any deviations from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.*
- *Annually a number of studies may be randomly selected for active monitoring.*
- *The date of approval indicates the first date that the study may be started.*
- *In the interest of ethical responsibility, the NWU-HREC reserves the right to:*

- request access to any information or data at any time during the course or after completion of the study;
- to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process;
- withdraw or postpone approval if:
 - any unethical principles or practices of the study are revealed or suspected;
 - it becomes apparent that any relevant information was withheld from the NWU-HREC or that information has been false or misrepresented;
 - submission of the annual monitoring report, the required amendments, or reporting of adverse events or incidents was not done in a timely manner and accurately; and/or
 - new institutional rules, national legislation or international conventions deem it necessary.
- NWU-HREC can be contacted for further information via Ethics-HRECApply@nwu.ac.za or 018 299 1206

The NWU-HREC would like to remain at your service and wishes you well with your study. Please do not hesitate to contact the NWU-HREC for any further enquiries or requests for assistance.

Yours sincerely,



Digitally signed by Petra Bester
DN: cn=Petra Bester,
o=AUTH, ou=NWU, Faculty
of Health Sciences,
email=petra.bester@nwu.ac.za,
c=ZA
Date: 2019.11.11 15:01:09
+0200

Chairperson NWU-HREC

Current details: (23236522) G:\My Drive\8. Research and Postgraduate Education\8.1.5.4 Templates\8.1.5.4.2_NWU-HREC_EAL.docm
20 August 2019

File Reference: 8.1.5.4.2

ADDENDUM 3

**Ethical approval from the Human Research Ethics Committee,
University of Witwatersrand, Johannesburg**





12 September 2017

Prof Marius Smuts
Faculty of Health Sciences
Centre of Excellence for Nutrition
North-West University (Potchefstroom Campus)

Sent by email to: marius.smuts@nwu.ac.za

Dear Prof Smuts

Re: Protocol Ref no: M150968
Protocol Title: Nutrition During Pregnancy and Early Development: The NuPED Study
Principal Investigator: Prof Marius Smuts et al
Protocol Amendment

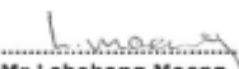
This letter serves to confirm that the Chairman of the Human Research Ethics Committee (Medical) has approved the protocol amendment on the abovementioned protocol, as detailed in your letter dated 08 August 2017.

The following documents were received:

- Cover Letter dated 08 August 2017.
- Participant Informed Consent version 1 dated 16 May 2016.
- Study Proposal version 7 dated 15 May 2017.

Thank you for keeping us informed and updated.

Yours Sincerely,


.....
Mr Lebohang Moeng
Administrative Assistant
Human Research Ethics Committee (Medical)



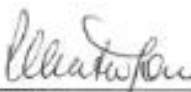


R14/49 Prof Marius Smuts et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M161045

NAME: Prof Marius Smuts et al
(Principal Investigator)
DEPARTMENT: Centre of Excellence for Nutrition, North-West University
Rahima Moosa Mother and Child Hospital
PROJECT TITLE: Nutrition in Pregnancy and Early Development:
The NuPED Postnatal Study
DATE CONSIDERED: 28/10/2016
DECISION: Approved unconditionally
CONDITIONS:
SUPERVISOR:

APPROVED BY: 
Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL: 01/02/2017

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

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third Floor, Faculty of Health Sciences, Philip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in October and will therefore be due in the month of October each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____

Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

ADDENDUM 4

Permission letter from the Gauteng Department of Health





GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

OUTCOME OF PROVINCIAL PROTOCOL REVIEW COMMITTEE (PPRC)

Researcher's Name (Principal investigator)	Prof. Marius Smuts
Organization / Institution	Centre of Excellence for Nutrition: North West University
Research Title	Nutrition During Pregnancy and Early Development (NuPED) study
Contact number	Address: N/A Contact no: 018 299 2086 Cell: Email: Marius.Smuts@nwu.ac.za
Protocol number	GP2015RP 38 473
Date submitted	26/10/2015
Date reviewed	26/11/2015
Outcome	Approved

It is a pleasure to inform you that the Gauteng Health Department has approved your research on "Nutrition During Pregnancy and Early Development (NuPED) study"

Study sites: JHB Metro, Rahima Moosa Hospital, Florida, Bosmont, Sophiatown and Zandspruit Clinics.

The Provincial Protocol Review Committee kindly requests that you to submit a report after completion of your study and present your findings to the Gauteng Health Department.

Recommended/Not Recommended


Dr. B. Ikalafeng
(on behalf of the PPRC)

Date: 27/11/2015

Approved/Not approved


Dr. LRR. Lebethe
Acting DDG: Clinical Service

Date: 03/12/15

ADDENDUM 5

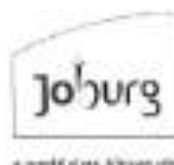
Permission letter from the City of Johannesburg District Research Committee





GAUTENG PROVINCE

REPUBLIC OF SOUTH AFRICA



JOHANNESBURG HEALTH DISTRICT

Enquiries

Hillbrow CHC Administration Building, Klein Street
Hillbrow, Johannesburg

E-mail:

Corat@joburg.org.za

johnnesburg.research@amr.ac.za

10 December 2015

Professor Marius Smuts
Nutrition
Potchefstroom Campus
E-mail: Marius.Smuts@ru.ac.za

Dear Professor Smuts,

Re: *Nutrition in Pregnancy and Early Development: The NuPED Study*

Your application dated 8 December 2015 refers. The District Research Committee has reviewed your application. This letter serves as an in-principle approval to access the Districts Health facilities (mentioned below) for the above project subject to following conditions:

- The facility to be visited: Florida, Bosmont, Sophiatown and Zandspruit Clinics
- The research can only commence after you submit an ethics clearance certificate from a recognized institution.
- Please contact the relevant RHDD prior to your visit to the facilities

Region	Regional Health Manager	Contact No.	Cell phone
B	Ms Paulinah Maepa	011 718 9856	082 551 5804
C	Mr. Tebogo Motsepe	011 761 0248	083 421 9405

- You will report to the Facility Manager before initiating the study.
- Participants' rights and confidentiality will be maintained all the time.
- No resources (Financial, material and human resources) from the above facilities will be used for the study. Neither the District nor the facility will incur any additional cost for this study.
- The study will comply with Publicly Financed Research and Development Act, 2008 (Act 51 of 2008) and its related Regulations.
- You will submit a copy (electronic and hard copy) of your final report. In addition, you will submit a six-monthly progress report to the District Research Committee. Your supervisor and University of South Africa will ensure that these reports are being submitted timeously to the District Research Committee.
- The District must be acknowledged in all the reports/publications generated from the research and a copy of these reports/publications must be submitted to the District Research Committee.

We reserve our right to withdraw our approval, if you breach any of the conditions mentioned above.

Please feel free to contact us, if you have any further queries. On behalf of the District Research Committee, we would like to thank you for choosing our District to conduct such an important study.

Regards,



Dr R Bismilla
Executive Director
City of Johannesburg

Date: 10/12/15

ADDENDUM 6

**Permission letter from the clinical manager at Rahima Moosa Mother
And Child Hospital**





GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA



RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

Enquiries: Dr E Hank

Tel: (011) 470 9030/9031

Fax: (011) 477 4117

Email: Edward.Hank@gauteng.gov.za

Ms Elize Symington

Centre of Excellence for Nutrition

North-West University (Potchefstroom Campus)

6 July 2015

Re: Nutrition in Pregnancy and Early Development: The NuPED study

Dear Ms Symington

Permission is granted for you to conduct the research as indicated in your request as per the title above.

The terms under which this permission is granted is contained in the Researcher Declaration form that you signed. Failure to comply with these conditions will result in the withdrawal of such permission.

Note that it is imperative that you notify the hospital of the actual start and end dates of your study by notifying Karen Marshall by email (Karen.Marshall@wits.ac.za).

Should the study commence more than 12 months from receipt of this letter then the Researcher Declaration form needs to be re-signed prior to commencement of the research. You are strongly advised to keep a signed copy of the declaration form so as to ensure that the terms of this agreement are complied with at all times.

Yours sincerely,


Clinical Manager

ADDRESS: cnr. FUEL & OUDSTHOORN STREET CORONATIONVILLE 2093 / PRIVATE BAG X20 NEWCLARE 2112 JHB

ADDENDUM 7

**Permission letter from the Head Of Department: Obstetrics And
Gyneacology at Rahima Moosa Mother and Child Hospital**





NORTH-WEST UNIVERSITY
YUNIBESITHI YA BOKONE-BOPHIRIMA
NOORDWES-UNIVERSITEIT

To: Head of Department Obstetrics and Gynaecology
Rahima Moosa Mother and Child Hospital

From: Prof Marius Smuts, Project Head
Centre of Excellence for Nutrition, North-West University, Potchefstroom
018 299 2086; Marius.Smuts@nwu.ac.za

3 September 2015

Permission letter for conducting research in the Department of Obstetrics and Gynaecology
Nutrition during Pregnancy and Early Development: The NuPED study

With reference to previous conversations and the attached permission letter by Dr E Hank, clinical manager of the hospital we are kindly requesting your permission for conducting the research project in your department.

The aim of the research project is to assess dietary intake and nutritional status of urban South African pregnant women and to determine associations with birth outcomes, maternal health and offspring health. Using a longitudinal observational research design, pregnant women (<16 weeks gestation) (min. n=250) will be recruited from primary healthcare clinics in Johannesburg and followed up at RMMCH. Dietary intake and nutrient status will be assessed at <16, 24 and 36 weeks gestation. At birth, maternal and neonatal health will be assessed. The following data will be obtained from medical records in your department:

- Medical history (parity; gravity, previously or currently diagnosed hypertension, diabetes, TB and HIV; bacterial vaginosis; early symptoms of pregnancy such as nausea and vomiting; smoking number of births, etc.)
- Blood pressure
- Ultrasound screen data
- Glucose tolerance test results

Kindly note that nursing staff will draw blood samples (additional tubes to be supplied by the research team) and analysed by external laboratories. Urine samples will be collected as per standard operating procedures, however, fieldworkers will take aliquots for research purposes.

The research team (trained fieldworkers) will be obtaining the socio-demographic data, anthropometrical measurements, diet history and general health questionnaires.

On behalf of the research team, we are herewith requesting your permission for conducting the research project in your department and obtaining the abovementioned data.

Prof Marius Smuts

Head: Department O&G

Outcome

29.9.15

Date

ADDENDUM 8

Informed Consent Form: Prenatal Phase of the NuPED Study





Health Research Ethics Committee

Faculty of Health Sciences
NORTH-WEST University
(Potchefstroom Campus)

2016 -04- 26

HREC Stamp

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM FOR ASSESSMENTS DURING PREGNANCY AND BIRTH

TITLE OF THE RESEARCH PROJECT:

Nutrition during Pregnancy and Early Development: The NuPED study

REFERENCE NUMBERS: NWU-00186-15-S1; M150968

PRINCIPAL INVESTIGATOR: Prof Marius Smuts

ADDRESS: School of Physiology, Nutrition and Consumer Sciences, Potchefstroom Campus, Building G16, Room 157

CONTACT NUMBER: 018 299 2086 / 082 451 0486

Good day

*You are invited to take part in a research project. Please take some time to read the information about this project. Please ask the researcher any questions if you do not fully understand. Your participation is **entirely voluntary** and you are free to say no. If you say no, this will not affect you negatively in any way. You are also free to withdraw from the study at any point, even if you agreed to take part at first.*

*This study has been approved by the **Health Research Ethics Committee of the Faculty of Health Sciences of the North-West University (NWU-00186-15-S1)** and the **Human Research Ethics Committee of the University of Witwatersrand (M150968)** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki and the ethical guidelines of the National Health Research Ethics Council. It might be necessary for the research ethics committee members or relevant authorities to inspect the research records. This study will be used by several students to obtain further academic qualifications.*

What is this research study all about?

A good diet during pregnancy is important for the healthy growth of the baby. A mother's diet can affect her baby's health. It is not very clear how different eating habits affect the baby's health.

The goals of this research are to describe the food intake and health of pregnant women throughout pregnancy and to determine if it relates to the babies' health.

Therefore, we would like to measure your diet (food intake) and health at early pregnancy, mid-pregnancy and late pregnancy. When you give birth, we will also measure how healthy your baby is. We may approach you after the study to further investigate the development and well-being of your baby, but then we will ask you to provide new consent. At least two hundred and fifty women will be included in this study.

Some of the blood that we will collect from you and the cord between you and your baby after birth will be used to look at some factors that you inherited from your parents and your baby inherited from you (genetic factors, such as DNA and RNA). Genetic factors are like a manual that tells your body how to work. Sometimes there are differences or changes that cause people to react differently to nutrients. We want to investigate these genetic changes to better understand how this works. We promise that all genetic tests and experiments will only focus on genetic factors to do with nutrient usage in the body and related to your and your baby's health.

Why have you been invited to participate?

You have been invited to take part because you are attending the antenatal clinic today.

You have also complied with the following inclusion criteria:

- You are a pregnant woman, born in South Africa, Lesotho, Swaziland, Zimbabwe, Botswana or Namibia.*
- You are planning to deliver your baby at Rahima Moosa Mother and Child Hospital.*
- You are able to communicate effectively in English, Afrikaans, Sotho, Xhosa or Zulu.*

You will be excluded if you:

- Are more than 18 weeks pregnant since we need to know your status in early pregnancy.*
- Are younger than 18 years of age or older than 39 years of age since age may influence the health of the baby.*
- Are stating that you are using illicit drugs since this may influence the growth of the baby.*
- Are carrying a multiple pregnancy, such as twins or triplets, since these babies are usually born smaller.*
- Have a known lifestyle disease such as diabetes, kidney disease, high blood cholesterol or high blood pressure or using medication for any of these, since this may influence the health of the baby.*
- Have a known infectious disease such as tuberculosis or hepatitis or using medication for any of these, since this may influence the health of the baby.*
- Have a known serious illness such as cancer, lupus or psychosis or using medication for any of these, since this may influence the health of the baby.*
- Are a smoker, or have been smoking in the past year since this influences the growth of the baby.*
- Note: You will not be excluded from the study if you have HIV, but will be asked if we can include your HIV status in our data.*

What will your responsibilities be?

If you agree to take part in the study, you will be expected to:

- *From here on have all your antenatal visits at Rahima Moosa Mother and Child hospital and not here at the clinic. You will be refunded for your travelling costs.*
- *Attend Rahima Moosa Mother and Child hospital next week, at 22 weeks pregnancy and at 36 weeks pregnancy for this research. The doctors or nurses may request you to attend other days as well for other medical reasons. Dates will be given to you for each visit.*
- *Answer questions about your age, education and living conditions only today.*
- *Answer questions about your diet and supplement use at each visit, as well as phone calls before and after the following visits.*
- *Answer questions about your general health, mood, allergy symptoms and medication usage at each visit.*
- *Indicate on a checklist how healthy you feel every day.*
- *Let us do some body measurements at each visit. We will only measure your weight by asking you to stand on a scale, your standing height against a height measure and your upper arm circumference with a tape measure.*
- *Get an ultrasound screen at each scheduled visit to the hospital.*
- *Give a urine sample at each visit.*
- *Give a blood sample at each visit. A total amount of 42ml (about three tablespoons full) will be drawn from your arm.*
- *Let us take your blood pressure at each visit.*
- *Do a diabetes test at around 24 weeks pregnancy. You have to fast from 10pm the previous night. The next morning you will be asked to drink a sweet drink at the hospital laboratory. Your blood sugar levels will be tested several times.*
- *Go to Rahima Moosa Mother and Child Hospital admissions when you feel labour pains. The nurse will then do some body measurements if possible.*
- *Allow us to take some body measurements of your newborn baby, such as weight, height and head circumference.*
- *Allow us to take some blood of the cord between you and your baby after the baby has been born and after the cord has been cut.*
- *Allow us to use your and your baby's medical records to check your health.*

Will you benefit from taking part in this research?

The direct benefits for you as a participant will be that you will receive the normal medical care from a gynaecologist and hospital staff. You will receive additional medical tests, such as an ultrasound screen and diabetes test. These services are not available at the clinic. You will receive immediate feedback on the measurements where results are available on the same day, such as blood pressure and the ultrasound screen. If there are any concerns, you can discuss this with the nurse or other medical professions. They can support you with the appropriate medical care.

The indirect benefit will be that you help us understand the dietary habits and health of pregnant women in South Africa and how that affects the health of their babies. By understanding more about this, we can help government to create policies that can address the health of South African pregnant women better.

Are there risks involved in you taking part in this research?

Most of the measurements that will be performed won't harm or hurt you in any way, but you might experience the following:

- 1. If you give permission to a blood sample, you might feel uncomfortable or scared. This will only last for a short while. We want to make sure that you are not hurt in any way and therefore the qualified professional will draw the blood from your arm. She will talk to you and explain to you everything that she is going to do.*
- 2. You may be concerned that the researchers will be testing your HIV status. The research team will not test your blood for HIV. The clinic nurse may test your blood for HIV as part of routine antenatal care. We do ask you permission that we get the result of this test which is transferred to your study number, thus it is anonymously used further on.*
- 3. During the body measurements you will be asked to remove some of your clothes keeping on only your underwear or light clothing. This might make you feel uncomfortable or shy. To help you feel less shy and uncomfortable, only females will take these measurements. Also, the area where these measurements will be done will be private and closed off. This means that no one else will be able to see you. Only the person that will take the measurements and someone to help her will be with you.*
- 4. When an ultrasound screen of your baby is taken, a clear gel will be squirted onto your belly. This will feel cold, but can do no harm. The medical professional conducting the ultrasound screen will talk you through the process.*
- 5. Being part of such a big research study can be frightening and overwhelming. To prevent us from wasting your time and to make sure that you know where to go and what to do, there will be people available at all times to help you and show you where you have to go every time.*
- 6. For the diabetes test, you will be asked not to eat or drink anything from 22:00 (ten o'clock) the night before. You will only be allowed to drink water. You should also not eat any breakfast on the morning of the study and not drink coffee, tea, juice or cold drink. Not eating or drinking anything might make you feel uncomfortable or light headed (dizzy or faint). When you arrive at around 7:00 on the day of your booking, the laboratory staff will give you a sweet sugary drink. This may taste too sweet for you, so the laboratory staff will give you diluted lemon juice to combat the sweetness. Your blood sugar levels will be tested first with a finger prick and by drawing about 3 ml blood from your arm at 1 and 2 hours after drinking the sugar drink. You will be provided with a food parcel to eat after the test.*
- 7. Doing all of the measurements on the days of the research study, will take most of the day. This might make you feel very tired. You will be provided with refreshments to eat and drink during the day.*
- 8. It is important that you indicate whether you have any food allergies. This will help the research team when providing meals to participants on research days.*

There are more benefits than dangers or risks when you take part in the study.

What will happen in the unlikely event of some harm/form of discomfort occurring as a direct result of you taking part in this research study?

Please let us know if you experience any physical or emotional discomfort during or after participating in the study and we will make appropriate arrangements for you to talk to a medical doctor or psychologist.

Who will have access to the data?

We will handle all your information as confidential as possible by allocating a study code to you and your baby when he/she is born. All samples will be labelled with this code and only the principal investigator and co-principal investigator will have access to the records containing your name. Only the researchers will work with your data. Data will be kept safe and secure by locking hard copies in locked cabinets at the clinic, until your baby is born. Thereafter, these documents will be kept secure in locked cabinets in the researcher's office and for electronic data it will be password protected. Reporting of findings will be anonymous.

What will happen with the data/samples?

Blood samples that will be sent overseas for laboratory analysis will be destroyed once all the pre-defined analyses have been completed. Blood and urine samples being analysed at North-West University will be stored for 7 years after completion of the study. Data will be stored for 15 years. There is the possibility that blood samples and data might be analysed by other researchers over time for the purpose as explained to you.

There is enough money to do the study and perform the most important analyses but some of the tests are very expensive and will only be done once more funding is obtained.

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

No, you will not be paid to take part in the study but your expenses for travelling to Rahima Moosa Mother and Child Hospital will be paid for study visits at <18, 22 and 36 weeks. At each visit you will receive a R5 cell phone voucher to enable you to make a call to the researchers or fieldworkers if you need to. Furthermore, you will be provided with a snack/lunch pack every two hours during assessments at <18, 22 and 36 weeks. You will receive a gift hamper to a value of R150 with goods for your baby as a token of appreciation.

Thus, if you take part there will be no costs involved for you.

Is there anything else that you should know or do?

- You can contact Prof. Marius Smuts at 018 299 2086 / 082 451 0486 or Elize Symington at 072 218 2184 if you have any further queries or encounter any problems.
- You can contact the Health Research Ethics Committee of North-West University via Mrs Carolien van Zyl at 018 299 2089; carolien.vanzyl@nwu.ac.za if you have any concerns or complaints that have not been adequately addressed by the researcher.
- You can also contact the Health Research Ethics Committee of the University of Witwatersrand via:
 - Prof Peter Cleaton-Jones, Chairperson of HREC (Medical) Tel: 011 717 2301 Email: peter.cleaton-jones1@wits.ac.za
 - Ms Zanele Ndlovu, HREC (Medical) Secretariat, Tel: 011 717 1252/2700/ 1234, Email: Zanele.ndlovu@wits.ac.za
- You will receive a copy of this information and consent form for your own records.

How will you know about the findings?

We will give you immediate feedback of results that we determine during the study, such as blood pressure and diabetes tests. However, take note that it will take time to perform the other analyses and that the results will only be available after several months. Once the study is completed and all the results are available, we will distribute the information to the clinics where you will attend for baby clinics. Should we find an abnormal value during our analyses that needs medical attention, we will inform you and the medical staff immediately for the necessary medical treatment.

Few questions (to be completed by the person obtaining the consent):

Did the participant understand the following questions?

If you take part in the study, where will your follow-up antenatal visits be done?

YES

NO

Will taking part in the study cost you any money?

If you take part in the study, from where will we take blood from your new born baby?

Declaration by participant

By signing below, I agree to take part in a research study entitled: *Nutrition during Pregnancy and Early Development: The NuPED study*. I declare that:

- I have read this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.
- I understand and agree that blood samples from me and from the umbilical cord may be sent outside South Africa for laboratory analysis.

Do you have any food allergies?

No ☐

Yes ☐ Which allergies? _____

Do you give permission that some of your blood samples may be analysed outside of South Africa?

Yes, I give permission ☐

No, I don't give permission ☐

Do you give permission that we may collect your genetic material?

Yes, I give permission to collect my genetic material ☐

No, I don't give permission to collect my genetic material ☐

Do you give permission that we may collect your baby's genetic material from the cord blood?

Yes, I give permission to collect my baby's genetic material ☐

No, I don't give permission to collect my baby's genetic material ☐

Do you give permission that the researchers have access to your HIV test results from the clinic?

Yes, I give permission ☐

No, I don't give permission ☐

Do you give permission to have access to your and your baby's medical records at hospital or clinic?

Yes, I give permission ☐

No, I don't give permission ☐

Do you give permission for the researchers to contact you after the birth of your baby for possible follow-up tests?

Yes, I give permission ☐

No, I don't give permission ☐

Do you give permission that other researchers use the blood samples and data at a later stage?

Yes, I give permission ☐

No, I don't give permission ☐

Signed at (place) on (date) 20....

.....
Signature of participant

.....
Signature of witness

Declaration by person obtaining consent:

I (name) declare that:

- I explained the information in this document to
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter.

Signed at (place) on (date) 20....

.....
Signature of investigator/fieldworker

.....
Signature of witness

.....
Signature of researcher

ADDENDUM 9

Informed Consent Form: Postnatal Phase of the NuPED Study





INFORMED CONSENT DOCUMENTATION

for NuPED ASSESSMENTS FROM BIRTH TO 12 MONTHS

TITLE OF THE RESEARCH PROJECT: *Nutrition during Pregnancy and Early Development: The NuPED study - postnatal*

ETHICS REFERENCE NUMBERS: NWU-00049-16-S1 and M161045

PRINCIPAL INVESTIGATOR: *Prof Marius Smuts, Dr Linda Malan, Dr Jeannine Baumgartner*

ADDRESS: *School of Physiology, Nutrition and Consumer Sciences, Potchefstroom Campus, Building G16, Room 157*

CONTACT NUMBER: 018 299 2086 / 082 451 0486
018 299 4237 / 084 402 3834
018 299 4018 / 076 436 4439

Good day

You and your baby are invited to take part in a research study. Please take some time to read the information presented here, which will explain the details of this study. Please ask the researcher or person explaining the research to you any questions about any part of this study that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research is about and how you might be involved. Also, your participation is **entirely voluntary** and you are free to say no to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, without penalty or loss of benefits, even if you do agree to take part now.

This study has been approved by the Health Research Ethics Committee of the Faculty of Health Sciences of the North-West University (NWU-00049-16-S1) and the University of the Witwatersrand (M161045) will be conducted according to the ethical guidelines and principles of Ethics in Health Research: Principles, Processes and Structures (DoH, 2015) and other international ethical guidelines applicable to this study. It might be necessary for the research ethics committee members or other relevant people to inspect the research records.

What is this research study all about?

Good nutrition during pregnancy is important for the healthy growth of the baby. A mother's nutritional status can affect her baby's health. It is not very clear how different eating habits affect the baby's health.

- *This study will be conducted at the Rahima Moosa Mother and Child Hospital and will involve questions about eating habits and health, and drawing blood, with experienced medical specialists and health researchers trained in nutrition. 250 participants will be included in this study.*
- *The goals of this research are to describe the dietary intake and nutritional status of pregnant women throughout pregnancy and to determine if it relates to the babies' health up to the age of 12 months.*

Therefore, we would like to measure how healthy you and your baby are after the baby's birth.

Why have you and your baby been invited to participate?

- *You and your baby have been invited to be part of this research because you are partaking in the NuPED study at the Rahima Moosa Mother and Child Hospital.*
- *You also fit the research because you are a mother taking part in the NuPED study.*
- *You will not be able to take part in this research if you have not been part of the NuPED study when you were pregnant.*

What will be expected of you?

If you agree to take part in the study, you will be expected to:

- *Attend to your baby's 6-month wellness visit at the Rahima Moosa Mother and Child Hospital instead of your usual clinic.*
- *Allow us to take some blood from the cord that connects you and your baby after the baby has been born and the cord has been cut.*
- *Allow us to use your baby's medical records to check your baby's health.*

- Answer questions about your diet, medicine and supplement (such as vitamin pills) use at each visit.
- Answer questions about how and what you feed your baby and at each visit.
- Answer questions about your general health, allergy symptoms and about your mood at each visit.
- Indicate on a checklist how healthy your baby is, and what supplements (such as vitamin drops) and medicine you gave to your baby every day.
- Let us do some body measurements on you and your baby (such as weight and height/length) at each visit.
- Let us do some developmental tests on your baby (like observe whether the baby can sit alone and crawl or walk, or play with some blocks)
- Give a urine sample at each visit and let us obtain a urine sample from your baby.
- Give us some breast milk (one to two teaspoons) after the birth of your baby and again at the 6 weeks and 6 months visit if you are still breast feeding.
- Give us a rectal (anus) swab sample and/or stool sample from yourself and your baby after birth and again when your baby is 6 months old.
- Give a blood sample (42 ml which is about 3 tablespoons full) six months after you gave birth and let us take a blood sample from your baby at 6, seven and a half and twelve months (3 ml, which is less than a teaspoon).
- Let us take your blood pressure when your baby is 6 and 12 months old.
- Visit the RMMC hospital when your baby is 6, seven and a half and 12 months old. You will be refunded for the travelling costs.
- Allow us to test you and your baby for allergies after the baby's birth (at 6 months or 7.5 months) with skin prick tests. You will be given a leaflet to explain the skin prick tests.

The blood, urine, stool and breast milk samples will be used to analyse how the food you and your baby eat (fat, vitamins, minerals) is taken up by your body and if you have allergies. The rectal swabs and stool samples will be tested for microorganisms (bacteria) that normally live in all people's guts (intestines). This is to see if your baby's microorganisms are the same as yours and how the food you and your baby eat might have changed it.

Will you and your baby benefit from taking part in this research?

- The gains for you and your baby are that you will receive extra medical care by specialists and also extra tests, such as tests that measure if you and your baby have enough iron in your blood and if you or your baby could be allergic to a food or something that can be inhaled like pollen. If we find any medical problems during the study, a specialist will see you or your baby during the study time.
- The other gains of the study will be that you will help us understand the dietary habits and health of pregnant women in South Africa and how that affects the health of their babies. By understanding more about this, we can help government to create policies that can manage the health of pregnant women better.

Are there risks involved in you taking part in this research and what will be done to prevent them?

Most of the measurements that will be performed won't harm or hurt you or your baby in any way, but you might experience the following:

If you give permission to blood samples, you and your baby might feel uncomfortable or scared. This will only last for a short while. We want to make sure that you or your baby is not hurt in any way and therefore a qualified nurse will draw the blood from you and your baby's arms. The nurse will also collect the urine and stool sample / rectal swab from you and your baby with a special bag, cup and something like an earbud. She will talk to you and explain to you everything that she is going to do.

For the skin allergy tests small pricks are made in the skin and might itch, but the nurse will apply a cream to stop the itching. A trained medical professional (nurse or doctor) will do the tests.

During some of the measurements you will be asked to remove some of your clothes keeping on only your underwear or light clothing. This might make you feel uncomfortable or shy. To help you feel less shy and uncomfortable, only females will take these measurements. Also, the area where these measurements will be done will be private and closed off. This means that no one else will be able to see you. Only the person that will take the measurements and someone to help her will be with you. Some measurements, like length and weight will also be taken from your baby and will make him/her a bit uncomfortable for a while.

Being part of such a big research study can be frightening and overwhelming. To prevent us from wasting your time and to make sure that you know where to go and what to do, there will be people available at all times to help you and show you where you have to go every time.

Doing all of the measurements on the days of the research study, will take most of the day (5 to 6 hours). This might make you feel very tired. You and your baby will be provided with refreshments to eat and drink during the day.

There are more benefits than dangers or risks when you and your baby take part in the study.

How will we protect your confidentiality and who will see your findings?

We will handle all your information as confidential as possible by allocating a study code to you and your baby when he/she is born. All samples will be labelled with this code and only the person who allocates the numbers (site-coordinator), the principal investigator and co-principal investigators will have access to the records containing you and your baby's names. If your results are abnormal, the research study medical doctors at Rahima Moosa Mother and Child Hospital will be given the information so that they can manage your treatment. Only the researchers will work with the data. Documents will be locked in cabinets at the Rahima Moosa Mother and Child Hospital and the clinic that you attend after the baby's birth and will be moved to cabinets in the researchers' university department. Electronic data will be password protected. Reporting of findings will be anonymous.

What will happen with the findings or samples?

Some blood samples will be sent overseas for laboratory analysis, but will be destroyed once all the tests have been completed. Blood and urine samples will be the responsibility of Dr Linda Malan (018 2994237 / 0844023834) and will be stored for 7 years after the study. Data will be stored for 7 years. There is enough money to do the study the most important tests, but some of the tests are very expensive and will only be done once more funding is found.

How will you know about the results of this research?

- We will give you the results of this research on the same day for some tests like blood pressure. If we find any abnormal results, the specialists in the study which works at the Rahima Moosa Mother and Child Hospital, will treat you.
- You will be informed of any new relevant findings at a meeting that will be held once the study is finished at the Rahima Moosa Mother and Child Hospital.

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

No, you will not be paid to take part in the study but your expenses for travelling to the RMMCH will be paid for. At each visit you will receive a R5 cell phone voucher to enable you to make a call to the researchers or fieldworkers if you need to. Furthermore, you and your baby (6 months and older) will be provided with a snack/lunch pack every two hours during assessments at the visits after the birth of your baby. At the 6, 7.5 and 12 month visit, you will receive gifts to a value of R50 with goods for your baby as a token of appreciation. Thus, if you take part there will be no costs involved for you.

Is there anything else that you should know or do?

You can contact Prof. Marius Smuts at 018 299 2086 / 082 451 0486 or Dr Linda Malan at 0844023834 or Dr Jeannine Baumgartner at 0764364439 if you have any further queries or encounter any problems.

You can contact the Health Research Ethics Committee of North-West University via Mrs Carolien van Zyl at 018 299 2089; carolien.vanzyl@nwu.ac.za if you have any concerns or complaints that have not been adequately addressed by the researcher.

You can also contact the Health Research Ethics Committee of the University of Witwatersrand via:

Prof Peter Cleaton-Jones, Chairperson of HREC (Medical) Tel: 011 717 2301 Email: peter.cleaton-jones1@wits.ac.za

Ms Zanele Ndlovu, HREC (Medical) Secretariat, Tel: 011 717 1252/2700/ 1234, Email: Zanele.ndlovu@wits.ac.za

You will receive a copy of this information and consent form for your own records.

A few questions (to be completed by the person obtaining the consent):

Subject understood the question?	YES	NO
If you take part in the study, will your baby be tested for allergies?		
Will taking part in the study cost you any money?		

Declaration by mother of participant (baby)

By signing below, I agree that my baby take part in the second (postnatal) part of the research study entitled: *Nutrition during Pregnancy and Early Development: The NuPED -postnatal study*. I declare that:

- I have read this information/it was explained to me by a trusted person in a language with which I am fluent and comfortable.
- The research was clearly explained to me.
- I have had a chance to ask questions to both the person getting the consent from me, as well as the researcher and all my questions have been answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be handled in a negative way if I do so.
- I may be asked to leave the study before it has finished, if the researcher feels it is in the best interest, or if I do not follow the study plan, as agreed to.
- I understand and agree that blood samples from my baby may be sent outside South Africa for laboratory analysis.

Do you give permission that some of your baby's blood samples may be analysed outside of South Africa?	
Yes, I give permission ☐	No, I don't give permission ☐
Do you give permission that the researchers have access to your baby's HIV test results?	
Yes, I give permission ☐	No, I don't give permission ☐
Do you give permission to have access to your baby's medical records at the hospital or clinic?	
Yes, I give permission ☐	No, I don't give permission ☐

Signed at (place) on (date) 20.....

.....
Signature of participant

.....
Signature of witness

Declaration by person obtaining consent

I (name) declare that:

- I clearly and in detail explained the information in this document to
- I did/did not use an interpreter.
- I encouraged her to ask questions and took adequate time to answer them.
- I am satisfied that she adequately understands all aspects of the research, as discussed above
- I gave her time to discuss it with others if she wished to do so.

Signed at (place) on (date) 20.....

.....
Signature of person obtaining consent

.....
Signature of witness

Declaration by researcher

I, ... declare that:

- I had it explained by who I trained for this purpose.
- I did/did not use an interpreter
- I was available should she want to ask any further questions.
- The informed consent was obtained by an independent person.
- I am satisfied that she adequately understands all aspects of the research, as described above.
- I am satisfied that she had time to discuss it with others if he/she wished to do so.

Signed at (place) on (date) 20.....

.....
Signature of researcher

.....
Signature of witness

Declaration by participant (mother)

By signing below, I
agree that I take part in the second (postnatal) part of the research study entitled: *Nutrition during Pregnancy and Early Development: The NuPED -postnatal study*. I declare that:

- I have read this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that my taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the researcher feels it is in my best interest, or if I do not follow the study plan, as agreed to.
- I understand and agree that blood samples from me and from the cord that connected me and baby before birth may be sent outside South Africa for laboratory analysis.

Do you give permission that some of your blood samples may be analysed outside of South Africa?

Yes, I give permission ☐ No, I don't give permission ☐

Do you give permission to have access to your medical records at the hospital or clinic?

Yes, I give permission ☐ No, I don't give permission ☐

Signed at (place) on (date) 20.....

.....
Signature of participant

.....
Signature of witness

Declaration by person obtaining consent

I (name) declare that:

- I clearly and in detail explained the information in this document to
- I did/did not use an interpreter.
- I encouraged her to ask questions and took adequate time to answer them.
- I am satisfied that she adequately understands all aspects of the research, as discussed above
- I gave her time to discuss it with others if she wished to do so.

Signed at (place) on (date) 20.....

.....
Signature of person obtaining consent

.....
Signature of witness

Declaration by researcher

I, ... declare that:

- I had it explained by who I trained for this purpose.
- I did/did not use an interpreter
- I was available should she want to ask any further questions.
- The informed consent was obtained by an independent person.
- I am satisfied that she adequately understands all aspects of the research, as described above.
- I am satisfied that she had time to discuss it with others if he/she wished to do so.

Signed at (place) on (date) 20.....

.....
Signature of researcher

.....
Signature of witness

ADDENDUM 10
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Article

A Priori and a Posteriori Dietary Patterns among Pregnant Women in Johannesburg, South Africa: The NuPED Study

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Abstract: Dietary pattern analyses allow assessment of the diet as a whole. Limited studies include both a priori and a posteriori dietary pattern analyses. This study aimed to explore the diet of pregnant women in urban South Africa through both a priori and a posteriori dietary pattern analyses and associated maternal and household factors. Dietary data were collected during early pregnancy using a quantified food frequency questionnaire from 250 pregnant women enrolled in the Nutrition During Pregnancy and Early Development (NuPED) cohort. A priori dietary patterns were determined using the Diet Quality Index-International (DQI-I), and a posteriori nutrient patterns using exploratory factor analysis. Based on the DQI-I, the study population followed a borderline low-quality diet. Three a posteriori nutrient patterns were identified: Pattern 1 “plant protein, iron, thiamine, and folic acid”; pattern 2 “animal protein, copper, vitamin A, and vitamin B₁₂”; pattern 3 “fatty acids and sodium”. Pattern 1 was associated with higher dietary quality ($p < 0.001$), lower maternal educational level ($p = 0.03$) and socioeconomic status ($p < 0.001$). Pattern 3 was significantly associated with lower dietary quality. The low dietary quality among pregnant women residing in urban South Africa should be addressed to ensure optimal maternal and offspring health outcomes.

Keywords: dietary patterns; a priori-defined dietary patterns; a posteriori-derived nutrient patterns; nutrition; pregnancy

1. Introduction

Maternal nutrition during pregnancy is building the foundation for offspring growth, development, and health [1]. With fetal growth being greatly determined by nutrient supply from the mother [2,3], poor maternal diet and lifestyle choices can have a negative effect on pregnancy outcomes and the health of the offspring [4]. Literature reports both maternal under- and overnutrition to influence an offspring's growth and development [5–7], with a poor maternal nutritional status during pregnancy affecting growth, neurodevelopment, and pulmonary, cardiometabolic, and immune function [6]. Long-term effects of maternal malnutrition include an increased risk for chronic illness later in life, and a decreased birth weight within the subsequent generation [6,8]. Pregnancy is thus regarded as a unique period in life during which the health and well-being of the next generation can be influenced [9].

Data on dietary intake among pregnant South African women are, however, sparse [10], with only four articles [11–14] having been published during the past decade. It is therefore yet unknown as to how the maternal diet affects health outcomes among the South African population. Although both Cormick et al. [11] and Krige et al. [13] found pregnant women to consume diets within the acceptable macronutrient distribution ranges but deficient in key micronutrients, they did not evaluate the overall quality of the diet.

Hu et al. [15] propose the use of dietary pattern analyses as a complementary method in assessing dietary intake. With nutrients not consumed in isolation but as part of a diet comprising of different foods, dietary pattern analyses account for the cumulative and interactive components of the diet to reflect the complexity of the human diet [15,16]. Dietary pattern analyses, therefore, provide a more predictive approach towards studying health outcomes [15] and is thus an imperative methodology in studying the role of the diet during pregnancy in maternal- and offspring health. However, it is only recently that dietary pattern analyses are being used to study the maternal diet during pregnancy. Most data available are from high-income countries with Raghavan et al. [17], indicating that the majority of research available is from healthy Caucasian women with access to medical care. Kibret et al. [18] concluded that research in low-income countries is needed to comprehend the impact of restricted resources on maternal dietary intake.

Dietary patterns can be derived either using the a priori or a posteriori method. The a priori method, also referred to as the hypothesis-oriented approach, entails the use of a dietary quality index to determine adherence to a predefined dietary pattern or dietary recommendation [15,19]. Conversely, the a posteriori method is a data-driven approach whereby dietary patterns are derived through statistical modeling techniques from empirical data [15,20]. A posteriori dietary patterns, therefore, provide insight into dietary behaviors as they reflect on actual food or nutrient intake [21]. Although these two methods are regarded to provide complementary information with regard to the overall diet [21], only a few studies [22–24] have used both methods to explore the maternal diet during pregnancy. Furthermore, to our knowledge, all studies reporting on a posteriori dietary patterns during pregnancy used foods or food groups as variables to determine patterns. Moskal et al. [20] though advocated for the use of nutrients as variables to determine empirical dietary patterns, as nutrients are universal in consumption, and allow for easier comparison between populations.

Only one study to date reported on maternal dietary patterns among pregnant South African women. Wrottesley et al. [14] found three distinct food patterns followed by their study population, namely, a “western”, “mixed”, and “traditional” food pattern. To address the sparsity of research, the purpose of this study was to explore the maternal diet of pregnant women residing in urban Johannesburg, South Africa, through both a priori and a posteriori dietary pattern analyses. Maternal- and household factors associated with these patterns are also determined.

2. Materials and Methods

2.1. Study Design and Participants

This study was embedded within the Nutrition During Pregnancy and Early Development (NuPED) cohort, a prospective study conducted in Johannesburg, South Africa. The details of the NuPED study have previously been described [25]. Data collection took place at early pregnancy (<18 weeks’ gestation), mid-pregnancy (± 22 weeks), late pregnancy (± 36 weeks), birth, as well as postnatally (6 weeks, 6 months, 7.5 months, and 12 months’ postnatal age). The current analysis reports on data collected at baseline (early pregnancy).

In brief, the recruitment of generally healthy urban pregnant women from primary health care clinics in Johannesburg took place between March 2016 and November 2017. Based on the South African socioeconomic profile, it is mainly the poorer proportion of the population that makes use of medical care provided by primary health care facilities [26]. Women were regarded as eligible for inclusion if they were 18 to 39 years old, less than 18 weeks of gestation with a singleton pregnancy, born within South Africa or in

a neighboring country (Lesotho, Swaziland, Zimbabwe, Botswana, or Namibia), and able to effectively communicate in the local languages (English, Afrikaans, Sotho, Zulu or Xhosa). Women born in a neighboring country had to have been living in South Africa for at least 12 months. Pregnant women diagnosed with a non-communicable disease (namely, hypertension, hypercholesterolemia, diabetes, and renal disease), infectious disease (namely, tuberculosis and hepatitis), or serious illness (namely, lupus, cancer, and psychosis) were excluded. Women were also excluded if they used illicit drugs (self-reported) and/or smoked (currently or in the past year). As South Africa has a high prevalence of human immunodeficiency virus (HIV) infections (22.7% of women of reproductive age [27]), HIV status was not considered exclusion criteria for enrolment.

Five-hundred and ninety-five pregnant women were invited to take part in the NuPED study of which 313 (53%) women volunteered. A further 63 women were excluded for not meeting the inclusion and exclusion criteria. In total, 250 pregnant women provided informed consent and were enrolled. Participants were followed-up at a tertiary hospital (Rahima Moosa Mother and Child Hospital) where data collection took place alongside routine maternal care. All 250 pregnant women completed data collection at baseline (<18 weeks' gestation).

2.2. Ethical Considerations

All women eligible and willing to partake in the study were provided with an informed consent form during recruitment. Written informed consent was obtained during the first study visit before any data were collected. The study was conducted according to the guidelines set out by the World Medical Association Declaration of Helsinki. Ethical approval was obtained from both the Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1) and the University of the Witwatersrand, Johannesburg (M 150968). The City of Johannesburg District Research Committee (Gauteng Department of Health) and the clinical manager at Rahima Moosa Mother and Child hospital provided permission for the study to take place in the relevant clinical setting.

2.3. Dietary Intake Assessment

Dietary intake was assessed during early pregnancy using an interviewer-administered quantified food-frequency questionnaire (QFFQ). The 140-item QFFQ was validated previously for energy and nutrient intake in an African population in South Africa [28], and its reproducibility was established [29,30]. Trained fieldworkers used standard probing questions [31] to inquire in as much detail as possible about the type/brand, cooking method, frequency, and amount of all foods and drinks consumed over the past four weeks. Household utensils, together with "dish-up and measure", food packaging material, and two- and three-dimensional food models, were used to quantify the portion sizes reported. Portion sizes were converted to grams by three registered dietitians/nutritionists using the South African Medical Research Council (SAMRC) Food Quantities Manual [32]. All foods and drinks were coded according to the South African Food Composition Database [33]. Daily energy, macro-, and micronutrient intake were calculated by the SAMRC by linking the coded and quantified dietary intake data to the most recent food composition database available at the time.

The daily dietary intake data are reflective of nutrient intake from food, excluding any micronutrient supplementation used. Maize meal and wheat flour are subject to mandatory micronutrient fortification as per South African legislation [34], and these fortified micronutrients (vitamin A, thiamine, riboflavin, niacin, pyridoxine, folic acid, iron, and zinc) were considered in the nutrient analysis. All participants provided complete dietary intake information.

2.3.1. A Priori Defined Dietary Patterns

The a priori dietary patterns were defined using the Diet Quality Index-International (DQI-I) [35]. Validated for international use and cross-national comparison of dietary

quality [36,37], the DQI-I is regarded as a valuable tool for exploring diet quality related to nutrition transition as it accounts for both dietary concerns contributing to chronic disease and undernutrition. South Africa is known to be undergoing a rapid nutrition transition alongside urbanization [38], contributing to a growing burden of malnutrition within the country [39]. In addition, being sensitive towards various dietary practices and allowing for the use of country-specific recommendations in the evaluation of the diet, the DQI-I serves as a good set of guidelines according to which dietary quality of populations can be evaluated [35].

The DQI-I describes all dimensions of a high-quality diet, namely variety, adequacy, moderation, and overall balance. Each of these categories contains components (including both nutrient and food-group indicators) according to which the diet is assessed, allowing for users to determine the aspect(s) of the diet which most likely needs improvement [40]. The four categories of the DQI-I amount to an overall score of 100, with a higher score indicating greater adherence to a higher quality diet. According to the criteria given by Kim et al. [35], a score of less than 60 out of a possible 100 is indicative of a poor quality diet.

The daily dietary intake for the study participants, based on the QFFQ, was scored as specified by Kim et al. [35]. Adjustments to the DQI-I criteria were made as follows: (1) serving sizes were determined both according to the guidelines provided by the South African Food-Based Dietary Guidelines [41] and the United States' Food Guide Pyramid serving size definitions [42]; (2) adequacy of micronutrient intake (iron, calcium, and vitamin C) was based on the Dietary Reference Intakes for pregnant women [43]; (3) the cut-off values for sodium were adjusted as the QFFQ used does not report on discretionary salt intake. According to a paper by Wentzel-Viljoen et al. [44], it is estimated that about 60% of the total salt intake among the South African population is from processed foods, with the remainder (40%) being the discretionary use of salt during food preparation and meals. Based on this observation, the sodium cut-off values were adjusted as follows: ≤ 1440 mg (6 points), >1440 – 2040 mg (3 points) and >2040 mg (0 points). The DQI-I scoring criteria, together with how the study participants scored, are indicated in Table 1.

2.3.2. A Posteriori-Derived Nutrient Patterns

Nutrient patterns were determined from 22 nutrients by exploratory factor analysis [45]. Using the dietary intake data obtained from the QFFQ, total protein was divided into animal- and plant protein, and total fat into saturated-, monounsaturated- and polyunsaturated fatty acids. Carbohydrate intake was reported as total carbohydrate- and total sugar intake. The correlation structure of the nutrient intake data was explored for stability using the Spearman and Pearson correlation coefficients. The difference between the coefficients was minimal (less than 0.1) and, therefore, raw nutrient data were used for the analysis. Nutrient data were energy-adjusted according to the nutrient density model proposed by Willet et al. [46]. The principal factor method was applied with the correlation matrix, and the reliability of the factor analysis verified using the Kaiser–Meyer–Olkin measure of sampling adequacy and Bartlett's test of sphericity. A Kaiser–Meyer–Olkin value of more than 0.5 and significance ($p < 0.05$) on Bartlett's test were regarded as adequate. Factors were retained and interpreted for further analysis according to the eigenvalues (more than 1.00), scree plot inspection, the proportion of the total variance explained, and the natural interpretability of the factors. Retained factors (patterns) were rotated by Varimax (orthogonal) rotation for a simpler structure and to improve interpretation. Patterns were named and interpreted according to nutrients with an absolute factor loading of equal or greater than 0.40. A positive factor loading indicates a nutrient to be positively associated with the nutrient pattern and a negative loading that a nutrient is negatively associated with the pattern. Factor scores were calculated for each participant to indicate the degree towards which a participant's nutrient intake conforms to the identified patterns. Factor scores were computed by weighting the standardized intakes of each nutrient with their factor loadings and then summing the nutrients within the respective patterns [47].

Table 1. Participant scores according to the Diet Quality Index-International (DQI-I) scoring criteria ($n = 250$) [35].

Category and Component		Scoring Criteria	<i>n</i> (%) ¹
Variety 0–20 points			
Overall food group variety (meat/poultry/fish/eggs; dairy beans; grain; fruit; vegetables)	0–15 points	>1 serving from each food group/ <i>d</i> = 15	92 (37)
		Any 1 food group missing/ <i>d</i> = 12	97 (39)
		Any 2 food groups missing/ <i>d</i> = 9	38 (15)
		Any 3 food groups missing/ <i>d</i> = 6	21 (8)
		>4 food groups missing/ <i>d</i> = 3	2 (1)
		None from any food groups = 0	0
Within-group variety for protein source (meat; poultry; fish; dairy/beans; eggs)	0–5 points	>3 different sources/ <i>d</i> = 5	137 (55)
		2 different sources/ <i>d</i> = 3	72 (29)
		From 1 source/ <i>d</i> = 1	31 (12)
		None = 0	10 (4)
Adequacy 0–40 points			
Vegetable group ^{2,3}	0–5 points	>3–5 servings/ <i>d</i> = 5, 0 servings/ <i>d</i> = 0	
		>100%	14 (6)
		50–100%	78 (31)
Fruit group ^{2,3}	0–5 points	<50%	158 (63)
		>2–4 servings/ <i>d</i> = 5, 0 servings/ <i>d</i> = 0	
		>100%	93 (37)
Grain group ^{2,3}	0–5 points	50–100%	97 (39)
		<50%	60 (24)
		>6–11 servings/ <i>d</i> = 5, 0 servings/ <i>d</i> = 0	
Fiber ^{2,3}	0–5 points	>100%	71 (28)
		50–100%	153 (61)
		<50%	26 (10)
Protein	0–5 points	>20–30 g/ <i>d</i> = 5, 0 g/ <i>d</i> = 0	
		>100%	149 (60)
		50–100%	97 (39)
Iron	0–5 points	<50%	4 (2)
		>10% of energy/ <i>d</i> = 5, 0% of energy/ <i>d</i> = 0	
		>100%	241 (96)
Calcium	0–5 points	50–100%	9 (4)
		<50%	0
		>100% RDA/ <i>d</i> = 5, 0% RDA/ <i>d</i> = 0	
Vitamin C	0–5 points	>100%	28 (11)
		50–100%	162 (65)
		<50%	60 (24)
Total fat	0–6 points	>100% AI/ <i>d</i> = 5, 0% AI/ <i>d</i> = 0	
		>100%	50 (20)
		50–100%	125 (50)
Saturated fat	0–6 points	<50%	75 (30)
		>100% RDA/ <i>d</i> = 5, 0% RDA/ <i>d</i> = 0	
		>100%	162 (65)
Cholesterol	0–6 points	50–100%	67 (27)
		<50%	21 (8)
		Moderation 0–30 points	
Total fat	0–6 points	<20% of total energy/ <i>d</i> = 6	15 (6)
		>20–30% of total energy/ <i>d</i> = 3	88 (35)
		>30% of total energy/ <i>d</i> = 0	147 (59)
Saturated fat	0–6 points	<7% of total energy/ <i>d</i> = 6	39 (16)
		>7–10% of total energy/ <i>d</i> = 3	111 (44)
		>10% of total energy/ <i>d</i> = 0	100 (40)
Cholesterol	0–6 points	<300 mg/ <i>d</i> = 6	102 (41)
		>300–400 mg/ <i>d</i> = 3	46 (18)
		>400 mg/ <i>d</i> = 0	102 (41)

Table 1. Cont.

Category and Component		Scoring Criteria	n (%) ¹
Sodium ⁴	0–6 points	<2400 mg/d = 6	44 (18)
		>2400–3400 mg/d = 3	53 (21)
		>3400 mg/d = 0	153 (61)
Empty calories	0–6 points	<3% of total energy/d = 6	47 (19)
		>3–10% of total energy/d = 3	131 (52)
		>10% of total energy/d = 0	72 (29)
Overall balance 0–10 points			
Macronutrient ratio ⁵ (carbohydrate:protein:fat)	0–6 points	55–65:10–15:15–25 = 6	10 (4)
		52–68:9–16:13–27 = 4	26 (10)
		50–70:8–17:12–30 = 2	43 (17)
		Otherwise = 0	171 (68)
Fatty acid ratio (PUFA:MUFA:SFA)	0–4 points	P/S = 1–1.5 and M/S = 1–1.5 = 4	54 (22)
		Else if P/S = 0.8–1.7 and M/S = 0.8–1.7 = 2	84 (34)
		Otherwise = 0	112 (45)

RDA: recommended dietary allowance; AI: adequate intakes; MUFA: monounsaturated fatty acids; SFA, saturated fatty acids; PUFA: polyunsaturated fatty acids; P/S, ratio of PUFA to SFA intake; M/S, ratio of MUFA to SFA intake. ¹ n = 250. ² Used as a continuous variable.

³ Based on 1700 kcal (7118 kJ)/2200 kcal (9211 kJ)/2700 kcal (11,304 kJ) diet; 1 kcal = 4.1868 kJ. ⁴ Based on sodium from food sources, excluding the discretionary use of table salt. ⁵ Ratio of energy from carbohydrate to protein to fat.

2.4. Assessment of Maternal and Household Factors

Several maternal and household factors were considered as possible determinants for dietary patterns during pregnancy. Interviewer-administered questionnaires were used to obtain sociodemographic and socioeconomic information, information on household-level food insecurity, medical history, and risk for prenatal depression and fatigue.

Sociodemographic and socioeconomic information obtained included maternal age, ethnicity, country of birth, marital status, educational level, employment status, and household beneficiaries of social support grants. Living standard data were also obtained to allow for classification of the socioeconomic status according to the Living Standard Measure in South Africa [48]. Food insecurity was assessed using the Community Childhood Hunger Identification Project (CCHIP) index [49,50]. This index investigates food insecurity as reflected by access to food on three levels, namely, the household-, adult/individual- and the child level. The extent of household food insecurity (CCHIP index total score) could not be determined as a great proportion of participants (n = 113; missing data n = 9) were not the parent or caretaker of a child in that household. We therefore only report on the three questions assessing household-level food insecurity, namely: (1) “does your household ever run out of money to buy food”; (2) “do you ever rely on a limited number of foods to feed your family because you are running out of money to buy food for a meal”; (3) “do you ever cut the size of meals or skip meals because there is not enough money for food” [49]. Households were regarded as “at risk for food insecurity” if the participant answered “yes” to one or more of the three questions; “no risk” was considered when the participant answered “no” to all three questions.

Medical history considered in this study included parity, pregnancy symptoms (nausea and/or vomiting experienced), and HIV status (routinely tested as part of antenatal care). Participants recorded pregnancy symptoms (nausea and/or vomiting) during the seven days after enrolment using a pictorial morbidity calendar. Gestational age was confirmed using fetal ultrasonography during early pregnancy. Prenatal fatigue and depression were assessed using the Multidimensional Assessment of Fatigue (MAF) scale [51] and the Edinburgh Postnatal Depression Score (EPDS) [52,53], respectively. MAF measures the severity of fatigue, distress, and the degree to which it influences daily activities. The global fatigue index (GFI) was calculated with higher scores indicating higher levels of fatigue, and a cut-off of 28 out of a possible 50 was used to define women with prenatal fatigue [54]. A cut-off value of ≥ 9 out of a possible 30 was used for the EPDS to indicate the risk for depressive symptoms [53].

Maternal anthropometric measures were also assessed although not considered as possible determinants for the dietary patterns in this analysis. The exclusion of maternal weight as a determinant is based on the observation by Doyle et al. [55] that the relationship between maternal weight and dietary patterns is more difficult to interpret as maternal weight can serve both as an outcome and a determinant of dietary patterns. Maternal height, weight, and mid-upper arm circumference (MUAC) were assessed during early pregnancy using the standardized methods indicated by the International Society for the Advancement of Kinanthropometry [56]. All measurements were taken twice and recorded to the nearest 0.05 kg for weight and 0.1 cm for height and MUAC. A calibrated scale was used for weight measurements (Seca 813, Hamburg, Germany), a mobile stadiometer for height (Seca 213, Hamburg, Germany), and a non-stretchable metal tape for the MUAC. As weight gain and edema during pregnancy decrease the reliability of the body mass index (BMI) [57], maternal weight at enrolment was adjusted (assuming that 2.5 kg was gained during the first 14 weeks of gestation) according to the gestational weight gain guidelines provided by the Institute of Medicine [58] to calculate an approximate pre-pregnancy BMI. The MUAC cut-offs for underweight and obesity as indicated by the South African Maternity Care guidelines [59] were also considered to evaluate maternal nutritional status, i.e., ≤ 23 cm considered as underweight and ≥ 33 cm as obese.

2.5. Statistical Analysis

The sample size was set as 250 participants; calculations of the sample size have been previously published [25]. IBM SPSS version 26 (SPSS Inc., Chicago, IL, USA) was used for data processing and statistical analysis. Dietary data were captured in Microsoft Excel, with all other raw data captured in Microsoft Access (Microsoft Corporation, Washington, DC, USA). All dietary data were double-checked to ensure accuracy of food codes used and amounts captured. Twenty percent of all other raw data were randomly checked for correctness.

Data were tested for normality using histograms, q-q plots, and the Shapiro–Wilk test. For normally distributed data, continued variables are reported as mean and standard deviation, and for non-normally distributed data as the median and interquartile range (IQR). Categorical data are reported as frequencies and percentages. Both the DQI-I total scores and nutrient pattern factor scores were divided into tertiles for further analysis. To determine food groups associated with each nutrient pattern, analysis of variance (ANOVA) was used to determine the difference between each food group and the nutrient pattern tertiles. The 140-items of the QFFQ were aggregated into 39 food groups expressed as a percentage of the total energy intake (Tables S1–S3). ANOVA was also used to determine differences between DQI-I scores and the nutrient pattern tertiles. In both instances, post-hoc comparisons for unequal variance were carried out using the Games–Howell test.

Hierarchical multiple linear regression models were applied to test for associations between the dietary patterns and maternal- and household factors. Hierarchical steps were based on the conceptual framework for multiple determinants of diet during pregnancy as proposed by Doyle et al. [55] and were as follows: step 1 investigates all sociodemographic factors (maternal age, level of education, and marital status), step 2 the sociodemographic and socioeconomic factors (employment, social grants received by the household, household-level food insecurity, and living standard measure), step 3 the sociodemographic-, socioeconomic-, pregnancy-related factors (parity, nausea- and/or vomiting experienced) and HIV status, and step 4 the sociodemographic-, socioeconomic-, pregnancy-related factors, HIV status and psychological factors. Significance was defined as $p < 0.05$.

3. Results

3.1. Characteristics of Study Participants

Characteristics of the study participants at early pregnancy are shown in Table 2.

The median (IQR) age was 27 (24–32) years and the median length of gestation at enrolment 14 (12–16) weeks. Most enrolled women were of black-African descent (88%), followed by women of mixed ancestry (11%). The distribution with regard to the number of previous pregnancies was equal as the same proportion of women (35%) were primiparous and multiparous, respectively. A quarter of the women (26%) had a positive HIV status, and almost half of the women reported experiencing nausea (52%) and vomiting (48%) within seven days after enrolment. Based on the calculated pre-pregnancy BMI, half of the women (52%) entered pregnancy either being overweight or obese. This was confirmed by the MUAC categories which indicated, when compared to the BMI categories, near similar proportions of the study participants to be underweight (4%) and obese (26%). A quarter of the study participants presented with a more severe level of prenatal fatigue (26%) and risk for prenatal depression (26%), respectively.

Table 2. Characteristics of study participants ($n = 250$) at early pregnancy (<18 weeks' gestation).

Subject Characteristics	Total Sample ¹ Median (IQR) or n (%)
Age (years)	27 (24–32)
Gestational age (weeks)	14 (12–16)
Parity	
Nulliparous	74 (30)
Primiparous	88 (35)
Multiparous	88 (35)
Calculated pre-pregnancy BMI (kg/m^2) ²	25 (22–30)
Underweight ($<18.5 \text{ kg}/\text{m}^2$)	14 (6)
Normal weight ($18.5\text{--}24.99 \text{ kg}/\text{m}^2$)	105 (42)
Overweight ($25\text{--}29.99 \text{ kg}/\text{m}^2$)	73 (29)
Obese ($\geq 30 \text{ kg}/\text{m}^2$)	57 (23)
MUAC (cm)	30 (27–33)
Underweight or chronic wasting ($\leq 23 \text{ cm}$)	10 (4)
Normal weight and overweight ($23.1\text{--}32.9 \text{ cm}$)	176 (70)
Obese ($\geq 33 \text{ cm}$)	64 (26)
HIV status	
Positive	64 (26)
Negative	186 (74)
Vomiting ³	
Experienced vomiting	111 (48)
Number of days	2 (1–4)
Nausea ³	
Experienced nausea	122 (52)
Number of days	2 (1–4)
Ethnicity	
Black African	219 (88)
Mixed ancestry	28 (11)
Indian	1 (<1)
White	1 (<1)
Country of birth	
South Africa	172 (72)
Zimbabwe	60 (25)
Lesotho	4 (2)
Swaziland	3 (1)

Table 2. Cont.

Subject Characteristics	Total Sample ¹ Median (IQR) or n (%)
Highest level of education	
Primary/None	9 (4)
Grade 8–10	37 (15)
Grade 11–12	145 (58)
Tertiary	58 (23)
Employment	
Unemployed	123 (49)
Self-employed	11 (4)
Wage-earner	111 (45)
Other	4 (2)
Marital status	
Unmarried	100 (40)
Married	68 (27)
Living together	57 (23)
Traditional marriage ⁴	22 (9)
Divorced/Separated	2 (1)
Social grant(s) received by household	
None	162 (67)
Child support	69 (29)
Social relief	3 (1)
Disability	2 (1)
Old-age pension	6 (3)
Living standard measure (LSM)	
Low (LSM 1–4)	17 (7)
Medium (LSM 5–7)	148 (59)
High (LSM 8–10)	85 (34)
Household-level food insecurity ⁵	
No risk for household food insecurity	130 (53)
At risk for household food insecurity	114 (47)
Risk for prenatal depression ⁶	5 (2–9)
No/low risk for prenatal depression	183 (74)
At risk for prenatal depression	63 (26)
Risk for prenatal fatigue ⁷	19 (1–28)
No/low severity for prenatal fatigue (GFI < 27.9)	179 (74)
More severe level of prenatal fatigue (GFI score ≥ 28)	62 (26)

IQR: interquartile range; BMI: body mass index; MUAC: mid upper arm circumference; HIV: human immunodeficiency virus; LSM: living standard measure; CCHIP: Community Childhood Hunger Identification Project; EPDS: Edinburgh Postnatal Depression Score; GFI: Global Fatigue Index. Data presented as n (%) for categorical variables and median (IQR) for continuous variables. ¹ Missing data: approximate pre-pregnancy BMI (n = 1); vomiting and nausea (n = 17); ethnicity (n = 1); country of birth (n = 11); level of education (n = 1); employment (n = 1); marital status (n = 1); social grants received by household (n = 8); household-level food security (n = 6); risk for prenatal depression (n = 4); risk for prenatal fatigue (n = 9). ² Maternal weight was adjusted according to the Institute of Medicine's guidelines [38] for gestational weight gain to determine an approximate pre-pregnancy BMI. ³ Nausea and vomiting experienced within 7 days after enrolment. ⁴ A traditional marriage does not require approval from an officer of validation but is rather entered between parties based on tradition. Recognised under customary law in South Africa, traditional marriage also allows for polygamous marriage. ⁵ Determined using the CCHIP index's questions on household-level food insecurity. ⁶ Determined using the Edinburgh Postnatal Depression Score [52,53]; a score of 9 or more out of a possible 30 is indicative of a risk for depressive symptoms. ⁷ Determined using the Multidimensional Assessment of Fatigue scale from which the Global Fatigue Index was calculated [51]; a cut-off value of 28 out of a possible 50 was used [54], with a higher score indicating greater severity of fatigue.

A quarter of women (23%) reported having tertiary education, with 73% having some form of secondary schooling. Half of the participants (49%) were unemployed at the time of the study, with two-thirds (67%) indicating that no social grants were received by the

household. Almost half of all households (47%) were thought at risk for food insecurity. Most women (59%) were categorized as have a medium living standard.

3.2. Dietary Pattern Analysis

3.2.1. A Priori Defined Dietary Patterns

The median total DQI-I score was 60 (54–66) out of a possible 100 (Table 3). The “variety” category had the highest achieved score, followed by the “adequacy” and “moderation” categories. The “overall balance” category was the weakest component of the diet, with a median score of 2 (0–4) out of a possible 10.

Table 3. Median (IQR) scores for DQI-I components ($n = 250$).

Category and Component	Score Range (Points)	Median (IQR)
Total DQI score	0–100 points	60 (54–66)
Variety	0–20 points	17 (14–20)
Overall food group variety	0–15 points	12 (12–15)
Within-group variety for protein sources	0–5 points	5 (3–5)
Adequacy	0–40 points	31 (28–33)
Vegetable group	0–5 points	2 (1–3)
Fruit group	0–5 points	4 (3–5)
Grain group	0–5 points	4 (3–5)
Fiber	0–5 points	5 (4–5)
Protein	0–5 points	5 (5–5)
Iron	0–5 points	3 (3–4)
Calcium	0–5 points	3 (2–5)
Vitamin C	0–5 points	5 (4–5)
Moderation	0–30 points	9 (6–15)
Total fat	0–6 points	0 (0–3)
Saturated fat	0–6 points	3 (0–3)
Cholesterol	0–6 points	3 (0–6)
Sodium [†]	0–6 points	0 (0–3)
Empty calories	0–6 points	3 (0–3)
Overall balance	0–10 points	2 (0–4)
Macronutrient ratio	0–6 points	0 (0–2)
Fatty acid ratio	0–4 points	2 (0–2)

IQR: interquartile range; DQI-I: Diet Quality Index-International. [†] Based on sodium from food sources, excluding the discretionary use of table salt.

About one-third (37%) of participants included at least one serving of each of the five food groups considered for overall food-group variety (meat/poultry/fish/eggs; dairy/beans; grain; fruit and vegetables), with 55% consuming protein from more than three different protein sources per day (Table 1). Vegetable intake was poorer than fruit intake; 63% of the women consumed less than half of the recommended amount of vegetables per day, while 24% consumed less than half of the recommended amount of fruit. A larger percentage of the participants had an intake of more than 50% of the recommendation for grain, fiber, protein, iron, calcium, and vitamin C. Only 11% and 20% achieved the Dietary Reference Intakes for pregnant women for iron and calcium, respectively, from food sources. With regard to the “moderation” category, most participants scored poorly for total fat, saturated fat, and sodium intakes. More than half (59%) of the women had a total fat intake of more than 30% of the total energy intake, with 40% of participants having a daily saturated fat intake of more than 10% of the total energy intake. Almost two-thirds of participants (61%) consumed foods with high sodium content. The high intake of total fat was reflected in the “overall balance” category as a high percentage of participants had a macronutrient (68%) and fatty acid (45%) intake outside of the ratios considered for optimal health.

3.2.2. A Posteriori-Derived Nutrient Patterns

Three nutrient patterns were retained by exploratory factor analysis, explaining 57% of the total variance in nutrient intake (eigenvalue > 2.5). Both the Kaiser-Meyer-Olkin measure (0.7) and Bartlett's test ($p < 0.001$) indicated the analysis to be appropriate for the study sample. Patterns were named according to the dominant nutrients (higher factor loadings) within each factor. The factor loadings and names assigned to each nutrient pattern are indicated in Table 4. The three nutrient patterns were further explored by determining associations between nutrient pattern tertiles and the consumption of food groups based on the percentage of total energy intake.

Table 4. Nutrient patterns and factor loadings extracted using factor analysis during early pregnancy ($n = 250$).

Nutrients and Variance Explained	Factors (Nutrient Patterns) ¹		
	Factor 1	Factor 2	Factor 3
	(Plant Protein, Iron, Thiamine, and Folic Acid)	(Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂)	(Fatty Acids and Sodium)
Animal protein	−0.46	0.53	0.32
Plant protein	0.86	−0.09	−0.00
Saturated fat	−0.68	0.08	0.44
Monounsaturated fat	−0.51	0.08	0.67
Polyunsaturated fat	−0.15	−0.08	0.57
Cholesterol	−0.09	0.88	0.32
Carbohydrates	0.61	−0.21	−0.70
Total sugars	−0.23	0.05	−0.68
Total fiber	0.70	0.10	−0.24
Calcium	−0.44	0.20	−0.34
Iron	0.76	0.35	0.02
Sodium	0.04	0.01	0.64
Zinc	0.45	0.44	0.30
Copper	0.25	0.79	−0.08
Vitamin A	0.12	0.81	−0.07
Thiamine	0.77	0.10	−0.05
Riboflavin	0.01	0.63	−0.14
Niacin	0.54	0.39	0.31
Vitamin B ₆	0.67	0.03	0.26
Folic acid	0.73	0.36	−0.07
Vitamin B ₁₂	0.10	0.86	−0.03
Vitamin E	0.04	0.03	0.41
% of variance			
Total variance: 57%	27%	18%	12%

¹ Factor analysis performed on 22 nutrients; estimates presented after rotation. Nutrients considered to have a strong association with the nutrient patterns (factor loading ≤ 0.4 and ≥ 0.4) are indicated in bold.

Pattern 1, named “plant protein, iron, thiamine, and folic acid”, had high positive loadings for plant protein, carbohydrates, fiber, iron, zinc, thiamine, niacin, vitamin B₆ and folic acid. Animal protein, saturated- and monounsaturated fatty acids, and calcium were negatively associated with this pattern. All micronutrients used for fortification according to South African legislation [34], except for vitamin A and riboflavin, reflected high positive loadings on this factor matrix. Pattern 1 explained 27% of the total variance in nutrient intakes. Based on the associations of this nutrient pattern with the food groups, intake of maize, whole wheat- and brown bread, and legumes were positively associated with nutrient pattern 1 (Table S1) as intake of these food groups was significantly higher across the nutrient pattern tertiles (higher tertile indicating that women are having a dietary intake closer to the respective nutrient pattern (higher factor scores)). Intake of maize increased the most from tertile 1 to tertile 3. Conversely, the intake of cakes, biscuits and pudding, cheese, dairy, fatty foods, fruit juice, processed- and red meat, rice and pasta, salad oils, salad vegetables, sugar-sweetened dairy and -drinks, and sweets and chocolates

were significantly lower across the nutrient pattern tertiles. Nutrient pattern 1 is therefore reflective of a “fortified grain and legume” dietary pattern.

Pattern 2, named “animal protein, copper, vitamin A, and vitamin B₁₂”, had high positive loadings for animal protein, cholesterol, zinc, copper, vitamin A, riboflavin, and vitamin B₁₂, and explained 18% of the total variance. Cheese, chicken, eggs, fish and seafood, nuts and nut spreads, and organ meat and offal were positively associated with nutrient pattern 2 as the intake of these foods was higher across the nutrient pattern tertiles (Table S2). Intake of fatty foods, roast potatoes and chips, sugar, and white bread was, though, significantly lower across the tertiles of nutrient pattern 2. Nutrient pattern 2 is, therefore, reflective of an “animal products” dietary pattern.

Pattern 3, named “fatty acids and sodium”, explained 12% of the variance and had high positive loadings for saturated-, monounsaturated- and polyunsaturated fatty acids, sodium, and vitamin E. Intake of cheese, fatty foods, nuts and nut spreads, processed- and red meat, salad oils, and sugar-sweetened drinks was positively associated with the nutrient pattern 3 (Table S3), with the intake of fatty foods increasing the most across the tertiles. Intake of dairy, fresh and dried fruit, maize, and other cooked porridges, and sugar was significantly lower across pattern 3 tertiles. Nutrient pattern 3 is, therefore, representative of a “fatty- and processed foods” dietary pattern.

3.2.3. Associations between the a Priori and a Posteriori Dietary Patterns

Table 5 indicates the median DQI-I scores for each of the nutrient patterns. One-way ANOVA with post-hoc comparisons indicated the DQI-I total scores (higher scores indicative of higher dietary quality) to significantly increase across the tertiles (tertile 3 presenting higher factor loadings) of nutrient pattern 1 (plant protein, iron, thiamine, and folic acid (fortified grain and legume)), but significantly decrease across nutrient pattern 3 (fatty acids and sodium (fatty- and processed foods)). The category scores “moderation” and “overall balance” were significantly higher across nutrient pattern 1, but significantly lower across the tertiles of nutrient pattern 2 (animal protein, copper, vitamin A, and vitamin B₁₂ (animal products)) and nutrient pattern 3. Conversely, the scores for the “variety” category were higher across the tertiles of nutrient pattern 2 ($p < 0.001$) and nutrient pattern 3 ($p < 0.001$), but significantly lower across nutrient pattern 1.

3.3. Factors Associated with Dietary Patterns

Table 6 shows the multiple regression coefficients of the dietary patterns retained for the maternal and household factors. When considering the sociodemographic-, socioeconomic-, pregnancy-related factors and HIV status (steps 1 to 3), having a maternal age equal to and older than 27 years (step 3: $\beta = -1.9$, $SE = 0.9$, $p = 0.046$), a lower level of education (<Grade 10) (step 3: $\beta = 2.0$, $SE = 1.0$, $p = 0.034$) and a lower level of living standard (step 3: $\beta = 2.0$, $SE = 1.0$, $p = 0.049$) were significantly associated with higher scores for nutrient pattern 1 (plant protein, iron, thiamine and folic acid (fortified grain and legume)). However, the association with maternal age did not hold when all maternal and household factors were included in the model (step 4), resulting in women of a lower education ($\beta = 2.1$, $SE = 1.0$, $p = 0.032$) and living standard measure ($\beta = 2.0$, $SE = 1.0$, $p = 0.049$) to have higher scores for nutrient pattern 1. For nutrient pattern 3 (fatty acids and sodium (fatty- and processed foods)), only step 1 (sociodemographic factors) had a significant model fit, but none of these factors were significantly associated with nutrient pattern 3 scores.

A maternal age equal to and older than 27 years was also significantly associated with the DQI-I. This association was retained throughout model steps 1 to 3 (step 4 had a non-significant model fit), indicating women equal and older than 27 years of age among our study population to have greater adherence to a diet with a higher dietary quality (step 3: $\beta = -5.8$, $SE = 1.6$, $p = 0.001$). No other maternal and household factors were significantly associated with the dietary patterns among our study population.

Table 5. DQI-I total and category scores by tertiles of nutrient pattern scores ($n = 250$).

DQI-I Categories	Nutrient Pattern 1 Scores						Nutrient Pattern 2 Scores						Nutrient Pattern 3 Scores					
	(Plant Protein, Iron, Thiamine, and Folic Acid)						(Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂)						(Fatty Acids and Sodium)					
	Tertile 1	Tertile 2	Tertile 3	Median (IQR)	Median (IQR)	p-Value	Tertile 1	Tertile 2	Tertile 3	Median (IQR)	Median (IQR)	p-Value	Tertile 1	Tertile 2	Tertile 3	Median (IQR)	Median (IQR)	p-Value
Total score	56.0 ^c (52.2–60.4)	60.4 ^b (55.3–64.9)	65.2 ^a (58.3–71.3)	17.0 ^a (15.0–20.0)	15.0 ^b (10.0–17.0)	<0.001	60.4 (52.7–65.8)	60.4 (54.7–65.2)	59.5 (54.0–66.2)	17.0 ^a (15.0–20.0)	17.0 ^a (15.0–20.0)	0.889	65.8 ^a (58.0–73.1)	59.8 ^b (54.8–64.1)	56.4 ^c (49.9–60.5)	17.0 ^a (14.0–20.0)	17.0 ^a (14.0–20.0)	<0.001
Variety	30.3 (27.8–33.9)	30.8 (27.6–35.1)	31.4 (29.0–32.7)	9.0 ^b (6.0–15.0)	9.0 ^b (9.0–21.0)	0.980	29.8 ^b (27.3–32.5)	31.0 ^{ab} (28.2–33.2)	31.7 ^a (29.0–35.1)	9.0 ^b (9.0–15.0)	9.0 ^b (9.0–15.0)	0.040	30.3 (27.4–32.5)	31.3 (28.4–34.6)	31.8 (28.0–34.2)	31.8 (28.0–34.2)	31.8 (28.0–34.2)	0.168
Adequacy	6.0 ^c (3.0–9.0)	9.0 ^b (6.0–15.0)	15.0 ^a (9.0–21.0)	4.0 ^a (2.0–6.0)	4.0 ^a (2.0–6.0)	<0.001	12.0 ^a (6.0–18.0)	9.0 ^b (6.0–15.0)	9.0 ^b (3.0–15.0)	9.0 ^b (3.0–15.0)	9.0 ^b (3.0–15.0)	0.009	18.0 ^a (12.0–24.0)	9.0 ^b (6.0–12.0)	6.0 ^c (3.0–9.0)	6.0 ^c (3.0–9.0)	6.0 ^c (3.0–9.0)	<0.001
Moderation	0.0 ^c (0.0–2.0)	2.0 ^b (2.0–4.0)	4.0 ^a (2.0–6.0)	2.0 ^b (2.0–4.0)	2.0 ^b (2.0–4.0)	<0.001	2.0 (2.0–4.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)	0.045	4.0 ^a (2.0–6.0)	2.0 ^b (0.0–4.0)	1.0 ^c (0.0–2.0)	1.0 ^c (0.0–2.0)	1.0 ^c (0.0–2.0)	<0.001
Overall balance																		

IQR: interquartile range. Significant difference between the median of the tertiles indicated in bold ($p < 0.05$) (according to Welsh test). Medians with a different letter in their superscript are significantly different at the 0.05 level according to the Games–Howell test.

Table 6. Associations of maternal and household factors with nutrient patterns and DQI-1¹.

	Nutrient Pattern 1 Plant Protein, Iron, Thiamine, and Folic Acid				Nutrient Pattern 2 Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂				Nutrient Pattern 3 Fatty Acids and Sodium				DQI-1			
	β	SE	p-Value		β	SE	p-Value		β	SE	p-Value		β	SE	p-Value	
Step 1²																
Maternal age																
<27 years vs. ≥ 27 years (RC)	−2.5	0.8	0.002		0.0	0.5	1.000		0.8	0.4	0.060		−5.0	1.3	<0.001	
Education																
$\leq$ Grade 10	2.4	1.0	0.012		−0.4	0.6	0.496		−0.8	0.5	0.128		−0.7	1.6	0.678	
Grade 11–12 (RC)																
Tertiary	−0.9	0.8	0.291		−0.2	0.5	0.695		0.6	0.5	0.168		−1.3	1.4	0.359	
Marital status																
Married/cohabitating vs. Single (RC)	0.7	0.7	0.321		−1.0	0.5	0.042		−0.6	0.4	0.157		−0.5	1.2	0.699	
Step 2²																
Maternal age																
<27 years vs. ≥ 27 years (RC)	−2.1	0.8	0.009		−0.2	0.5	0.749		0.7	0.4	0.103		−4.8	1.4	0.001	
Education																
$\leq$ Grade 10	1.9	1.0	0.051		−0.3	0.6	0.593		−0.8	0.5	0.149		−0.2	1.6	0.483	
Grade 11–12 (RC)																
Tertiary	−0.4	0.9	0.687		−0.4	0.6	0.518		0.6	0.5	0.186		−0.8	1.5	0.616	
Marital status																
Married/cohabitating vs. Single (RC)	0.7	0.8	0.336		−0.9	0.5	0.067		−0.6	0.4	0.154		−0.5	1.3	0.678	
Employment																
Unemployed vs. Employed (RC)	−0.8	0.7	0.256		0.6	0.5	0.209		0.4	0.4	0.290		−0.5	1.2	0.707	
Grants received by the household																
Not received vs. Received (RC)	−0.9	0.8	0.279		−0.2	0.5	0.728		0.0	0.4	0.934		−1.0	1.4	0.451	
Step 3²																
Household-level food insecurity																
No risk vs. At risk (RC)	−0.8	0.7	0.282		−0.1	0.5	0.823		−0.2	0.4	0.687		−1.8	1.3	0.170	
Living standard measure																
Low living standard measure (1–5) vs.																
High living standard measure (6–10) (RC)	2.1	1.0	0.030		−0.9	0.6	0.159		−0.3	0.5	0.618		0.8	1.7	0.639	
Step 3²																
Maternal age																
<27 years vs. ≥ 27 years (RC)	−1.9	0.9	0.046		0.1	0.6	0.918		0.6	0.5	0.249		−5.8	1.6	0.001	

Table 6. Cont.

	Nutrient Pattern 1 Plant Protein, Iron, Thiamine, and Folic Acid		Nutrient Pattern 2 Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂		Nutrient Pattern 3 Fatty Acids and Sodium		DQI-4					
Education												
≤Grade 10	2.0	1.0	0.004	−0.3	0.6	0.620	−0.8	0.5	0.129	−0.9	1.7	0.593
Grade 11–12 (RC)	−0.1	0.9	0.889	−0.2	0.6	0.201	0.6	0.5	0.257	−1.1	1.6	0.501
Tertiary	1.2	0.8	0.128	−0.7	0.5	0.161	−0.7	0.4	0.084	−0.5	1.3	0.699
Marital status												
Married/cohabitating vs. Single (RC)	−0.8	0.7	0.278	0.5	0.5	0.262	0.4	0.4	0.316	−0.1	1.3	0.920
Employment												
Unemployed vs. Employed (RC)	−1.0	0.8	0.219	−0.3	0.5	0.387	0.1	0.4	0.889	−0.7	1.4	0.611
Grants received by the household												
Not received vs. Received (RC)	−0.8	0.7	0.278	−0.1	0.5	0.890	−0.2	0.4	0.710	−1.9	1.3	0.139
Household-level food insecurity												
No risk vs. At risk (RC)	2.0	1.0	0.049	−1.1	0.6	0.101	−0.3	0.5	0.503	1.0	1.7	0.572
Living standard measure												
Low living standard measure (1–5) vs. High living standard measure (6–10) (RC)	−1.1	1.0	0.253	−0.6	0.6	0.341	0.5	0.5	0.385	1.3	1.7	0.435
Parity												
Nulliparous vs. Primiparous and multiparous (RC)	−1.0	0.7	0.185	−0.3	0.5	0.391	0.3	0.4	0.414	−0.7	1.3	0.508
Nausea experienced³												
Yes vs. No (RC)	0.6	0.7	0.793	0.5	0.5	0.263	0.1	0.4	0.765	−0.2	1.3	0.862
Vomiting experienced³												
Yes vs. No (RC)	1.6	0.8	0.055	0.3	0.5	0.802	−0.6	0.5	0.205	1.9	1.4	0.180
HIV status												
Negative vs. Positive (RC)	Step 4 ³											
Maternal age												
<27 years vs. ≥27 years (RC)	−1.9	0.9	0.050	0.1	0.6	0.362	0.6	0.5	0.253	−5.7	1.6	0.001
Education												
≤Grade 10	2.1	1.0	0.032	−0.3	0.6	0.485	−0.8	0.5	0.131	−0.8	1.7	0.612
Grade 11–12 (RC)	−0.1	0.9	0.914	−0.2	0.6	0.744	0.6	0.5	0.262	−1.0	1.6	0.513
Tertiary	1.2	0.8	0.120	−0.7	0.5	0.153	−0.7	0.4	0.063	−0.5	1.4	0.699
Marital status												
Married/cohabitating vs. Single (RC)	−0.8	0.7	0.297	0.5	0.5	0.269	0.4	0.4	0.331	−0.1	1.3	0.914
Employment												
Unemployed vs. Employed (RC)												

Table 6. Cont.

	Nutrient Pattern 1 Plant Protein, Iron, Thiamine, and Folic Acid			Nutrient Pattern 2 Animal Protein, Copper, Vitamin A, and Vitamin B ₁₂			Nutrient Pattern 3 Fatty Acids and Sodium			DQI-I	
	β	SE	p-Value	β	SE	p-Value	β	SE	p-Value	β	p-Value
Grants received by the household											
Not received vs. Received (RC)	−1.0	0.8	0.206	−0.3	0.5	0.501	0.1	0.4	0.849	−0.8	1.4
Household-level food insecurity											
No risk vs. At risk (RC)	−0.8	0.7	0.292	0.0	0.5	0.953	−0.2	0.4	0.712	−1.9	1.3
Living standard measure											
Low living standard measure (1–5) vs. High living standard measure (6–10) (RC)	2.0	1.0	0.049	−1.2	0.6	0.068	−0.3	0.5	0.577	0.9	1.7
Parity											
Nulliparous vs. Primi- and multiparous (RC)	−1.1	1.0	0.238	−0.6	0.6	0.314	0.5	0.5	0.379	1.2	1.7
Nausea experienced ³											
Yes vs. No (RC)	−0.9	0.7	0.239	−0.1	0.5	0.789	0.3	0.4	0.436	−0.6	1.3
Vomiting experienced ³											
Yes vs. No (RC)	0.6	0.7	0.454	0.5	0.5	0.258	0.1	0.4	0.751	−0.2	1.3
HIV status											
Negative vs. Positive (RC)	1.5	0.8	0.073	0.3	0.5	0.617	−0.6	0.5	0.220	1.9	1.5
Risk for prenatal depression											
At risk vs. No risk (RC)	0.8	1.5	0.598	2.6	1.0	0.008	0.1	0.8	0.891	1.8	2.6
Risk for prenatal fatigue											
Global Fatigue Index (continues)	0.6	0.8	0.445	0.1	0.5	0.873	−0.2	0.4	0.716	0.1	0.961

β : unstandardized coefficients; SE: standard errors; RC: reference category after categorical coding in regression analysis (dummy variables); HIV: human immunodeficiency virus. ¹ Grey sections indicates regression coefficients of models which did not have a significant model fit. ² Step 1: sociodemographic and socioeconomic factors; step 2: sociodemographic and socioeconomic factors; step 3: sociodemographic, socioeconomic, and pregnancy-related factors and HIV status; step 4: sociodemographic, socioeconomic, and pregnancy-related factors, HIV status and psychological factors. ³ Nausea and vomiting experienced within 7 days after enrolment. Significance ($p < 0.05$) indicated in bold. Background colour indicates that these models did not have a significant model fit during the statistical analysis.

4. Discussion

We explored the diet of pregnant women living in an urban South African setting during early pregnancy using both a priori and a posteriori dietary pattern analyses. Three distinct dietary patterns were identified, namely, pattern 1 “plant protein, iron, thiamine, and folic acid”; pattern 2 animal protein, copper, vitamin A, and vitamin B₁₂; pattern 3 “fatty acids and sodium”. These nutrient patterns, based on their associations with food groups, represent a “fortified grain and legume”, “animal products”, and “fatty-and processed foods” dietary pattern, respectively. Based on the a priori index, our study population had a borderline low-quality diet (DQI-I total score of 60). Nutrient pattern 1 was positively associated and nutrient pattern 3 negatively associated with dietary quality indicated by the a priori index. Possible determinants for the dietary patterns were found to be maternal age, level of education, and socioeconomic status.

The borderline low-quality diet observed in this study population can be attributed to low scores on the “moderation” and “overall balance” categories of the DQI-I as most participants consumed a diet high in total- and saturated fat, and foods high in sodium. Poor scorings on the total- and saturated fat categories could be due to the use of the stringent cut-off values proposed by Kim et al. [38]. However, these cut-off values are in line with that advocated by the South African Food-Based Dietary Guidelines and were chosen to emphasize the importance of moderate fat intake. A high intake of total fat among pregnant urban South African women was also reported by Krige et al. [13] with two-thirds of their study population consuming more than 30% of their total energy intake from fat. Jordaan [60] indicated similar findings when evaluating the dietary intake among two ethnic groups (including males and females between the ages of 20 and 30 years) of varying socioeconomic backgrounds residing in urban areas. A fat intake of more than 30% of the total energy intake among the urban South African population was indicated by Vorster et al. [38] as an adverse effect of the nutrition transition occurring due to urbanization. A high sodium intake among the South African population is also well described [61,62], hence the implementation of the mandatory legislation in 2016 to reduce the sodium content of certain foodstuffs [63].

In a recent publication, the World Health Organization recommended the intake of total fat to not exceed 30% of total energy as a higher fat intake is often a contributing factor towards unhealthy weight gain in adults [64]. Total fat intake was, however, found to only have a weak positive association with weight gain in the Nurses’ Health Study, with saturated-, trans-, and polyunsaturated fat having stronger positive relationships with bodyweight [65]. Rosqvist et al. [66] found in an overfeeding trial participants to gain similar amounts of weight regardless of consuming a diet high in saturated- or polyunsaturated fat. A diet high in saturated fat though resulted in more visceral adipose fat and liver fat being gained, whereas high intakes of polyunsaturated fat were found to increase lean body tissue [66]. It is, hence, important to consider the quality and type of dietary fat when evaluating health and disease risk [67]. The consensus is that saturated fat should rather be replaced with naturally occurring unsaturated fat, with the intake of industrially produced trans-fat excluded from the diet [64,67]. It should also be considered that often when people follow a diet high in saturated- and trans-fat, other unhealthy lifestyle factors such as a high intake of fast foods and sugar-sweetened beverages, which can contribute to poor health outcomes, are often followed [65].

Nutrient pattern 1 (plant protein, iron, thiamine, and folic acid), which is reflective of a “fortified grain and legume” pattern, represents a more traditional South African diet. The traditional South African diet, which is associated with a lower prevalence of degenerative diseases [68], is characterized by a high fiber and low fat intake as a result of a high plant protein (particularly legumes) and starchy food consumption [29,69]. The representation of nutrient pattern 1 of the traditional diet is supported by a high positive loading for total fiber and high negative loadings for saturated- and monounsaturated fat on the factor matrix, as well as the higher consumption of legumes and lower consumption of products of animal origin and processed foods. Upon determining the associations between

the a posteriori-derived nutrient patterns and a priori dietary patterns, nutrient pattern 1 was found to be associated with higher dietary quality. This higher dietary quality is attributed to more favorable scores in the “moderation” and “overall balance” categories of the DQI-I, which is also supported by the loadings of the factor matrix and the lower intake of products of animal origin and processed foods. Dietary variety was negatively associated with this pattern since traditional diets are typically more monotonous [70].

Nutrient pattern 2 (animal protein, copper, vitamin A, and vitamin B₁₂) and 3 (fatty acids and sodium) are, conversely, reflective of the nutrition transition. The nutrition transition is described as the increase in the intake of foods of animal origin and processed foods high in fat and sodium as populations adapt to a more modern lifestyle often due to urbanization and economic- and social development [38,71]. These changes in dietary intake are well documented and have been associated with the increasing prevalence of obesity and non-communicable diseases [38]. Although the food groups associated with nutrient pattern 2 were mainly animal products, nutrient pattern 2 was not found to be associated with dietary quality. Nutrient pattern 3, reflecting a “fatty- and processed foods” pattern, was found to be associated with a lower dietary quality, which was mainly driven by poor scorings in the “moderation” and “overall balance” categories. This is supported by high positive loadings on fat (saturated-, monounsaturated- and polyunsaturated fatty acids) and sodium on the factor matrix, together with the higher consumption of fatty foods, processed- and red meat, cheese, nuts and nut spreads, and sugar-sweetened beverages.

Nutrient pattern 1 was found to be adhered to by women with a lower level of education and a poorer socioeconomic status. Considering the positive association between nutrient pattern 1 scores and dietary quality, maternal age (≥ 27 years) can also be regarded as a determinant for this pattern. In a systematic review on determinants of dietary patterns and dietary quality during pregnancy, Doyle et al. [55] described a social gradient whereby women of older age, a higher education, a higher income, and/or other markers indicating affluence are more likely to follow a healthier dietary pattern [55]. Although our findings were similar with regard to maternal age, a higher quality diet was followed by less affluent women among our study population. This higher dietary quality can be explained by the higher intake of whole wheat- and brown bread, legumes, and maize, which are generally more affordable when compared to fatty foods and processed animal products. Bourne et al. [68] found that individuals within nutrition transition who were more traditionally orientated to frequently be under-employed and therefore have time available to prepare the lower costing maize meal and legume-based dishes, which have relatively long cooking times. Equally, employed city dwellers tend to more frequently choose unhealthy fast foods and convenience foods, which are generally refined and higher in fat due to long commuting times to and from work [68]. Nevertheless, it is important to note that the finding by Doyle et al. [55], in which women of a higher social gradient followed a diet of higher quality, was based on data mainly from high-income countries. This disparity in findings with regard to determinants for dietary patterns between high-income and middle-income countries was also reported by López-Olmedo et al. [72] who indicated individuals from a lower socioeconomic status in Mexico to follow a higher quality diet than individuals from higher socioeconomic status.

In a recently published review, Chia et al. [73] grouped both a priori and a posteriori dietary patterns to identify “healthy” and “unhealthy” patterns to conduct a meta-analysis on the associations between maternal dietary patterns during pregnancy and birth outcomes. A healthier dietary pattern was reported to be associated with a lower risk for preterm birth, with an unhealthy dietary pattern associated with a higher risk for preterm birth and low-birth weight. Considering the associations between the nutrient patterns and dietary quality identified by our study, nutrient pattern 1 reflects a more “healthy” dietary pattern, with nutrient pattern 3 reflecting an “unhealthy” dietary pattern. Based on the findings by Chia et al. [73], it is likely that women with higher adherence to nutrient pattern 3 have an increased risk for adverse pregnancy outcomes. A possible rationale for this is that nutrient pattern 3, which is reflective of a “fatty and processed food” pattern and nutrition

transition, increases the risk for overweight, obesity, and non-communicable disease [38]. In one of the only studies to evaluate the change in dietary patterns from before pregnancy and during pregnancy, Crozier et al. [74] found that, although there was a slight difference in the food products consumed, the dietary patterns remain mainly unchanged from before pregnancy. Women following an unhealthy dietary pattern during pregnancy are, therefore, likely to have followed an unhealthy pattern before conception too. Overweight, obesity, and non-communicable diseases both before and during pregnancy are well described to increase the risk for morbidity (gestational diabetes, preeclampsia, and macrosomia) and mortality during pregnancy [7,75–77].

A limitation to our study is that the dietary data used to score the a priori dietary patterns were obtained using a QFFQ. As the QFFQ reports on a range of foods or food groups consumed over a long period [78], it is likely that when converting the dietary data to intake per day, a greater variety of foods was reported, which could have led to an overestimation of the “variety” and “adequacy” scorings of the DQI-I. In addition, the QFFQ is not always accurate with regard to the estimated portion sizes consumed as this questionnaire relies heavily on memory [78]. However, the scoring of the DQI-I was performed stringently according to the guidelines given by Kim et al. [35], and we are confident that the results represent an accurate overview of the maternal dietary quality. Furthermore, the associations investigated between the maternal and household factors and the dietary patterns were likely to have been influenced by the relatively small sample size (multiple testing correction was not applied) of our study, as well as our study population being mainly from an urban setting.

5. Conclusions

We present a comprehensive analysis of the diet of pregnant women residing in an urban South African setting by including both a priori and a posteriori dietary pattern analyses. Although three distinct a posteriori dietary patterns were followed by participants in our study population, the overall dietary quality was poor. Considering possible poor maternal outcomes associated with lower dietary quality, the poor dietary quality among pregnant South African women, especially women of younger age, should be addressed through nutritional education. It is also advised that further research be carried out to truly understand the impact of the maternal diet on health outcomes among the South African population. Our study also confirms that the a priori and a posteriori methods, based on their methodological construction, evaluate the diet by different means and, therefore, provide complementary and useful information in exploring the diet as a whole. Determining associations between the a priori and a posteriori dietary patterns is also worthwhile as this aids in the better understanding of the a posteriori patterns that are representative of the actual dietary intake.

Supplementary Materials: The following are available online at <https://www.mdpi.com/2072-6643/13/2/565/s1>, Table S1: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 1 ($n = 250$), Table S2: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 2 ($n = 250$), Table S3: Consumption of food groups as a percentage of total energy intake (median and interquartile range) according to nutrient pattern 3 ($n = 250$).

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by both the Human Research Ethics Committees of the North-West University, Potchefstroom (NWU-00186-15-A1) and the University of the Witwatersrand, Johannesburg (M 150968). The City of Johannesburg District Research Committee (Gauteng Department of Health) and the clinical manager at Rahima Moosa Mother and Child hospital provided permission for the study to take place in the relevant clinical setting.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: As required by the Human Research Ethics Committee of the North-West University, South Africa, the researcher signed confidentiality agreements in which they agreed "not to disclose confidential information to anyone other than North West University unless required to do so by law or by court order". Participant consent forms were also clear for the purposes of data usage. Permission to obtain the data can be obtained from the North-West University Health Research Ethics Committee, Wayne Towers: wayne.towers@nwu.ac.za.

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ADDENDUM 11
Dietary Requirements During Pregnancy



Recommendations for weight gain and energy intake during pregnancy

Recommendations for weight gain during pregnancy				
Gestational weight gain ¹	Weight category	Single fetus		Multiple Fetuses
		Range of total weight gain (kg)	Mean (range) weight gain per week during the 2 nd and 3 rd trimester (kg/week) ²	Range of total weight gain (kg)
	Underweight (BMI < 18.5kg/ m ²)	12.5 – 18	0.51 (0.44 – 0.58)	- ³
	Normal weight (BMI 18.5 – 24.9 kg/m ²)	11.5 – 16	0.42 (0.35 – 0.50)	17 – 25
	Overweight (BMI 25 – 29.9kg/m ²)	7 – 11.5	0.28 (0.23 – 0.33)	14 – 23
	Obese (BMI > 30kg/m ²)	5 – 9	0.22 (0.17 – 0.27)	11 - 19
Recommendations for maternal energy intake				
Energy ⁴	1 st trimester: EER ⁵ = non-pregnant EER + 0 kCal 2 nd trimester: EER ⁵ = non-pregnant EER + 340 kCal 3 rd trimester: EER ⁵ = non-pregnant EER + 452 kCal			

BMI: Body mass index; kg: kilogram; EER: estimated energy requirements; kCal: kilocalorie (1 kCal equals 4.184 kilojoules)

¹ Recommendations as from the Institute of Medicine (Institute of Medicine & National Research Council, 2009)

² Calculations of mean weight gain per week assume that 0.5 – 2kg weight was gained during the 1st trimester

³ As yet, insufficient information is available to develop a guideline for weight gain for underweight women with multiple fetuses

⁴ Guidelines on energy intake for pregnant women as from the Institute of Medicine's guidelines (Institute of Medicine, 2006)

⁵ Estimated energy requirements (EER) reflects, as defined by age, weight, height and the level of physical activity, the average energy intake to maintain an energy balance in a healthy adult. Calculated as $EER (kCal/day) = 354 - (6.91 \times \text{age [year]}) + PA \times [(9.36 \times \text{weight [kg]}) + (726 \times \text{height [m]})]$.

Recommendations for nutrient intake during pregnancy

Recommendations for maternal nutrient intake ¹			
Macronutrients			
AMDR ^{2, 3}	Carbohydrates: 45 – 65% of TE Protein: 10 – 35% of TE Total fat: 20 – 35% of TE <i>MUFA</i> : Determined as $MUFA (\%TE) = \text{total fat } (\%TE) - SFA (\%TE) - PUFA (\%TE) - TFA (\%TE)$; Can be 15 – 20% depending on total fat intake <i>PUFA</i> : 6 – 11% of TE <i>Omega-6 PUFA</i> : 5 – 10% of TE; <i>Omega 3 PUFA</i> : 0.6 – 1.2 % of TE		
	Recommendations ⁴	Function	Food sources
Carbohydrates	RDA: 175g per day	Energy source (glucose) for bodily cells, including that of the growing fetus; the central nervous system and red blood cells have a necessity for glucose to function.	Carbohydrates are in starchy foods such as corn, cereals, pasta, rice, potatoes and starchy vegetables. It is recommended that whole grain and unrefined options are rather selected.
Free sugars	<10% of TE intake; <5% of TE is associated with better health outcomes		Sugar added by the cook or consumer; sugar added by manufacturer to foods or drinks; sugars naturally present in foods, such as honey, syrups, fruit juices and fruit juice concentrates.
Fibre	AI: 14g per 1000 kCal	Aids in laxation and hence assists in prevention/ treatment of constipation during pregnancy; promotes the feeling of satiety; assists in the control of blood glucose levels; and regulates blood cholesterol levels.	Mainly found in fruit, vegetables, legumes, nuts and whole (high-fibre) grains.
Protein	RDA: 0.8g per kg per day during 1 st half of pregnancy (56g per day) RDA: 1.1g per kg per day during the 2 nd half of the pregnancy (71g per day)	Structural component of each cell in the body; also has a functional role as protein serves as a precursor for, amongst others, co-enzymes, enzymes and hormones.	Animal sources include meat, poultry, fish, milk, yoghurt, cheese and eggs (also referred to as complete proteins as animal sources contain all essential amino acids). Legumes and nuts are also a source of protein, although considered as an incomplete source as legumes do not contain all essential amino acids.
Total fat	DRI not determined; AMDR as above recommended	Main source of energy; assists in the absorption of fat-soluble vitamins (vitamin A, D, E and K) and carotenoids	

Recommendations for nutrient intake during pregnancy (continued)

	Recommendations ⁴	Function	Food sources
SFA	<10% of TE intake	Source of energy; physical component of cell membranes; and assists in the functioning of body proteins	Mainly animal products such as cream, whole milk, butter, cheese and fatty meats. Plant sources include coconut, palm and palm kernel oil.
MUFA	DRI not determined; AMDR as above recommended	Main component of the structural lipids of membranes, especially the myelin of nervous tissue	Plant-based sources are canola and olive oil.
PUFA	DRI not determined; AMDR as above recommended		
<i>Omega 6 PUFA</i>	AI: 13g.per day	Substance for eicosanoid (including prostaglandins) synthesis; precursor for arachidonic acid; component of structural lipids of membranes; involved in the regulation of fatty acid synthesis.	Vegetable oils such as sunflower, safflower and soybean oil; other sources include nuts and seeds.
<i>Omega 3 PUFA</i>	AI: 1.4g per day	Precursors for eicosapentaenoic acid and docosahexaenoic acid synthesis – both of which play an important role in the optimal development of the fetal brain and retina.	Fatty fish and fish oil are main sources. Canola and flaxseed oil also contain omega-3 fatty acids.
TFA	Avoid as far as possible (<1% of TE)		Mainly found in fried foods, pastries and french fries; margarine and vegetable oils exposed to partial hydrogenation are also a source.

Recommendations for nutrient intake during pregnancy (continued)

Micronutrients			
	Recommendations ⁴	Function	Food sources
Vitamin A	RDA: 770 µg RAE per day	Fat-soluble vitamin important for reproduction, embryonic development, growth, optimal vision, gene expression and immune functioning.	Animal sources which are a source of vitamin A (retinol) include liver, eggs, fatty fish and dairy. Plant source contains carotenoids which are converted in the body to vitamin A. These food sources include orange and yellow vegetables and fruits (e.g. orange-fleshed sweet potatoes, carrots, pumpkin, mango and papaya) and dark green leafy vegetables (e.g. spinach and chard). In South Africa, maize meal and bread flour are fortified with vitamin A ⁵ .
Vitamin D	AI: 5 µg per day <i>Primarily obtained from ultraviolet B rays from sunlight via cutaneous synthesis.</i>	Involved in bone health as it is essential for calcium and phosphorus absorption; also important in regulating calcium and phosphorus levels in the body.	As it is a fat-soluble vitamin it is mainly found in fatty fish and fish-liver oils. Some margarines in South Africa contain added vitamin D.
Vitamin E	RDA: 15 mg per day	Serves as an antioxidant and hence prevents the spread of free-radical reactions.	Mainly found in vegetable oils, including sunflower, canola and olive oil. Other sources include nuts, the fatty portion of meat, unprocessed cereal grains, fruits and vegetables.
Vitamin K	AI: 90 µg per day	Acts as a coenzyme for biological reactions involved in bone metabolism and blood coagulation.	Mainly found in green leafy vegetables (spinach, salad greens, broccoli, Brussels sprouts and cabbage).
Vitamin B ₁ (Thiamine)	RDA: 1.4 mg per day	Serves as a co-enzyme for the metabolism of carbohydrates and branch-chain amino acids.	Grain products; pork; and fortified maize meal and bread flour ⁵
Vitamin B ₂ (Riboflavin)	RDA: 1.4 mg per day	Acts as a co-enzyme in oxidation-reduction reactions during energy production and metabolic pathways.	Milk and milk products; bread products; and fortified maize meal and bread flour ⁵

Recommendations for nutrient intake during pregnancy (continued)

	Recommendations ⁴	Function	Food sources
Vitamin B ₃ (Niacin)	RDA: 18 mg per day	Acts as a hydrogen ion donor or acceptor in various biological reduction-oxidation reactions (synthesis of fatty acids and steroids; fuel molecule oxidation; intracellular respiration).	Niacin-rich sources include meat, poultry, liver and fish. Maize meal and bread flour are also fortified with niacin ⁵ .
Vitamin B ₅ (Pantothenic acid)	AI: 6 mg per day	Involved in co-enzyme A synthesis. Co-enzyme A is required for the synthesis of, amongst others, amino acids, steroid hormones, fatty acids, membrane phospholipids and neurotransmitters.	Main sources include beef, chicken, liver, kidney, egg yolk, potatoes, oat cereals, whole grains, and broccoli and tomato products.
Vitamin B ₆ (Pyridoxine)	RDA: 1.9 mg per day	Serves as a co-enzyme for the metabolism of amino acids and glycogen.	Fortified maize meal and bread flour ⁵ ; beef liver and other organ meats.
Vitamin B ₇ (Biotin)	AI: 30 µg per day	Co-enzyme within bicarbonate-dependent carboxylation reactions.	As yet, limited information available on biotin. Content within food is therefore generally not documented, but biotin is known to be found in natural (unprocessed) foods.
Vitamin B ₉ (Folic acid)	RDA: 600 µg per day	Important for reducing the risk of neural tube defects during pregnancy. Also acts as a co-enzyme in nucleic and amino acid metabolism.	Fortified maize meal and bread flour ⁵ ; dark green leafy vegetables; and legumes.
Vitamin B ₁₂ (Cobalamin)	RDA: 2.6 µg per day	Important in blood formation and neurological function. Acts as a co-enzyme in the homocysteine–methionine reaction, as well as the metabolism of fatty acids and amino acids.	Mainly found in animal foods, namely organ meats (liver), venison, shellfish and sardines.
Vitamin C	RDA: 85 mg per day	Powerful antioxidant and hence acts as a scavenger of free radicals; acts as a cofactor for several enzymes which are involved in the synthesis of neurotransmitters, collagen and carnitine.	Mainly fruits and vegetables – citrus fruit and juice, tomatoes and tomato juice, sweet peppers (red and green), broccoli and strawberries are particularly good sources.

Recommendations for nutrient intake during pregnancy (continued)

	Recommendations ⁴	Function	Food sources
Iron	RDA: 27 mg per day	Forms part of various proteins (haemoglobin, myoglobin, cytochromes and enzymes). Mainly, however, found in haemoglobin, which is part of erythrocytes and transports oxygen within the body.	Available in two forms: heme-iron and non-heme iron. Heme-iron (highly bioavailable) is found in meat, poultry and fish. Non-heme iron (lower bio-availability) is found mainly in plant-source foods, namely vegetables, fruit, and whole grain bread. In South Africa, fortified maize meal and bread flour ⁵ are also a source of non-heme iron.
Calcium	AI: 1000 mg per day	Primarily forms part of the structure of bones and teeth. Also involved in neural transmission, muscle contraction, and vascular constriction and vasodilation.	Main food sources include dairy and dairy products, namely milk, cheese and yoghurt.
Iodine	RDA: 220 µg per day	Forms an integral part of thyroid hormones. These hormones regulate many vital biological reactions which affect processes in the brain, heart, muscles, kidneys and pituitary gland.	Content in most foods is low. High concentrations found in seafood. Table salt in South Africa is, however, iodated, making table salt an important source of iodine ⁶
Zinc	RDA: 11 mg per day	It is essential for optimal growth and development as it plays a structural, regulatory and catalytic role in the body.	Red meat; whole grains; fortified maize meal and bread flour ⁵ ; and some seafood.
Magnesium	RDA: 350 mg per day	Involved in various enzymatic processes; important for the regulation of intracellular potassium and calcium; also plays an important role in the development and maintenance of bone and calcified tissue.	High concentrations are found in green leafy vegetables, whole grains, and nuts. Milk, meat and starches also provide moderate amounts of magnesium.

AMDR: acceptable macronutrient distribution ranges; TE: total energy; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; SFA: saturated fatty acids; TFA: trans fatty acids; RDA: recommended dietary allowance; kCal: kilocalorie (1 kCal equals 4.184 kilojoules); DRI: Dietary reference intakes; AI: adequate intake.¹ Guidelines on recommended nutrient intake during pregnancy as indicated by the Institute of Medicine's guidelines (Institute of Medicine, 2006); free sugars recommendation are from WHO (World Health Organization) (2018), and the recommendations on saturated- (SFA), monounsaturated- (MUFA), polyunsaturated- (PUFA) and trans (TFA) fatty acid intake are from FAO (Food and Agriculture Organization) (2010).

² Acceptable macronutrient distribution ranges (AMDR) indicates the percentage of energy from a specific macronutrient which ensures adequate essential nutrient intake; these ranges are also associated with a decreased risk of chronic disease.

³ As yet, there are no specific guidelines for pregnant women, and hence guidelines for adults are reported.

⁴ Recommendations expressed as recommended dietary allowance (RDA) or Adequate Intake (AI) for pregnant women aged 19 to 50 years (magnesium is, however, for pregnant women 19 to 30 years of age). RDA is recommended as a reference guide for nutrient intake as an intake at RDA has a low probability of inadequate intake. AI is indicated for nutrients where there is as yet insufficient evidence available to determine the RDA; intake at AI is likely to either meet or exceed the individual's requirements.

⁵ According to South African legislation, the food industry must fortify maize meal (sifted, unsifted, super, special) and bread flour (white and brown bread flour) with eight micronutrients: vitamin A, thiamine, riboflavin, niacin, folic acid, pyridoxine, iron and zinc (Department of Health, 2003)

⁶ Department of Health (2001)

ADDENDUM 12
Overview Of The Diet Quality Index - International



SCORING CRITERIA FOR THE DIET QUALITY INDEX-INTERNATIONAL

Dietary methodology suggested

Although the DQI-I was constructed using dietary data from 24-hour recalls, the International Dietary Data Expansion Project indicates that dietary data can also be obtained from food frequency questionnaires or weighted food records (INDDEX Project, 2018). Mariscal-Arcas *et al.* (2007) and Tur *et al.* (2005) used dietary data obtained from both 24-hour recalls and quantified food frequency questionnaires. Data from the food frequency questionnaires were used to evaluate food consumption patterns and hence the components under the variety category were scored using the frequency dietary data. Information on daily nutrient intake was obtained from the dietary data obtained from the 24-hour recalls. Ferranti *et al.* (2016), Chan *et al.* (2015) and Veugeliers *et al.* (2005), however, used only data obtained from quantified food frequency questionnaires. Consumption, reported as gram per week or month, was converted to intake per 24 hours, before scoring the DQI-I in the individual studies.

Scoring criteria

The DQI-I has an overall score of 100 (a score of 0 being the lowest and 100 the highest). The scores of each component of a category are summed to provide a score per category; the scores of the 4 categories are then summed to provide an overall score (Kim *et al.*, 2003). According to the criteria given by Kim *et al.* (2003), a score of less than 60 out of a possible 100 indicates a poor dietary quality. Following is a short overview of the scoring criteria for each category (Kim *et al.*, 2003):

- **Variety:** The variety of a diet is evaluated in two ways, namely (1) the overall variety and (2) the within food-group variety (protein sources). This allows for assessing whether nutrients are consumed from diverse sources both across food groups and within food groups.
 - The food groups to determine *overall variety* include (1) meat/ poultry/fish/ eggs; (2) dairy/ beans^a; (3) grains; (4) fruit; and (5) vegetables. The inclusion of at least one serving^b of each of the five food groups allows for a maximum score of 15. For every food group for which one serving is missing, the total score is reduced by 3 points.
 - *Variety within protein-sources* is dependent upon the intake of (1) meat, (2) poultry, (3) fish, (4) dairy/ beans and (5) eggs. The intake of at least a half serving of each protein source is regarded to be a meaningful consumption. A meaningful intake of 3 or more sources amounts to the maximum score of 5. The score reduces to 3, 1 or 0 when the number of sources decreases to 2, 1 or 0, respectively.
- **Adequacy:** Eight components are scored within this category, allowing for the diet to be evaluated according to foods and nutrients required for a healthy diet. The scores for these

eight components are assigned on a continuous scale based upon the percentage attainment of the recommended intake.

- *Fruits, vegetables, grains and fibre*: The recommended intake for these food groups is based upon energy intake. The three energy levels given by Kim *et al.* (2003) are 1700kCal (7118kJ), 2200kCal (9211kJ) and 2700kCal (11304kJ).

Depending on the energy levels, daily intake of ≥ 2 , 3 or 4 servings of fruit, and ≥ 3 , 4 or 5 servings of vegetables amount to the highest score of 5 points.

A daily intake of ≥ 6 , 9 or 11 servings of grains and >20 g, 25g or 30g of fibre, also depending on the energy levels, amounts to a maximum score of 5 points.

- *Daily protein intake*: Intake is considered adequate (maximum score of 5 points) if the total intake is $>10\%$ of the total daily energy intake.
- *Daily iron, calcium and vitamin C intake*: recommended intake is based upon Dietary Reference Intake levels (for age and gender). An intake of $\geq 100\%$ of the recommended Dietary Reference Intake amounts to a maximum score of 5 points.

- *Moderation*: With this category, foods and nutrients related to chronic disease and which may need restriction are evaluated. The intake levels are based on three tiers according to the possible effect on health.

Lowest tier: An intake below this level will show no harmful effect on health in a healthy individual.

Highest tier: Intake at this level and above might be related to chronic health outcomes.

Middle tier: Intake between that of the lowest and highest tier.

A score of 6 is given to the lowest tier, 3 for the middle tier and 0 for the highest tier.

- *Total fat and saturated fat intake*: To emphasise the importance of a moderate intake, stringent cut-off values for total fat and saturated fat are used. A daily intake of $\leq 20\%$ of total energy intake permits the highest possible score (6 points), and intake of $>30\%$ the lowest score (0 points). A saturated fat intake of $\leq 7\%$ of total daily energy intake allows for the highest score, and $>10\%$ of total daily energy intake for a 0 score. These cut-off values are, however, in line with what the WHO recommends as part of a healthy diet (WHO, 2018) and the recommendations given per the South African Food-Based Dietary Guidelines (Smuts & Wolmarans, 2013).
- *Cholesterol and sodium*: An intake equal to or less than 300mg of cholesterol and 2400mg of sodium per day, individually, equals a high score of 6 points. An intake of more than 400mg and 3400mg for cholesterol and sodium, respectively, scores the lowest score of 0.
- *Empty calorie foods*: With this component, the percentage of energy consumption from foods of low nutrient density is evaluated. Nutrient density is determined according to

the ratio of nutrients to energy in an amount of food consumed compared with the recommended levels. For example:

$$\begin{aligned} &\text{Vitamin C density per 100g apple (consumed by a 20-year-old female)} \\ &= (5.7\text{mg} / 75\text{mg}^c) / (247\text{kJ} / 9211\text{kJ}^d) \\ &= 2.83 \end{aligned}$$

A nutrient ratio of more than 1 indicates that the food has a higher nutrient composition compared to energy.

For the DQI-I, the sum of nutrients evaluated in the examined food should score more than 1 to indicate that the food is nutrient dense. Kim *et al.* (2003) indicate that mainly table sugar, oil and alcohol classify as low nutrient-dense foods according to this method.

A score of 6 points is given should the total energy consumed from low nutrient-dense foods be less than 10%.

- *Overall balance:* In this category, the overall balance of the diet with regard to the proportionality of energy intake (macronutrient ratio) and fatty acid composition are evaluated.
 - *Macronutrient ratio (carbohydrates: protein: fat):* This illustrates the ratio of energy of carbohydrates to protein to fat. A maximum score of 6 points, dependent upon the optimal macronutrient range (see ranges in the table), is allocated to this component.
 - *Fatty acid ratio:* A maximum score of 4 points is possible in this component, based upon the PUFA:MUFA:SFA^e ratio (ranges given in the table below).

^aBeans and dairy are included within the same group to allow for cross-national comparison. As beans are the main source of calcium in many countries (for example Asia), dairy alone will present a misrepresentation of the intake of calcium-rich foods in some countries.

^bKim *et al.* (2003) used the United States Food Guide Pyramid serving size definitions.

^cActual levels of vitamin C and energy within the apple.

^dRecommended vitamin C and energy intake for a 20-year-old individual.

^ePUFA: polyunsaturated fatty acids; MUFA: monounsaturated fatty acids; SFA, saturated fatty acids

Adjustments made to the DQI-I scoring criteria

As the cut-off points used within the DQI-I allow for the adjustment of the DQI-I according to the study population under investigation, various authors have recommended or made adjustments to the DQI-I scoring. One of the recommended adaptations regarding the DQI-I was published by Tur *et al.* (2005). Tur *et al.* (2005) applied the DQI-I to Spanish nationals living on the Balearic Islands to assess whether the DQI-I can be used to evaluate the quality of a Mediterranean diet. The authors concluded that the cut-off values recommended by Kim *et al.* (2003) were too stringent and new cut-off values in line with the Mediterranean dietary pattern were recommended: intake of total fat between 30 and 35% of total energy was regarded as more appropriate, olive oil and wine were not included in the calculation of foods contributing to the intake of empty calories, and the fatty acid ratio was adjusted to evaluate the sum of polyunsaturated and monounsaturated fatty acids to saturated fatty acids (Tur *et al.*, 2005).

This DQI-I version adapted for the Mediterranean dietary pattern was used by Mariscal-Arcas *et al.* (2007) to evaluate the diet quality of young people living in the southern parts of Spain. Mariscal-Arcas *et al.* (2007), however, also included the Spanish recommended daily nutrient intakes as cut-off values and further adjusted the criteria for empty-calorie foods. Chan *et al.* (2015), however, could not determine the percentage of energy consumed from empty calorie foods, and this component was excluded. The DQI-I version hence used by Chan *et al.* (2015) scored out of a possible 94 rather than 100.

Diet Quality Index-International scores and components (Kim *et al.*, 2003)

Category & Component	Scoring Criteria		Score
Variety	0 – 20 points		
Overall food group variety: - meat/ poultry/fish/eggs - dairy/ beans - grain - fruit - vegetables	0– 15 points	≥ 1 serving from each food group/d = 15 Any 1 food group missing/d = 12 Any 2 food groups missing/d = 9 Any 3 food groups missing/d = 6 ≥ 4 food groups missing/d = 3 None from any food groups = 0	
Within-group variety for protein source (meat, poultry, fish, dairy/ beans, eggs)	0 – 5 points	≥ 3 different sources/d = 5 2 different sources/d = 3 From 1 source/d = 1 None = 0	
Adequacy	0 - 40 points		
Vegetable group ^{1, 2}	0 – 5 points	≥ 3 –5 servings/d = 5, 0 servings/d = 0	
Fruit group ^{1, 2}	0 – 5 points	≥ 2 –4 servings/d = 5 0 servings/d = 0	
Grain group ^{1, 2}	0 – 5 points	≥ 6 –11 servings/d = 5 0 servings/d = 0	
Fiber ^{1, 2}	0 – 5 points	≥ 20 -30g /d = 5 0 g/d = 0	
Protein	0 – 5 points	$\geq 10\%$ of energy/ d = 5 0% of energy/d = 0	
Iron	0 – 5 points	$\geq 100\%$ RDA (AI)/ d = 5 0% RDA (AI)/d = 0	
Calcium	0 – 5 points	$\geq 100\%$ AI/ d = 5 0% AI/d = 0	
Vitamin C	0 – 5 points	$\geq 100\%$ RDA (RNI)/d = 5 0% RDA (RNI)/d = 0	

Diet Quality Index-International scores and components (continued) (Kim *et al.*, 2003)

Category & Component	Scoring Criteria		Score
Moderation	0 – 30 points		
Total fat	0 – 6 points	$\leq 20\%$ of total energy/d = 6 $>20\text{--}30\%$ of total energy/d = 3 $\geq 30\%$ of total energy/d = 0	
Saturated fat	0 – 6 points	$\leq 7\%$ of total energy/d = 6 $>7\text{--}10\%$ of total energy/d = 3 $\geq 10\%$ of total energy/d = 0	
Cholesterol	0 – 6 points	≤ 300 mg/d = 6 $>300\text{--}400$ mg/d = 3 ≥ 400 mg/d = 0	
Sodium	0 – 6 points	≤ 2400 mg/d = 6 $>2400\text{--}3400$ mg/d = 3 ≥ 3400 mg/d = 0	
Empty calories	0 – 6 points	$\leq 3\%$ of total energy/d = 6 $>3\text{--}10\%$ of total energy/d = 3 $\geq 10\%$ of total energy/d = 0	
Macronutrient ratio ³ (carbohydrate: protein: fat)	0 – 6 points	55 ~ 65 : 10 ~ 15 : 15 ~ 25 = 6 52 ~ 68 : 9 ~ 16 : 13 ~ 27 = 4 50 ~ 70 : 8 ~ 17 : 12 ~ 30 = 2 Otherwise = 0	
Fatty acid ratio (PUFA: MUFA: SFA)	0 – 4 points	P/S = 1 ~ 1.5 and M/S = 1 ~ 1.5 = 4 Else if P/S = 0.8 ~ 1.7 and M/S = 0.8 ~ 1.7 = 2 Otherwise = 0	

RDA: Recommended Dietary Allowance; AI: Adequate Intakes; RNI: Recommended Nutrient Intake; MUFA: monounsaturated fatty acids; SFA: saturated fatty acids; PUFA: polyunsaturated fatty acids; P/S, ratio of PUFA to SFA intake; M/S, ratio of MUFA to SFA intake.

¹Used as a continuous variable.

²Based on 1700 kcal (7118 kJ)/ 2200kCal (9211kJ)/ 2700kCal (11304kJ) diet; 1kCal = 4.1868kJ

³Ratio of energy of carbohydrate to protein to fat.

ADDENDUM 13
Questionnaires Used For Exposure And Outcome Variables





NuPED

Nutrition during Pregnancy and Early Development

Quantitative Food Frequency Questionnaire

Name of fieldworker:

Participant number

Phase

Today's date:

2	0	1	

Day of the week:

year

month

day

Please think carefully about the food and drink you have consumed during the **PAST MONTH** (four weeks).

We have divided the foods into different groups for example all the porridges and cereals together. I will go through a list of food groups and drinks with you and I would like you to tell me:

- Which foods you eat in each of the different food groups
- How the food is prepared
- How much of the food you eat at a time
- How many times a day you eat it and if you do not eat it everyday, how many times a week or a month you eat it.

To help you to describe the amount of a food you eat, I will show you pictures of different amounts of the food as well as other food models, containers, etc.

There are no right or wrong answers.

Everything you tell me is confidential. Only your subject number appears on the form.

Is there anything you want to ask now?

Are you willing to go on with the questions?

Before we start I would like to find out what type of margarine, oil and milk you **USUALLY** use in your home.

1. What type of **MARGARINE** do you USUALLY use in your home? Give brand name if possible. Mark ONE.

☐ Tub/Soft margarine (brand name)

☐ Brick/Hard margarine (brand name)

☐ I don't know

☐ Do not use margarine in home

☐ Butter (brand name)

2. What type of **OIL** do you USUALLY use in the preparation of food in your home? Mark ONE.

☐ Sunflower oil (give brand name) _____

☐ Canola oil (give brand name) _____

☐ Olive oil (give brand name) _____

☐ Other (give brand name) _____

☐ Oil previously used _____

☐ I don't know

☐ Do not use OIL ever in the home

3. What type of **MILK** do you USUALLY use in your home? Mark only ONE

☐ Full cream milk / Fresh cow's milk/ Box milk full cream

☐ Low fat milk / 2% milk / Box low fat or 2% milk

☐ Fat free milk / Skim milk / Box fat free or skim milk

☐ Powder milk (eg Elite; give brand name)

☐ I don't know

☐

Do not use milk

4. What type of **CREAMER** do you USUALLY use in your home?

☐

Cremora, Ellis Brown, Coffee Mate, Tea Mate etc

☐

Cremora Lite

☐

I don't know

☐

Do not use creamer

QUANTIFIED FOOD FREQUENCY QUESTIONNAIRE

INSTRUCTIONS: Circle the subject's answer. Fill in the amount and times eaten in the appropriate columns.

I shall now ask you about the type and the amount of food you have been eating in the **LAST MONTH**. Please tell if you eat the food, how much you eat and how often you eat it. We shall start with maize meal porridge.

In the last **four weeks**, did you eat...?

MAIZE MEAL, COOKED PORRIDGES AND BREAKFAST CEREALS								
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Maize-meal porridge	Stiff (pap)						4401	
	Soft porridge (slappap)						4400	
	Crumbly (phutu)						4402	
Sour porridge (Tini)	Maize meal						9829	
	Mabella						9827	
	Other:							
Mabella	Stiff						3437	
	Soft							
Oats							3239	
Tastee wheat	Soft						3240	
Other cooked porridge	Type							
Morvite	Soft						9804	
Breakfast cereals	All bran flakes						3242	
	Corn flakes plain						3243	
	Weetbix						3244	
	Rice crispies plain						3252	
	Other:							

If yes, in the last **four weeks**, how often did you eat the food?

Do you pour milk on your maize meal (e.g. stiff, phutu soft porridge), cooked porridge or cereal?

Ye

1

No

2

If yes, what type of milk (whole fresh, sour, 1%, fat free, milk blend, etc)

If no, go directly to the "sugar" section.

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / WEEK
			Complete one column					
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
If yes, how much milk	Whole milk/full cream milk/ fresh cow's milk						2718	
	Maas/sour milk						2787	
	Low fat / 2% milk						2772	
	Fat free / skim milk						2775	
	Other							

Do you put sugar on your porridge or cereal?

If no, go directly to the next question "do you put anything else in your porridge?".

Ye

No

If no, go directly to the next question: do you eat anything else in your porridge? :								
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / WEEK
			Complete one column					
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
If yes, how much sugar WHITE or BROWN	Cooked porridge						3989	
	Cereal						3989	
	Other porridge / cereal						3989	
	Other							

Do you put anything else in your porridge?

1

Ye

2

No

If yes, what? _____ How much? _____

OTHER STARCH								
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Samp	Bought Self ground						3250	
Samp and beans	Give ratio of samp:beans						3402 (1:1)	
Samp and other (e.g. peanuts)	Give ratio of samp:other Specify other:						3250 (samp)	
Rice	White						3247	
	Brown						3315	
	Maize Rice						3250	
	Any fat added?							
Pasta	Macaroni, plain						3262	
	Spaghetti, plain						3262	
	Spaghetti, canned in tomato sauce						3258	
	Macaroni & cheese Cheese: Milk: Fat:							
	Other specify							
Pizza	Home made: Specify topping						3353 (base+ch +tom+oliv)	
	Bought: Specify topping						3353 (base+ch +tom+oliv)	

You are being very helpful. Can I now ask you about meat?

CHICKEN, MEAT, FISH

How many times do you eat meat (beef, mutton, pork, chicken, fish) per week?

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Chicken	Meat & skin, boiled						2926	
	Meat without skin, boiled						2963	
	Meat & skin, roasted/ grilled						2925	
	Meat without skin, roasted/ grilled						2950	
	Kentucky / Chicken Licken (Fried in batter/crums)						3018	
	Nando's						2925	
	Other							
Chicken stew	With potato and onion WITH skin						9813	
	With tomato and onion WITH skin						2985	
	With vegetables WITH skin						3005	
	With tomato and onion NO skin						4379	
	With vegetables NO skin						4378	
Chicken BONE stew	With potato, onion and tomato						9814	
	Other							
Chicken feet	Nothing added						2997	
	Stew with potato, onion and tomato						9815	
Chicken head							2999	
Chicken offal	Stew with tomato and onion and sunflower oil						9816	
	Liver, cooked						2970	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/d ay	Weekly Times/ week	Monthly Times/ month	No		
RED MEAT	How do you like your meat? With fat OR Fat trimmed							
Red meat BEEF	BRISKET, boiled/fried without added fat						4363	
	BRISKET, fried in added fat						4363	
	Type of fat: Beef, stewed with cabbage						3006	
	Beef, stewed with potato, onion and tomato						9817	
	Beef, stewed with vegetables						3020	
	Mince (lean/ topside), nothing added						2921	
	Mince (regular), nothing added						4363	
	Mince, tomato & onion added						2987	
	Beef BONE stew with potato and onion and oil						9819	
	Other							
MUTTON	Meat, with fat, cooked						2947	
	Mutton, no fat, cooked						3036	
	Mutton, chop, grilled						2927	
	Mutton, stewed with vegetables						2916	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / WEEK
			Complete one column					
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Beef/mutton Offal	Offal, cooked						3003	
	Stewed with vegetables							
	Liver, beef, fried/cooked						2920	
	Liver, sheep, fried/cooked						2955	
	Kidney, beef, cooked						2923	
	Kidney, sheep, cooked						2956	
	Brain, sheep, cooked						2952	
	Lung, beef, cooked						3019	
	Lung, sheep, cooked						4337	
	“Gemaldes” (lung & fat)						4409	
	Heart, beef, cooked						2968	
	Heart, sheep, cooked						2969	
	Other							
Goat meat	Grilled/roasted/cook ed						4281	
	Stewed with vegetables							
	Other							
Venison/ Wild buck							2913	
Horse/Donke y							9807	
Rabbit							4327	
Other type of meat	Specify							

What type of vegetables is usually put into meat stews?

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Wors / Sausage	Beef & pork, boerewors						2931	
Bacon							2906	
Patties	Beef, fried						2984	
	Chicken, fried						3011	
Cold meats AND Processed meats	Polony						2919	
	Ham						2967	
	Vienna						2936	
	Frankfurter, beef & pork						2937	
	Frankfurter/Sausa ge, chicken						3012	
	Russian/Salami						2948	
	Other							
Canned meat	Bully beef, plain						2940	
	Bully beef with potato & onion & oil						2994	
	Other							
Meat pie BOUGHT Or HOMEMADE	Beef						2939	
	Steak and kidney						2957	
	Sausage roll						2939	
	Cornish						2953	
	Chicken						2954	
	Other							
Hamburger	Bought						9818	
	Other							
Biltong	Beef (with fat OR without fat)						3021	
Dried wors Dried sausage	Beef						2949	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Dried beans	Baked beans in tomato sauce						3176	
	Bean salad / Sousbone						3174	
	Soup with dried beans, beef and vegetables						3145	
	Sugar beans, cooked						3205	
	Other							
Lentils	Whole, cooked						3203	
	Lentil soup with beef and vegetables						3153	
Soya products eg. Imana, Knorr, Jileleke, Toppers	Cooked						3196	
	Soup/Gravy made with soya products						9831	
	Stewed with extra potato, onion and tomato						9830	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Pilchards in tomato sauce or chilli or brine	Whole						3102	
	Mashed with fried onion						3102 (70%) 3730 (30%)	
	With tomato and onion						9820	
	Other							
Fish	Hake, fried with batter/crumbs in sunflower oil						3072	
	Hake, fried in sunflower oil						3060	
	Hake, steamed						4373	
	Moddervis / Yellow fish* fried in oil						3084	
	Moddervis / Yellow fish baked with onion (NO oil added)						3089	
	Other							
Other canned fish	Tuna in oil						3056	
	Sardines in oil						3104	
	Sardines in tomato sauce						3087	
	Other							
Fish cakes	Bought: Fried						3080	
	Home made with potato, fried in sunflower oil						3098	
Fish fingers	Bought (baked)						3081	
Eggs	Boiled/poached						2867	
	Scrambled (full cream milk & brick margarine)						2890	
	Scrambled (NO milk, ONLY oil added)						2869	
	Scrambled (NO oil, ONLY full cream milk)						2872	
	Fried in oil						2869	
	Fried in brick margarine						2877	
	Other							

VEGETABLES								
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Cabbage	How do you cook cabbage?							
	Boiled, nothing added						3756	
	Boiled with potato and onion and sunflower oil						3815	
	Boiled with potato and onion and brick margarine						3813	
	Fried in oil						3812	
	Fried in brick margarine						3810	
	Boiled with potato, onion and tomato and oil						9821	
	Raw with nothing added						3704	
	Other							
Spinach or morogo or beetroot leaves or other green leafy	How do you cook spinach?							
	Boiled, nothing added						3913	
	Boiled with oil added							
	Boiled with brick margarine added						3898	
	Boiled with tub margarine added						3899	
	Boiled with potato, onion and tomato and oil						9822	
	Other							
Tomato and onion gravy	With oil						9823	
	Without fat, without sugar						3925	
	Canned						4192	
	Thickened with packet soup powder						9832	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Pumpkin (yellow) Butternut Hubbard squash Table Queen Etc	Boiled, nothing added						4164	
	Boiled with sugar only (NO fat)						3728	
	Boiled with brick margarine & sugar						3893	
	Boiled with tub margarine and sugar						9833	
	Boiled with oil and sugar						9828	
	Other							
Carrots	Boiled, nothing added						3757	
	Boiled with oil added							
	Boiled with brick margarine added						3816	
	Boiled with tub margarine added						3817	
	Boiled with sugar only						3818	
	Boiled with oil and sugar							
	Boiled with brick margarine and sugar						3819	
	Boiled with tub margarine and sugar						3820	
	Boiled with potato, onion and sunflower oil						3824	
	Boiled with potato, onion and brick margarine						3822	
	Boiled with potato, onion and tub margarine							
	Chakalaka						9812	
	Raw, nothing added						3709	
	Other							
Mealies/ Sweet corn	On cob – fat added Fat:						3725	
	On cob – no fat added						3725	
	Creamed sweet corn / canned						3726	
	Whole kernel/canned						3942	
	Whole kernel, frozen, boiled						4132	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Beetroot	Salad						3699	
	Boiled, nothing added						3698	
How do you cook potatoes?								
Potatoes	Boiled/baked with skin						4155	
	Boiled/baked without skin						3737	
	Boiled with sunflower oil added						3873	
	Boiled with brick margarine added						3867	
	Boiled with tub margarine added						3868	
	Mashed with whole milk and brick margarine						3876	
	Mashed with whole milk and oil							
	Roasted in beef fat						3878	
	Roasted in sunflower oil						3979	
	French fries (chips) / Fried potatoes						3740	
	Other							
Sweet potatoes	How do you cook sweet potatoes?							
	Boiled/baked with skin						3748	
	Boiled/baked without skin						3903	
	Boiled with sugar and oil added						9834	
	Boiled with sugar and brick margarine added						3749	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Broccoli	Boiled						3701	
	Raw						3702	
Cauliflower	Boiled						3716	
Green beans	Boiled, nothing added						3696	
	Cooked with potato, onion and sunflower oil						3794	
	Cooked with potato, onion and brick margarine						3792	
	Other							
Mixed vegetables	Canned						4264	
	Frozen, boiled (carrot, corn, peas, green beans)						3727	
	Frozen, boiled (carrot, cauliflower, green beans)						4265	
	Other							
Salad vegetables	Mixed salad: tomato, lettuce and cucumber (no dressing)						3921	
	Raw tomato						3750	
	Cucumber, raw						4119	
	Coleslaw (cabbage) (mayonnaise)						3705	
	Coleslaw (cabbage) (commercial)						3707	
	Potato salad (mayonnaise)						3928	
	Baked bean salad						9824	
	Other salad vegetables							
Mayonnaise / salad dressing	Mayonnaise						3488	
	Vinegar, oil						3487	
	Low oil salad dressing						3505	
	Salad cream						3489	
	Other: Specify							
Other vegetables (specify prep)								

FRUIT								
Now we come to fruit								
Do you like fruit?			☐ Ye ¹ ☐ No ²					
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Apples							3592	
Banana							3540	
Pears							3582	
Oranges							3560	
Naartjie							3558	
Grapes							3550	
Peaches	Fresh						3565	
	Canned						3567	
Apricots	Fresh						3534	
	Canned						3535	
Mangoes							3556	
Guavas	Fresh						3551	
	Canned						3553	
Watermelon	Fresh						3576	
Fruit salad	Fresh						3588	
	Canned						3580	
Fig (Vye)							3544	
Avocado							3656	
Wild fruit/berries	Specify type							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Dried fruit	Apple, dried, raw						3600	
	Peach, dried, raw						3568	
	Mixed fruit, dried, raw						3593	
	Mixed fruit, dried and cooked with sugar						3590	
	Fruit roll, dried (all types)						3655	
	Other							
Other fruit								

Let me ask you about ***Custard***.

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Custard	Homemade, full cream milk or fresh cow's milk						2716	
	Homemade, lowfat milk						2779	
	Homemade, skim milk						2717	
	Commercial eg Ultramel						2716	
	Other							
Custard with other food (e.g. with jelly, fruit salad, baked pudding)								

BREAD AND BREAD SPREADS								
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Bread / Bread rolls	White						3210	
	Brown						3211	
	Whole wheat						3212	
Do you spread anything on the bread?			Always		Sometimes		Never	
Margarine	What brand do you have at home now?							
	Tub, regular						3496	
	Tub, medium fat						9806	
	Tub, light/low fat						3524	
	Brick, regular						3484	
	Brick, medium fat						9805	
	Brick, lite/low fat						3528	
	Other							
Peanut butter						3485		
Jam/syrup/honey						3985		
Marmite / Fraybentos / Oxo						4058		
Fish/meat paste						3109		
Cheese	Cheddar						2722	
	Gouda						2723	
	Other							
Sandwich spread						3522		
Achaar						3117		
Other spreads	Specify							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Dumpling	White flour						9835	
	Whole wheat flour						3212	
Vetkoek	White flour						3257	
	Whole wheat flour						3324	
Provita, crackers, etc	Provita						3235	
	Cream crackers						3230	
	Other savoury biscuits like Bacon kips, wheat crackers, etc						3331	

DRINKS								
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Tea	English (normal)						4038	
	Rooibos						4054	
Coffee							4037	
White sugar	Tea						3989	
	Coffee						3989	
Brown sugar	Tea						4005	
	Coffee						4005	
Milk per cup of TEA	Do you use milk in your TEA? ☐ Yes ☐ No If YES, What type of milk do you use in TEA? If no, go to milk in coffee.							
	Fresh / long life whole/full cream						2718	
	Fresh/long life: 2%/low fat						2772	
	Fresh/long life: fat free / skim milk						2775	
	Creamer/whitener like Ellis Brown / Cremora						2751	
	Cremora Lite							
	Condensed milk						2714	
	Evaporated milk						2715	
	Other							
	None							
Milk per cup of COFFEE	Do you use milk in your COFFEE? ☐ Yes ☐ No If YES, What type of milk do you use in COFFEE? If no, go to milk as such							
	Fresh/long life: whole/full						2718	
	Fresh/long life: 2%/low fat						2772	
	Fresh/long life: fat free						2775	
	Creamer/whitener like Ellis Brown						2751	
	Cremora Lite							
	Condensed milk						2714	
	Evaporated milk						2715	
	Other							
FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Milk as such	What type of milk do you drink milk as such?							
	Fresh/long life: whole / full cream milk						2718	
	Fresh/long life: 2% milk / low fat milk						2772	
	Fresh/long life: fat free / skim milk						2775	
	Condensed milk						2714	

	Sour/maas						2787	
	Other							
Milk drinks	Flavoured milk						2774	
	Milo made with full cream milk						2735	
	Milo made with skim milk						2747	
	Drinking chocolate made with water						4287	
	Other							
Yoghurt	Drinking yoghurt low fat						2756	
	Plain low fat						2734	
	Low fat sweetened with fruit						2732	
Squash	Sweet O						4027	
	Six O							
	Oros/Lecol – with sugar or other						3982	
	- artificially sweetener						3990	
	KoolAid (powder mixed with water)						4027	
	Other							
Fizzy drinks Coke, fanta, etc	Sweetened						3981	
	Diet							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Fruit juice	Fresh/Liquifruit /Ceres						2866	
	Tropica (Dairy –fruit juice mix)						2791	
	Other							
Mageu/Motogo							4056	
Home brew beer							4039	
Beer							4031	
Cider	Sweet						4057	
Spirits Eg Brandy, gin, vodka, whisky, cane, etc							4035	
Wine red							4033	
Wine White							4033	
Other specify								
WATER	Tap, borehole, dam, river, etc						4042	
	Bottled						4042	

SNACKS AND SWEETS								
FOOD	DESCRIPTION	AMOUNT	TIMES EATENComplete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Potato crisps							3417	
Peanuts	Raw						4285	
	Roasted						3458	
Other nuts								
Savoury snack e.g. Fritos, Doritos, Cheese curls, Niknaks							3267	
Raisins							3552	
Peanuts and raisins								
Chocolates	Milk chocolate, plain						3987	
	Kit Kat/ Tex (with wafers) etc						4024	
	Chocolate coated bars like Bar One, TV bar, etc						3997	
	Other							
Popcorn	Plain						3332	
	Sugar- coated/candied						3359	
Candies/Sweets	Sugus, gums, hard sweets, etc						4000	
Toffees / Fudge / caramels							3991	
Biscuits/cookies	Homemade, plain						3233	
	Commercial, plain						3216	
	Commercial, with filling						3217	
	Other							
Cakes	Butter cake, homemade with whole milk and brick margarine NO icing						3288	
	Chocolate cake, homemade with whole milk and brick margarine NO icing						3289	
	Icing for cake made with brick margarine						4014	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Tarts	Apple tart with a batter made with whole milk and brick margarine						3327	
	Other							
Scones	Plain made with whole milk and brick margarine						3237	
	Other							
Muffin	Bran						3407	
	Plain						3408	
	Other							
Rusks	Buttermilk, commercial						3329	
	Homemade, white						3222	
	Other							
Savouries	Sausage rolls, small						2939	
	Samoosas: Meat filling						3355	
	Samoosas: Vegetable filling						3414	
	Biscuits eg bacon kips						3331	
	Other							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Jelly	Jelly						3983	
	Custard added made with whole milk	Yes/No					2716	
	Other							
Baked pudding	Baked in a syrup						3312	
	Baked without a syrup						3429	
	Custard added made with whole milk	Yes/No					2716	
	Other							
Instant pudding	Made with whole milk						3266	
	Made with low fat milk						3395	
	Other							
Ice cream	Regular						3483	
	Soft serve						3518	
	Other							
Sorbet							3491	
Other specify								

SAUCES, GRAVIES AND CONDIMENTS

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		
Tomato sauce							3139	
Worcester sauce							4309	
Chutney							3168	
Pickles							3866	
White sauce	Made with whole milk and brick margarine						3142	
Packet soups	Dry powder (all types)						3158	
	Made with water (all types)						3165	
Gravy	Made from meat and thickened						3120	
Other								

WILD FRUITS, WILD BIRDS, ANIMALS OR INSECTS (hunted in rural areas or on farms)

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN Complete one column				CODE	AMOUNT / WEEK
			Daily Times/ day	Weekly Times/ week	Monthly Times/ month	No		

MISCELLANEOUS: Please mention ANY OTHER FOODS used more than once/two times a week which we have NOT talked about

INDIGENOUS/TRADITIONAL FOODS/PLANTS/ANIMALS

Please tell me if you use any indigenous plants OR other indigenous foods like mopani worms, locusts ect to eat

PLEASE GIVE DETAILS



NuPED

Nutrition during Pregnancy and Early Development

Obstetric ultrasonography sheet

Participant nr

	Phase 1 (<18wks)	Phase 2 (±22wks)	Phase 3 (±36wks)
DATE			
Name of sonographer:			
Number of foetuses:			
Fetal heart present (Y/N):			
Gestational age (GA):	/ Weeks/days	/ Weeks/days	/ Weeks/days
Crown-rump length (CRL):	mm	mm	mm
Biparietal diameter (BPD):	mm	mm	mm
Head circumference (HC):	mm	mm	mm
Abdominal circumference (AC):	mm	mm	mm
Femur length (FL):	mm	mm	mm
Estimated fetal weight (EFW):	g	g	g
EDD:			
Amniotic fluid volume:	cm		cm
	decreased	adequate	increased
	decreased	adequate	increased

Evaluation of the maternal uterus, tubes, ovaries, and surrounding structures:

Comments on fetus and cord:

Plan for follow up scan

Only for phase 2 (22 wks gestation) and phase 3 (36 wks gestation) measurements

Location and appearance of the placenta:



NuPED

Nutrition during Pregnancy and Early De

Anthropometry – Baby



Participant nr:

DATE:																												
FIELDWORKER:																												
WEIGHT (kg)	Phase 5	Phase 6	Phase 7	Phase 8																								
<i>1st Measurement</i>	<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.		
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<i>2nd Measurement</i>	<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.		
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<i>3rd (if needed)</i>	<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.		
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*If difference between 1st and 2nd measurement is more than 0.05 kg, take the 3rd measurement.

Oedema*	Yes	1		Yes	1		Yes	1		Yes	1	
<i>(*If yes, record as AE)</i>	No	2		No	2		No	2		No	2	

Length (cm)	Phase 5	Phase 6	Phase 7	Phase 8																								
<i>1st measurement</i>	<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.			<table border="1" style="width: 100%; text-align: center;"><tr><td></td><td></td><td></td><td>.</td><td></td><td></td></tr></table>				.		
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*If difference between 1st and 2nd measurement is more than 0.2 cm, take the 3rd measurement.

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NuPED

Nutrition during Pregnancy and Early Development

Protocol for Child Monitoring – phase 8 (12 months)

Data collector: _____

Participant no:

Phase:

Date:

	Day	Month	Year
Baby's Date of Birth			
Baby's Age			

Introduce the mother:

“We are going to play some games” (show some materials; explain that games will be played, and that you want the child to enjoy them). The games are chosen for children of all ages, and the purpose of the assessment is to find out which activities your child enjoys and can play. There are no right or wrong answers. We want the child to have fun. It is important for the child to try the games. S/he will try harder if it is enjoyable.”

Explain to the family member who accompanies the child their role – which is to:

- Provide comfort to their child by their presence.
- Encourage the child to participate.
- (If necessary) Help communicate the instructions to the child to help them to understand the game, but NOT to assist the child to complete items.

A. Gross Motor Introduce this section to the child by saying: ENG:“Let us play some games showing me how strong you are.”			
PCM1	IF SITTING=0 Upper body control. Head control (observation). If you observe the child holding his/her head erect without support and turning his/her head to the right and to the left, score this item at the highest level (3).	0	The child is unable to lift his/her head up. The parent must continually support the child's head.
		1	The child is able to hold to lift his/her head erect on his/her own for at least 5 seconds.
		2	The child is able to hold his/her head erect for more than 5 seconds. The parent supports the child's head at any point during the interview. The child is not able to turn his/her head to the right and to the left.
		3	The child is able to hold his/her head up without support throughout the interview. The child is able to control his/her head and turns it to the left and to the right.
PCM2	IF SITTING=0 Lifts upper body. This item should not be administered to a child who is able to walk on his/her own. For children who are not able to sit, place the child on his/her stomach on a flat surface saying: ENG:“Let's lie down like this.” Shake a rattle in front of the child to encourage him/her to lift the front part of the body. Observe and score appropriately.	0	The child is not able to lift his/her upper body.
		1	The child only lifts his/her upper body briefly.
		2	The child attempts to push up his/her chest while lying on his/her stomach.
		3	The child pushes up with his/her arms and holds his/her chest off the ground.

PCM3	IF SITTING=0 Rolls. Place the child on his/her stomach with his/her face turned away from the parent or assessor. Observe and record child's behavior. Softly call out the child's name or use a rattle to encourage the child to turn to face you.	0	The child is not able to roll.
		1	The child rolls from stomach to side.
		2	The child rolls from stomach to back.
		3	The child rolls from side to side.
PCM4	IF STANDING=0 OR WALKING=0 Sitting. Sits with support. Watch the child sitting on the floor, or on the parent's lap. If the child allows you, place the child on your lap and feel the child's strength in the shoulders, neck and lower back.	0	The child falls over or flops forward if left unsupported
		1	The child sits at an angle (leaning on parent) when supported in his/her parent's lap.
		2	The child sits on his/her own with minimal support, e.g. leaning on something, or propped up with pillows, and does not fall over.
		3	The child maintains balance by leaning forward on one or both arms outstretched in a tripod position without falling over.
PCM5	IF STANDING=0 OR WALKING=0 Sits without support. Ask the parent: ENG: "Can the child sit on his/her own? Can s/he sit without falling over, or does s/he need support?"	0	The child is not able to sit without support.
		1	The child can sit briefly without arm support but falls over to the side or backwards after a short while.
		2	The child is able to sit alone for up to 30 seconds at a time before toppling over.
		3	The child is able to sit unsupported (with his/her back straight) for prolonged periods of time. The child's arms are free for exploration.
PCM6	IF STANDING=0 OR WALKING=0 Can reach out and return to sitting position. Place a toy in front of the child an arm's length away. Tell the child: ENG: "Take the toy" The child must move forward to pick up the toy	0	The child is not able.
		1	The child attempts but is unsuccessful.
		2	The child can reach out with two hands but is not stable.
		3	The child can steadily reach out and return to a sitting position and uses only one hand.

	and then return to a sitting position, without losing balance or needing a hand to remain upright. To score at the highest level, the child must pick the toy with one hand. Child can retrieve a toy that is beyond his reach, turn around on his tummy or crawl to reach it.		
PCM7	IF STANDING=0 OR WALKING=0 Moving. Crawls. Establish from the parent what happens when her child wants something that is far from him/her. Ask the parent: ENG:“How does your child move around?”	0	The child is not able to move along the floor.
		1	The child attempts to crawl but is unsuccessful.
		2	The child moves but his/her mid-section is on the ground.
		3	The child is able to make 3 continuous movements in any direction either on his/her hands and knees or on his/hands and bottom (with stomach off the ground).
PCM8	IF STANDING=0 OR WALKING=0 Can move from lying to sitting. Say to the child: ENG:“Come and lie down.” Demonstrate to the child how to lie on the back and then move from lying to sitting without using hands. ENG:“Can you copy me?”	0	The child is not able.
		1	The child needs to be pulled up by the hands to move from lying to sitting; uses much effort or extra support.
		2	The child uses some effort/extra support or his/her hands for balance to move from lying to sitting.
		3	The child moves easily from lying to sitting and does not rely on hands for balance.

PCM9	IF STANDING=0 OR WALKING=0 Static balance. Stands with support. For children younger than 12 months and who are not able to stand on their own, hold the child standing taking all the weight under the child's arms. Gradually release until the child is holding his/her own weight.	0	The child is not able to take his/her full weight or to firmly place both feet flat on the floor when held upright.
		1	The child pushes down with feet on the floor when held.
		2	The child supports his/her whole weight on legs when held.
		3	The child stands while holding on to furniture or object for 10 seconds or more.
PCM10	IF STANDING=0 OR WALKING=0 Stands without support. For children older than 12 months, observe the child as they come into the assessment area. If they come in walking, score this item automatically at the highest level. For children who are just beginning to stand, ask the parent: ENG: "When you leave the child standing, how long does it take before they sit or fall down?" Observe if the child can lean or bend forward to retrieve an object from the floor and then raise himself with or without support.	0	The child is not able. →skip to GMV1
		1	The child stands alone for about 10 seconds.
		2	The child stands alone for 10 seconds to 30 seconds .
		3	The child stands alone steadily for more than 30 seconds .
PCM11	Moves from sitting to standing. Sit on the floor with the child and say to him/her: ENG: "Let's get up." Demonstrate moving from sitting to standing without using hands. Practice with the child and then encourage him/her to do it alone. Observe (does the child twist and turn before getting up?) and record the child's performance.	0	The child is not able to.
		1	The child pulls him/herself into a standing position while holding on to an object for support.
		2	The child twists and turns before getting up; rolls over and up.
		3	The child moves steadily from sitting to standing and does not use hands.
PCM12		0	The child is not able to.

	Can sit down steadily from a standing position. This item should be administered immediately after PCM11 so that the assessor asks the child: ENG: "Now let's sit down again, see my hands, can you copy me? " Demonstrate to the child how to sit down without using hands. Practice with the child and then let him/her do it on his/her own. Observe and record the child's performance.	1	The child sits down unsteadily from a standing position and/or with extra support.
		2	The child uses his/her hands for support.
		3	The child sits down steadily/smoothly from a standing position without using hands.
PCM13	Walks with support. This item aims to establish if the child has good control of the lower limbs and someone only helps with his/her balance. Observe the child moving during the course of the assessment.	0	The child cannot take a few steps forward even when someone is holding on to both hands.
		1	The child moves sideways while holding onto furniture for support (cruising).
		2	The child walks when one or both hands are held, for less than length of mat.
		3	The child walks when one or both hands are held, for length of mat.
PCM14	Walks without support. Does the child move freely on his/her two feet?	0	The child is not able to walk on his/her own; cannot maintain balance. → skip to PCM22
		1	The child attempts to walk alone but is not able to take at least one step. → skip to PCM22
		2	The child walks on his/her own for less than the length of mat. → skip to PCM22
		3	The child walks on his/her own for the length of mat. → go to PCM15
PCM15	Climbs up. Look for and appropriate chair or table, or other large piece of furniture. If no convenient piece of furniture exists ask the parent: ENG: "Does your child climb on a chair to reach	0	The child does not attempt onto furniture, or fails to climb up.
		1	The child climbs up on his her stomach.

	something he wants? What does s/he do to get up, and to get down?" (get the parent to demonstrate if necessary). IF THERE IS furniture: Ask the child: ENG: "Can you climb up there?" Pulling and climbing means the child uses another part of the body to support him/herself (e.g., arms, stomach, belly or bottom). Stepping up means getting up on to the platform like a step, with one foot after the other.	2	The child can climb up, carefully, pulling him or herself up.
		3	The child climbs up, using minimal support for balance.

VALIDITY – GROSS MOTOR			
GMV1	For child assessment sections: Do you believe the test is valid?	0	No
		1	Yes-> SKIP TO END
		88	Not Applicable-> SKIP TO END
GMV2	If not, why not	1	Child was sick
		2	Child was tired or asleep
		3	Child was not cooperative
		4	Child was too shy to engage
		5	Child was upset and crying
		6	Child was not cognitively or physically competent to complete the test
		7	Other, Explain, _____
END	"If gross motor assessment is complete, finalise form to upload and note time of assessment completion."		

PROTOCOL FOR CHILD MONITORING B. FINE MOTOR (PCM37-PCM47)					
START RULE	Standing support	without	☐ ¹ No, Start at PCM 37 ☐ ⁰ Yes → skip to PCM 39		
For Children who start at PCM 37 -- TWO 0s in a row → skip to end					
At the beginning of this section, say to the child: ENG: "Let's sit down to play some more games, come and see the toys I have."					
Stop rule – Stop after failing 2 TASKS (some tasks have more than one item)					
PCM37	Reaches out for moving object. Ask the parent to sit the child on her lap. Hold a wooden ring in front of the child, at the level of his/her nose, within reach. Watch the eyes. Then swing the ring slowly from side to side and ask or encourage the child to: ENG: "Take the ring." Observe and record the child's behavior.		0	The child does not track the moving object. → SKIP TO PCM39	
			1	The child tracks, but unable to grasp object. → SKIP TO PCM39	
			2	The child reaches out, can grasp the still ring, but not the moving ring.	
			3	The child grasps the moving object successfully.	
PCM38	IF PCM37=2 OR PCM37=3 Manipulates object. Observe the child's holding the ring and note if it is passed from hand to hand. Mark the highest activity achieved.		0	The child does not take the object.	
			1	The child brings object toward the mouth for oral contact.	
			2	The child holds and examines object.	
			3	The child passes the object from hand to hand	
PCM39	Picks up object. Say to the child: ENG: "Let's play with these blocks." Place a wooden block on the ground or mat. Point to the block saying: ENG: "Pick up this block." Observe how the child picks up the block.		0	The child is not able to pick up objects on his/her own. Someone must place the object in the child's hands.	
			1	The child is able to pick up the block using the whole hand (with the block on the palm).	
			2	The child picks the block using the thumb and three or four fingers. (Not the palm).	

	For older children this turns into the Tower.PCM42	3	The child picks the block with the thumb and one or two fingers.
PCM40	Retains one object. Offer the child two blocks, one after the other and say: ENG:“Take these blocks.” The child should hold the cubes in either hand, without holding them against his/her body for support. For this item score what happens with the first two blocks.	0	The child is not able to retain one cube. → SKIP TO PCM42
		1	The child attempts to retain one cube but it keeps falling. → SKIP TO PCM42
		2	The child retains the cube in either hand when given.
		3	The child retains one cube when a second one is offered.
PCM41	IF PCM40=2 OR PCM40=3 Retains multiple objects. After offering the third block, watch to see if the child can retain 2 in one hand, and one in another.	0	The child is not able to retain multiple objects.
		1	The child attempts, but can only hold one cube in each hand.
		2	The child can hold 2 cubes in one hand. But cannot take the third without dropping one.
		3	The child retains 2 cubes when a third one is offered.
PCM42	Builds tower. Place 12 cubes in front of the child and say to the child: ENG: “Let’s build a tower.” Demonstrate building a tower by putting one block on top of another. Encourage the child to join in. Break down the tower and say to the child: ENG:“Now you make a big tower.” Encourage the child to continue building the tower. If the blocks fall, encourage the child to build again, up to 3 trials.	0	The child does not/is not able to build a tower.
		1	The child builds a tower of up to 4 cubes.
		2	The child builds a tower of 5-8 cubes.
		3	The child builds a tower of 9-12 cubes.
PCM43 Coin Box. These items test the child’s ability to manipulate small objects, using coins and a moneybox. Place the coin box, with the slot lying from right to left, in front of the child, and 3 coins between the child and the box and say to the child, ENG:“Let’s play with this box and coins.”			

Demonstrate with another coin putting the coin in the slot, then say:			
ENG:“Now you do it.”			
Observe how the child picks the coins, and which hand they chose to use first.			
Place 3 the coins on side of the box of the child’s favoured hand, and say:			
ENG “Now you put in these coins”			
Then swap to the other side, repeat the instruction and watch the other hand.			
PCM43.1	Puts the coins in the box with the slit horizontal, using the right hand.	0	The child is not able to place coins using the right hand.
		1	The child attempts to put the coins in the box but is unsuccessful.
		2	The child puts in 3 coins, trial and error (bumping the box).
		3	The child puts in all 3 coins smoothly.
PCM43.2	Puts the coins in the box using the left hand with the slit horizontal.	0	The child is not able to place coins using the left hand.
		1	The child attempts to put the coins in the box but is unsuccessful.
		2	The child puts in 3 coins, trial and error (bumping the box).
		3	The child puts in all 3 coins smoothly.
IF (PCM43.1=0 OR 1) AND (PCM 43.2=0 OR 1) THEN SKIP TO PCM45			
PCM43.3	IF PCM43.1=2 OR PCM43.1=3 Puts coins in box using the right hand with the slit vertical (rotated box).	0	The child is not able to place coins using the right hand.
		1	The child attempts to put the coins in the box but is unsuccessful.
		2	The child puts in 3 coins, trial and error (bumping the box).
		3	³ The child puts in all 3 coins smoothly.
PCM43.4	IF PCM43.2=2 OR PCM43.2=3 Puts coins in box using the left hand with the slit vertical (rotated box).	0	The child is not able to place coins using the left hand.
		1	The child attempts to put the coins in the box but is unsuccessful.
		2	The child puts in 3 coins, trial and error (bumping the box).

		3	³ The child puts in all 3 coins smoothly.
PCM45 PINCER GRASP. Present 12 beads in a wide mouthed container or bowl. Place another container with a narrow mouth, (such as a small bottle of drinking water, about 4 cms) in front of the child. Say to the child: ENG:“Let’s play with these.” Demonstrate picking the bead with your index finger and thumb using a pincer grasp and say to the child: ENG:“Pick up the bead like this and drop it into this container.” Drop the bead slowly and purposefully into the container. Encourage the child to pick and drop the beads into the container. Observe the child’s performance and record. Do not leave the child unattended with the beads within their reach.			
PCM45. 1	Picks up beads.	0	The child does not pick up any beads. → skip to FMV1
		1	The child attempts to pick up a bead but is unsuccessful. → skip to FMV1
		2	The child uses all his/her fingers and thumb to pick up beads.
		3	The child picks up beads between his/her thumb and forefinger (pincer grasp).
PCM45. 2	Drops beads into container.	0	The child does not attempt. → skip to FMV1
		1	The child attempts to drop beads into container but is unsuccessful. → skip to FMV1
		2	The child makes a clumsy and jerky release of beads into the container.
		3	The child uses a fluid movement to drop several beads into the container.

VALIDITY – FINE MOTOR			
FMV1	For child assessment sections: Do you believe the test is valid?	0	No
		1	Yes → SKIP TO END
FMV2	If not, why not	1	Child was sick
		2	Child was tired or asleep
		3	Child was not cooperative
		4	Child was too shy to engage
		5	Child was upset and crying
		6	Child was not cognitively or physically competent to complete the test
		7	Other, Explain, _____
END	“If gross motor assessment is complete, finalise form to upload and note time of assessment completion.”		

PROTOCOL FOR CHILD MONITORING C.COGNITION (PCM48-PCM52)			
PCM48 Items test the child's recognition of a writing implement (pen, pencil or crayon) and attempt to make a controlled mark on the paper.			
PCM48.1	Holds a pen purposefully. Place the pen/pencil/crayon and paper on a hard surface and say to the child: ENG:“Let's draw.” Ask the child: ENG: “Can you do this?” Observe the manner in which the child picks and holds the pen and record the child's performance	0	The child bangs the pen against the floor or table or uses it another way that is to write or draw. → SKIP TO PCM49
		1	The child holds the pen in a fist or in another way, and attempts to make a mark on the paper.
		2	The child holds the pen with control, but cannot yet copy the shapes.
		3	The child holds a pen with control and can copy shapes.
PCM48.2	IF PCM48.1=1 OR PCM48.1=2 OR PCM48.1=3 Can draw shapes with a pen. ENG:“Can you copy these shapes ? Watch me.” Draw a straight line on the paper, moving from your right to your left. Then draw a circle.	0	The child is not able to make any marks on the paper.
		1	The child can make any kind of mark on paper (scribbles).
		2	The child can copy a straight line.
		3	The child can copy a circle.

Introduce this section by saying:

ENG: "We will play some games of building blocks and matching colours."

PCM49	Removes cubes from containers. Rattle the yellow container in front of the child and then ask the child: ENG: "What's inside?" Give the child the container. With another container demonstrate how to open the lid and remove the cubes. Watch the see if the child copies you. Put back the cubes into the container, cover with the lid, give the container to the child and say: ENG: "Now you try and take them out." Observe and record the child's performance. Observe if the child rattles the container deliberately to make a noise. The child gets the idea that there is something inside the box and intentionally lifts the lid off the container. Observe if the child deliberately takes 1 cube out of the container. (Do not count if the block falls out accidentally.) If the child puts the container upside down so that the cubes fall out, it shows they have adopted an easy strategy to get them out. Give a score at the highest level.	0	The child is not able
		1	The child rattles the box and lifts the lid off box (not knocking over).
		2	The child tries and manages to take one cube out of the box.
		3	The child removes both cubes from the container.
PCM50	Puts cubes into container. Place all three containers in front of the child, and empty them all (if he child joins in spontaneously let them complete the task). ENG: "Let's put all the blocks back now." If necessary demonstrate how to put them back, including replacing the lid. Re-empty the container you have filled, and let the child complete the task alone. Saying, ok, you do it now.	0	The child is not able to return the cubes.
		1	The child puts 1 cube into at least one container.
		2	The child puts 2 cubes into at least one single container.
		3	The child fills all the containers.
PCM51	Puts lid back on container. For the same activity score how the child replaces the lid. Watch the child's eyes and the movement of his/her hands.	0	The child does not follow the instructions (no attempt made to replace the lid).
		1	The child attempts to replace the lid but is not able to.
		2	The child puts lids back, but bangs the lid at the wrong angle before being able to. This level does not require total success,

			only a purposefully attempts to put the cubes and lid back.
		3	The child puts lid back by adjusting the lid to fit the container smoothly. Score at this level if the child deliberately turns the wrist to fit the lid to the container, or twists the box to fit the angle of the lid.
VALIDITY – COGNITION			
COGV1	For child assessment sections: Do you believe the test is valid?	0	No
		1	Yes → SKIP TO END
		88	Not applicable → SKIP TO END
COGV2	If not, why not	1	Child was sick
		2	Child was tired or asleep
		3	Child was not cooperative
		4	Child was too shy to engage
		5	Child was upset and crying
		6	Child was not cognitively or physically competent to complete the test
		7	Other, Explain,

PROTOCOL FOR CHILD MONITORING

D. EXECUTIVE FUNCTION (PCM53-PCM57)

The executive function subscale is made up of two tasks – the Self-control (inhibition) and a working memory task. For younger children (up to 36 months), this is the A-not-B task. For children over 36 months this is the Self-Ordered Pointing Task. The first trial of the Self-control task is administered before, while the second trial is administered after the age relevant working memory task.

PCM53	ALL Self- control, TRIAL 1. Place the board in front of the child. Show the child the reward and say: ENG:“This is your reward. I'll put it on the board. Don't take it until I tell you.” Place reward on well and cover with transparent cup. Back off from the table and act busy. Observe discreetly and record how long it takes the child to go for the reward. If the child waits for more than 30 seconds say: ENG:“Now you can take it.”	0	The child is not interested in the reward.
		1	The child takes the reward immediately.
		2	The child takes the reward after 10 seconds and before 20 seconds.
		3	The child takes a reward after 20 seconds and before 30 seconds

PCM54	A not – B task (10 trials)	
Before you begin this test, ensure the child is sitting comfortably. The child should be seated facing the platform and opposite the assessor. For younger children, it is recommended that the child be placed on his/her parent's lap. Avoid any breaks as far as possible and deal with any potential distractors. Place the board, with the two cups covering the wells, in front of the child and say: ENG:"Do you like this treat? Now look where I'm hiding it." The trial begins when the child looks at the treat and watches where it is being hidden. Open the 2 cups at the same time and slide the treat onto one of the wells. Systematically swap start point for each child you assess, so that you do not always start on the same side. Quickly cover both wells with the cups. Remove the board out of the child's sight, and distract him/her by singing or clapping for the following length of time. 3 seconds for children less than 12 months (say, <i>taatata ta!</i>); 5 seconds for those between 12 and 24 months (count, 1, 2, 3, 4, 5 at the rate of about one number per second); 10 seconds for children aged 25 to 36 months. (sing, <i>A, E, I, O, U, hiziniherufitu!</i>) Return the board to the table and say to the child: ENG:"Now show me where I have hidden it." Let the child remove the cup. If the child looks towards, points or reaches out for one cup, remove the cup so that the child can see if the treat is hidden under it. Mark "correct" if the child successfully retrieves the treat, and "incorrect" if not successful. Repeat the same procedure on the same side until the child gets 2 correct in a row. After two consecutive successful retrievals hide the object in the alternate location. If the child does not respond within 30 seconds, record 'no response.' If the child gets very upset and within 30 seconds cannot be persuaded to look at the treat being hidden, suspend the trials and record 'refusal to participate.'		
Mark		
1. Where the initial treat is with a dot, 2. Where the child chooses (tick for correct, cross for incorrect/error R for no response in both boxes)		
	Left	Right
1		
2		
3		
4		
5		
6		
7		
8		

	9				
	10				
PCM54.1	Total number of valid trials				
	Total number of trials where the child has selected a cup, both correct & incorrect				
PCM54.2	Total number of trials on which a refusal was registered				
PCM54.3	Trial number on which first set was achieved (trial number on which the child achieves the second correct response in a row)				
PCM54.4	Total number correct	0	No correct trials.		
		1	1-5 trials correct.		
		2	6-9 trials correct.		
		3	10 trials correct.		
PCM54.5	Perseverative errors (Count number of times child continues to choose old hiding place after you have swapped sides – that is Errors after each correct set).	0	7-8 perseverative errors.		
		1	3-6 perseverative errors.		
		2	1-2 perseverative errors.		
		3	No perseverative errors.		
PCM54.6	Maximum error run (length of longest run of crosses/errors)	0	10 errors.		
		1	6-9 errors		
		2	1-5 errors.		
		3	No errors.		
PCM54.7	Total number of errors	0	7-8 errors.		
		1	3-6 errors.		
		2	1-2 errors.		
		3	No errors.		

VALIDITY – EXECUTIVE FUNCTION			
EFV1	For child assessment sections: Do you believe the test is valid?	0	No
		1	Yes → SKIP TO END
EFV2	If not, why not	1	Child was sick
		2	Child was tired or asleep
		3	Child was not cooperative
		4	Child was too shy to engage
		5	Child was upset and crying
		6	Child was not cognitively or physically competent to complete the test
		7	Other, Explain, _____

PROTOCOL FOR CHILD MONITORING E. LANGUAGE (PCM58 to PCM79)			
We will use a mixture of parental responses and observation to complete this section. If you have seen/heard the child communicate, use this knowledge to complete the items, and check with the parent about the child's level of development in the home setting.			
EARLY COMMUNICATION SKILLS Before beginning this section, introduce it by saying to the parent: ENG: "I will now ask you a few questions to understand how your child is communicating using sounds, words and gestures." During the assessment, take note of the child's vocalizations. As you play with the child ask questions, give instructions and listen carefully. For younger children, who are not yet speaking repeat different sounds such as aa aa aa, mama, papa, gagaga etc. and observe if the child. If you hear the child making vowel and/or syllable sounds, ask the parent: ENG: "How long the child has been making these sounds/talking?" If you do not notice these sounds during the assessment, ask the mother: ENG: "Does your child make any sounds?" ENG: "What sounds does s/he make?" ENG: "If you talk to him/her and say 'aa aa aa, or 'ba ba ba,' what does s/he say?"			
PCM59 Does the child use recognizable words?			
If PCM59 No (0) Start with PCM 60 If PCM 59 = 1 – Skip to PCM 62 If PCM 59 = 2 Skip to PCM 65			
PCM60	IF PCM59 =0 Repeats vowels in strings. (e.g. aa aaa, or bbbb)	0	The child does not make any sounds, only crying sounds.
		1	The child babbles or mimics one vowel sound.
		2	The child can mimic several vowels sounds.
		3	The child babbles vowels sounds spontaneously much of the time.
PCM61	IF PCM59=0 Repeats syllables in string. (e.g.ma ma ma)	0	The child does not produce any syllable sounds or only makes vowel sounds
		1	The child can make or mimic a sound that consists of both a consonant and vowel, e.g. ba, ma, da.
		2	The child can mimic a babble with 2-4 syllable e.g. mamama, gagaga

		3	The child regularly, several times a day, mimics a babble with 2-4 syllable e.g. mamama, gagaga.
PCM62	IF PCM59=1 Understands gestures to request something. Observation: During the assessment, stretch out your hand and ask the child to pass you an object in front of you both, do not look at or point the object. Then ask the parent: ENG: "If you stretch out your hand to ask the child for something, does s/he always give it to you?"	0	There is no sign that the child understands the gesture
		1	The child understandS the gestures, but makes an inappropriate response.
		2	The child gives the caregiver what has been requested, sometimes.
		3	The child always responds appropriately either by giving the parent the request items, or refuses but shows they understand what the parent wants
PCM63	IF PCM59=1 Uses gestures to communicate. If you have already seen this mark it, but then also check with the parent: ENG: "When your child wants to show you something, what does s/he do?" ENG: "When your child wants something, how does s/he tell you?"	0	The child does not use gestures to communicate. The child only cries when s/he wants something.
		1	The child uses a gesture from time to time.
		2	The child always uses one gesture consistently, and has only one or two more that s/he uses inconsistently.
		3	The child uses several gestures to communicate, which s/he uses consistently.
PCM64	IF PCM59=1 Using sounds instead of words. ENG: "Does the child imitate or has the child ever Imitated animal and other sounds, e.g. 'mee' for goat, 'moo' for cow, 'woowoo' for dog, 'vroom' for car, etc."	0	The child does not make animal sound or other sounds that reflect objects (eg vroom for car) . -> SKIP TO END
		1	The child makes a sound that does not reflect what they hear, imitates incorrectly. (eg moo for car) -> SKIP TO END
		2	The child make a sound that reflects an object accurately but only one animal or object
		3	The child makes sounds that reflect several objects that they see or hear.
PCM 65	START IF PCM 59=2 Demonstrates by word or gesture that s/he understands when told 'no' that s/he should stop. The instruction must be verbal and or accompanied by a gesture. Take note that	0	The child does not pause at/stop what s/he is doing/ give any indication of having understood the word NO.
		1	The child responds to the action of the finger pointing to say no, but not to the word on its own.

	sometimes children understand the command (no) but do not stop because they are disobedient. For example, if s/he pauses and looks at the person who says no, then continues to do what s/he was doing, that shows that s/he understands. This question is about understanding NO, firstly with the gesture, and then the word. The child may also show defiance and get upset that s/he is being told no. does he respond to your tone of voice and stop doing it, even if just for a moment, we are not asking if the child OBEYS, just that they understand the communication. Again start by observing, and then check out the consistency of what you have seen by asking the parent: ENG: "What does your child do when you say 'no' to stop an action that the child is carrying out? (such as touching, pulling scratching, putting things in his/her mouth.)"	2	Sometimes the child will stop what s/he is doing, when s/he hears the word NO, but generally also needs the gesture, the finger as well.
		3	The child consistently demonstrates (by stopping or looking at you or nodding or shaking the head) when the person says 'no'.
PCM66	Understands simple instruction like "come here" or "go away". Ask the parent: ENG: "What does your child do when you say 'come here' or 'go away'?" ENG: "Does s/he understand when you tell him/her to do something simple?" Ask the parent: ENG: "What other instructions can your child follow?"	0	The child cannot follow instructions.
		1	The child can follow simple instructions, but not many and not consistently.
		2	The child follows a few instructions consistently.
		3	The child follows several simple instructions consistently.
PCM 71	Use the following categories to prompt the parent further: ENG: "Apart from the words in the list I read out), are there any other words the child uses for animals, foods, kitchen items, people, clothes, body parts?"		
PCM72	Number of words that child uses. (use information from Vocabulary Section)	0	Uses 1 or 2 words. The child might not pronounce the word correctly but s/he uses the word consistently to refer to the same thing.
		1	Uses up to 10 words, consistently.
		2	Between 11 and 50 words.
		3	More than 50 words.
PCM73	ENG: "Identifies familiar objects."	0	The child cannot identify any object.
		1	1- 5 objects.
		2	6- 10 objects.

		3	More than 10 objects.
PCM 74	ENG: "Identifies body parts."	0	The child is not able to identify any body part.
		1	1-2 body parts.
		2	3-5 body parts.
		3	More than 5 body parts.
PCM76	Uses 3 word combinations. During the assessment, listen for any 3 component sentences that the child uses spontaneously and appropriately in reference to a specific object or person, e.g. 'red cup' or 'mummy here.' If you do not hear any words during the assessment, ask the parent: ENG: "If your child wants something, how does s/he say it?" ENG: "Have you heard him say two/three words together to try and make a sentence?"	0	The child says only one word at the time. (The child can say 2 words but they do not go together in a sentences, for example mama, dada.)
		1	The child regularly uses two words together in the early form of sentences, for e.g. "give water" or "want that".
		2	The child uses a mixture of 2 and 3 part sentences.
		3	The consistently uses sentences with at least 3 parts when appropriate. (I want milk, I am sleepy.)
PCM77	Can sing songs. Ask the parent: ENG "Can your child sing a song? Does s/he use the correct words?"	0	The child does not sing with words.
		1	The child can join in a song with some words.
		2	The child can sing a song, but does not get all the words correct.
		3	The child can sing a whole song correctly. (At least one.)

LAEND END TIME: : 24 hour clock.			
VALIDITY – LANGUAGE			
LAV1	For caregiver report sections: Do you believe the test is valid?	0	No
		1	Yes
LAV2	If not, why not	1	Caregiver did not appear to understand questions
		2	Caregiver report did not seem accurate with examiner observations
		3	Caregiver did not seem interested
		4	Caregiver seemed to give answers to please the examiner
		5	Caregiver did not seem to know child well enough to answer with accuracy
		6	Other, Explain, _____
LAV3	For child assessment sections: Do you believe the test is valid?	O ¹ Yes O ⁰ No	
LAV4	If not, why not	1	Child was sick
		2	Child was tired or asleep
		3	Child was not cooperative
		4	Child was too shy to engage
		5	Child was upset and crying
		6	Child was not cognitively or physically competent to complete the test
		7	Other, Explain, _____

PROTOCOL FOR CHILD MONITORING			
H. EMOTIONAL DEVELOPMENT			
PCM103	Feeding. ENG: "Tell me about the appetite of your child. What happens when you feed your child? How was your child eating in the last one month time? When comparing your child with other children of the same age can you say whether your child likes eating or not?" (Can also refers to drinking when not on solids yet)	0	Always major issue. Runs away at the sight of food/ has to be forced to eat at every meal/ may spit food out.
		1	Mild issue. Sometimes refuses different types of foods and/ or needs managing at mealtimes.
		2	Not an issue. Eats all foods/happy to eat, maybe only an odd exception (e.g. specific dislikes).
PCM104	Going to bed. ENG: "How will you know your child is sleepy? Children shows different behaviours when they are sleepy, some may cry, some may just lie down on the ground anywhere and sleep, and others easily go to bed to sleep. How does your child behave when he/she is sleepy? Does your child behave the same way most of the times or always?"	0	Trouble sleeping happens every night. The child requires special and extensive routine to go to sleep.
		1	May have trouble falling asleep but only once in a while.
		2	O ² Has no trouble falling asleep.
PCM108	Jealousy. ENG: "Does your child show jealousy of others some of the time? When you carry another child apart from your child or give to other children your child's toys to play with, how does your child respond to that?"	0	Hits, bites or kick the parent or the items of jealousy. Cries or throws a tantrum on seeing the parent carrying another child. Pushes or attacks the person they think is taking their place.
		1	Sometimes, some particular instances trigger displays of jealousy, but the jealousy is not violently expressed e.g the child may just cry or lean on the parent complaining or wanting to be carried.
		2	Is not jealous in instances that may trigger jealousy.
PCM109	Reaction to parent's departure. <i>For children 11 months and younger it is important that they do show distress. For these children some distress 01 = 0 , 02 = 1 and 00 = 2</i>	0	The child cries when the parent is leaving and this continues even after the parent's departure. The child hangs on to the parent and delays the parent's departure. The parent has to hide to get away. (Ask for the regularity).
		1	Okay sometimes. The child can cries a bit and needs to be distracted. Keeps quiet after you leave and can stay comfortable after that. The child does not show extreme distress.

	ENG: "What happens to your child when sees you going?"	2	The child shows little or no distress at the caregiver's departure but settles down before you leave. Distress does not delay departure.
PCM110	Independence in daily tasks. (This is about how much help they seek, not what they can and cannot do) ENG: "What are the things your child tries to do for him or herself? Does h/she demand help for activities that they can do for themselves. These are things like eating, dressing and drinking. Does your child try to do some of these things by him or herself? Or does he/she want it done for him/her by someone else? Is there something your child can do by him/herself but refuse to do? Or because he/she wants you or someone else to assist?"	0	Sits there and expects everything to be done for him/her, even those tasks that the child CAN do alone.
		1	Sometimes tries to help themselves with daily living tasks.
		2	The child tries to do things on her/his own e.g. attempts to feed self, tries to remove panty for the younger child. For the older child, e.g. dressing, washing, tidying up. Exception is when the child is sick.
PCM115	Anger management. ENG: "what does your child do when she/he is angry? Does he/she get angry quickly? Is s/he short tempered?"	0	Often gets very upset/ angry. Could be several times a day, and takes a while to calm down.
		1	Can get upset or angry, but not often, and then needs some consoling to calm down.
		2	Can get upset, but not very upset/ angry; easily consolable.
PCM114	Hits, bites or kicks you, or other parents. ENG: "How does your child behave when his/her toys are taken away by you or any other parent, or s/he is stopped from going out, or denied something like a ball, or any other thing? Does s/he ever hit or kick you? When did he/she do that?"	0	Does it daily.
		1	Sometimes, for some reason or in context e.g. like when denied something very important to him/her
		2	Never been observed.
PCM 116	Cries or throws tantrums until s/he is exhausted. ENG: "Does your child screams loud and rolling on the ground when crying or when angry? When was the last time she/he did that? How long does he/she take to calm down? (duration)"	0	Very frequent or daily tantrums that endanger the physical wellbeing of the child/child is very violent to the point of exhaustion.
		1	Tantrums but very occasionally (not even weekly).
		2	May cry but no tantrums/ violent expression of anger when upset/angry.

PCM117	Solving disputes. ENG: "Who can calm the child down? What does your child do when playing with some other children then one of them upset him/her while you are not around?"	0	Not able to regulate emotion even with help, difficult to console
		1	The child's first response is to look for the parent/caregiver in the face of adversity and s/he never even attempts to solve own problem and quarrels, tries to escape
		2	Young child: Easily calmed, Depends on your proximity to him/her but can sometime comfort self. Older child: Does not rely on you to solve their quarrels/can comfort self.
PCM124	Mood: Inappropriate happiness or sadness ENG: "What are the things that make your child happy or sad? In the past one month was he/she happy or sad often? Was he/she laughing or crying without a reason?(frequency)	0	Extreme problem requiring major change to family organization
		1	Some/ limited problem, perhaps requiring some changes in family structure or some extra guidance, monitoring and support
		2	Family sees the child as even tempered, not requiring special support or strategies.
PCM 92	Follows a moving person with eyes. ENG: "If someone else is holding the baby and you are talking while moving around the room, how will the baby react?" Have you seen the baby try to search for you and follow you with his/her eyes?	0	Does not look in your direction or show interest.
		1	Follows a moving person with his/her eyes only very briefly.
		2	Shows interest by looking at you when you are in front of them, but rarely follows you as you move away.
		3	Follows a moving person with eyes and shows interest in her.
PCM93	Responds to vocalization. ENG: "When you talk to your child, what does s/he do?" (Does/he smile or talk back at you?)"	0	The child does not react in anyway.
		1	The child smiles in response to the parent talking to him/her.
		2	The child sometimes vocalizes when talked to.
		3	The child always vocalizes when talked to.
PCM94	Child can select a person to comfort them. ENG: "When your child is upset and you try to comfort him/her, what does s/he do?"	0	The child is not comforted by any adult.
		1	The child can be comforted by an adult, and reacts to all adults, including the parent, in the same way.
		2	If the child is crying or fussing, the child prefers to be comforted by a familiar person, particularly the parent.
		3	When upset the child looks for a specific person to comfort her/him.

PCM95	Recognizes other people. ENG: "Does your child know other people? How do you know that?"	0	The child react the same way to both family members and visitors; the child does not distinguish one from the other.
		1	The child can distinguish strangers from the familiar people; for instance, the child may cry when held by a stranger.
		2	The child seeks contact from familiar people; for instance, if the parents come back home, the child reaches out for them to hold him/her.
		3	
PCM96	Reacts to own name. Call the child's name and observe his/her reaction. If the child turns and looks at you: ENG: "How long has the child been doing this? If you call your child's name, what does/he do?" Ask the caregiver " Call the child's name."	0	The child does not react to his/her name.
		1	The child reacts in the same way as to any other name or word.
		2	The child clearly reacts to his/her name and recognizes that s/he is being called. For e.g. the child turns his/her head toward the person who is called his/her name.
		3	The child turns toward the person and vocalizes a response.
PCM97	Plays with others. This item is about how close they are to others when they play, it is not about how well they co-operate (such as fights etc). That is covered in emotional development below. ENG: "What happens when your child is playing and other children are around? Have you seen your child look at what other children are doing and show an interest in them? Have you seen him/her play next to other children? Have you seen him/her join in games and play together with other children?"	0	The child sits alone and does not watch other children who are nearby. The child shows no interest in others playing around him/her.
		1	The child watches other children who are playing. The child is interested in what other children are doing.
		2	The child plays next to other children and watches them. Each child plays individual games but they are playing next to each other and watching each other
		3	The child plays games with other children. The children are interested in playing the game together.
PCM80	Dresses self. Ask the parent: ENG: "How does your child get dressed? How much help do you give?" "Is your child able to get dressed by him/herself without any help? What does your child do when you want to dress him/her? Does s/he reach	0	The child is unable to dress him/herself.
		1	The child tries to raise or reach out hands to help the person dressing him/her.
		2	The child is able to put on most of his/her clothes but need help with some things, for example. Buttons/ zippers or lacing up shoes.

	out his/her hand to help dress him/herself? Does he push his arm through once it is in the sleeve? Can put on his own shirt, sweater or coat, if you put his pants, underwear or skirt at his feet, can your child pull the clothes on completely until his/her waist is reached?"		
		3	The child can completely dresses on his/her own without any help, even with buttons and zippers and tying shoes.
PCM81	Undresses self. Ask the parent: ENG:"Is your child able to take his/her clothes off on his/ her own? Can child undress himself by taking off clothing such as socks, cap, shoes or gloves? " Removing something simple like a hat or kicking off very loose socks does not qualify as undressing self.	0	The child is unable to undress him/herself or can only remove something simple like a hat.
		1	The child tries to get out of clothes when being undressed.
		2	The child is able to remove his/her pants or socks without help from another person.
		3	The child undresses him/herself completely on his/her own without help from another person.
PCM82	Drinks from a cup. Ask the parent: ENG:"How does your child drink liquid? Does your child drink anything from a cup? How much help does the child need?"	0	The child is not able to drink from a cup
		1	The child is able to drink from a cup, but with many spillage
		2	The child can partially hold the cup and drink from it but still needs help from the parent.
		3	The child can hold the cup to his/her lips and drink on her/his own. The parent does not need to help in any way.
PCM83	Feeds self. Ask the parent: ENG:"Is child able to feed him/herself? Does s/he use her/his hands or a spoon? Does some of the food spill when s/he is eating?"	0	The child is unable to feed him/herself.
		1	The child tries to feed him/herself with fingers, but often drops the food. Spillage allowed.
		2	The child can use a spoon. Some spillage allowed.
		3	The child is able to use his/her hands or a spoon to feed him/herself without any spillage.
PCM84	Controls bladder. ENG: "How long before you have to change your child's undergarments? Can your child stay dry for an hour without peeing on him/herself? "	0	Not able to stay dry.
		1	Stays dry for most of the day / The child may still wet the bed at night.
		2	The child stays dry for most of the day and most nights.
		3	Stays dry for the whole day/ and most nights.
PCM85	Indicates when wet ENG:"Does your child indicate when s/he has peed on	0	Does not indicate, parent always has to check.
		1	Cries or gets fussy when wet, sometimes.
		2	Always cries or gets fussy when wet.

	her/himself and s/he is wet? For instance, does your child cry, get fussy or tell you when s/he's wet?"	3	Tries to remove the wet item of clothing.
PCM86	Indicates when wants to pee. ENG: "What does your child do when s/she wants to pee? Does s/he get fussy or point to the toilet?" (Does s/he tell you with words?) "	0	The child does not indicate in any way that s/he wants to pee.
		1	The child cries, gets fussy or pointed to the toilet when s/he wants to pee.
		2	The child tells someone with words that s/he want to pee.
		3	The child goes to the toilet by him/herself.
PCM87	CONTROLS BOWEL MOVEMENTS. ENG: "Does your child ever soil him/herself? Is s/he clean all of the time? "	0	The child still soils him/herself.
		1	The child sometimes has one or two accidents in a day
		2	The child is rarely dirty by day and is clean most of the time.
		3	The child's bladder and bowel control is complete and s/he is rarely dirty by day or night.
PCM88	Activity/ tiredness/ lethargy Instruction: Ask the mother, ENG: "At what level does your child perform regular activities?" "How often does s/he show lethargy in regular activities?"	0	Low energy level, child unable to take part regularly in activities
		1	Child can only attempt activities of a short length
		2	Child active, but needs encouragement to start and or complete activities
		3	Child very active, begins activities alone, and keeps going until completed or has moved to another activity

EDEND END TIME: : 24 hour clock.			
VALIDITY – LANGUAGE			
LAV1	For caregiver report sections: Do you believe the test is valid?	0	No
		1	Yes
LAV2	If not, why not	1	Caregiver did not appear to understand questions
		2	Caregiver report did not seem accurate with examiner observations
		3	Caregiver did not seem interested
		4	Caregiver seemed to give answers to please the examiner
		5	Caregiver did not seem to know child well enough to answer with accuracy
		6	Other, Explain, _____
LAV3	For child assessment sections: Do you believe the test is valid?	O ¹ Yes O ⁰ No	
LAV4	If not, why not	1	Child was sick
		2	Child was tired or asleep
		3	Child was not cooperative
		4	Child was too shy to engage
		5	Child was upset and crying
		6	Child was not cognitively or physically competent to complete the test
		7	Other, Explain, _____