

Associations of dietary patterns during pregnancy with perinatal fatigue and depression among urban women in South Africa: The NuPED study

V Smith
21676496



orcid.org/0000-0001-5573-3955

Research proposal for the Dissertation submitted in *partial* fulfilment of the requirements for the degree *MSc* in Dietetics at the North-West University

Supervisor: Prof Jeannine Baumgartner
Co-supervisor: Ms Cornelia Conradie

18 December 2020

SOLEMN DECLARATION AND PERMISSION TO SUBMIT

1. Solemn declaration by student

I, **Vincent Smith**

declare herewith that the thesis/dissertation/mini-dissertation/article entitled (**exactly as registered/approved title**),

Associations of dietary patterns during pregnancy with perinatal fatigue and depression among urban women in South Africa: The NuPED study

which I herewith submit to the North-West University is in compliance/partial compliance with the requirements set for the degree:

Magister Scientiae (MSc) in Dietetics

is my own work, has been text-edited in accordance with the requirements and has not already been submitted to any other university.

LATE SUBMISSION: If a thesis/dissertation/mini-dissertation/article of a student is submitted after the deadline for submission, the period available for examination is limited. No guarantee can therefore be given that (should the examiner reports be positive) the degree will be conferred at the next applicable graduation ceremony. It may also imply that the student would have to re-register for the following academic year.

Ethics number:

NWU-00186-15-A1-06

ORCID:

0 0 0 0 - 0 0 0 1 - 5 5 7 3 - 3 9 5 5

Signature of Student

**Vincent
Smith**

Digitally signed by
Vincent Smith
Date: 2020.12.09
14:09:50 +02'00'

University Number

2 1 6 7 6 4 9 6

Signed on this day of of 20

2. Permission to submit and solemn declaration by supervisor/promoter

The undersigned declares that the thesis/dissertation/mini-dissertation/article:

- ☒ complies with the A-rules and the technical requirements provided for in the Manual for Master's and Doctoral studies and in faculty rules;
- ☒ has been checked by me for plagiarism (by making use of TurnItIn software for example) and a satisfactory report has been obtained;
- ☒ and that the work was language edited before submission for examination.

Faculty specific requirements as per A-rules: 1.3.2, 433, 4.2.4, 4.10.4, 5.3.2

- ☒ complies with regards to faculty rules on submission or acceptance by an accredited scientific journal;
- ☒ complies with regards to faculty rules on peer reviewed conference proceedings;
- ☒ the student is hereby granted permission to submit his/her article/mini-dissertation/ dissertation/thesis for examination.

Signatures of supervisor(s) and Promoter(s): (only compulsory in cases where there are co- or assistant- supervisor(s/promoters))

**Jeannine
Baumgartner**
Supervisor/Promoter
Digitally signed by
Jeannine Baumgartner
Date: 2020.12.16
16:35:31 +01'00'

**Cornelia
Conradie**
Co-Supervisor/Co-Promoter
Digitally signed by
Cornelia Conradie
Date: 2020.12.16
21:22:18 +02'00'

Assistant-Supervisor
Assistant-Promoter

ACKNOWLEDGEMENTS

Without Prof Marius Smuts, this study wouldn't have been possible. Not only because he was the principal investigator but also because of his role in this sub-study specifically. Thank you, Prof Smuts, for not only inspiring me to pursue a postgraduate degree but also motivating me to do so.

I was very fortunate to have a supervisor familiar with the emerging field of nutritional neuroscience (nutritional psychiatry). Thank you, Prof Jeannine Baumgartner for sharing your expertise and providing guidance with regards to data management, statistical analysis and academic writing.

My co-supervisor, Ms Cornelia Conradie was also instrumental in this work. Thank you for assisting with statistical analysis as well as academic writing. Thank you for all your input with regards to editing and teaching me the finer points of academic writing.

I would like to thank my family starting with my parents, Robert and Waldette Smith. You have always supported, encouraged and motivated me in my studies. Thank you for your always believing in me. Thank you to my brother, John-Robbert Smith and my sister-in-law, Sandra Lawrenson who always supported me and reminded me of the importance of a healthy work-leisure balance.

To my friend, Tenique van Der Merwe, thank you very much for all your support and motivation through this process. I admired your inquisitive nature regarding my research and I enjoyed explaining the smaller intricate details to you.

Finally, to my husband Steyn Geldenhuys, thank you for listening to my ideas and for your constant support. You kept a constant coffee supply from dusk till dawn, which helped significantly. Thank you for your compassion and motivation.

ABSTRACT

Background: Perinatal depression is a serious problem worldwide and the prevalence is higher in low- and middle-income countries (LMIC) than in high-income countries (HIC). The South African prevalence of perinatal depression is estimated to be four times the global average. One of the potential risk factors for depression is an unhealthy diet, which women from LMIC have a higher risk of developing than women from HIC. An “unhealthier” diet has been associated with higher depressive symptoms during the perinatal period. Perinatal fatigue is common and has also been shown to have a bi-directional relationship with depression.

Objectives: The aim of this study was to investigate the association between dietary patterns during early pregnancy and perinatal depression and fatigue among women.

Methods: Forming part of the Nutrition during Pregnancy and Early Development (NuPED) study, dietary data were obtained at enrolment (< 18 weeks gestation) using a quantified food frequency questionnaire from which nutrient patterns were determined by means of exploratory factor analysis. The Edinburgh Postnatal Depression Scale (EPDS) was used to assess depressive symptoms and the Multidimensional Assessment of Fatigue (MAF) scale to measure fatigue at three time points during pregnancy and two postnatally.

Results: The prevalence of perinatal depression ranged from 17.3% to 26.4% and perinatal fatigue ranged from 8.4% to 18.8% across the various time points. Three nutrient patterns were identified: 1) “Plant protein, iron, thiamine and folate”, which decreased the risk of fatigue at 6 months postnatally. This decrease in risk was attributed to the B-vitamins, iron and zinc present in the nutrient pattern; 2) “Animal protein, vitamin A, vitamin B₁₂ and copper”, which increased the risk of depression at 12 months postnatally. The increased risk of depression may be due to the high meat content of the nutrient pattern; 3) “Fatty acids and sodium” which increased the risk for depression at 6 months postnatally. A possible reason for this increased risk of depression may be the high amount of saturated fatty acids in the nutrient pattern. Perinatal fatigue was also found to be positively associated with perinatal depression.

Conclusion: This research illustrates the potential role of maternal diet during pregnancy in the development of maternal fatigue and depression.

Keywords: perinatal fatigue, perinatal depression, dietary patterns, nutrient patterns, antenatal, pregnancy.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS.....	ii
ABSTRACT.....	iii
LIST OF TABLES	VIII
LIST OF FIGURES.....	IX
LIST OF ABBREVIATIONS	X
LIST OF DEFINITIONS.....	XI
CHAPTER 1: INTRODUCTION.....	1
1.1 Rationale for the study	1
1.2 Background.....	2
1.2.1 The use of dietary and nutrient pattern analysis in investigating the role of maternal diet in perinatal fatigue and depression	3
1.3 Research aim and objectives.....	4
1.3.1 Research aim	4
1.3.2 Research objectives.....	4
1.4 The larger NuPED study	5
1.5 Ethical approval.....	6
1.6 Dissertation outline	6
1.7 Research team	7
REFERENCES.....	8

CHAPTER 2: LITERATURE REVIEW	11
2.1 Perinatal depression	11
2.2 Prevalence of perinatal depression	11
2.3 Potential causes of perinatal depression	13
2.4 Consequences of perinatal depression	16
2.4.1 Pregnancy and birth outcomes	17
2.4.2 Early developmental outcomes	18
2.5 Screening tools for perinatal depression	21
2.6 Perinatal fatigue	22
2.7 Prevalence of perinatal fatigue	22
2.8 Potential causes of perinatal fatigue	23
2.9 Consequences of perinatal fatigue	24
2.10 Screening tools for perinatal fatigue	24
2.11 The role of maternal diet in perinatal depression and fatigue	25
2.12 Dietary trajectory across pregnancy	25
2.13 Dietary patterns and perinatal depression and fatigue	26
REFERENCES	32
CHAPTER 3: STUDY ARTICLE	42
1. INTRODUCTION	42
2. MATERIALS AND METHODS	44
2.1. Study design and participants	44

2.2. OUTCOME MEASUREMENTS.....	44
2.3. EXPOSURE MEASUREMENTS	44
2.4. COVARIATES.....	45
2.5. STATISTICAL METHODS.....	45
2.6. ETHICAL CONSIDERATIONS.....	46
3. RESULTS.....	46
3.1. Subject Characteristics	46
3.2. Nutrient patterns	46
3.3. Depression and Fatigue	47
3.4. Associations of fatigue scores with dietary data.....	49
3.5. Associations of depression scores with dietary data	50
3.6. Associations of depression scores with fatigue scores.....	51
4. DISCUSSION	51
5. CONCLUSIONS.....	53
REFERENCES.....	53
CHAPTER 4: SUMMARY AND CONCLUSION	59
4.1 Summary	59
4.2 Strengths and limitations.....	59
4.3 Recommendations on future research.....	60

REFERENCES.....	61
APPENDIX 1: SOCIO-DEMOGRAPHIC QUESTIONNAIRE	62
APPENDIX 2: MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE.....	64
APPENDIX 3: EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS-10).....	67

LIST OF TABLES

Table 1: NuPED inclusion and exclusion criteria at sampling.....	5
Table 2: Characteristics of participants at the time of enrolment (< 18 weeks) into the NuPED study.....	47
Table 3: Nutrient patterns and factor loadings extracted through factor analysis (n = 250)	48
Table 4: Associations between perinatal fatigue (GFI total score) and nutrient patterns (factor scores)	49
Table 5: Associations between perinatal fatigue (GFI > 28) and nutrient patterns (factor scores)	49
Table 6: Associations between perinatal depression (EPDS total score) and nutrient patterns (factor scores).....	50
Table 7: Associations between perinatal depression (EPDS ≥ 9) and nutrient patterns (factor score)	51
Table 8: Associations between perinatal fatigue (GFI scores) and depression (EPDS scores)	51

LIST OF FIGURES

Figure 1: Possible underlying mechanisms responsible for the associations between child
outcomes and parental psychiatric disorders (Stein *et al.*, 2014:1813) 16

Figure 2: Prevalence of perinatal depression, suicidal ideation and fatigue across various time
points. 48

LIST OF ABBREVIATIONS

HIC:	High Income Countries
LMIC:	Low- and Middle-Income Countries
SA:	South Africa
HIV:	Human Immunodeficiency Virus
WHO:	World Health Organization
RMMCH:	Rahima Moosa Mother and Child Hospital
MDGs:	Millennium Development Goals
UN:	United Nations
SDGs:	Sustainable Development Goals
KZN:	KwaZulu Natal
HPA:	Hypothalamic-Pituitary-Adrenal
CRH:	Corticotrophin-Releasing Hormone
BMI:	Body Mass Index
NICUs:	Neonatal Intensive Care Units
ALSPAC:	The Avon Longitudinal Study of Parents and Children

LIST OF DEFINITIONS

Antenatal/Prenatal:	The period during pregnancy
Postnatal/Postpartum:	The period after pregnancy
Perinatal/Peripartum:	The period during and/or up to one year after pregnancy (the antenatal and post-natal period combined)
Unipolar depression:	Clinical depression/major depressive disorder/major depression
Relapse:	A deterioration in an individual's state of (mental) health after a temporary improvement
Gravidity:	A woman's number of previous pregnancies
Parity:	A woman's number of previous births
Non-perinatal:	Not occurring within the perinatal period
Apgar score:	A method to quickly summarize the health of new-born children against infant mortality
Undervaccination:	Selective, partial or delayed vaccination
Plasticity:	The capacity of an individual organism to alter its behaviour, morphology and physiology/gene expression in direct response to changing environmental conditions

CHAPTER 1: INTRODUCTION

1.1 Rationale for the study

Depression within the perinatal period is a serious health problem worldwide (Woody *et al.*, 2017:89). In low- and middle-income countries (LMIC) the prevalence of perinatal depression is higher than in high-income countries (HIC) (Manikkam & Burns, 2012:940). This might be due to maternal mental health being largely neglected in LMIC (Honikman *et al.*, 2012:1). In South Africa (SA) the prevalence has been estimated to be as high as four times the global average (Manikkam & Burns, 2012:940; Rochat *et al.*, 2011:362; Tuthill *et al.*, 2017:5; van Heyningen *et al.*, 2016:7). Maternal fatigue is also concerning and seems to have a bi-directional relationship with perinatal depression (Giallo *et al.*, 2016:32; Kuo *et al.*, 2012:216).

Poor dietary quality has been identified as a potential risk factor for perinatal depression (Baskin *et al.*, 2015:42; Pina-Camacho *et al.*, 2015:1857). The risk of poor dietary quality during pregnancy is higher in LMIC than in HIC (Baskin *et al.*, 2015:46; Fowles *et al.*, 2012:6). The relationship between diet quality and mental health is hypothesised to be bi-directional whereby they both influence each other (Baskin *et al.*, 2015:46).

It is of major public health relevance that research into the association between antenatal diet and maternal mental health outcomes continues (Baskin *et al.*, 2015:46). In order to fully explain the relationship between maternal perinatal diet and mental health, more high quality studies are required (Silva *et al.*, 2019:12).

Recent epidemiological studies are focusing on dietary pattern (eating pattern) analysis. Dietary pattern analysis is a composite measure of dietary quality (Cespedes & Hu, 2015:899). Dietary patterns can be generated empirically by means of statistical methods without the need of researchers to define a healthy eating pattern (Newby & Tucker, 2004:177). Statistical methods commonly used to empirically derive dietary patterns include principal component analysis, factor analysis and cluster analysis (Cespedes & Hu, 2015:899; Newby & Tucker, 2004:177). Dietary patterns encompass the totality of the diet while also allowing multiple ways to achieve a healthy diet. Public health recommendations and guidelines could be most easily translated into eating behaviours when described by dietary patterns (Cespedes & Hu, 2015:899).

1.2 Background

Perinatal depression refers to the occurrence of depression during the antenatal and/or postnatal period (up to 12 months after delivery) (Leung & Kaplan, 2009:1566). Perinatal depression shares signs and symptoms with unipolar depression (clinical depression) in the general population. These symptoms include depressed mood, feelings of low self-worth or guilt, changes in appetite, disturbed sleep, fatigue, loss of interest or pleasure in all or most activities, and poor concentration (Gelaye *et al.*, 2016:2; Howard *et al.*, 2014:1777; Leung & Kaplan, 2009:1566). A complex, multi-factorial aetiology has been highlighted by many studies investigating risk factors involved in the onset of antenatal (during pregnancy) depression and anxiety (Biaggi *et al.*, 2016:74). Biaggi *et al.* (2016:64) identified various environmental, psychosocial, antenatal and obstetric related risk factors for developing antenatal depression and anxiety.

Gelaye *et al.* (2016:2), employing a systematic review, found the prevalence of antenatal depression to range between 7% and 15% in HIC and between 19% and 25% in LMIC. The prevalence is significantly higher in LMIC compared to HIC (Fisher *et al.*, 2012:143; Gelaye *et al.*, 2016:2; Lara *et al.*, 2015:18; Redinger *et al.*, 2018:31; Woody *et al.*, 2017:89). The South African prevalence of perinatal depression varies across studies, ranging from 22% to 49% (Manikkam & Burns, 2012:940; Rochat *et al.*, 2011:362; Tuthill *et al.*, 2017:5; van Heyningen *et al.*, 2016:7). Risk factors identified in SA include the increasing threat of human immunodeficiency virus (HIV), intimate partner violence, high-risk suicide, food insecurity and hazardous drinking (Dewing *et al.*, 2013:5; Tsai *et al.*, 2016:9; Tsai *et al.*, 2014:9).

Antenatal depression is associated with an increased likelihood of epidural analgesia during labour as well as an increased likelihood of planned caesarean delivery (Gentile, 2015:4; Goodman, 2019:218). Postnatal depression affects the caregiving ability of the mother, which can have long-term effects on her child (Glover, 2014:31; Hartley *et al.*, 2011:1; Honikman *et al.*, 2012:1; Woody *et al.*, 2017:86).

Antenatal fatigue has been associated with poor foetal development, early-onset labour, caesarean section, as well as poor child motor- and mental development (Cheng *et al.*, 2015:64; Cheng & Pickler, 2014:1). Antenatal stress has also been shown to cause negative obstetric outcomes including pregnancy-induced hypertension, poor foetal development, earlier delivery, and lower birth weight for gestational age (Cheng & Pickler, 2014:1; Glover, 2014:26).

1.2.1 The use of dietary and nutrient pattern analysis in investigating the role of maternal diet in perinatal fatigue and depression

Nutrient demands from the foetus, which constantly change over various developmental stages, necessitate the need for a maternal diet during the antenatal period with enhanced nutrient density. Some micronutrients, such as zinc, iron, vitamin D, selenium and folate, were found to be inversely associated with depressive symptoms (Baskin *et al.*, 2015:42).

Within dietary data there is a large number of correlated dietary variables (food groups, individual foods, nutrients or biomarkers) (Moskal *et al.*, 2014:2). Nutrition research has traditionally mainly focused on single nutrients or specific foods (Cespedes & Hu, 2015:899). This approach has methodological limitations, such as the inability to detect small effects from single nutrients, as well as failing to account for interactions and intercorrelations between nutrients (Newby & Tucker, 2004:177). A conceptual limitation is that people don't consume nutrients in isolation; they consume meals comprised of a variety of foods and a complex combination of nutrients (Hu, 2002:3; Newby & Tucker, 2004:178). Therefore, studies using traditional methods cannot account for how these elements may act in combination and is inelegant in providing tangible dietary advice (Newby & Tucker, 2004:178).

More recently, epidemiological studies started focusing on dietary pattern analysis, as dietary patterns aim to describe the diet as a whole (Previdelli *et al.*, 2016:1). Dietary patterns are defined as “the quantities, proportions, variety, or combination of different foods, drinks, and nutrients in diets, and the frequency with which they are habitually consumed”. In terms of overall disease risk reduction, dietary components (nutrients) are the same as dietary patterns (Dietary Guidelines Advisory Committee, 2020:4). This gives researchers the opportunity to use a range of foods to customize the dietary patterns to meet their needs. Foods can be included to align with cultural and religious practices, food availability, sensory appeal and income. This pattern is flexible and customizable irrespective of the designated research label (Dietary Guidelines Advisory Committee, 2020:8). As a complementary strategy to a single food or nutrient approach, dietary pattern analysis captures the intrinsic complexity of the diet, the inter-relationship between different components and the heterogeneity in food or nutrient patterns (Moskal *et al.*, 2014:2). Dietary pattern analysis is an alternative method of measuring dietary exposure due to limitations of the traditional approach (Newby & Tucker, 2004:177). Additionally, dietary patterns may have a stronger association with outcomes than any individual items contributing towards it (Hodge & Bassett, 2016:191).

Dietary pattern analysis can be approached in two main ways, *a priori* and *a posteriori* (Hodge & Bassett, 2016:191). *A priori* methods define dietary patterns theoretically and is often referred to as “measures of dietary quality” (Hodge & Bassett, 2016:191; Newby & Tucker, 2004:177). This is

usually achieved by predetermining an “ideal” diet and assessing agreement between dietary data and the “ideal” diet. This agreement is typically assessed using scores or indices (Hodge & Bassett, 2016:191). Various indices have been proposed for assessing overall dietary quality and are typically based on dietary recommendations (Hu, 2002:4).

Statistical methods are used in *a posteriori* methods to look for patterns empirically within the study population (Hodge & Bassett, 2016:191). These empirical dietary patterns can be identified by using exploratory dimension reduction methods such as principal component analysis and factor analysis. These multivariate statistical approaches intend to summarise these variables into fewer independent components that explain most of the dietary variability despite variations within and between subjects (Moskal *et al.*, 2014:2).

Limited work has been done on nutrient pattern analysis compared to food pattern analysis. However, studying nutrient patterns has several advantages. In contrast to food patterns, nutrients are to a large extent universal and may characterise specific nutritional profiles in such a way that it is easier to compare populations. Furthermore, an enhanced mirroring of bioactive nutrients in complex biological mechanisms associated with diseases is obtained by nutrient patterns compared to food patterns (Moskal *et al.*, 2014:2).

Pina-Camacho *et al.* (2015:1851) found that an unhealthier diet during the perinatal period was associated with depression. The “Rhea” cohort study conversely demonstrated that following a “health-conscious” diet, which included fruit and vegetables, nuts, pulses, dairy, fish, seafood and olive oil, over a “Western” diet, which comprised mainly of meat and meat products, potatoes, cereals, sweets and sugar, salty snacks, eggs, sauces and beverages, during the antenatal period was associated with lower depressive scores (Chatzi *et al.*, 2011:1163).

1.3 Research aim and objectives

1.3.1 Research aim

The aim of this study is to investigate the associations between dietary patterns during early pregnancy and perinatal fatigue and depression among women in Johannesburg, South Africa (SA).

1.3.2 Research objectives

The objectives of this study are, in urban women residing in Johannesburg, SA:

- To determine maternal dietary patterns during early pregnancy by means of exploratory factor analysis using dietary intake data collected prior to 18 weeks gestation (via quantitative food frequency questionnaire [QFFQ]).

- To assess the prevalence of perinatal depression at various time points during pregnancy and after delivery (<18, 22 and 36 weeks gestation, and postnatally at six and twelve months) using the Edinburgh Postnatal Depression Scale (EPDS).
- To assess the severity of maternal fatigue at various time points during pregnancy and after delivery (<18, 22 and 36 weeks gestation, and postnatally at six and twelve months) using the Multidimensional Assessment of Fatigue (MAF) scale.
- To determine associations of dietary patterns during early pregnancy with EPDS scores and the prevalence of perinatal depression.
- To determine associations of dietary patterns during early pregnancy with severity of maternal perinatal fatigue.
- To determine associations of perinatal fatigue with perinatal depression.

1.4 The larger NuPED study

The prospective Nutrition during Pregnancy and Early Development (NuPED) cohort study aimed to assess nutritional status and dietary intake of urban pregnant women in Johannesburg, South Africa. Further, the study aimed to determine associations of nutritional status and dietary intake with birth outcomes, maternal health as well as offspring health and development. The NuPED study recruited 250 pregnant women (<18 weeks gestation) (Symington *et al.*, 2018:1). The inclusion and exclusion criteria are summarised in table 1 below.

Table 1: NuPED inclusion and exclusion criteria at sampling

Inclusion criteria	Exclusion criteria
Confirmed pregnancy with intent to deliver baby at RMMCH	>18 weeks gestational age (maximum 18 weeks)
<18 weeks gestational age	<18 years and >39 years
Born in South Africa, Lesotho, Swaziland, Zimbabwe, Botswana or Namibia	Multiple pregnancy
Able to communicate effectively in one of the following languages: English; Afrikaans; Sotho; Zulu or Xhosa	Women using illicit drugs (self-confessed)
	Smoking (current and/or in past year)
	Known non-communicable diseases (NCDs) such as diabetes, renal disease, history of high blood cholesterol, and hypertension
	Known infectious diseases* such as tuberculosis and hepatitis

	Known serious illnesses such as cancer, lupus or psychosis.
--	---

*HIV positive women will be included in the study. This is due to the high prevalence of HIV in the country (36% in women aged 30-34 years) (Symington *et al.*, 2018:4).

The women were followed up until 12 months postpartum. Antenatal assessments that were conducted at <18, 22 and 36 weeks gestation included maternal nutritional status and dietary intake (Symington *et al.*, 2018:1). Further antenatal assessments included measurement of anthropometric indices, blood pressure, foetal growth using obstetric ultrasound, antenatal depression, antenatal fatigue, immune function, allergy and gestational diabetes. Postnatal assessments, including the measurement of postnatal fatigue and depression, were done at six months and 12 months postpartum, along with other measurements (Symington *et al.*, 2018:1).

1.5 Ethical approval

The larger NuPED study was approved by the Health Research Ethical Committee (HREC) of the North-West University (NWU), Potchefstroom campus (NWU-00049-16-A1) as well as the Medical Human Research Ethics Committee of the University of the Witwatersrand (M150968). This MSc sub-study has been approved by the Health Research Ethical Committee (HREC) of the North-West University (NWU), Potchefstroom campus (NWU-00186-15-A1-06).

1.6 Dissertation outline

This mini-dissertation is presented according to the NWU postgraduate manual. All referencing is in accordance with the NWU Harvard style.

The mini-dissertation will consist of four chapters:

Chapter 1 contains a brief introduction to the study along with the study rationale. Also included in this chapter are the problem statement and research aims and objectives. An overview of the Nutrition during Pregnancy and Early Development (NuPED) study as well as an introduction of the research team completes Chapter 1.

Chapter 2 is a detailed literature review of the available literature regarding perinatal depression and fatigue, its prevalence rates, potential causes and consequences. The literature review also examines the role of dietary components and more specifically dietary patterns in the development of perinatal depression and fatigue.

Chapter 3 puts forward the findings in article form, for publication in the *Nutrients* journal. The article titled “The association of nutrient patterns during pregnancy with perinatal fatigue and depression among urban women in South Africa: The NuPED study” is formatted as per the journal's guidelines.

Chapter 4 summarises the findings of the study, the conclusion as well as limitations and recommendations for future studies.

1.7 Research team

The current study is a sub-study to the larger NuPED study (including the pregnancy and postnatal studies). Indicated below is only the research team for this sub-study. All members of the research team for the complete NuPED study are indicated in the NuPED larger study protocols.

Partner name	Team member	Qualification	Professional registration	Role and responsibility
NWU	Prof. Marius Smuts	PhD Biochemistry	HPCSA: Nutritionist	Principal investigator (PI) of the larger study
NWU & ETH Zürich, Switzerland	Prof. Jeannine Baumgartner	PhD in Human Nutrition	None	Co-PI of the larger study, supervisor of MSc student; expertise in the role of nutrition in brain development and health
NWU	Cornelia Conradie (PhD candidate)	(PhD candidate) MSc in Dietetics	HPCSA: Dietitian	Supervisor of MSc student, responsible for coding, capturing and cleaning of dietary data.
NWU	Vincent Smith (MSc student)	BSc (Dietetics)	HPCSA: Dietitian	MSc student (part-time), responsible for statistical data analysis and writing of dissertation.

REFERENCES

- Baskin, R., Hill, B., Jacka, F.N., O'Neil, A. & Skouteris, H. 2015. The association between diet quality and mental health during the perinatal period. A systematic review. *Appetite*, 91:41-47.
- Biaggi, A., Conroy, S., Pawlby, S. & Pariante, C.M. 2016. Identifying the women at risk of antenatal anxiety and depression: A systematic review. *Journal of Affective Disorders*, 191:62-77.
- Cespedes, E.M. & Hu, F.B. 2015. Dietary patterns: from nutritional epidemiologic analysis to national guidelines. *The American Journal of Clinical Nutrition*, 101(5):899-900.
- Chatzi, L., Melaki, V., Sarri, K., Apostolaki, I., Roumeliotaki, T., Georgiou, V., Vassilaki, M., Koutis, A., Bitsios, P. & Kogevinas, M. 2011. Dietary patterns during pregnancy and the risk of postpartum depression: the mother-child 'Rhea' cohort in Crete, Greece. *Public Health Nutrition*, 14(9):1663-1670.
- Cheng, C.Y., Chou, Y.H., Wang, P., Tsai, J.M. & Liou, S.R. 2015. Survey of trend and factors in perinatal maternal fatigue. *Nursing & Health Sciences*, 17(1):64-70.
- Cheng, C.Y. & Pickler, R.H. 2014. Perinatal stress, fatigue, depressive symptoms, and immune modulation in late pregnancy and one month postpartum. *The Scientific World Journal*, 2014:1-8.
- Dewing, S., Tomlinson, M., le Roux, I.M., Chopra, M. & Tsai, A.C. 2013. Food insecurity and its association with co-occurring postnatal depression, hazardous drinking, and suicidality among women in peri-urban South Africa. *Journal of Affective Disorders*, 150(2):1-14.
- Dietary Guidelines Advisory Committee. 2020. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and Secretary Health and Human Services. Washington, DC: U.S. Department of Agriculture Agricultural Research Service.
- Fisher, J., Cabral de Mello, M., Patel, V., Rahman, A., Tran, T., Holton, S. & Holmes, W. 2012. Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bulletin of the World Health Organization*, 90(2):139-149.
- Gelaye, B., Rondon, M.B., Araya, R. & Williams, M.A. 2016. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. *The Lancet Psychiatry*, 3(10):1-28.
- Gentile, S. 2015. Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. *Neuroscience*, 342:154-166.
- Giallo, R., Gartland, D., Woolhouse, H. & Brown, S. 2016. "I didn't know it was possible to feel that tired": exploring the complex bidirectional associations between maternal depressive symptoms and fatigue in a prospective pregnancy cohort study. *Archives of Women's Mental Health*, 19(1):25-34.

Glover, V. 2014. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 28(1):25-35.

Goodman, J.H. 2019. Perinatal depression and infant mental health. *Archives of Psychiatric Nursing*, 33(3):217-224.

Hartley, M., Tomlinson, M., Greco, E., Comulada, W.S., Stewart, J., le Roux, I., Mbewu, N. & Rotheram-Borus, M.J. 2011. Depressed mood in pregnancy: Prevalence and correlates in two Cape Town peri-urban settlements. *Reproductive Health*, 8(9):1-7.

Hodge, A. & Bassett, J. 2016. What can we learn from dietary pattern analysis? *Public Health Nutrition*, 19(2):191-194.

Honikman, S., van Heyningen, T., Field, S., Baron, E. & Tomlinson, M. 2012. Stepped care for maternal mental health: a case study of the perinatal mental health project in South Africa. *PLoS Medicine*, 9(5):1-6.

Howard, L.M., Molyneaux, E., Dennis, C.-L., Rochat, T., Stein, A. & Milgrom, J. 2014. Non-psychotic mental disorders in the perinatal period. *The Lancet*, 384(9956):1775-1788.

Hu, F.B. 2002. Dietary pattern analysis: a new direction in nutritional epidemiology. *Current Opinion in Lipidology*, 13:3-9.

Kuo, S.Y., Yang, Y.L., Kuo, P.C., Tseng, C.M. & Tzeng, Y.L. 2012. Trajectories of depressive symptoms and fatigue among postpartum women. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 41(2):216-226.

Lara, M.A., Navarrete, L., Nieto, L., Barba Martín, J.P., Navarro, J.L. & Lara-Tapia, H. 2015. Prevalence and incidence of perinatal depression and depressive symptoms among Mexican women. *Journal of Affective Disorders*, 175:18-24.

Leung, B.M. & Kaplan, B.J. 2009. Perinatal depression: prevalence, risks, and the nutrition link--a review of the literature. *Journal of the American Dietetic Association*, 109(9):1566-1575.

Manikkam, L. & Burns, J.K. 2012. Antenatal depression and its risk factors: an urban prevalence study in KwaZulu-Natal. *South African Medical Journal*, 102(12):940-944.

Moskal, A., Pisa, P.T., Ferrari, P., Byrnes, G., Freisling, H., Boutron-Ruault, M.C., Cadeau, C., Nailler, L., Wendt, A., Kuhn, T., Boeing, H., Buijsse, B., Tjonneland, A., Halkjaer, J., Dahm, C.C., Chiuve, S.E., Quiros, J.R., Buckland, G., Molina-Montes, E., Amiano, P., Huerta Castano, J.M., Gurrea, A.B., Khaw, K.T., Lentjes, M.A., Key, T.J., Romaguera, D., Vergnaud, A.C., Trichopoulou, A., Bamia, C., Orfanos, P., Palli, D., Pala, V., Tumino, R., Sacerdote, C., de Magistris, M.S., Bueno-de-Mesquita, H.B., Ocke, M.C., Beulens, J.W., Ericson, U., Drake, I., Nilsson, L.M., Winkvist, A., Weiderpass, E., Hjartaker, A., Riboli, E. & Slimani, N. 2014. Nutrient patterns and their food sources in an International Study Setting: report from the EPIC study. *PLoS One*, 9(6):e98647.

Newby, P.K. & Tucker, K.L. 2004. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutrition Reviews*, 62(5):177-203.

- Pina-Camacho, L., Jensen, S.K., Gaysina, D. & Barker, E.D. 2015. Maternal depression symptoms, unhealthy diet and child emotional-behavioural dysregulation. *Psychological Medicine*, 45(9):1851-1860.
- Previdelli, A.N., de Andrade, S.C., Fisberg, R.M. & Marchioni, D.M. 2016. Using Two Different Approaches to Assess Dietary Patterns: Hypothesis-Driven and Data-Driven Analysis. *Nutrients*, 8(10):1-15.
- Redinger, S., Norris, S.A., Pearson, R.M., Richter, L. & Rochat, T. 2018. First trimester antenatal depression and anxiety: prevalence and associated factors in an urban population in Soweto, South Africa. *Journal of Developmental Origins of Health and Disease*, 9(1):30-40.
- Rochat, T.J., Tomlinson, M., Barnighausen, T., Newell, M.L. & Stein, A. 2011. The prevalence and clinical presentation of antenatal depression in rural South Africa. *Journal of Affective Disorders*, 135(1-3):362-373.
- Silva, D.F.O., Cobucci, R.N., Gonçalves, A.K. & Lima, S.C.V.C. 2019. Systematic review of the association between dietary patterns and perinatal anxiety and depression. *BMC Pregnancy and Childbirth*, 19(1):1-13.
- Symington, E.A., Baumgartner, J., Malan, L., Zandberg, L., Ricci, C. & Smuts, C.M. 2018. Nutrition during pregnancy and early development (NuPED) in urban South Africa: a study protocol for a prospective cohort. *BMC Pregnancy and Childbirth*, 18(1):308.
- Tsai, A.C., Tomlinson, M., Comulada, W.S. & Rotheram-Borus, M.J. 2016. Food insufficiency, depression, and the modifying role of social support: Evidence from a population-based, prospective cohort of pregnant women in peri-urban South Africa. *Social Science and Medicine*, 151:69-77.
- Tsai, A.C., Tomlinson, M., Dewing, S., le Roux, I.M., Harwood, J.M., Chopra, M. & Rotheram-Borus, M.J. 2014. Antenatal depression case finding by community health workers in South Africa: feasibility of a mobile phone application. *Archives of Women's Mental Health*, 17(5):423-431.
- Tuthill, E.L., Pellowski, J.A., Young, S.L. & Butler, L.M. 2017. Perinatal Depression Among HIV-Infected Women in KwaZulu-Natal South Africa: Prenatal Depression Predicts Lower Rates of Exclusive Breastfeeding. *AIDS and Behavior*, 21(6):1691-1698.
- van Heyningen, T.V., Myer, L., Onah, M., Tomlinson, M., Field, S. & Honikman, S. 2016. Antenatal depression and adversity in urban South Africa. *Journal of Affective Disorders*, 203:121-129.
- Woody, C.A., Ferrari, A.J., Siskind, D.J., Whiteford, H.A. & Harris, M.G. 2017. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. *Journal of Affective Disorders*, 219:86-92.

CHAPTER 2: LITERATURE REVIEW

2.1 Perinatal depression

Perinatal depression has the same signs and symptoms as unipolar depression (clinical depression) (Howard *et al.*, 2014:1777). This includes depressed mood, feelings of guilt or low self-worth, disturbed sleep, changes in appetite, fatigue, loss of interest or pleasure in all or most activities, as well as poor concentration (Howard *et al.*, 2014:1777; Leung & Kaplan, 2009:1566). Although perinatal depression includes both the antenatal and postnatal period, it is important to note that longitudinal studies have found that depression is more prevalent in the antenatal period than the postnatal period (Bowen *et al.*, 2012:161; Paulson *et al.*, 2016:2). Additionally, in most cases, postnatal depression was preceded by antenatal depression (Bowen *et al.*, 2012:161; Heron *et al.*, 2004:65; Lee & Chung, 2007:183; Paulson *et al.*, 2016:2).

Poor maternal mental health during the postpartum period has become a major public health issue due to the growing evidence of the negative impacts on child development (Falah-Hassani *et al.*, 2016:142; Muzik & Borovska, 2010:240). In September 2000, the World Health Organisation (WHO) recognised maternal health as a major public health issue (WHO, 2008). Its improvement formed part of the WHO's Millennium Development Goals (MDGs), which concluded in 2015 (Bauer *et al.*, 2016:83). It was included under Goal 5: "Improving maternal health" (WHO, 2008). Following the conclusion of the MDGs, the United Nations (UN) developed the 2030 Agenda for the Sustainable Development Goals (SDGs) in 2015 (Costanza *et al.*, 2016:350; Izutsu *et al.*, 2015:1052). This offered detailed goals, targets and indicators applicable to all countries (Costanza *et al.*, 2016:350). Lessons learnt and gaps identified through the implementation of the MDGs were incorporated into the SDGs as well as newly emerging developmental challenges. Mental health is included in the SDGs under Goal 3: "Ensure healthy lives and promote wellbeing for all at all ages" (Izutsu *et al.*, 2015:1052).

2.2 Prevalence of perinatal depression

A review of the available literature, at the time, reported that the likelihood of developing depression throughout life is twice as likely for women as it is for men (Luskin *et al.*, 2007:480). Not only is depression viewed as one of the most common mental health problems for women of childbearing age, but this also extends through the perinatal period (Howard *et al.*, 2014:1775; Roomruangwong & Epperson, 2011:179). During the antenatal period, women with a history of mental health disorders are at risk of relapse (deterioration in an individual's state of health after a temporary improvement) while others are at risk of experiencing their first depressive episode (Biaggi *et al.*, 2016:74). Antenatal depression rates later in pregnancy are said to be comparable, if not higher, than the rates

of postnatal depression (Baskin *et al.*, 2017:1). More specifically, some studies reported peaks in rates of depression during the first and third trimester (Banti *et al.*, 2011:344; Kitamura *et al.*, 1993:967; Kumar & Robson, 1984:35).

A recent systematic review and meta-regression estimated the global prevalence of perinatal depression to be 11.9%. The same study estimated the prevalence of perinatal depression to be 13.1% for LMIC and 11.4% for HIC (Woody *et al.*, 2017:89). The contrast between LMIC and HIC, in terms of perinatal depression prevalence, seems far greater when viewing other studies, which report prevalence rates between 3% and 20% for HIC and 4.9% to 59.4% for LMIC (Fisher *et al.*, 2012:143; Gelaye *et al.*, 2016:2; Howard *et al.*, 2014:1775; Lara *et al.*, 2015:18; Redinger *et al.*, 2018:31; Woody *et al.*, 2017:89). A systematic review by Woody *et al.* (2017:86) stated that a limitation in determining the prevalence of perinatal depression was the lack of data from LMIC. This limitation demonstrated the necessity for more epidemiological research in LMIC on the prevalence of perinatal depression (Woody *et al.*, 2017:86).

The prevalence of postnatal depression in HIC was reported by a Canadian study to be between 20.4% and 29.6% (Falah-Hassani *et al.*, 2016:144). A Chinese study reported a prevalence of 6.4% (Lee *et al.*, 2004:93), while a Turkish study reported a prevalence of 27.5% for antenatal depression (Golbasi *et al.*, 2010:488). A study from Brazil investigating the prevalence of perinatal depression in two different settings reported a prevalence of 24.3% for antenatal depression and 10.8% for postnatal depression (Melo *et al.*, 2012:1204). The South African prevalence of perinatal depression varies greatly based on study design, location (rural, peri-urban or urban) and other inter-study variations. Across studies, the prevalence ranges from 22% to 48.5% (Manikkam & Burns, 2012:940; Rochat *et al.*, 2011:362; Tuthill *et al.*, 2017:5; van Heyningen *et al.*, 2016:7). A study performed in Khayelitsha, Cape Town, reported the prevalence of postnatal depression to be 32% amongst predominantly Xhosa-speaking black African women (Dewing *et al.*, 2013:5). Within the same demographic group, a year later, antenatal depression was reported to be between 42% and 46% (Tsai *et al.*, 2014:5). A third cross-sectional study performed in Cape Town found that 22% of participants were diagnosed with depression on their first antenatal visit (van Heyningen *et al.*, 2016:7). In urban KwaZulu Natal (KZN), researchers found that 38.5% of the study population presented with perinatal depression (Manikkam & Burns, 2012:940). Another study from KZN, investigating pregnant women infected with HIV, found a 48.5% prevalence of perinatal depression (Tuthill *et al.*, 2017:5). In keeping with this, another study in the same geographical area reported a 47% prevalence in antenatal depression amongst a similar study population (Rochat *et al.*, 2011:366). There are little/not much data on the prevalence of perinatal depression in the Johannesburg area. Most studies are performed in the urban and peri-urban areas of Cape Town and KZN.

2.3 Potential causes of perinatal depression

Relapse is likely among women with a history of perinatal and non-perinatal depression (occurring outside of the perinatal period) (Gentile, 2015:3). Additionally, a history of non-perinatal anxiety and bipolar disorder are major risk factors for perinatal depression (Goodman, 2019:217). Although the aetiology of perinatal depression is unknown (Bennett *et al.*, 2004:160; Doyle *et al.*, 2018:6), the risk of depressive episodes may be increased due to pregnancy itself (Gentile, 2015:3). Normal physiological changes during the antenatal and early postnatal period may cause somatic depressive symptoms (Howard *et al.*, 2014:1775).

Hormonal hypotheses have received the most attention, even though psychological and biological explanations have also been proposed (Bonair *et al.*, 2004:727). During pregnancy a woman's hypothalamic-pituitary-adrenal (HPA) axis undergoes gradual change due to an increase in production of corticotrophin-releasing hormone (CRH) by the placenta (Doyle *et al.*, 2018:6). One of the principal regulators of the HPA axis is CRH (Bennett *et al.*, 2004:160). Disturbances of the HPA axis have a central role in the aetiology of mood disorders in general and in particular perinatal depression (Bennett *et al.*, 2004:160; Doyle *et al.*, 2018:6).

A systematic review found that women who have been victims of abuse (psychical, sexual or psychological) during any point in their lifetime are at elevated risk of developing perinatal depression when compared to women with no lifetime abuse (Alvarez-Segura *et al.*, 2014:354). The Centre for Disease Control and Prevention and The Nations Children's Emergency Fund conducted a survey in seven LMIC between 2007 and 2013 to establish the prevalence of childhood sexual abuse. The study reported that 25% of girls in LMIC have been victims of sexual abuse (Sumner *et al.*, 2015:565). Child abuse (childhood maltreatment) is defined as all forms of physical, sexual and psychological maltreatment that poses harm to a child's dignity, development and health. Other childhood maltreatment such as neglect, and emotional abuse tend to co-occur with child abuse. Childhood sexual abuse is one of the most widely studied types of child abuse (Gelaye *et al.*, 2016:5). The underlying biological mechanisms responsible for associations between child abuse and perinatal depression are thought to be related to the disruptions of neurobiological stress response systems including the HPA axis, the serotonin system as well as the sympathetic nervous system (Gelaye *et al.*, 2016:5). In individuals who have experienced child abuse, a greater inflammatory response to stressors is observed. In pregnant women, lower levels of oxytocin have been seen. Oxytocin is important in maternal-infant bonding and has anti-inflammatory properties. The combination of higher proinflammatory cytokines and lower oxytocin during pregnancy may elevate risk for perinatal depression (Garfield *et al.*, 2016:333).

Inflammation has been linked with increased depressive symptoms as well as clinical depression in non-pregnant individuals (Garfield *et al.*, 2016:333). Increased immune markers, such as increased circulatory proinflammatory cytokines and immune signalling levels, have been observed in psychiatric patients which suggests immune system association in mental illness (Leff-Gelman *et al.*, 2016:399). Once these proinflammatory cytokines access the brain, they initiate a cascade of reactions which increase glutamatergic effects and lower serotonin levels. The deficit of serotonergic neurotransmission and enhanced glutamate receptor *N*-methyl-d-aspartate activation is characteristic of depression (Garfield *et al.*, 2016:333). Tryptophan, which is a precursor to serotonin, is degraded by indoleamine 2,3-dioxygenase activated by proinflammatory cytokines. Indoleamine 2,3-dioxygenase further facilitates competition with the serotonin pathway by shunting tryptophan toward the production of kynurenine. Proinflammatory cytokines promote the development of depressive symptoms via these mechanisms (Garfield *et al.*, 2016:333). Treatment aimed at reducing depressive symptoms is correlated with normalization of immune signalling levels (Leff-Gelman *et al.*, 2016:399).

The levels of proinflammatory molecules, both circulating and uterine, are altered during pregnancy (Garfield *et al.*, 2016:333). This causes the first and third trimester to be dominated by a proinflammatory environment and the second trimester with an anti-inflammatory environment (Garfield *et al.*, 2016:333; Kendall-Tackett, 2010:7). The inflammatory response in the first trimester is due to a local inflammatory response in the uterus as a result of implantation. The pro-inflammatory state continues through implantation into the uterine wall and vascularisation establishing placental-foetal blood supply. In aid of rapid foetal development, the second trimester is an anti-inflammatory state (Garfield *et al.*, 2016:333). During the third trimester pro-inflammatory cytokines aid in uterine contractions, wound healing and fighting off infection, in preparation for birth (Garfield *et al.*, 2016:333; Kendall-Tackett, 2010:8). If this proinflammatory cytokine cascade during pregnancy is inappropriately escalated it may contribute to the development of depression. Available data suggest that inflammation seems to be one of many possible contributors to the development and maintenance of depressive symptoms, rather than depression being an inflammatory disorder (Garfield *et al.*, 2016:333).

Intimate partner violence is a common type of abuse experienced by about a third of all women worldwide (Mitchell *et al.*, 2016:452). Intimate partner violence is defined as any physical, psychological or sexual abuse perpetrated towards a partner in an intimate relationship (Gelaye *et al.*, 2016:5; Mitchell *et al.*, 2016:452). In a multi-country study conducted in nine LMIC and Japan by the WHO, the prevalence of physical intimate partner violence aimed towards women ranged between 10% and 69% (Krug *et al.*, 2002:1085). Psychological abuse is often present along with physical intimate partner violence, with a third to a half of physical intimate partner violence cases

also including sexual abuse (Gelaye *et al.*, 2016:6; Watts & Zimmerman, 2002:1233). A more recent multi-country study conducted by the WHO on intimate partner violence found that between 15% and 71% of women reported lifetime physical or sexual violence by a partner (Garcia-Moreno *et al.*, 2006:1264). Intimate partner violence is also an important public health concern in South Africa according to the Domestic Violence Act (116 of 1998) (South Africa, 1998:1). The underlying mechanism responsible for associations between intimate partner violence and perinatal depression include physical, social and emotional isolation, loss, separation and the unpredictability exerted by the abuser (Gelaye *et al.*, 2016:6).

Among people living with HIV, mental health problems are known to be high (Mitchell *et al.*, 2016:452). Depressive symptoms in these individuals are associated with psychological, biological and clinical characteristics affecting the disease progression of HIV (Yousuf *et al.*, 2019:153). Compared to people living with HIV that never experienced depression, those who were chronically depressed, especially women, are twice as likely to die from Acquired Immunodeficiency Syndrome (AIDS) (Yousuf *et al.*, 2019:156). Pregnant women with HIV have very specific psychosocial issues related to pregnancy and the new child, including fear of infecting the foetus, maternal guilt, stress, stigma, poverty, insufficient social network and issues around diagnostic disclosure. In HIV-infected women, perinatal depression might be caused primarily by a biological mechanism (Arseniou *et al.*, 2014:100).

A systematic review and meta-analysis concluded that women who are obese, with a body mass index (BMI) greater than 30kg/m² at conception, have a higher likelihood of experiencing perinatal depression, compared to normal-weight and intermediate risk for overweight women (Molyneaux *et al.*, 2014:1). The adverse perinatal outcomes associated with maternal obesity have not yet been explained by one unifying mechanism. Based on available data, there are numerous factors that seem to contribute to early placental and foetal dysfunction leading to adverse outcomes. These factors are, oxidative stress, inflammation, increased antenatal maternal insulin resistance and accompanying hyperinsulinemia (Catalano & Shankar, 2017:1).

Not only is antenatal depression a strong risk factor for postnatal depression (Banti *et al.*, 2011:343), the physical and emotional demands of childbirth may also put women at risk for developing postnatal depression (Bozoky & Corwin, 2002:437). A Turkish study found higher depression scores to be positively, mildly correlated with higher gravidity (number of previous pregnancies), parity (number of previous births), number of living children and maternal age (Golbasi *et al.*, 2010:488).

The higher prevalence of perinatal depression in LMIC vs HIC could be attributed to increased social and economic adversity (van Heyningen *et al.*, 2016:9). Not only is the prevalence higher, but women from LMIC are more exposed to risk factors known to influence the development of perinatal

depression. These factors include low income, war, disaster, intimate partner violence, food insecurity, sanitation deficiencies, child abuse, shortage of access to quality health care, difficulty in accessing contraception and high prevalence of disease such as HIV, malaria and tuberculosis. Knowledge regarding the underlying mechanisms contributing to perinatal depression in LMIC are scarce (Herba *et al.*, 2016:1).

2.4 Consequences of perinatal depression

Perinatal depression does not only affect the mother, but it can also have devastating consequences for her family and unborn child (Gavin *et al.*, 2005:1071). A biologically mediated antenatal disorder (through in-utero effects) would have effects specifically on the mother and the neurodevelopment of her foetus. But if either parent has a psychiatric disorder, the child may be affected by means of postnatal and genetic factors (Stein *et al.*, 2014:1808). Figure 1 is a summarised model of the possible underlying mechanisms responsible for the associations between child outcomes and parental psychiatric disorders. The association between child susceptibility to mental illness and parental mental disorders at any time (including the perinatal period) may be partly due to shared genetic risk factors (inherited from both parents). There is evidence to support a strong environmental contribution in the cause of mental illness (Stein *et al.*, 2014:1808). A proportion of variance in associations between parental disorders and child outcomes could be accounted for by correlations between genetic and environmental factors through genetic confounding (Stein *et al.*, 2014:1811).

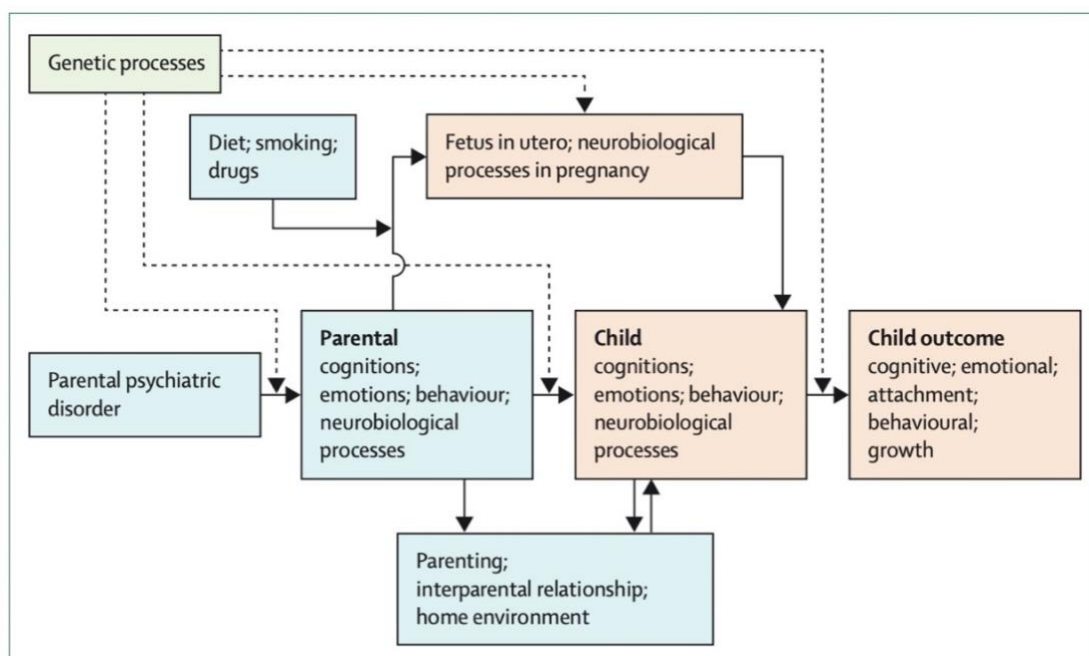


Figure 1: Possible underlying mechanisms responsible for the associations between child outcomes and parental psychiatric disorders (Stein *et al.*, 2014:1813)

Child effects are in the orange blocks. Parental effects are in the blue blocks. Green refers to genetic processes. Solid lines indicate interactions. Dotted lines indicate genetic processes.

Early life experiences (including the perinatal environment) have long-lasting effects on biological and behavioural phenotypes. A proposed mechanism to explain this is epigenetic change where gene expression is modified without altering the genetic sequence. It is hypothesised that maternal disorders and child outcomes are mediated by epigenetic pathways, however this hypothesis has not been formally tested (Stein *et al.*, 2014:1811). Foetal and maternal programming has been proposed as mediating factors in perinatal depression (Stein *et al.*, 2014:1812).

The phenomenon of foetal programming is well established when it comes to physical foetal outcomes (Glover, 2014:26). Foetal programming happens during vulnerable developmental periods of the foetus. As a result of over or under nutrition in pregnancy there is a possible “programming” effect or “switching on” of certain genes in the foetus leading to a genetic predisposition to chronic disease later in life (Carolan-Olah *et al.*, 2015:3717). For example, Glover (2014:26) found that perinatal depression can increase the risk of children developing asthma later in life. The maternal changes responsible for the changes in foetal brain development are not clear. There is evidence in both rodent models and humans that exposure to cortisol *in utero* can affect foetal brain development. The placenta is hypothesised to also be involved due to being rich in serotonin, which has shown to alter foetal brain development in increased concentrations (Herba *et al.*, 2016:3).

Chronic exposure (continued or recurrent) of children to a mother’s mental disorders has been found to mediate the effects of perinatal depression. Variance within the association between child outcomes and perinatal depression is a result of the persistence of the depression. There is evidence to suggest that quality of parenting is the most important potential mediators in perinatal depression (Stein *et al.*, 2014:1812). Data for the various components of this mediating pathway show that the quality of parenting is compromised by perinatal disorder and symptoms. Disturbances in child development are associated with compromised early parenting. The association between child outcomes and perinatal mental health is mediated by disrupted parenting (Stein *et al.*, 2014:1812).

2.4.1 Pregnancy and birth outcomes

Antenatal depression can lead to difficulty in performing usual activities, and has also been associated with poor utilisation of antenatal services and poor health behaviour, such as risk-taking behaviour, substance abuse (tobacco, alcohol and drugs) and inadequate diet (Gentile, 2015:3; Goodman, 2019:217; Woody *et al.*, 2017:86). If left untreated, depression during pregnancy may lead to suicide in the perinatal period (Golbasi *et al.*, 2010:485; Lusskin *et al.*, 2007:483). As a cause of maternal mortality, suicide surpasses haemorrhage and hypertensive disorders during the perinatal period (Goodman, 2019:217). The prevalence of suicidal attempts in adolescent mothers may be as high as 20% (Gentile, 2015:3). In HIC, the leading cause of death during the perinatal period is maternal suicide (Honikman *et al.*, 2012:1).

Antenatal depression has also been associated with an increased risk for premature delivery (<37 weeks gestation) (Goodman, 2019:218; Stein *et al.*, 2014:1801). Premature delivery is a complex process with multiple risk factors including reproductive history, medical disorders, mental health problems, health behaviours and genetics. Psychosocial stress during pregnancy in the aetiology of preterm delivery is supported by a growing body of literature. Multiple pathways such as inflammatory, neuroendocrine and maternal behavioural and lifestyle pathways connect psychosocial stress and premature delivery (Shapiro *et al.*, 2013:2).

Perinatal depression increases the risk for low birth-weight delivery (Bauer *et al.*, 2016:83). Two mechanisms have been hypothesised: foetal undernutrition and overexposure to glucocorticoids. Foetal undernutrition (especially protein deprivation) alters the foetus' exposure to cortisol (Meaney *et al.*, 2007:269). Birth weight is influenced by intrauterine growth and gestational age, making low birth weight a consequence of preterm delivery or intrauterine growth retardation (de Mola *et al.*, 2014:340). This association is higher in LMIC than in HIC. It is possible that low birthweight is a substantial factor in LMIC but not in HIC due to socioeconomical disadvantages. Pre-eclampsia, Apgar scores and admissions to neonatal intensive-care units (NICUs) were not associated with antenatal depression (Stein *et al.*, 2014:1801). A systematic review concluded that, despite substantial research into depression and birth outcomes, the evidence remains ambiguous (Accortt *et al.*, 2015:12).

2.4.2 Early developmental outcomes

A range of negative child outcomes have been associated with perinatal depression (Honikman *et al.*, 2012:1; Rochat *et al.*, 2011:362). Child well-being is impacted by maternal depression through interpersonal, genetic and environmental mechanisms (Flynn *et al.*, 2004:316). A systematic review from the United Kingdom (a HIC) found that children from mothers with perinatal mental illness were at greater risk of reduced growth (Bauer *et al.*, 2016:83). A study from India (a LMIC) found, after adjusting for low birth-weight and maternal education, that perinatal depression was significantly associated with poorer growth outcomes at six months (Patel *et al.*, 2003:35). The authors ascribed this poor growth to impairment of the mothering role by symptoms of depression. Depressive symptoms (such as fatigue, tiredness, irritability, agitation, psychomotor delay, feelings of worthlessness or guilt, loss of concentration and loss of interest in daily activities) raise the probability of early breastfeeding cessation, which has been identified as a factor in infant undernutrition and may mediate poor growth outcomes (Patel *et al.*, 2003:36). However, the evidence that links infant growth to maternal depressive symptoms is mixed (Nasreen *et al.*, 2013:254).

Mothers suffering from perinatal depression are less likely to breastfeed (Goodman, 2019:217). In LMIC only 37% of children under six months of age are exclusively breastfed (Tuthill *et al.*, 2020:2).

A South African study found poor exclusive breastfeeding rates among HIV positive mothers with postnatal depression (Tuthill *et al.*, 2017:6). Risk factors that possibly limit exclusive breastfeeding in a low-resource setting include HIV status, poor psychosocial health (particularly lack of assistance from partners in terms of infant care) and food insecurity (Machado *et al.*, 2014:989; Tuthill *et al.*, 2020:2). Machado *et al.* (2014:992) found that mothers who breastfed exclusively, but did not receive assistance from their partner in terms of infant care, abandoned exclusive breast feeding. Longer duration of breastfeeding was observed when the father had a positive attitude and showed support towards breastfeeding. Furthermore, mothers are more likely to continue exclusive breastfeeding for six months when they talk to their partner about infant health (Machado *et al.*, 2014:992).

One of the many positive outcomes of exclusive breastfeeding is that it can positively impact maternal mental health in mother-infant attachment. Thus, factors hindering exclusive breastfeeding can also negatively impact on maternal mental health facilitated by exclusive breastfeeding (Tuthill *et al.*, 2017:6). The exact mechanism of how these risk factors interact to influence breastfeeding behaviours remain unstudied and have not been well described (Tuthill *et al.*, 2020:2). Mechanisms underpinning the link between life stress during pregnancy and breastfeeding duration need to be explored in future research (Li *et al.*, 2008:223).

Caring for a new-born infant can cause physical and emotional stress which can be exacerbated by depression (Golbasi *et al.*, 2010:485). Postnatal depression can also influence a mother's ability to maintain relationships with significant others (Woody *et al.*, 2017:86), possibly making it difficult to relate to the child's father (Banti *et al.*, 2011:343). It is interesting to note that emerging literature suggests that new and expecting fathers also have an elevated depressive risk which can lead to relative impairments in parenting (Paulson *et al.*, 2016:2).

Perinatal depression has been suggested to inhibit mothers' bonding with their infants (Banti *et al.*, 2011:343). A systematic review found an association between perinatal depression and lower quality interactions between mothers and their children (Gavin *et al.*, 2005:1071). Although the underlying mechanism of action is unclear, conclusive evidence has found that mother-infant interactions mediate adverse outcomes (Moehler *et al.*, 2006:274). Maternal postnatal behaviour that expresses bonding include gaze, smiling, proximity seeking, contact, touch, positive expression, baby talk and cuddling. Higher autonomic stress response to distress stimuli in children was associated with adverse parental bonding (Nonnenmacher *et al.*, 2016:927). The precise relationship between bonding and postnatal depression remains unclear (Nonnenmacher *et al.*, 2016:928).

Due to perinatal depression, new mothers may be less likely to follow infant safety recommendations (such as using home safety devices and placing the infant in the back-to-sleep position) (Goodman, 2019:218). Furthermore, perinatal depression has also been associated with missed paediatric

appointments and more frequent use of emergency department services (Gavin *et al.*, 2005:1071; Roomruangwong & Epperson, 2011:179). It has been hypothesised that depressed mothers are more likely to seek care for acute illness due to heightened levels of worry about the child, decreased comfort in their own ability to manage illness, increased psychosocial concerns and decreased ability to interpret symptoms (Minkovitz *et al.*, 2005:307). Appointments for preventative care are often missed due to difficulty in keeping appointments or difficulty in advanced planning. As a consequence, it has been hypothesised that depressed mothers are more likely to have undervaccinated (selective, partial or delayed vaccinated) children (Minkovitz *et al.*, 2005:307).

In terms of neurodevelopment, an increased risk of cognitive, behavioural and emotional problems have been associated with perinatal depression (Bauer *et al.*, 2016:83; Glover, 2014:26). Furthermore, a large prospective cohort study found an association between child emotional-behavioural dysregulation (up to the age of seven years) and maternal depressive symptoms (Pina-Camacho *et al.*, 2015:1851). Associations have also been found between perinatal depression and a higher level of psychiatric disturbances among children (Herba *et al.*, 2016:2; Roomruangwong & Epperson, 2011:179; Stein *et al.*, 2014:1804).

A systematic review by Honikman *et al.* (2012:1) found the prevalence of maternal mental disorders to be three times higher in LMIC than in HIC. In LMIC maternal competence in child care likely plays a greater role in the child's physical wellbeing and chances of survival, due to the environment frequently being more hostile than in HIC (Rahman, 2005:71). In LMIC specifically, negative child outcomes associated with perinatal depression include higher risk for infant diarrhoea, poor child growth and poor mental development (Hartley *et al.*, 2011:1). These outcomes have been attributed to circumstances that are common in LMIC such as poor sanitation, overcrowding and food insecurity. When these factors are combined with sub-optimal maternal care it may result in a detriment to the child's physical health (Rahman, 2005:71). Three mechanisms of action have been proposed. The first involves the risk of antenatal depression towards the unborn infant. Women with depression are more likely to obtain inadequate antenatal care compared to women without depression (Rahman, 2005:73). Secondly, mothers with depression tend to have negative views of themselves as parents, where they feel that they are less able to positively influence their child and have less control over their child's development. Thirdly, mothers who are depressed may act in ways that increase the probability of their children experiencing adversity. This is through exposure to more stressors than infants of mothers without depression, such as family discord (Rahman, 2005:74).

A new concept in early childhood development is that of nurturing care which is characterised by a home environment that is developmentally stimulating, sensitive to children's nutritional and health needs, and emotionally supportive with opportunities for play and exploration without adversity. In

the Life-Course Conceptual Framework for Early Childhood Development published in the 2017 Lancet series for early childhood development, it was reported that nurturing care is built upon foundational capacities established as early as pre-conception (Black *et al.*, 2017:4). Maternal nutrition during pregnancy along with parental physical and mental health are included among factors that form the basis of nurturing care. Nurturing care has demonstrated with neuroscientific evidence that it promotes children's health, growth and development. It can even attenuate the detrimental effects of low socioeconomic status on the brain (Black *et al.*, 2017:4).

2.5 Screening tools for perinatal depression

Within the perinatal period, various screening tools have been utilised to identify generic depression including the General Health Questionnaire, the Hospital Anxiety and Depression Scale, the Beck Depression Inventory and Zung's Self-rating Depression Scale. The most widely used validated tools, however, are the Postpartum Depression Screening Scale (PDSS) and the Edinburgh Postnatal Depression Scale (EPDS) (Milgrom & Gemmill, 2014:15). Compared to other screening tools, the EPDS is favoured as it has been judged to be a "simple, safe, precise and validated screening test" with established cut-offs (Milgrom & Gemmill, 2014:16).

The EPDS is a self-report scale including 10 statements related to symptoms of depression occurring within the past week (Hartley *et al.*, 2011:2; Milgrom & Gemmill, 2014:16). Each statement can have one of four possible responses to yield a maximum score of 30. Some somatic symptoms, like changes in appetite and sleep, are deliberately excluded from the EPDS as these are common in the perinatal period in the absence of mental disorders (Milgrom & Gemmill, 2014:15). Women with an EPDS score of ≥ 13 need to be evaluated for depression or other mental disorder (Glover, 2014:32).

The EPDS has been validated against the DSM-IV diagnosis of depression (amongst women in postnatal care) (de Bruin *et al.*, 2004:114). The EPDS has been found to be acceptable to most women and health professionals by an Australian report on the acceptability of routine screening for perinatal depression (Buist *et al.*, 2006:233). It has been found to be suitable for screening and measuring perinatal depression in African countries (Tsai *et al.*, 2013:1). It has been specifically validated for the screening and assessment of postnatal and also antenatal depression in South African women (de Bruin *et al.*, 2004:114; Lawrie *et al.*, 1998:1343; Manikkam & Burns, 2012:941). A cut-off of EPDS ≥ 9 has been proposed, as it has a high sensitivity and specificity to detect depression in South African women (Tsai *et al.*, 2013:5).

2.6 Perinatal fatigue

The relationship between perinatal fatigue and depressive symptoms has been described as complex, reciprocal and bidirectional (Giallo *et al.*, 2016:32; Kuo *et al.*, 2012:216). Although perinatal fatigue and depressive symptoms are related, the two should be seen as distinct symptoms (Kuo *et al.*, 2012:225). Perinatal fatigue has been described as a persistent, overwhelming sense of physical as well as mental exhaustion, not alleviated by adequate rest. Signs and symptoms of postnatal fatigue also include muscle weakness, lack of energy and impairments in concentration (Giallo *et al.*, 2015:258).

A study examining antenatal sleep impairment, found that this specific type of fatigue is characterized by impaired motor and cognitive skills along with reduced motivation (Pires *et al.*, 2010:579). Postnatal fatigue, which has long been identified as a common health problem (Taylor & Johnson, 2010:368), can start to subside as early as eight weeks postpartum or last as long as four months postpartum (Fairbrother *et al.*, 2008:150). In a Swedish study, 87.7% of women with antenatal depression and 86.3% of women with postpartum depression reported fatigue or loss of energy (Andersson *et al.*, 2006:940). A study examining maternal fatigue in two independent samples found that fatigue during the postnatal period has been suggested to be predicative of postnatal depression (Fairbrother *et al.*, 2008:150).

2.7 Prevalence of perinatal fatigue

The prevalence of perinatal fatigue varies greatly depending on the measurement tool used, time points during pregnancy in which measurements were taken, as well as the country being studied (Cheng *et al.*, 2015:64). A survey conducted in Sweden found a prevalence of 30% to 65% across various gestational periods (Rodriguez *et al.*, 2001:216). A Taiwanese study found a prevalence of 94.6% among women 20-36 weeks pregnancy (Chien & Ko, 2004:489). Researchers from South Korea found that 82% of women reported fatigue three months postpartum (Song *et al.*, 2014:339). Japanese data shows that 67% of mothers reported fatigue one month postnatally (Iwata *et al.*, 2018:187). Amongst Australian mothers at six to seven months postnatally, 69% reported fatigue (Brown & Lumley, 2000:1197). In the Netherlands researchers found that postnatal fatigue was still present in 26% of mothers six months postnatally and in 18% of mothers one year postnatally (Bakker *et al.*, 2014:387).

Compared to early pregnancy, fatigue levels are higher later in pregnancy and postnatally. Perinatal fatigue in its entirety (antenatal and up to one year postnatal) has only been investigated by a few studies (Cheng *et al.*, 2015:64). Fatigue in LMIC is often assumed to be due to nutritional deficiencies or infectious disease (Smartt *et al.*, 2016:368). Further research in LMIC is needed to improve evidence-based guidelines for the management of perinatal fatigue (Smartt *et al.*, 2016:371).

2.8 Potential causes of perinatal fatigue

Antenatal fatigue may start as early as 11 to 12 weeks gestation and increases in severity during the last trimester (Cheng *et al.*, 2015:64; Cheng & Pickler, 2014:1). A predisposition towards fatigue during the antenatal period can be attributed to psychological, emotional and physical changes (Mortazavi & Borzooee, 2019:e45).

In preparation of motherhood, a considerable amount of plasticity (the capacity of an individual organism to alter its behaviour, morphology and physiology/gene expression in direct response to changing environmental conditions) occurs during the perinatal period. Maternal behavioural plasticity is accompanied by substantial brain plasticity which manifests as changes in cognition. It has been hypothesised that this adaptive process conserves energy to be used for functions promoting offspring survival (Workman *et al.*, 2012:54). Antenatally there are changes in the morphology, physiology and function of various brain structures involved in the induction of maternal behaviour due to drastic fluctuations in peptide and steroid hormone levels. The hippocampus and cortex undergo alterations and are involved in mediating learning and memory. The morphology and structure of the hippocampus is dramatically altered during the perinatal period which may have behavioural implications (Workman *et al.*, 2012:54). A high concentration of steroid and peptide hormone receptors renders the hippocampus sensitive to hormonal fluctuations during the perinatal period (Workman *et al.*, 2012:55).

The prevalence of antenatal sleep disturbances is high (Mindell *et al.*, 2015:483). Not only is there a later observed bedtime later in pregnancy (Mindell *et al.*, 2015:485), there is also an increase in interrupted sleep (Naghi *et al.*, 2011:489). More specifically there is an increase in the number and duration of night awakenings as well as less total sleep (Mindell *et al.*, 2015:485). As one might expect, sleep dissatisfaction has been related to postpartum fatigue (Cheng *et al.*, 2015:64).

Women remain at a higher risk for developing fatigue up to one year postnatally (Giallo *et al.*, 2015:528). After assessing patterns of maternal fatigue, a few studies reported that there is a fairly consistent pattern of increase in fatigue following childbirth (Fairbrother *et al.*, 2008:150). Fatigue during the postnatal period has been viewed as normal and can be attributed to the physical demands (infant care and feeding), sleep disruption, less active coping styles and adaptations of motherhood (Bakker *et al.*, 2014:389; Bozoky & Corwin, 2002:437; Giallo *et al.*, 2015:529). Most mothers reported less fatigue in the mornings and more towards evenings (Cheng *et al.*, 2015:64; Cheng & Pickler, 2014:1). Commonly reported feelings from new mothers include feeling drained, mentally tired and exhausted (Fairbrother *et al.*, 2008:150). A study investigating the trajectory of maternal and paternal fatigue found that both parents' fatigue increase following the birth of their

infant. Maternal and paternal fatigue was associated with stress, poor sleep quality and depression (Loutzenhiser *et al.*, 2015:15).

2.9 Consequences of perinatal fatigue

Some negative outcomes, such as poor foetal development, earlier delivery and poor child motor and mental development have been associated with antenatal stress, usually reported as tiredness or fatigue (Cheng & Pickler, 2014:1). Perinatal fatigue may adversely affect not only women's well-being but also their daily functioning and parent-child interactions (Giallo *et al.*, 2015:529; Mortazavi & Borzoe, 2019:e45).

One study found that antenatal and birth factors, such as mode of delivery, health during pregnancy and breastfeeding are likely to be associated with postpartum fatigue levels (Giallo *et al.*, 2015:540). A longer labour duration and increased likelihood to undergo a caesarean section were reported in women with sleep problems (Naghi *et al.*, 2011:491). Positive correlations have also been found between fatigue and lower social interactions as well as sexual activity (Mortazavi & Borzoe, 2019:e45).

2.10 Screening tools for perinatal fatigue

In order for medical professionals to design adequate interventions, measuring fatigue and associated risk factors is of great importance (Mortazavi & Borzoe, 2019:e45). The Multidimensional Assessment of Fatigue (MAF) scale has been validated for use in subjects that are considered to be vulnerable to fatigue (Fairbrother *et al.*, 2008:151). The MAF has demonstrated good psychometric properties (Whitehead, 2009:123) and adequate sensitivity (Whitehead, 2009:124). Validity as well as reliability of the MAF were supported when administered to women in the perinatal period (Cheng *et al.*, 2015:66). Among women in the perinatal period, the MAF has been found to be a useful measure of fatigue (Fairbrother *et al.*, 2008:157).

This scale assesses multiple aspects of the subjective experience of fatigue; it is brief and easy to use. A recent systematic review found that the MAF scale has been used in 17 different countries and 32 different disease conditions. To this end, it has also been translated into nine languages (Mortazavi & Borzoe, 2019:e45). The MAF scale measures four dimensions of fatigue experienced during the preceding week by making use of a set of 16 Likert-type items. Items 1 and 2 measure severity, item 3 measures distress, items 4 to 14 measures the degree of interference in activities of daily living and items 15 and 16 measure timing of fatigue (Fairbrother *et al.*, 2008:151). Most often the MAF is used to calculate a single score, namely the Global Fatigue Index (GFI). To calculate GFI, item 15 is converted to a 10-point scale by multiplying the score for this item by 2.5. The mean of items 4 to 15 is then added to items 1 to 3. Item 16 is not included in the calculation of

GFI (Fairbrother *et al.*, 2008:151). Generally, a cut-off of 28 is indicative of fatigue (Cheng *et al.*, 2015:66).

2.11 The role of maternal diet in perinatal depression and fatigue

Across various developmental stages, the nutrient demands from the foetus change (Leung & Kaplan, 2009:1569). These demands from a growing foetus increase physiological stress on the mother's body, making her susceptible to nutrient deficiencies (Marx *et al.*, 2017:430). For optimal pregnancy outcomes and proper metabolic activities that support tissue growth and functioning in the developing foetus, micronutrients are critical. If micronutrient deficiencies are left unaddressed it can threaten the well-being and survival of mothers as well as their infants. Due to the intergenerational transfer of malnutrition, subsequent generations of children may also be at risk (Oh *et al.*, 2020:2).

Pre-existing micronutrient deficiencies become worse during pregnancy (Oh *et al.*, 2020:1), and poor quality diets may exacerbate nutrient deficiencies (Marx *et al.*, 2017:430). Micronutrient deficiencies are more common in people from LMIC (Oh *et al.*, 2020:1). Dietary nutrients have a potential role in the biochemical pathways of mental illness whereby deficiencies during pregnancy may explain perinatal depression (Marx *et al.*, 2017:430). It is therefore crucial that pregnant women consume foods with enhanced nutrient density to avoid nutritional deficiencies (Leung & Kaplan, 2009:1569). With the link between nutrient deficiency and depression along with the evidence of dietary inadequacy in pregnancy, one can reasonably theorise the potential influence of nutrient deficiencies on the incidence of perinatal depression (Leung & Kaplan, 2009:1571).

According to literature, at all stages of life, diet is likely relevant to mental health (Marx *et al.*, 2017:430). In a position paper by the Academy of Nutrition and Dietetics, it's stated that a lifestyle optimizing health and reducing the risk of birth defects should be adopted by women of childbearing age. The authors continue that in order to achieve healthy pregnancy components, such as healthy pregnancy weight and appropriate weight gain, women should consume a wide variety of foods as well as appropriate vitamin and mineral supplementation. They concluded that the ideal prenatal diet prevents undernutrition for the foetus and limits overconsumption for the mother (Procter & Campbell, 2014:1099).

2.12 Dietary trajectory across pregnancy

Nausea and vomiting are the most common medical conditions during pregnancy affecting up to 90% of expecting mothers (Ebrahimi *et al.*, 2010:241). A recent meta-analysis found that 32.7% of pregnant women had nausea without vomiting and 23.5% had nausea with vomiting continuing into the third trimester (Einarson *et al.*, 2013:e171). The Southampton Women's Survey was based on

2270 participants and analysed dietary data from food frequency questionnaires taken before pregnancy, at 11 weeks and 34 weeks gestation. The study found that nausea and vomiting during pregnancy were transient and not related to changes in dietary quality (Crozier *et al.*, 2017:1).

A Swedish study, which obtained dietary data mid-pregnancy, found that dietary changes are more likely to be made in the first trimester and that restrictions tend to be eased later on in pregnancy (Wennberg *et al.*, 2013:1032). The Southampton Women's Survey is based on 1 490 women who gave information before pregnancy and again at 11 and 34 weeks gestation between 1998 and 2003. An analysis of the survey conducted in 2009 found that the greatest changes in maternal diet occurred in the first trimester and was mostly a reduction in the amount of alcoholic and caffeinated beverages. There was only a 1% change in the intake of fruits and vegetables across trimesters (Crozier *et al.*, 2009:446).

An Irish study found that expecting mothers' diets tend to remain within the same pattern across trimesters. In the study, a three-day food diary during each trimester was completed by 285 participants. In 72% of participants the "unhealthy" dietary pattern persisted from the first to second trimester and in 56.6% of participants it extended from the second to third trimester (McGowan & McAuliffe, 2012:104). A study from the United States of America reported no significant difference in terms of food items and food group intake means between the first and second trimester (Rifas-Shiman *et al.*, 2006:4). There was, however, a significant increase in iron and folic acid intake attributed to the use of antenatal micronutrient supplements (Rifas-Shiman *et al.*, 2006:4).

2.13 Dietary patterns and perinatal depression and fatigue

In the past, nutrition research has mainly focused on single nutrients or specific foods, even though these foods are not consumed in isolation (Cespedes & Hu, 2015:899). In terms of measuring dietary exposure in nutritional epidemiology, the single food or nutrient approach has limitations (Newby & Tucker, 2004:177). Among studies focusing on single nutrients or specific foods, one author noted that there was a lack of studies that brought together the broader picture of multiple nutrient intakes (Abu-Saad & Fraser, 2010:5). Dietary (eating pattern) analysis describes the diet as a whole, combinations and variety of foods, food groups, the included nutrients, as well as the quantity and frequency in which they are habitually consumed (Cespedes & Hu, 2015:899).

These patterns can be defined theoretically or empirically. For theoretical pattern analysis a set of *a priori* criteria of nutritional health is used to group nutritional variables. Empirical analysis involves statistical manipulation that reduces nutritional variables into a smaller number of variables with evaluation *a posteriori*. With empirically derived dietary patterns there is no need to define patterns *a priori*, rather, patterns are generated from collected dietary data through statistical methods (Newby & Tucker, 2004:177). Although principal component analysis is widely used, factor analysis

and cluster analysis are two other methods commonly used in nutritional epidemiology to derive a *posteriori* dietary patterns (Cespedes & Hu, 2015:899; Newby & Tucker, 2004:177). Factor analysis uses intercorrelations between dietary items to reduce data into patterns. Cluster analysis, on the other hand, uses individual differences in mean intakes to reduce data into patterns (Newby & Tucker, 2004:177).

A recent systematic review investigated associations between dietary patterns and perinatal depression. Ten studies were included in the review, in which various methods were used to assess dietary intake (food frequency questionnaire, food history questionnaire and three-day food record) at various time points (six months before pregnancy, during pregnancy and the postpartum period) (Silva *et al.*, 2019:2). The methods used for assessing depressive symptoms (Primary Care Evaluation of Mental Disorders, Centre for Epidemiologic Studies Depression Scale and the EPDS) also varied among the included studies. In terms of statistical analysis, most of the studies used factor analysis to identify dietary patterns; only one made use of cluster analysis. The authors concluded that there is no definitive evidence regarding the relationship between “Western” dietary patterns and perinatal depression (Silva *et al.*, 2019:7). Negative associations with perinatal depression were seen in a “healthy” dietary pattern as well as “traditional Japanese” and “traditional-Indian-Confinement” dietary patterns (Silva *et al.*, 2019:12).

The Growing up in Singapore towards Healthy Outcomes (GUSTO) study was done prospectively on associations of postpartum maternal dietary patterns with postpartum depression ($n = 490$). Researchers identified four main dietary patterns (Traditional-Chinese-Confinement, Traditional-Indian-Confinement, Eat-Out, and Soup-Vegetable-Fruits) by grouping foods into 84 groups based on similarities in nutritional characteristics (Teo *et al.*, 2018:3). Dietary intake was assessed using three-day food diaries, and depressive symptoms were measured using the EPDS. Exploratory factor analysis with principal component extraction was used to derive patterns (Teo *et al.*, 2018:4).

Multivariate models showed that greater adherence to “Traditional-Indian-Confinement” was associated with fewer symptoms of postpartum depression. A non-significant trend towards fewer postpartum depressive symptoms was seen in the “Soup-Vegetable-Fruits” pattern. There were no associations found between the “Eat-Out” and “Traditional-Chinese-Confinement” patterns and postpartum depression (Teo *et al.*, 2018:7).

The “Soup-Vegetable-Fruits” pattern possibly protects against symptoms of depression by regulating oxidative damage due to oxidative stress. The “Soup-Vegetable-Fruits” pattern is high in fruit and vegetables, which are rich in antioxidants such as β -carotene, vitamin C and vitamin E. Neural protection is provided by antioxidants, counterbalancing the effect of free radical oxidants and reducing oxidative damage (Teo *et al.*, 2018:10). This pattern is also high in fish (non-fried), of which

some are rich in omega-3 fatty acids. The role of omega-3 fatty acids in the brain includes maintaining permeability and fluidity of neuronal membranes as well as regulation of function and metabolism of serotonin. Furthermore, omega-3 fatty acids have anti-oxidative and anti-inflammatory properties (Teo *et al.*, 2018:10).

The “Traditional-Indian-Confinement” dietary pattern contains curry dishes prepared with saffron, fenugreek and curcumin. These herbs and spices possibly alleviate depressive symptoms through anti-inflammatory, serotonergic, neuroprotective and HPA axis regulatory effects which have been previously reported (Lopresti *et al.*, 2012:1520; Sanmukhani *et al.*, 2014:585; Teo *et al.*, 2018:10). This dietary pattern also contains legumes, pulses and breads rich in B-vitamins which are essential for the synthesis of monoamine neurotransmitters, which may also protect against perinatal depression (Teo *et al.*, 2018:10).

Barker *et al.* (2013:418) used a food frequency questionnaire (FFQ) and then delineated “healthy” and “unhealthy” groups. A confirmatory factor analysis was then used to examine the internal reliability of these groupings. Three first-order latent factors, namely vegetables, non-meat protein, and fish, were considered as “healthy” foods, while two second-order latent factors, fried and processed foods, were labelled as “unhealthy”. After delineation of the two food groups, the reliability of the groupings was examined using confirmatory factor analysis. Path analysis of data from the Avon Longitudinal Study of Parents and Children (ALSPAC) was done to examine inter-relationships between maternal depression symptoms and “unhealthy” diet using the food groups described by Barker *et al.*, (2013:418) above ($n = 13\,867$). The study reported that higher intake of unhealthy food and lower intake of healthy food were related to higher depressive symptoms. The study did not identify any causative relationship and did not examine biological mechanisms (Barker *et al.*, 2013:418).

A research group using data from the ALSPAC study applied bivariate logistic regression analysis ($n = 9\,530$) and found that “health-conscious” and “traditional” dietary patterns were associated with protective effects against anxiety symptoms, while a vegetarian pattern was associated with an increased possibility of anxiety symptoms during pregnancy (Vaz *et al.*, 2013:1). Another study also found that a “vegetarian” dietary pattern was associated with an increased possibility of anxiety symptoms (Chen *et al.*, 2016:18). A possible explanation could be a low vitamin B₁₂ intake due to the absence of meat (which is the richest source of vitamin B₁₂ in the modern diet, according to the authors), as well as low omega-3 fatty acid intake, especially docosahexaenoic acid, due to the absence of fish in the “vegetarian” pattern (Vaz *et al.*, 2013:7). Optimal neurological function requires both these nutrients (Chen *et al.*, 2016:18). The study by Vaz *et al.* (2013:7) did not comment on the potential role of other sources of vitamin B₁₂ (such as dairy) or other micronutrients (such as iron).

The Rhea cohort study from Greece ($n = 529$) demonstrated that choosing a “health-conscious” diet, which includes fruit and vegetables, nuts, pulses, dairy, fish, seafood and olive oil, over a Western diet, which comprises mainly of meat and meat products, potatoes, cereals, sweets and sugar, salty snacks, eggs, sauces and beverages, during pregnancy was associated with lower EPDS scores (Chatzi *et al.*, 2011:1163). Diet plays a significant role in maternal mental health during the perinatal period according to emerging evidence. Regarding the exact way in which this relationship operates, however, little is known (Baskin *et al.*, 2015:46). Several oxidative stress-related disturbances have been reported in depression, such as oxidative deoxyribonucleic acid damage, oxidative damage of erythrocytic membranes, elevated lipid peroxidation products, reduced serum levels of vitamins C and E, and increased concentrations of asymmetric dimethyl-arginine, which is an endogenous inhibitor of endothelial nitrous oxide synthase leading to decreased levels of nitrous oxide (Chatzi *et al.*, 2011:1668). The “health-conscious” pattern from the Rhea cohort included foods that are rich in antioxidants such as vitamin C, E, selenium, carotenoids and flavonoids. The authors state that by correcting several depression-related oxidative markers in the cortex, it is plausible that the “health-conscious” food pattern may exert protective effects against depression (Chatzi *et al.*, 2011:1668).

A prospective cohort study in Brazil ($n = 248$) found that a “healthy” dietary pattern pre-pregnancy was inversely associated with depressive symptoms not only throughout pregnancy, but even to early postpartum (Vilela *et al.*, 2014:1616). Foods that comprised the “healthy” dietary pattern included pasta, noodles, roots and tubers, fruit, fruit juices, dairy, tea, fish and legumes. This resulted in a high dietary intake of antioxidants (vitamins, minerals and flavonoids), which protects the brain from oxidative stress implicated in depression. The “healthy” dietary patterns also provided omega-3 fatty acids (from fish), known to be critical for optimal neurological functioning. The authors concluded that the “healthy” dietary pattern prevents neurocognitive impairments which manifests as mood changes, such as depressive symptoms, during pregnancy (Vilela *et al.*, 2014:1617).

Another study, also from Brazil ($n = 712$), found an association between a “healthy” diet that includes fruit, vegetables and beans and a lower prevalence of common mental disorders during pregnancy (Paskulin *et al.*, 2017:214). The authors attributed this beneficial effect to antioxidant compounds from fruit and vegetable intake. These antioxidant compounds include vitamin C, E, carotenoids, flavonoids, iron, magnesium, zinc and folate. Antioxidants seem to be effective in reducing or preventing pathophysiological and cognitive alterations. There is evidence that these compounds may modulate the risk of neurostructural and cognitive alterations in the brain with a strong biological plausibility in affecting modulation of mood as well as brain function (Paskulin *et al.*, 2017:214). The same study reported that a “common-Brazilian” dietary pattern was associated with a higher occurrence of depression when compared to the “varied” pattern. Foods comprising the “common-Brazilian” pattern were foods popular in Brazilian culture, such as French rolls, noodles, rice,

boneless beef or chicken, eggs, beans, margarine, coffee with sugar, and artificial juices (Paskulin *et al.*, 2017:210). The “common-Brazilian” dietary pattern is similar to the “Western” pattern reported in other studies, in the sense that both are composed of foods rich in refined carbohydrates and have a high glycaemic load. An association has been suggested between these types of foods and higher levels of C-reactive protein, which is a sensitive biomarker of inflammation (Paskulin *et al.*, 2017:213). A typical “Western” diet could influence brain structure and function by deregulating the expression of brain-derived neurotrophic factor as according to experimental studies. Brain-derived neurotrophic factor promotes neurogenesis, protects neurons and plays a central role in depression (Paskulin *et al.*, 2017:213). Fibre is important in the modulation of the gut microbiota; a lack thereof may influence the ability for gut bacteria to be transferred from mother to child. Recent evidence shows that the gut microbiota possibly mediates the link between diet and depression through the gut-brain axis (Paskulin *et al.*, 2017:213).

“Healthy” and “Brazilian traditional” dietary patterns have been inversely associated with depression during pregnancy ($n = 784$). These dietary patterns include high consumption of minimally processed foods and low consumption of ultra-processed products (Badanai *et al.*, 2019:589). Natural and minimally processed foods contain micronutrients which have been identified as possible protectors against antenatal depression such as vitamin D, folate selenium, iron and zinc (Badanai *et al.*, 2019:588).

During pregnancy as well as the postnatal period, an “unhealthier” diet has been associated with higher depressive symptoms ($n = 7\ 814$). An “unhealthy” diet was defined by means of confirmatory factor analysis as previously described by Barker *et al.* (2013:418) (Pina-Camacho *et al.*, 2015:1851). There is evidence to suggest that individuals with depression choose high-fat, high-sugar foods over fruits and vegetables. Thus, there is usually a higher intake of unhealthy food and an insufficient intake of nutrient-dense (healthy) food. High-fat and high-sugar foods can have a direct noxious effect on the brain and body. Via different pathways, nutrient and fibre deficiency may also present negative outcomes (Pina-Camacho *et al.*, 2015:1858).

A recent systematic review on the role of diet and nutritional supplementation in perinatal depression concluded that future studies should ensure nutrition and depression measurements at baseline as well as several time points throughout the perinatal period. Additionally, reverse causality between dietary intake and perinatal depression could be overcome by conducting high-quality longitudinal studies (Sparling *et al.*, 2017:18)

Perinatal depression can have devastating consequences on mothers as well as their offspring (Gavin *et al.*, 2005:1071). Although the aetiology of perinatal depression is largely unknown (Bennett *et al.*, 2004:160; Doyle *et al.*, 2018:6), perinatal fatigue seems to have a bi-directional relationship

with perinatal depression (Giallo *et al.*, 2016:32; Kuo *et al.*, 2012:216). Seeing as perinatal depression is a problem, especially in LMIC (Manikkam & Burns, 2012:940), and the potential role that diet and fatigue may play (Giallo *et al.*, 2016:32; Kuo *et al.*, 2012:216; Silva *et al.*, 2019:7). It is imperative that research into the role of diet and fatigue in depression, especially in the perinatal period, be pursued. Studies in to the role of fatigue specifically is lacking (Cheng *et al.*, 2015:64).

REFERENCES

- Abu-Saad, K. & Fraser, D. 2010. Maternal Nutrition and Birth Outcomes. *Epidemiological Reviews*, 32:5-25.
- Accortt, E.E., Cheadle, A.C. & Dunkel Schetter, C. 2015. Prenatal depression and adverse birth outcomes: an updated systematic review. *Maternal Child Health Journal*, 19(6):1306-1337.
- Alvarez-Segura, M., Garcia-Esteve, L., Torres, A., Plaza, A., Imaz, M.L., Hermida-Barros, L., San, L. & Burtchen, N. 2014. Are women with a history of abuse more vulnerable to perinatal depressive symptoms? A systematic review. *Archives of Women's Mental Health*, 17(5):343-357.
- Andersson, L., Sundstrom-Poromaa, I., Wulff, M., Astrom, M. & Bixo, M. 2006. Depression and anxiety during pregnancy and six months postpartum: a follow-up study. *Acta Obstetrica et Gynecologica*, 85(8):937-944.
- Arseniou, S., Arvaniti, A. & Samakouri, M. 2014. HIV infection and depression. *Psychiatry and Clinical Neuroscience*, 68(2):96-109.
- Badanai, N.d.L., Zuccolotto, D.C.C., Crivellenti, L.C. & Sartorelli, D.S. 2019. Association of dietary patterns and degree of food processing with feelings of depression in pregnancy. *Revista Brasileira de Saúde Materno Infantil*, 19(3):581-590.
- Bakker, M., van der Beek, A.J., Hendriksen, I.J., Bruinvels, D.J. & van Poppel, M.N. 2014. Predictive factors of postpartum fatigue: a prospective cohort study among working women. *Journal of Psychosomatic Research*, 77(5):385-390.
- Banti, S., Mauri, M., Oppo, A., Borri, C., Rambelli, C., Ramacciotti, D., Montagnani, M.S., Camilleri, V., Cortopassi, S., Rucci, P. & Cassano, G.B. 2011. From the third month of pregnancy to 1 year postpartum. Prevalence, incidence, recurrence, and new onset of depression. Results from the perinatal depression-research & screening unit study. *Comprehensive Psychiatry*, 52(4):343-351.
- Barker, E.D., Kirkham, N., Ng, J. & Jensen, S.K. 2013. Prenatal maternal depression symptoms and nutrition, and child cognitive function. *The British Journal of Psychiatry*, 203(6):417-421.
- Baskin, R., Hill, B., Jacka, F.N., O'Neil, A. & Skouteris, H. 2015. The association between diet quality and mental health during the perinatal period. A systematic review. *Appetite*, 91:41-47.
- Baskin, R., Hill, B., Jacka, F.N., O'Neil, A. & Skouteris, H. 2017. Antenatal dietary patterns and depressive symptoms during pregnancy and early post-partum. *Maternal & Child Nutrition*, 13(1).
- Bauer, A., Knapp, M. & Parsonage, M. 2016. Lifetime costs of perinatal anxiety and depression. *Journal of Affective Disorders*, 192:83-90.
- Bennett, H.A., Einarson, A., Taddio, A., Koren, G. & Einarson, T.R. 2004. Depression during Pregnancy. *Clinical Drug Investigation*, 23(3):157-179.

- Biaggi, A., Conroy, S., Pawlby, S. & Pariante, C.M. 2016. Identifying the women at risk of antenatal anxiety and depression: A systematic review. *Journal of Affective Disorders*, 191:62-77.
- Black, M.M., Walker, S.P., Fernald, L.C.H., Andersen, C.T., DiGirolamo, A.M., Lu, C., McCoy, D.C., Fink, G., Shawar, Y.R., Shiffman, J., Devercelli, A.E., Wodon, Q.T., Vargas-Barón, E. & Grantham-McGregor, S. 2017. Early childhood development coming of age: science through the life course. *The Lancet*, 389(10064):77-90.
- Bonair, L., Pinto, N., Ahn, E., Einarson, A., Steiner, M. & Koren, G. 2004. Perinatal Risk of Untreated Depression During Pregnancy. *Canadian Journal of Psychiatry*, 49(11):726-735.
- Bowen, A., Bowen, R., Butt, P., Rahman, K. & Mauhajarine, N. 2012. Patterns of Depression and Treatment in Pregnant and Postpartum Women. *The Canadian Journal of Psychiatry*, 57(3):161-167.
- Bozoky, I. & Corwin, E.J. 2002. Fatigue as a Predictor of Postpartum Depression. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 31(4):436-443.
- Brown, S. & Lumley, J. 2000. Physical health problems after childbirth and maternal depression at six to seven months postpartum. *British Journal of Obstetrics and Gynaecology*, 107:1194-1201.
- Buist, A., Condon, J., Brooks, J., Speelman, C., Milgrom, J., Hayes, B., Ellwood, D., Barnett, B., Kowalenko, N., Matthey, S., Austin, M.P. & Bilszta, J. 2006. Acceptability of routine screening for perinatal depression. *Journal of Affective Disorders*, 93(1-3):233-237.
- Carolan-Olah, M., Duarte-Gardea, M. & Lechuga, J. 2015. A critical review: early life nutrition and prenatal programming for adult disease. *Journal of Clinical Nursing*, 24(23-24):3716-3729.
- Catalano, P.M. & Shankar, K. 2017. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *The British Medical Journal* 360:1-16.
- Cespedes, E.M. & Hu, F.B. 2015. Dietary patterns: from nutritional epidemiologic analysis to national guidelines. *The American Journal of Clinical Nutrition*, 101(5):899-900.
- Chatzi, L., Melaki, V., Sarri, K., Apostolaki, I., Roumeliotaki, T., Georgiou, V., Vassilaki, M., Koutis, A., Bitsios, P. & Kogevinas, M. 2011. Dietary patterns during pregnancy and the risk of postpartum depression: the mother-child 'Rhea' cohort in Crete, Greece. *Public Health Nutrition*, 14(9):1663-1670.
- Chen, X., Zhao, D., Mao, X., Xia, Y., Baker, P.N. & Zhang, H. 2016. Maternal Dietary Patterns and Pregnancy Outcome. *Nutrients*, 8(6):1-26.
- Cheng, C.Y., Chou, Y.H., Wang, P., Tsai, J.M. & Liou, S.R. 2015. Survey of trend and factors in perinatal maternal fatigue. *Nursing & Health Sciences*, 17(1):64-70.
- Cheng, C.Y. & Pickler, R.H. 2014. Perinatal stress, fatigue, depressive symptoms, and immune modulation in late pregnancy and one month postpartum. *The Scientific World Journal*, 2014:1-8.

- Chien, L. & Ko, Y. 2004. Fatigue during pregnancy predicts caesarean deliveries. *Issues and Innovations in Nursing Practice*, 45(5):487-494.
- Costanza, R., Daly, L., Fioramonti, L., Giovannini, E., Kubiszewski, I., Mortensen, L.F., Pickett, K.E., Ragnarsdottir, K.V., De Vogli, R. & Wilkinson, R. 2016. Modelling and measuring sustainable wellbeing in connection with the UN Sustainable Development Goals. *Ecological Economics*, 130:350-355.
- Crozier, S.R., Inskip, H.M., Godfrey, K.M., Cooper, C., Robinson, S.M. & Group, S.W.S.S. 2017. Nausea and vomiting in early pregnancy: Effects on food intake and diet quality. *Maternal & Child Nutrition*, 13(4):1-10.
- Crozier, S.R., Robinson, S.M., Borland, S.E., Godfrey, K.M., Cooper, C., Inskip, H.M. & Group, S.W.S.S. 2009. Do women change their health behaviours in pregnancy? Findings from the Southampton Women's Survey. *Paediatric and Perinatal Epidemiology*, 23(5):446-453.
- de Bruin, G.P., Swartz, L., Tomlinson, M., Cooper, P.J. & Molteno, C. 2004. The Factor Structure of the Edinburgh Postnatal Depression Scale in a South African Peri-Urban Settlement. *South African Journal of Psychology*, 34(1):113-121.
- de Mola, C.L., de Franca, G.V.A., Quevedo, L.D. & Horta, B.L. 2014. Low birth weight, preterm birth and small for gestational age association with adult depression: systematic review and meta-analysis. *The British Journal of Psychiatry*, 205(5):340-347.
- Dewing, S., Tomlinson, M., le Roux, I.M., Chopra, M. & Tsai, A.C. 2013. Food insecurity and its association with co-occurring postnatal depression, hazardous drinking, and suicidality among women in peri-urban South Africa. *Journal of Affective Disorders*, 150(2):1-14.
- Doyle, M., Carballido, A. & O'Keane, V. 2018. Perinatal depression and psychosis: an update. *BJPsych Advances*, 21(1):5-14.
- Ebrahimi, N., Maltepe, C. & Einarson, A. 2010. Optimal management of nausea and vomiting of pregnancy. *International Journal of Women's Health*, 2:241-248.
- Einarson, T.R., Piwko, C. & Koren, G. 2013. Quantifying the global rates of nausea and vomiting of pregnancy: A meta-analysis. *Journal of Population Therapeutics and Clinical Pharmacology*, 20(2):e171-e183.
- Fairbrother, N., Hutton, E.K., Stoll, K., Hall, W. & Kluka, S. 2008. Psychometric evaluation of the Multidimensional Assessment of Fatigue scale for use with pregnant and postpartum women. *Psychological Assessment*, 20(2):150-158.
- Falah-Hassani, K., Shiri, R. & Dennis, C.L. 2016. Prevalence and risk factors for comorbid postpartum depressive symptomatology and anxiety. *Journal of Affective Disorders*, 198:142-147.
- Fisher, J., Cabral de Mello, M., Patel, V., Rahman, A., Tran, T., Holton, S. & Holmes, W. 2012. Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bulletin of the World Health Organization*, 90(2):139-149.

- Flynn, H.A., Davis, M., Marcus, S.M., Cunningham, R. & Blow, F.C. 2004. Rates of maternal depression in pediatric emergency department and relationship to child service utilization. *General Hospital Psychiatry*, 26(4):316-322.
- Garcia-Moreno, C., Jansen, H.A.F.M., Ellsberg, M., Heise, L. & Watts, C.H. 2006. Prevalence of intimate partner violence: findings from the WHO multi-country study on women's health and domestic violence. *The Lancet*, 368(9543):1260-1269.
- Garfield, L., Mathews, H.L. & Witek Janusek, L. 2016. Inflammatory and Epigenetic Pathways for Perinatal Depression. *Biological Research for Nursing*, 18(3):331-343.
- Gavin, N.I., Gaynes, B.N., Lohr, K.N., Meltzer-Brody, S., Gartlehner, G. & Swinson, T. 2005. Perinatal Depression A Systematic Review of Prevalence and Incidence. *Obstetrics and Gynecology*, 106(5):1071-1083.
- Gelaye, B., Rondon, M.B., Araya, R. & Williams, M.A. 2016. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. *The Lancet Psychiatry*, 3(10):1-28.
- Gentile, S. 2015. Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. *Neuroscience*, 342:154-166.
- Giallo, R., Gartland, D., Woolhouse, H. & Brown, S. 2016. "I didn't know it was possible to feel that tired": exploring the complex bidirectional associations between maternal depressive symptoms and fatigue in a prospective pregnancy cohort study. *Archives of Women's Mental Health*, 19(1):25-34.
- Giallo, R., Seymour, M., Dunning, M., Cooklin, A., Loutzenhiser, L. & McAuslan, P. 2015. Factors associated with the course of maternal fatigue across the early postpartum period. *Journal of Reproductive and Infant Psychology*, 33(5):528-544.
- Glover, V. 2014. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 28(1):25-35.
- Golbasi, Z., Kelleci, M., Kisacik, G. & Cetin, A. 2010. Prevalence and correlates of depression in pregnancy among Turkish women. *Maternal and Child Health Journal*, 14(4):485-491.
- Goodman, J.H. 2019. Perinatal depression and infant mental health. *Archives of Psychiatric Nursing*, 33(3):217-224.
- Hartley, M., Tomlinson, M., Greco, E., Comulada, W.S., Stewart, J., le Roux, I., Mbewu, N. & Rotheram-Borus, M.J. 2011. Depressed mood in pregnancy: Prevalence and correlates in two Cape Town peri-urban settlements. *Reproductive Health*, 8(9):1-7.
- Herba, C.M., Glover, V., Ramchandani, P.G. & Rondon, M.B. 2016. Maternal depression and mental health in early childhood: an examination of underlying mechanisms in low-income and middle-income countries. *The Lancet Psychiatry*, 3(10):983-992.

- Heron, J., O'Connor, T.G., Evans, J., Golding, J., Glover, V. & Team, A.S. 2004. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *Journal of Affective Disorders*, 80(1):65-73.
- Honikman, S., van Heyningen, T., Field, S., Baron, E. & Tomlinson, M. 2012. Stepped care for maternal mental health: a case study of the perinatal mental health project in South Africa. *PLoS Medicine*, 9(5):1-6.
- Howard, L.M., Molyneaux, E., Dennis, C.-L., Rochat, T., Stein, A. & Milgrom, J. 2014. Non-psychotic mental disorders in the perinatal period. *The Lancet*, 384(9956):1775-1788.
- Iwata, H., Mori, E., Sakajo, A., Aoki, K., Maehara, K. & Tamakoshi, K. 2018. Course of maternal fatigue and its associated factors during the first 6 months postpartum: a prospective cohort study. *Nursing Open*, 5(2):186-196.
- Izutsu, T., Tsutsumi, A., Minas, H., Thornicroft, G., Patel, V. & Ito, A. 2015. Mental health and wellbeing in the Sustainable Development Goals. *The Lancet Psychiatry*, 2(12):1052-1054.
- Kendall-Tackett, K. 2010. Four research findings that will change what we think about perinatal depression. *The Journal of Perinatal Education*, 19(4):7-9.
- Kitamura, T., Shima, S., Sugawara, M. & Toda, M.A. 1993. Psychological and social correlates of the onset of affective disorders among pregnant women. *Psychological Medicine*, 23(4):967-975.
- Krug, E.G., Mercy, J.A., Dahlberg, L.L. & Zwi, A.B. 2002. The world report on violence and health. *The Lancet*, 360(9339):1083-1088.
- Kumar, R. & Robson, K.M. 1984. A Prospective Study of Emotional Disorders in Childbearing Women. *The British Journal of Psychiatry*, 144(1):53-47.
- Kuo, S.Y., Yang, Y.L., Kuo, P.C., Tseng, C.M. & Tzeng, Y.L. 2012. Trajectories of depressive symptoms and fatigue among postpartum women. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 41(2):216-226.
- Lara, M.A., Navarrete, L., Nieto, L., Barba Martín, J.P., Navarro, J.L. & Lara-Tapia, H. 2015. Prevalence and incidence of perinatal depression and depressive symptoms among Mexican women. *Journal of Affective Disorders*, 175:18-24.
- Lawrie, T.A., Hofmeyer, G.J., de Jager, M. & Berk, M. 1998. Validation of the Edeinburgh Postnatal Depression Scale on a cohort of South African women *South African Medical Journal*, 88(10):1340-1344.
- Lee, D.T., Chan, S.S., Sahota, D.S., Yip, A.S., Tsui, M. & Chung, T.K. 2004. A prevalence study of antenatal depression among Chinese women. *Journal of Affective Disorders*, 82(1):93-99.
- Lee, D.T. & Chung, T.K. 2007. Postnatal depression: an update. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 21(2):183-191.

- Leff-Gelman, P., Mancilla-Herrera, I., Flores-Ramos, M., Cruz-Fuentes, C., Reyes-Grajeda, J.P., Garcia-Cuetara Mdel, P., Bugnot-Perez, M.D. & Pulido-Ascencio, D.E. 2016. The Immune System and the Role of Inflammation in Perinatal Depression. *Neuroscience Bulletin*, 32(4):398-420.
- Leung, B.M. & Kaplan, B.J. 2009. Perinatal depression: prevalence, risks, and the nutrition link--a review of the literature. *Journal of the American Dietetic Association*, 109(9):1566-1575.
- Li, J., Kendall, G.E., Henderson, S., Downie, J., Landsborough, L. & Oddy, W.H. 2008. Maternal psychosocial well-being in pregnancy and breastfeeding duration. *Acta Paediatrica*, 97(2):221-225.
- Lopresti, A.L., Hood, S.D. & Drummond, P.D. 2012. Multiple antidepressant potential modes of action of curcumin: a review of its anti-inflammatory, monoaminergic, antioxidant, immune-modulating and neuroprotective effects. *Journal of Psychopharmacology*, 26(12):1512-1524.
- Loutzenhiser, L., McAuslan, P. & Sharpe, D.P. 2015. The trajectory of maternal and paternal fatigue and factors associated with fatigue across the transition to parenthood. *Clinical Psychologist*, 19(1):15-27.
- Luskin, S.I., Pundiak, T.M. & Habibi, S.M. 2007. Perinatal Depression: Hiding in Plain Sight. *The Canadian Journal of Psychiatry*, 52(8):479-488.
- Machado, M.C., Assis, K.F., Oliveira Fde, C., Ribeiro, A.Q., Araujo, R.M., Cury, A.F., Priore, S.E. & Franceschini Sdo, C. 2014. Determinants of the exclusive breastfeeding abandonment: psychosocial factors. *Public Health Practice*, 48(6):985-994.
- Manikkam, L. & Burns, J.K. 2012. Antenatal depression and its risk factors: an urban prevalence study in KwaZulu-Natal. *South African Medical Journal*, 102(12):940-944.
- Marx, W., Moseley, G., Berk, M. & Jacka, F. 2017. Nutritional psychiatry: the present state of the evidence. *Proceedings of the Nutrition Society*, 76(4):427-436.
- McGowan, C.A. & McAuliffe, F.M. 2012. Maternal dietary patterns and associated nutrient intakes during each trimester of pregnancy. *Public Health Nutrition*, 16(1):97-107.
- Meaney, M.J., Szyf, M. & Seckl, J.R. 2007. Epigenetic mechanisms of perinatal programming of hypothalamic-pituitary-adrenal function and health. *Trends in Molecular Medicine*, 13(7):269-277.
- Melo, E.F., Jr., Cecatti, J.G., Pacagnella, R.C., Leite, D.F., Vulcani, D.E. & Makuch, M.Y. 2012. The prevalence of perinatal depression and its associated factors in two different settings in Brazil. *Journal of Affective Disorders*, 136(3):1204-1208.
- Milgrom, J. & Gemmill, A.W. 2014. Screening for perinatal depression. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 28(1):13-23.
- Mindell, J.A., Cook, R.A. & Nikolovski, J. 2015. Sleep patterns and sleep disturbances across pregnancy. *Sleep Medicine*, 16(4):483-488.

- Minkovitz, C.S., Strobino, D., Scharfstein, D., Hou, W., Miller, T., Mistry, K.B. & Swartz, K. 2005. Maternal depressive symptoms and children's receipt of health care in the first 3 years of life. *Pediatrics*, 115(2):306-314.
- Mitchell, J., Wight, M., Van Heerden, A. & Rochat, T.J. 2016. Intimate partner violence, HIV, and mental health: a triple epidemic of global proportions. *International Review of Psychiatry*, 28(5):452-463.
- Moehler, E., Brunner, R., Wiebel, A., Reck, C. & Resch, F. 2006. Maternal depressive symptoms in the postnatal period are associated with long-term impairment of mother-child bonding. *Archives of Women's Mental Health*, 9(5):273-278.
- Molyneaux, E., Poston, L., Ashurst-Williams, S. & Howard, L.M. 2014. Obesity and mental disorders during pregnancy and postpartum: a systematic review and meta-analysis. *Obstetrics and Gynecology*, 123(4):857-867.
- Mortazavi, F. & Borzooee, F. 2019. Fatigue in Pregnancy: The validity and reliability of the Farsi Multidimensional Assessment of Fatigue scale. *Sultan Qaboos University Medical Journal*, 19(1):e44-e50.
- Muzik, M. & Borovska, S. 2010. Perinatal depression: implications for child mental health. *Mental Health in Family Medicine*, 7:239-247.
- Naghi, I., Keypour, F., Ahari, S.B., Tavalai, S.A. & Khak, M. 2011. Sleep disturbance in late pregnancy and type and duration of labour. *Journal of Obstetrics and Gynaecology*, 31(6):489-491.
- Nasreen, H.E., Kabir, Z.N., Forsell, Y. & Edhborg, M. 2013. Impact of maternal depressive symptoms and infant temperament on early infant growth and motor development: results from a population based study in Bangladesh. *Journal of Affective Disorders*, 146(2):254-261.
- Newby, P.K. & Tucker, K.L. 2004. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutrition Reviews*, 62(5):177-203.
- Nonnenmacher, N., Noe, D., Ehrenthal, J.C. & Reck, C. 2016. Postpartum bonding: the impact of maternal depression and adult attachment style. *Archives of Women's Mental Health*, 19(5):927-935.
- Oh, C., Keats, E.C. & Bhutta, Z.A. 2020. Vitamin and Mineral Supplementation During Pregnancy on Maternal, Birth, Child Health and Development Outcomes in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. *Nutrients*, 12(2).
- Paskulin, J.T.A., Drehmer, M., Olinto, M.T., Hoffmann, J.F., Pinheiro, A.P., Schmidt, M.I. & Nunes, M.A. 2017. Association between dietary patterns and mental disorders in pregnant women in Southern Brazil. *Revista Brasileira de Psiquiatria*, 39(3):208-215.
- Patel, V., DeSouza, N. & Rodrigues, M. 2003. Postnatal depression and infant growth and development in low income countries: a cohort study from Goa, India. *Archives of Disease in Childhood*, 88:34-37.

- Paulson, J.F., Bazemore, S.D., Goodman, J.H. & Leiferman, J.A. 2016. The course and interrelationship of maternal and paternal perinatal depression. *Archives of Women's Mental Health*, 19(4):655-663.
- Pina-Camacho, L., Jensen, S.K., Gaysina, D. & Barker, E.D. 2015. Maternal depression symptoms, unhealthy diet and child emotional-behavioural dysregulation. *Psychological Medicine*, 45(9):1851-1860.
- Pires, G.N., Andersen, M.L., Giovenardi, M. & Tufik, S. 2010. Sleep impairment during pregnancy: possible implications on mother-infant relationship. *Medical Hypotheses*, 75(6):578-582.
- Procter, S.B. & Campbell, C.G. 2014. Position of the Academy of Nutrition and Dietetics: nutrition and lifestyle for a healthy pregnancy outcome. *Journal of the Academy of Nutrition and Dietetics*, 114(7):1099-1103.
- Rahman, A. 2005. Maternal Depression and Child Health: The Need for Holistic Health Policies in Developing Countries. *Harvard Health Policy Review*, 6(2):70-80.
- Redinger, S., Norris, S.A., Pearson, R.M., Richter, L. & Rochat, T. 2018. First trimester antenatal depression and anxiety: prevalence and associated factors in an urban population in Soweto, South Africa. *Journal of Developmental Origins of Health and Disease*, 9(1):30-40.
- Rifas-Shiman, S.L., Rich-Edwards, J.W., Willett, W.C., Kleinman, K.P., Oken, E. & Gillman, M.W. 2006. Changes in dietary intake from the first to the second trimester of pregnancy. *Paediatric and Perinatal Epidemiology*, 20(1):35-42.
- Rochat, T.J., Tomlinson, M., Barnighausen, T., Newell, M.L. & Stein, A. 2011. The prevalence and clinical presentation of antenatal depression in rural South Africa. *Journal of Affective Disorders*, 135(1-3):362-373.
- Rodriguez, A., Bohlin, G. & Lindmark, G. 2001. Symptoms across pregnancy in relation to psychosocial and biomedical factors. *Acta Obstetrica et Gynecologica Scandinavica*, 80:213-223.
- Roomruangwong, C. & Epperson, C.N. 2011. Perinatal depression in Asian women: prevalence, associated factors, and cultural aspects. *Asian Biomedicine*, 5(2):179-193.
- Sanmukhani, J., Satodia, V., Trivedi, J., Patel, T., Tiwari, D., Panchal, B., Goel, A. & Tripathi, C.B. 2014. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. *Phytotherapy Research*, 28(4):579-585.
- Shapiro, G.D., Fraser, W.D., Frasch, M.G. & Seguin, J.R. 2013. Psychosocial stress in pregnancy and preterm birth: associations and mechanisms. *Journal of Perinatal Medicine*, 41(6):631-645.
- Silva, D.F.O., Cobucci, R.N., Gonçalves, A.K. & Lima, S.C.V.C. 2019. Systematic review of the association between dietary patterns and perinatal anxiety and depression. *BMC Pregnancy and Childbirth*, 19(1):1-13.

Smartt, C., Medhin, G., Alem, A., Patel, V., Dewey, M., Prince, M. & Hanlon, C. 2016. Fatigue as a manifestation of psychosocial distress in a low-income country: a population-based panel study. *Tropical Medicine and International Health*, 21(3):365-372.

Song, J.E., Chae, H.J. & Kim, C.H. 2014. Changes in perceived health status, physical symptoms, and sleep satisfaction of postpartum women over time. *Nursing & Health Sciences*, 16(3):335-342.

South Africa. 1998. Domestic Violence Act 116 of 1998:1-14.

Sparling, T.M., Henschke, N., Nesbitt, R.C. & Gabrysch, S. 2017. The role of diet and nutritional supplementation in perinatal depression: a systematic review. *Maternal & Child Nutrition*, 13(1):1-36.

Stein, A., Pearson, R.M., Goodman, S.H., Rapa, E., Rahman, A., McCallum, M., Howard, L.M. & Pariante, C.M. 2014. Effects of perinatal mental disorders on the fetus and child. *The Lancet*, 384(9956):1800-1819.

Sumner, S.A., Mercy, J.A., Saul, J., Motsa-Nzuza, N., Kwessigabo, G., Buluma, R., Marcelin, L.H., Lina, H., Shawa, M., Moloney-Kitts, M., Kilbane, T., Sommarin, C., Ligiero, D.P., Brookmeyer, K., Chiang, L., Lea, V., Lee, J., Kress, H. & Hills, S.D. 2015. Prevalence of Sexual Violence Against Children and Use of Social Services - Seven Countries, 2007-2013. *Morbidity and Mortality Weekly Report*, 64(21):565-569.

Taylor, J. & Johnson, M. 2010. How women manage fatigue after childbirth. *Midwifery*, 26(3):367-375.

Teo, C., Chia, A.-R., Colega, M., Chen, L.-W., Fok, D., Pang, W., Godfrey, K., Tan, K., Yap, F., Shek, L., Chong, Y.-S., Meaney, M., Chen, H. & Chong, M. 2018. Prospective Associations of Maternal Dietary Patterns and Postpartum Mental Health in a Multi-Ethnic Asian Cohort: The Growing up in Singapore towards Healthy Outcomes (GUSTO) Study. *Nutrients*, 10(3):299.

Tsai, A.C., Scott, J.A., Hung, K.J., Zhu, J.Q., Matthews, L.T., Psaros, C. & Tomlinson, M. 2013. Reliability and validity of instruments for assessing perinatal depression in African settings: systematic review and meta-analysis. *PloS One*, 8(12):1-13.

Tsai, A.C., Tomlinson, M., Dewing, S., le Roux, I.M., Harwood, J.M., Chopra, M. & Rotheram-Borus, M.J. 2014. Antenatal depression case finding by community health workers in South Africa: feasibility of a mobile phone application. *Archives of Women's Mental Health*, 17(5):423-431.

Tuthill, E.L., Miller, J.D., Collins, S.M., Widen, E.M., Onono, M. & Young, S.L. 2020. HIV infection, hunger, breastfeeding self-efficacy, and depressive symptoms are associated with exclusive breastfeeding to six months among women in western Kenya: a longitudinal observational study. *International Breastfeeding Journal*, 15(1):4.

Tuthill, E.L., Pellowski, J.A., Young, S.L. & Butler, L.M. 2017. Perinatal Depression Among HIV-Infected Women in KwaZulu-Natal South Africa: Prenatal Depression Predicts Lower Rates of Exclusive Breastfeeding. *AIDS and Behavior*, 21(6):1691-1698.

van Heyningen, T.V., Myer, L., Onah, M., Tomlinson, M., Field, S. & Honikman, S. 2016. Antenatal depression and adversity in urban South Africa. *Journal of Affective Disorders*, 203:121-129.

Vaz, J.D., Kac, G., Emmett, P., Davis, J.M., Golding, J. & Hibbeln, J.R. 2013. Dietary patterns, n-3 fatty acids intake from seafood and high levels of anxiety symptoms during pregnancy: findings from the Avon Longitudinal Study of Parents and Children. *PloS One*, 8(7):1-9.

Vilela, A.A., Farias, D.R., Eshriqui, I., Vaz Jdos, S., Franco-Sena, A.B., Castro, M.B., Olinto, M.T., Machado, S.P., Moura da Silva, A.A. & Kac, G. 2014. Prepregnancy healthy dietary pattern is inversely associated with depressive symptoms among pregnant Brazilian women. *The Journal of Nutrition*, 144(10):1612-1618.

Watts, C. & Zimmerman, C. 2002. Violence against women: global scope and magnitude. *The Lancet*, 359(9313):1232-1237.

Wennberg, A.L., Lundqvist, A., Hogberg, U., Sandstrom, H. & Hamberg, K. 2013. Women's experiences of dietary advice and dietary changes during pregnancy. *Midwifery*, 29(9):1027-1034.

Whitehead, L. 2009. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. *Journal of Pain and Symptom Management*, 37(1):107-128.

WHO. 2008. Millennium Development Goal 5—improving maternal health. *World Health Organization*.

Woody, C.A., Ferrari, A.J., Siskind, D.J., Whiteford, H.A. & Harris, M.G. 2017. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. *Journal of Affective Disorders*, 219:86-92.

Workman, J.L., Barha, C.K. & Galea, L.A. 2012. Endocrine substrates of cognitive and affective changes during pregnancy and postpartum. *Behavioral Neuroscience*, 126(1):54-72.

Yousuf, A., Mohd Arifin, S.R., Musa, R. & Md Isa, M.L. 2019. Depression and HIV Disease Progression: A Mini-Review. *Clinical Practice and Epidemiology in Mental Health*, 15:153-159.

Associations of nutrient patterns during pregnancy with perinatal fatigue and depression among urban women in South Africa: The NuPED study

Vincent Smith ¹ , Cornelia Conradie ¹ , Marius Smuts ¹  and Jeannine Baumgartner ^{1,2,*} 

¹ Centre of Excellence for Nutrition (CEN), North-West University, 11 Hoffman street, 2520, South Africa; vincent.smith1990@gmail.com (V.S.); cornelia.conradie@nwu.ac.za (C.C.); marius.smuts@nwu.ac.za (M.S.)

² Laboratory of Human Nutrition, Institute of Food, Nutrition and Health, ETH Zurich, Schmelzbergstrasse 7, 8092 Zurich, Switzerland; jeannine.baumgartner@hest.ethz.ch

* Correspondence: jeannine.baumgartner@hest.ethz.ch; +41 44 632 86 32

Received: date; Accepted: date; Published: date

Abstract: Perinatal depression is a global public health problem with a higher prevalence in low- and middle-income countries (LMIC) compared to high-income countries. Women from LMIC are at greater risk of having an unhealthy diet during pregnancy, which is a known risk factor for depression. The aim of this study was to investigate associations of nutrient patterns early in pregnancy with perinatal fatigue and depression among women residing in urban Johannesburg, South Africa. As part of the Nutrition during Pregnancy and Early Development (NuPED) study, dietary data (n = 250) were obtained at enrolment (< 18 weeks' gestation) using a quantified food frequency questionnaire from which nutrient patterns were determined using exploratory factor analysis. Depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS) and fatigue using the Multidimensional Assessment of Fatigue (MAF) at three time points during pregnancy and two postnatally. Three nutrient patterns were identified: 1) “*Plant protein, iron, thiamine and folate*”, which decreased the risk for perinatal fatigue at 6 months postnatally (OR: 0.79; 95% CI: 0.63, 0.97; $p = 0.03$); 2) “*Animal protein, vitamin A, vitamin B₁₂ and copper*”, which increased the risk of depression at 12 months postnatally (OR: 1.24; 95% CI: 1.03, 1.48; $p = 0.02$), and; 3) “*Fatty acids and sodium*”, which increased the risk for depression at 6 months postnatally (OR: 1.29; 95% CI: 1.00, 1.67; $p = 0.06$). These results indicate a potential role of the maternal diet during pregnancy in the development of maternal fatigue and depression.

Keywords: perinatal depression; perinatal fatigue; dietary patterns; nutrient patterns; pregnancy; antenatal.

1. Introduction

Depression during the perinatal period (pregnancy and up to one year postnatally) is a debilitating health problem worldwide, affecting around 11.9% women [1]. In low- and middle-income countries (LMIC) the prevalence is higher than in high-income countries (HIC) [2]. Prevalence rates in HIC range between 3% and 20%, and in LMIC between 4.9% and 59.4% [1,3–7]. In South Africa (SA) the prevalence has been estimated to be four times higher than the global average [2,8–10]. This might be due to maternal mental health being largely neglected in LMIC [11]. The higher risk for perinatal depression in LMIC can be attributed to poverty, lack of social support and substance abuse [12]. In SA specifically, human immunodeficiency virus (HIV) and partner violence have been identified as additional risk factors [8]. Fatigue during the perinatal period is common and was shown to have a bi-directional relationship with perinatal depression [13,14].

Antenatal depression is associated with an increased likelihood of epidural analgesia during labour as well as an increased likelihood of planned caesarean delivery [15,16]. In LMIC specifically, there is a higher risk for infant diarrhoea, poor child growth and poor mental development [17]. Maternal depressive symptoms have been associated with child emotional-behavioural dysregulation (up to the age of seven) [18]. Associations have also been found between perinatal depression and a higher level of psychiatric disturbances among children [19-21]. Perinatal depression has been associated with missed paediatric appointments and more frequent use of emergency department services [20,22]. It has been hypothesized that mothers with depression are more likely to have undervaccinated (selective, partial or delayed vaccinated) children [23]. Postnatal depression affects the caregiving ability of the mother, which can have long-term effects on her child [1,11,17,24]. Antenatal fatigue has been associated with poor foetal development, early-onset labour, caesarean section, as well as poor child motor- and mental development [25,26]. Antenatal stress, usually reported as tiredness or fatigue, has been shown to cause negative obstetric outcomes including pregnancy-induced hypertension, poor foetal development, early delivery, and lower birth weight for gestational age [24,26].

The plausibility of a relationship between an unhealthy diet and perinatal depression has been shown in a large prospective birth cohort study of 7814 mother-child pairs [18]. Nutrient demands from the foetus, which constantly change over various developmental stages, necessitate the need for the maternal diet during the antenatal period to be of enhanced nutrient density. Some micronutrients, such as zinc, iron, vitamin D, selenium and folate were found to be inversely associated with depressive symptoms [12].

Recent epidemiological studies are focusing on dietary pattern (eating pattern) analysis. Dietary pattern analysis is a composite measure of dietary quality [27]. Dietary patterns can be generated empirically by means of statistical methods without the need of researchers to define a healthy eating pattern [28]. Dietary patterns encompass the totality of the diet while also allowing multiple ways to achieve a healthy diet. Public health recommendations and guidelines could be most easily translated into eating behaviours when described by dietary patterns [27].

In terms of overall disease risk reduction, dietary components (nutrients) are the same as dietary patterns. This gives researchers the opportunity to use a range of foods to customize the dietary patterns to meet their needs. Foods can be included to align with cultural and religious practices, food availability, sensory appeal and income. This pattern is flexible and customizable irrespective of the designated research label [29]. Studying nutrient patterns has several advantages. In contrast to food patterns, nutrients are to a large extent universal and may characterize specific nutritional profiles in such a way that it is easier to compare populations. Furthermore, an enhanced mirroring of bioactive nutrients in complex biological mechanisms associated with disease is obtained by nutrient patterns compared to food patterns [30].

The “Rhea” prospective mother-child cohort study which included 529 pregnant women from Greece aimed to identify associations between dietary patterns and postnatal depression. The study demonstrated that following a “health-conscious” diet over a “Western” diet during the antenatal period was associated with lower depressive scores [31]. A study conducted in Singapore found that a “Traditional-Indian-Confinement” pattern was associated with fewer symptoms of postpartum depression. The authors ascribed this to the herbs and spices (saffron, fenugreek and curcumin) commonly used, which have shown to have anti-inflammatory, serotonergic, neuroprotective and HPA axis regulatory effects [32-34]. Another group of researchers delineated between “healthy” and “unhealthy” food group before analysis. They concluded that a higher intake of “unhealthy” foods and lower intake of “healthy” foods were related to higher depressive symptoms [35]. A Brazilian study found that a “healthy” dietary pattern pre-pregnancy was inversely associated with depressive symptoms throughout the perinatal period [36]. Another Brazilian study found that a “healthy” diet lowered the prevalence of common mental disorders during pregnancy [37]. Dietary patterns which include high consumption of minimally processed foods and low consumption of ultra-processed foods were inversely associated with perinatal depression [38].

As perinatal depression is a major health problem in SA [10] and diet plays a potential role [12], it is warranted to investigate the potential role of the rapid nutritional transition in SA in the development of perinatal depression [39]. This nutrition transition, which is the result of social- and economic-development as well as urbanization, is described as the increase consumption of processed and animal-derived foods [40,41]. This resulted in a double burden of under- and over-nutrition [42], as well as an increased prevalence

of obesity and non-communicable diseases [40]. The aim of this study was therefore to investigate associations of nutrient patterns early in pregnancy with perinatal fatigue and depression among women residing in urban Johannesburg, South Africa.

2. Materials and Methods

2.1. Study design and participants

This study formed part of the prospective Nutrition during Pregnancy and Early Development (NuPED) cohort conducted in Johannesburg, South Africa. The study protocol has previously been published [43]. In brief, pregnant women were recruited from primary health clinics in Johannesburg. Women were included in the study if they had a confirmed pregnancy, were less than 18 weeks' gestation and intended to deliver the baby at Rahima Moosa Mother and Child Hospital (RMMCH). Only participants from South Africa and selected neighbouring countries (Namibia, Botswana, Swaziland and Lesotho) were included and participants had to be able to effectively communicate in either English, Afrikaans, Zulu, Xhosa or Sotho. Women were excluded if they were less than 18 or more than 39 years of age or if they were having a multiple pregnancy. Women who self-confessed to illicit drug use or were smoking tobacco products (currently or in the past year) were also excluded from the study. Potential participants who had a known non-communicable (hypertension, diabetes, high blood cholesterol or renal disease) disease or serious illness (psychosis, lupus or cancer) were excluded from the study. In terms of infectious disease (tuberculosis or hepatitis), women were excluded except if they had HIV. Due to South Africa's high prevalence of HIV (36% in women aged 30 - 34 years [44]), women who were HIV positive were included in the study in order for it to be a better representation of the general population.

Women included in the study were followed-up at the antenatal clinic of RMMCH. Data were collected during pregnancy (< 18-, 22- and 36-weeks' gestation) as well as the postnatal period (6 and 12 months postpartum).

2.2. Outcome measurements

The primary outcome variables in this study were perinatal fatigue and depression. Fatigue was measured using the self-administered Multidimensional Assessment of Fatigue (MAF) scale. Data derived from the MAF were used to calculate the Global Fatigue Index (GFI). A cut off of > 28 was used as it has been previously shown to be indicative of fatigue [25]. The Edinburgh Postnatal Depression scale (EPDS) was administered by field workers in order to assess perinatal depressive symptoms. Many studies use an EPDS cut-off of ≥ 13 to classify perinatal depression as this number identifies women in need of evaluation for possible depression [24]. Although higher cut-offs allow for greater specificity it is at the cost of sensitivity [45]. A cut off of ≥ 9 has been shown to enhance sensitivity [45] and was used in this study to classify women as being at risk of depression.

2.3. Exposure measurements

An interviewer-administered Quantified Food Frequency Questionnaire (QFFQ) was conducted by trained field workers at the baseline visit (< 18 weeks' gestation). The QFFQ has been validated [46], and its reproducibility proven within the population being studied [46,47]. During the QFFQ, participants were asked regarding 140 food items in as much detail as possible with regards to the brand used, cooking methods, portion size and frequency. Standard measuring equipment, common size containers (cups, bowls and glasses) along with two- and three-dimensional food models were used to assist in quantifying portion sizes. The QFFQ examined all food and drink consumed in the past four weeks. Portion sizes were converted to grams per week by three registered dietitians/nutritionists using the South African Medical Research Council (SAMRC) food quantities manual [48] and coded using the SAMRC food composition database [49]. Nutrient analysis to determine daily intakes were done by the SAMRC by linking the coded dataset to the latest database available at the time. Although the larger NuPED study collected dietary data at more than one time point, only dietary data from one time point was used for the purpose of this analysis as Crozier *et al.* [50] demonstrated that there is little overall change in dietary patterns throughout pregnancy.

Exploratory factor analysis was used to determine nutrient patterns from 22 nutrients obtained from the QFFQ [51]. Total protein was reported as plant- and animal protein, total fat as saturated-, monounsaturated- and polyunsaturated fatty acids and carbohydrates as total carbohydrate and total sugar intake. Spearman and Pearson correlation coefficients were used to explore the correlation structure of the nutrient intake. Raw nutrient data were used for the analysis as the difference between the coefficients was minimal (<0.1). Energy adjustment was done for nutrients according to the nutrient density model previously published by Willet *et al.* [52]. The principal factor method with correlation matrix was applied, and the reliability of the factor analysis was verified using the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy as well as Bartlett's test of sphericity. A KMO value of >0.5 and significance ($p < 0.05$) on Bartlett's test were regarded as adequate. Scree plots, eigenvalues (>1.00), the interpretability of the factors and the proportion of variance explained were used to interpret retained factors for further analysis. Nutrient patterns (retained factors) were rotated by Varimax (orthogonal) rotation for simpler structure and improved interpretation. The naming and interpretation of patterns were based on the nutrients with an absolute loading ≥ 0.40 . Positive loadings indicate that a nutrient is positively associated with the nutrient pattern and a negative loading shows a negative association with the pattern. For each participant, factor scores were calculated to indicate the degree to which a participant's nutrient intake conforms to the identified patterns. To compute factor scores, the standardized intakes of each nutrient was weighted with their factor loading after which the nutrients were summed within the respective patterns [28].

2.4. Covariates

At the baseline visit (<18 weeks' gestation) maternal socio-demographic and -economic data were obtained through an interviewer-administered questionnaire. This included maternal age, country of birth, ethnicity, educational level, marital status, employment status and the number of household members who were beneficiaries of a social support grant. Data on living standard were also obtained in order to classify participants' socioeconomic status according to the Living Standard Measure (LSM) [53].

Maternal anthropometric data were collected using methods as standardized by the International Society for the Advancement of Kinanthropometry [54]. Weight, height and mid-upper arm circumference (MUAC) measurements were obtained at all time points. All measurements were taken twice and recorded to the nearest 0.1 cm for height and MUAC and 0.05 kg for weight. Weight measurements were done using a calibrated scale (Seca 813, Hamburg, Germany), height with a mobile stadiometer (Seca 213, Hamburg, Germany) and a metal non-stretchable measuring tape (Seca 201, Hamburg, Germany) for MUAC. Body Mass Index (BMI) was obtained by dividing weight (kg) by height (m) squared.

Although more data were obtained for the larger NuPED study, these were selected for this analysis in order to describe the population and control for potential confounders in statistical models.

2.5. Statistical methods

The number of subjects to sample was calculated by means of a priori sample size calculation in the G*Power 3.1.9.2 statistical program [55]. The calculation was based on a small effect size F_2 of 0.05; probability of error (α) of 5%; a power of 80%. The outcome was that 160 subjects would be required. Considering an opt-out rate of 30% the minimum subjects required would be 208. In order to increase the power of the inclusion of other maternal and offspring health outcomes, 250 subjects were enrolled.

Data processing and analysis was done using SPSS 24 (SPSS Inc, Chicago, IL, USA) with the level of significance set at $p < 0.05$. All data were tested for outliers and normality through visual inspection of Q-Q plots and Kolmogorov-Smirnov test prior to data analysis and description. Normally distributed data were presented as means $\pm$ standard deviation (SD) with 95% confidence intervals (CI). Non-normally distributed data were reported as medians (25th – 75th centiles). Categorical variables were reported as frequencies and percentages.

Descriptive statistics were conducted to obtain information on possible confounders or covariates. Multiple linear regression analyses were done to determine associations between nutrient patterns (factor scores) and depressive symptoms (EPDS scores) and fatigue (GFI) scores. The β coefficient as well as the CI were reported. Binary logistic regression analyses were conducted to determine associations between nutrient patterns (factor scores) and depression (EPDS ≥ 9) and fatigue (GFI > 28). Odds Ratios (OR) and CI were reported. All regression models (linear and logistic) were adjusted for maternal age, educational level, employment status and LSM score.

2.6. Ethical considerations

Potential subjects were supplied with an informed consent form. Before data collection, written consent was obtained from all participants. This study was conducted in accordance with the Declaration of Helsinki and all procedures were approved by the Health Research Ethics Committee of the North-West University, Potchefstroom (NWU-00186-15-A1-06) as well as the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg (M150968). Permission to conduct this research at the indicated clinical setting was granted by the Gauteng Health Department, City of Johannesburg District Research Committee and the Clinical Manager of RMMCH.

3. Results

3.1. Subject Characteristics

In total, 595 women living in Johannesburg, South Africa, were recruited and invited to take part in the NuPED study. More than half (53%) volunteered to take part in the study and signed written informed consent. Following screening, 63 women were excluded as per the inclusion and exclusion criteria. A total of 250 women were enrolled in the study and completed data collection at baseline (< 18 weeks gestation) with only 246 completing the EPDS and 241 the MAF. At the first follow-up (22 weeks gestation), 230 women completed the EPDS and 225 the MAF. This number decreased to 197 women completing the EPDS and 195 completing the MAF at the third time point (36 weeks gestation). At the first postnatal visit (6 months postnatal), 87 women completed the EPDS and 92 the MAF. During the final visit (12 months postnatal), 92 women completed the EPDS and 87 the MAF.

Table 2 summarizes the characteristics of the women included in the study along with socio-economic and lifestyle indicators at the time of enrolment. The median maternal age was 27 years (24 - 32) and mean gestational age 14.3 weeks (9.4 - 16.1). Most of the participants (88%) were of Black African descent and born in South Africa (72%). More than a quarter of participants were HIV positive. Although most of the participants (58.2%) have completed grade 11 or 12 in terms of education, almost half (49.4%) of the participants were unemployed. In terms of LSM score, most participants (59.2%) were classified as having a "medium" and over a third (34%) as having a "high" living standard.

3.2. Nutrient patterns

Three nutrient patterns were retained, which accounted for 56.57% of the total variance (eigenvalue > 2.5). The analysis was appropriate for the study based on the KMO measure (0.7) and Bartlett's test ($p < 0.001$). Table 3 summarizes nutrient patterns and factor loadings extracted using factor analysis. Dominant nutrients within each factor were used to name the patterns. Factor one was named "*Plant protein, iron, thiamine and folate*" and had high loading for plant protein, carbohydrates, fibre, zinc, iron, thiamine, niacin, vitamin B₆ and folate. This nutrient pattern was negatively associated with animal protein, saturated- and monounsaturated fatty acids as well as calcium. Factor two was named "*Animal protein, vitamin A, vitamin B₁₂ and copper*" and had positive loading for cholesterol, riboflavin and zinc. Factor three was named "*Fatty acids and sodium*" and had high positive loadings for saturated-, monounsaturated- and polyunsaturated fatty acids, vitamin E and sodium.

Table 2: Characteristics of participants at the time of enrolment (< 18 weeks) into the NuPED study.

Characteristics		Median (IQR) or n (%)
Maternal age (years)		27 (24 – 32)
Gestational age at enrolment (weeks)		14.3 (9.4 – 16.1)
Weight at enrolment (kg)		67.4 (58.0 – 91.6)
BMI at enrolment (kg/m ²)		26.3 (23.0 – 30.6)
People per household		3 (2 – 4)
Ethnicity	Black African	219 (88.0)
	Mixed ancestry	28 (11.2)
	Indian	1 (0.4)
	White	1 (0.4)
Country of birth	South Africa	172 (72.0)
	Zimbabwe	60 (25.1)
	Lesotho	4 (1.7)
	Swaziland	3 (1.3)
Education level	Primary school / None	9 (3.6)
	Grade 8 – 10	37 (14.9)
	Grade 11 – 12	145 (58.2)
	Tertiary	58 (23.3)
Employment status	Unemployed	123 (49.4)
	Wage-earner	111 (44.6)
	Self-employed	10 (4)
	Self-employed professional	1 (0.4)
	Other	4 (1.6)
HIV status	Positive	64 (25.6)
	Negative	186 (74.4)
LSM score	Low (1 – 4)	17 (6.8)
	Medium (5 – 7)	148 (59.2)
	High (8 – 10)	85 (34.0)

IQR: interquartile range; HIV: human immunodeficiency virus; LSM: living standards measure

3.3. Depression and Fatigue

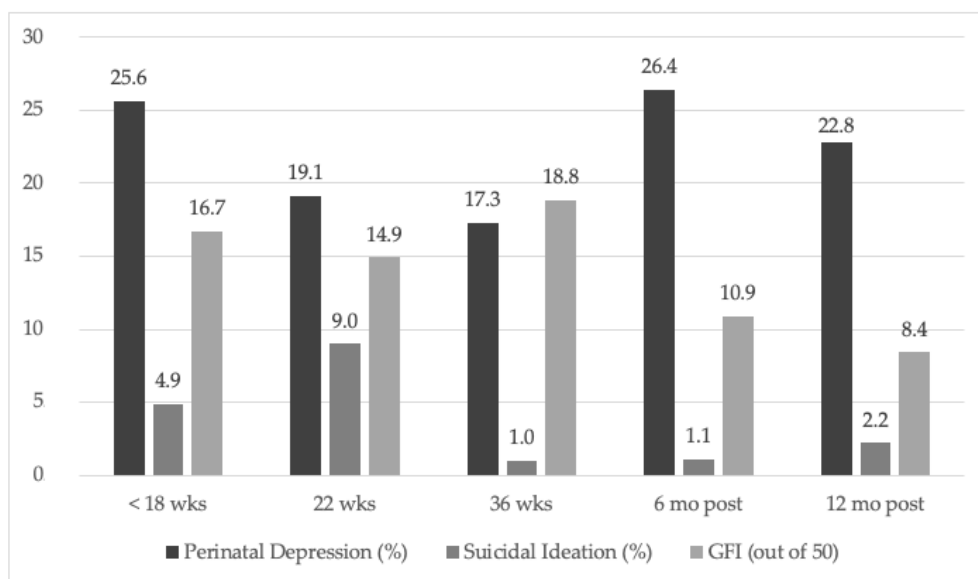
The prevalence of perinatal depression, suicidal ideation and fatigue varied across time points. Figure 2 summarizes the trajectory of these variables across the various time points. Prevalence rates for depression ranged from 17.3% to 26.4%, and prevalence rates for fatigue ranged from 8.4% to 18.8% across the perinatal period. Similarities in trend can be seen between perinatal depression and fatigue antenatally. Suicidal ideation does not seem to have similarities with the trends of perinatal depression or fatigue.

Table 3: Nutrient patterns and factor loadings extracted through factor analysis (n = 250)

Nutrients and variance	Factors (nutrient patterns) ¹		
	Factor 1 (Plant protein, iron, thiamine and folate)	Factor 2 (Animal protein, vitamin A, vitamin B ₁₂ and copper)	Factor 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
Folate	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 ²	27%	18%	11.5%

¹ Factor analysis included 22 nutrients; factor scores presented after rotation of the data. Nutrients considered to have strong association with the nutrient patterns (factor loadings ≤ -0.4 or ≥ 0.4) are indicated in **bold**.

² Total variance: 56.5%



wks: weeks gestation; mo post: months postnatal; GFI: global fatigue index

Figure 2: Prevalence of perinatal depression, suicidal ideation and fatigue across various time points.

3.4. Associations of fatigue scores with dietary data

Multiple linear regression analyses were conducted to determine associations between nutrient patterns (factor scores) and fatigue (GFI) scores, using fatigue as a continuous variable, at the different antenatal and postnatal time points (Table 4). The “*Plant protein, iron, thiamine and folate*” nutrient pattern (Factor 1) tended to be negatively associated with maternal fatigue at 6 months postnatally ($\beta = -0.56$; 95% CI: -1.18, 0.06; $p = 0.07$), but no other time points.

Binary logistic regression analyses were conducted to identify possible associations of the identified nutrient patterns (factor scores) with perinatal fatigue (GFI > 28), using fatigue as a categorical variable. These results are summarized in Table 5. The “*Plant protein, iron, thiamine and folate*” nutrient pattern (Factor 1) was associated with a decreased risk for perinatal fatigue only at 6 months postnatally (OR: 0.79; 95% CI: 0.63, 0.97; $p = 0.03$).

Table 4: Associations between perinatal fatigue (GFI total score) and nutrient patterns (factor scores)
(Multiple linear regression, β -values and 95% confidence intervals)

Perinatal fatigue (GFI)				
Time	Predictor	β	95% CI	p
< 18 weeks gestation	Factor 1	-0.23	-0.62, 0.15	0.24
	Factor 2	0.02	-0.55, 0.58	0.96
	Factor 3	0.08	0.66, 0.83	0.83
22 weeks' gestation	Factor 1	-0.16	-0.54, 0.22	0.41
	Factor 2	-0.11	-0.66, 0.45	0.71
	Factor 3	0.06	-0.67, 0.79	0.87
36 weeks' gestation	Factor 1	0.00	-0.42, 0.42	0.99
	Factor 2	-0.21	-0.82, 0.41	0.51
	Factor 3	0.10	-0.71, 0.90	0.81
6 months postnatal	Factor 1	-0.56	-1.18, 0.06	0.07
	Factor 2	0.46	-0.44, 1.36	0.31
	Factor 3	0.53	-0.66, 1.71	0.38
12 months postnatal	Factor 1	0.05	-0.56, 0.66	0.87
	Factor 2	0.07	-0.82, 0.95	0.88
	Factor 3	0.08	-1.09, 1.25	0.89

GFI: global fatigue index; CI: confidence interval

Table 5: Associations between perinatal fatigue (GFI > 28) and nutrient patterns (factor scores)
(Binary logistic regression, odds ratios and 95% confidence intervals)

Perinatal fatigue (GFI > 28)				
Time	Predictor	OR	95% CI	p
< 18 weeks gestation	Factor 1	0.95	0.88, 1.02	0.14
	Factor 2	1.00	0.88, 1.13	0.96
	Factor 3	1.02	0.89, 1.17	0.77
22 weeks' gestation	Factor 1	0.96	0.88, 1.05	0.41
	Factor 2	1.05	0.93, 1.19	0.45
	Factor 3	1.01	0.87, 1.18	0.86
36 weeks' gestation	Factor 1	0.98	0.91, 1.06	0.65
	Factor 2	1.02	0.91, 1.13	0.77
	Factor 3	1.01	0.88, 1.15	0.94
6 months postnatal	Factor 1	0.79	0.63, 0.97	0.03
	Factor 2	0.88	0.64, 1.21	0.44
	Factor 3	1.29	0.90, 1.84	0.16
12 months postnatal	Factor 1	1.03	0.87, 1.21	0.75
	Factor 2	1.16	0.92, 1.47	0.22
	Factor 3	0.91	0.63, 1.32	0.62

3.5. Associations of depression scores with dietary data

Multiple linear regression analyses were conducted in order to determine associations between perinatal depression (EPDS total score) and nutrient patterns (factor scores). The results are summarised in Table 6. The “Fatty acids and sodium” nutrient pattern (Factor 3) was positively associated with perinatal depression at six months postnatally (postnatally ($\beta = 0.55$; 95% CI: 0.12, 0.98; $p = 0.01$). This association was not seen at any other time points. The “Animal protein, vitamin A, vitamin B₁₂ and copper” nutrient pattern (Factor 2) was positively associated with perinatal depression at 12 months postnatally ($\beta = 0.40$; 95% CI: 0.08, 0.73; $p = 0.02$) and no other time points. Binary logistic regression analyses were conducted to identify possible associations between nutrient patterns (factor scores) and perinatal depression (EPDS of ≥ 9). Table 7 below summarizes the findings. The “Fatty acids and sodium” nutrient pattern (Factor 3), tended to increase risk for perinatal depression only at six months postnatally (OR: 1.29; 95% CI: 1.00, 1.67; $p = 0.06$). Women consuming an “Animal protein, vitamin A, vitamin B₁₂ and copper” dietary pattern (Factor 2) were at a higher risk of developing depression 12 months postnatally (OR: 1.24; 95% CI: 1.03, 1.48; $p = 0.02$), but not at any other time point.

Table 6: Associations between perinatal depression (EPDS total score) and nutrient patterns (factor scores)
(Multiple linear regression, β -values and 95% confidence intervals)

Perinatal depression (EPDS)				
Time	Predictor	β	95% CI	p
< 18 weeks gestation	Factor 1	-0.04	-0.18, 0.11	0.62
	Factor 2	0.05	-0.16, 0.26	0.66
	Factor 3	0.11	-0.17, 0.39	0.43
22 weeks' gestation	Factor 1	-0.04	-0.16, 0.08	0.51
	Factor 2	-0.05	-0.22, 0.13	0.61
	Factor 3	0.06	-0.18, 0.29	0.64
36 weeks' gestation	Factor 1	-0.04	-0.18, 0.10	0.56
	Factor 2	0.04	0.16, 0.24	0.68
	Factor 3	0.15	-0.11, 0.41	0.27
6 months postnatal	Factor 1	0.01	-0.22, 0.24	0.94
	Factor 2	0.19	-0.14, 0.52	0.26
	Factor 3	0.55	0.12, 0.98	0.01
12 months postnatal	Factor 1	-0.02	-0.25, 0.20	0.85
	Factor 2	0.40	0.08, 0.73	0.02
	Factor 3	0.19	-0.24, 0.62	0.38

EPDS: Edinburgh postnatal depression scale; CI: confidence interval

Table 7: Associations between perinatal depression (EPDS ≥ 9) and nutrient patterns (factor score)
(Binary logistic regression, odds ratios and 95% confidence intervals)

Time	Predictor	Perinatal depression (EPDS ≥ 9)		
		OR	95% CI	<i>p</i>
< 18 weeks gestation	Factor 1	0.99	0.93, 1.07	0.84
	Factor 2	1.03	0.94, 1.14	0.51
	Factor 3	1.04	0.92, 1.19	0.51
22 weeks' gestation	Factor 1	1.03	0.95, 1.12	0.48
	Factor 2	0.94	0.82, 1.08	0.39
	Factor 3	1.13	0.97, 1.32	0.12
36 weeks' gestation	Factor 1	0.99	0.90, 1.08	0.77
	Factor 2	0.87	0.72, 1.06	0.16
	Factor 3	1.14	0.95, 1.35	0.16
6 months postnatal	Factor 1	1.10	0.96, 1.27	0.17
	Factor 2	1.15	0.97, 1.36	0.11
	Factor 3	1.29	1.00, 1.67	0.06
12 months postnatal	Factor 1	1.04	0.92, 1.19	0.53
	Factor 2	1.24	1.03, 1.48	0.02
	Factor 3	1.01	0.79, 1.30	0.93

EPDS: Edinburgh postnatal depression scale; OR: odds ratio; CI: confidence interval

3.6. Associations of depression scores with fatigue scores

In order to identify associations between depression scores (EPDS) and fatigue scores (GFI), multiple linear regression analyses were performed. Table 8 below summarizes these results. Perinatal fatigue (GFI scores) was significantly associated with perinatal depression (EPDS scores) throughout pregnancy and up to six months postnatally ($p < 0.001$) but not at 12 months postnatally.

Table 8: Associations between perinatal fatigue (GFI scores) and depression (EPDS scores)
(Binary logistic regression, β -values and 95% confidence intervals)

Time	Perinatal depression (EPDS score)		
	β	95% CI	<i>p</i>
< 18 weeks' gestation	1.14	0.93, 0.18	<0.001
22 weeks' gestation	1.11	0.07, 0.15	<0.001
36 weeks' gestation	0.11	0.06, 0.15	<0.001
6 months postnatal	0.13	0.06, 0.63	<0.001
12 months postnatal	0.04	-0.06, 0.13	0.46

GFI: global fatigue index; EPDS: Edinburgh postnatal depression scale; CI: confidence interval;

4. Discussion

In this cohort of pregnant women residing in urban Johannesburg, we determined that a “Plant protein, iron, thiamine and folate” nutrient pattern may reduce the likelihood perinatal fatigue in the early postnatal period. Additionally, it was determined that a “Fatty acids and sodium” nutrient pattern may increase the risk for perinatal depression in the early postnatal period, and that an “Animal protein, vitamin A, vitamin B₁₂ and copper” nutrient pattern may increase the risk for perinatal depression later in the postnatal period. We also determined that perinatal fatigue is associated with perinatal depression.

The prevalence of fatigue was 16.7% at baseline (< 18 weeks gestation), decreasing to 14.9% at 22 weeks gestation. The prevalence of fatigue in this sample of women peaked again at 36 weeks gestation (18.8%) after which prevalence lowered to 10.9% at six months postnatally and 8.4% at 12 months postnatally. Over a quarter (25.6%) of women were depressed at baseline (<18 weeks gestation), and by 22 weeks gestation less than a fifth (19.1%) were depressed. Depression prevalence continued along a downward trend to 17.3% at 36 weeks gestation. At six months postnatally a sharp increase was observed to 26.4%, which lowered to 22.8%

at 12 months postnatally. These findings are inconsistent with previous findings which indicate that late antenatal depression rates are comparable (if not higher) than postnatal depression rates [56]. This may, however, be explained by other research that found antenatal depression to be a strong risk factor for postnatal depression [57]. Moreover, the physical and emotional demands of childbirth may further increase a women's risk for developing postnatal depression [58]. Women from LMIC are exposed to more risk factors known to influence the development of perinatal depression. These risk factors include intimate partner violence, food insecurity, sanitation deficiencies, childhood abuse and high prevalence of disease (such as HIV and malaria) [19].

We identified three nutrient patterns: 1) "*Plant protein, iron thiamine and folate*" (Factor 1); 2) "*Animal protein, vitamin A, vitamin B₁₂ and copper*" (Factor 2); 3) "*Fatty acids and sodium*" (Factor 3). We found a significant negative association between the "*Plant protein, iron, thiamine and folate*" nutrient pattern (Factor 1) and perinatal fatigue 6 months postnatally. Positive associations were found between the "*Fatty acids and sodium*" nutrient pattern (Factor 3) and perinatal depression six months postnatally, and the "*Animal protein, vitamin A, vitamin B₁₂ and copper*" nutrient pattern (Factor 2) and perinatal depression 12 months postnatally.

The negative association between the "*Plant protein, iron, thiamine and folate*" nutrient pattern (Factor 1) and perinatal fatigue may be due to the micronutrients present in this nutrient pattern (thiamine, niacin, folate, vitamin B₆, iron and zinc). B vitamins (thiamine, niacin, folate and B₆) in general are required for proper functioning of the energy-production system [59]. Animal studies have shown that a thiamine (vitamin B₁) deficiency leads to a reduction in the concentration of a specific neurotransmitter, GABA (γ -aminobutyric acid) [60], which regulates sleep and has a potential to evoke fatigue [61]. Fatigue has been observed in iron deficient individuals and fatigue improved after supplementation with iron [62]. As deficiencies of these nutrients may lead to fatigue, one can hypothesise that a diet providing adequate amounts would decrease the risk of fatigue.

An increased risk for depression associated with the "*Fatty acids and sodium*" nutrient pattern (Factor 3) might be due to the high content of fatty acids, especially saturated fatty acids (SFA). In the "*Western*" diet, monounsaturated fatty acids (MUFA) and PUFA are replaced by SFA [63]. This nutrient pattern may indicate this happening in South Africa as well, potentially due to the nutrition transition. A large cohort study found a positive association between total fat and depression, and a negative association between MUFA and PUFA and depression [63]. A potential mechanism whereby a high fat diet leads to brain inflammation has been indicated by previous research [64]. In rodents, depressive-like behaviour induced by a high fat diet has been positively associated with brain inflammation [65]. There is a lack of evidence on the relationship between sodium intake and depression in humans. Existing evidence demonstrated that depression may lead to a preference for salt [66]. No studies could be found investigating sodium as a contributing or causative factor in depression.

The "*Animal protein, vitamin A, vitamin B₁₂ and copper*" nutrient pattern (Factor 2) increasing the risk of depression at six months postnatally, maybe due to the high loading for animal protein. High meat intake has been shown to moderately increase the risk of depression despite limited research on the topic [67]. With regards to the high loading for dietary cholesterol, most research on cholesterol and depression have been on serum cholesterol levels and not dietary intakes. These studies found that lower serum cholesterol was associated with a higher risk of suicide or violence-related death [68,69].

One needs to keep in mind that dietary patterns do not significantly change over the perinatal period [50,70,71]. Thus, one could assume that the diet followed early in pregnancy would probably be continued into the postnatal period, thereby explaining how dietary measurements from early pregnancy may describe postnatal depressive symptoms. The positive factor loading for micronutrients (zinc, copper, vitamin A, riboflavin and vitamin B₁₂) probably did not contribute to depression. This is due to lower concentrations of serum zinc increasing the risk of depression [72]. Individuals with copper intakes that meet the Recommended Dietary Allowance were shown to have a significantly lower risk of developing depression [73]. Studies further suggest that the consumption of riboflavin-rich foods decreases the risk of perinatal depression [74,75]. It has also been shown that vitamin B₁₂ deficiency may result in severe depression, suicidal behaviour and psychosis [76].

Strengths of this study include an appropriate sample size to determine prevalence of fatigue and depression, its prospective design and the use of validated measurement instruments.

One of the limitations of this study was a low retention rate in long-term follow-up.

5. Conclusions

These results indicate a potential role of maternal diet during pregnancy in the development of maternal fatigue and depression during and after pregnancy. We have demonstrated the importance of adequate micronutrient and omega-3 fatty acid intake during pregnancy which emphasizes the need for antenatal micronutrient supplementation. More research is needed to further elucidate the relationship between diet during pregnancy with fatigue and depression. Future studies should consider nutrient analysis and empirically derived dietary or nutrient patterns. This will eliminate researcher bias in terms of defining an *a priori* “healthy” diet [28]. Nutrient patterns are also universal [30], making recommendations internationally relevant.

Author Contributions: Conceptualization, V.S., J.B., C.C. and M.S.; methodology, J.B. and M.S.; software, V.S., J.B. and C.C.; validation, J.B. and C.C.; formal analysis, C.C. and V.S.; investigation, M.S.; resources, J.B. and C.C.; data curation, J.B., C.C. and V.S.; writing—original draft preparation, V.S.; writing—review and editing, J.B., C.C. and V.S.; visualization, V.S.; supervision, J.B. and C.C.; project administration, V.S.; funding acquisition, J.B. and M.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research was partly funded by THE NATIONAL RESEARCH FOUNDATION OF SOUTH AFRICA, grant number 99374. Funding was received from THE SOUTH AFRICAN MEDICAL RESEARCH COUNCIL in the form of a self-initiated research grant. Further financial support was received from THE UNIVERSITY OF SOUTH AFRICA’S RESEARCH DEPARTMENT for the grant *Academic Qualification Improvement Programme*.

Acknowledgments: We would like to thank all our participants for their time and participation. We acknowledge all nursing staff from RMMCH and primary health clinics in Johannesburg as well as midwives, field workers and all other medical professionals involved in data collection.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

1. Woody, C.A.; Ferrari, A.J.; Siskind, D.J.; Whiteford, H.A.; Harris, M.G. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. *J Affect Disord* **2017**, *219*, pp. 86-92.
2. Manikkam, L.; Burns, J.K. Antenatal depression and its risk factors: an urban prevalence study in KwaZulu-Natal. *S Afr Med J* **2012**, *102*, pp. 940-944.
3. Fisher, J.; Cabral de Mello, M.; Patel, V.; Rahman, A.; Tran, T.; Holton, S.; Holmes, W. Prevalence and determinants of common perinatal mental disorders in women in low- and lower-middle-income countries: a systematic review. *Bull World Health Organ* **2012**, *90*, pp. 139-149.
4. Gelaye, B.; Rondon, M.B.; Araya, R.; Williams, M.A. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. *The Lancet Psychiatry* **2016**, *3*, pp. 1-28.
5. Howard, L.M.; Molyneaux, E.; Dennis, C.-L.; Rochat, T.; Stein, A.; Milgrom, J. Non-psychotic mental disorders in the perinatal period. *The Lancet* **2014**, *384*, pp. 1775-1788.
6. Lara, M.A.; Navarrete, L.; Nieto, L.; Barba Martín, J.P.; Navarro, J.L.; Lara-Tapia, H. Prevalence and incidence of perinatal depression and depressive symptoms among Mexican women. *J Affect Disord* **2015**, *175*, pp. 18-24.
7. Redinger, S.; Norris, S.A.; Pearson, R.M.; Richter, L.; Rochat, T. First trimester antenatal depression and anxiety: prevalence and associated factors in an urban population in Soweto, South Africa. *J Dev Orig Health Dis* **2018**, *9*, pp. 30-40.

8. Rochat, T.J.; Tomlinson, M.; Barnighausen, T.; Newell, M.L.; Stein, A. The prevalence and clinical presentation of antenatal depression in rural South Africa. *J Affect Disord* **2011**, *135*, pp. 362-373.
9. Tuthill, E.L.; Pellowski, J.A.; Young, S.L.; Butler, L.M. Perinatal Depression Among HIV-Infected Women in KwaZulu-Natal South Africa: Prenatal Depression Predicts Lower Rates of Exclusive Breastfeeding. *AIDS and Behavior* **2017**, *21*, pp. 1691-1698.
10. van Heyningen, T.V.; Myer, L.; Onah, M.; Tomlinson, M.; Field, S.; Honikman, S. Antenatal depression and adversity in urban South Africa. *J Affect Disord* **2016**, *203*, pp. 121-129.
11. Honikman, S.; van Heyningen, T.; Field, S.; Baron, E.; Tomlinson, M. Stepped care for maternal mental health: a case study of the perinatal mental health project in South Africa. *PLoS Med* **2012**, *9*, pp. 1-6.
12. Baskin, R.; Hill, B.; Jacka, F.N.; O'Neil, A.; Skouteris, H. The association between diet quality and mental health during the perinatal period. A systematic review. *Appetite* **2015**, *91*, pp. 41-47.
13. Giallo, R.; Gartland, D.; Woolhouse, H.; Brown, S. "I didn't know it was possible to feel that tired": exploring the complex bidirectional associations between maternal depressive symptoms and fatigue in a prospective pregnancy cohort study. *Archives of Women's Mental Health* **2016**, *19*, pp. 25-34.
14. Kuo, S.Y.; Yang, Y.L.; Kuo, P.C.; Tseng, C.M.; Tzeng, Y.L. Trajectories of depressive symptoms and fatigue among postpartum women. *J Obstet Gynecol Neonatal Nurs* **2012**, *41*, pp. 216-226.
15. Gentile, S. Untreated depression during pregnancy: Short- and long-term effects in offspring. A systematic review. *Neuroscience* **2015**, *342*, pp. 154-166.
16. Goodman, J.H. Perinatal depression and infant mental health. *Arch Psychiatr Nurs* **2019**, *33*, pp. 217-224.
17. Hartley, M.; Tomlinson, M.; Greco, E.; Comulada, W.S.; Stewart, J.; le Roux, I.; Mbewu, N.; Rotheram-Borus, M.J. Depressed mood in pregnancy: Prevalence and correlates in two Cape Town peri-urban settlements. *Reproductive Health* **2011**, *8*, pp. 1-7.
18. Pina-Camacho, L.; Jensen, S.K.; Gaysina, D.; Barker, E.D. Maternal depression symptoms, unhealthy diet and child emotional-behavioural dysregulation. *Psychol Med* **2015**, *45*, pp. 1851-1860.
19. Herba, C.M.; Glover, V.; Ramchandani, P.G.; Rondon, M.B. Maternal depression and mental health in early childhood: an examination of underlying mechanisms in low-income and middle-income countries. *The Lancet Psychiatry* **2016**, *3*, pp. 983-992.
20. Roomruangwong, C.; Epperson, C.N. Perinatal depression in Asian women: prevalence, associated factors, and cultural aspects. *Asian Biomedicine* **2011**, *5*, pp. 179-193.
21. Stein, A.; Pearson, R.M.; Goodman, S.H.; Rapa, E.; Rahman, A.; McCallum, M.; Howard, L.M.; Pariante, C.M. Effects of perinatal mental disorders on the fetus and child. *The Lancet* **2014**, *384*, pp. 1800-1819.
22. Gavin, N.I.; Gaynes, B.N.; Lohr, K.N.; Meltzer-Brody, S.; Gartlehner, G.; Swinson, T. Perinatal Depression A Systematic Review of Prevalence and Incidence. *Obstet Gynecol* **2005**, *106*, pp. 1071-1083.
23. Minkovitz, C.S.; Strobino, D.; Scharfstein, D.; Hou, W.; Miller, T.; Mistry, K.B.; Swartz, K. Maternal depressive symptoms and children's receipt of health care in the first 3 years of life. *Pediatrics* **2005**, *115*, pp. 306-314.
24. Glover, V. Maternal depression, anxiety and stress during pregnancy and child outcome; what needs to be done. *Best Practice & Research Clinical Obstetrics and Gynaecology* **2014**, *28*, pp. 25-35.

25. Cheng, C.Y.; Chou, Y.H.; Wang, P.; Tsai, J.M.; Liou, S.R. Survey of trend and factors in perinatal maternal fatigue. *Nurs Health Sci* **2015**, *17*, pp. 64-70.
26. Cheng, C.Y.; Pickler, R.H. Perinatal stress, fatigue, depressive symptoms, and immune modulation in late pregnancy and one month postpartum. *The Scientific World Journal* **2014**, *2014*, pp. 1-8.
27. Cespedes, E.M.; Hu, F.B. Dietary patterns: from nutritional epidemiologic analysis to national guidelines. *The American Journal of Clinical Nutrition* **2015**, *101*, pp. 899-900.
28. Newby, P.K.; Tucker, K.L. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutr Rev* **2004**, *62*, pp. 177-203.
29. Dietary Guidelines Advisory Committee. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and Secretary Health and Human Services*; U.S. Department of Agriculture Agricultural Research Service: Washington, DC, 2020.
30. Moskal, A.; Pisa, P.T.; Ferrari, P.; Byrnes, G.; Freisling, H.; Boutron-Ruault, M.C.; Cadeau, C.; Nailler, L.; Wendt, A.; Kuhn, T., et al. Nutrient patterns and their food sources in an International Study Setting: report from the EPIC study. *PLoS One* **2014**, *9*, pp. e98647.
31. Chatzi, L.; Melaki, V.; Sarri, K.; Apostolaki, I.; Roumeliotaki, T.; Georgiou, V.; Vassilaki, M.; Koutis, A.; Bitsios, P.; Kogevinas, M. Dietary patterns during pregnancy and the risk of postpartum depression: the mother-child 'Rhea' cohort in Crete, Greece. *Public Health Nutr* **2011**, *14*, pp. 1663-1670.
32. Lopresti, A.L.; Hood, S.D.; Drummond, P.D. Multiple antidepressant potential modes of action of curcumin: a review of its anti-inflammatory, monoaminergic, antioxidant, immune-modulating and neuroprotective effects. *J Psychopharmacol (Oxf)* **2012**, *26*, pp. 1512-1524.
33. Sanmukhani, J.; Satodia, V.; Trivedi, J.; Patel, T.; Tiwari, D.; Panchal, B.; Goel, A.; Tripathi, C.B. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. *Phytother Res* **2014**, *28*, pp. 579-585.
34. Teo, C.; Chia, A.-R.; Colega, M.; Chen, L.-W.; Fok, D.; Pang, W.; Godfrey, K.; Tan, K.; Yap, F.; Shek, L., et al. Prospective Associations of Maternal Dietary Patterns and Postpartum Mental Health in a Multi-Ethnic Asian Cohort: The Growing up in Singapore towards Healthy Outcomes (GUSTO) Study. *Nutrients* **2018**, *10*, pp. 299.
35. Barker, E.D.; Kirkham, N.; Ng, J.; Jensen, S.K. Prenatal maternal depression symptoms and nutrition, and child cognitive function. *Br J Psychiatry* **2013**, *203*, pp. 417-421.
36. Vilela, A.A.; Farias, D.R.; Eshriqui, I.; Vaz Jdos, S.; Franco-Sena, A.B.; Castro, M.B.; Olinto, M.T.; Machado, S.P.; Moura da Silva, A.A.; Kac, G. Prepregnancy healthy dietary pattern is inversely associated with depressive symptoms among pregnant Brazilian women. *The Journal of Nutrition* **2014**, *144*, pp. 1612-1618.
37. Paskulin, J.T.A.; Drehmer, M.; Olinto, M.T.; Hoffmann, J.F.; Pinheiro, A.P.; Schmidt, M.I.; Nunes, M.A. Association between dietary patterns and mental disorders in pregnant women in Southern Brazil. *Revista Brasileira de Psiquiatria* **2017**, *39*, pp. 208-215.
38. Badanai, N.d.L.; Zuccolotto, D.C.C.; Crivellenti, L.C.; Sartorelli, D.S. Association of dietary patterns and degree of food processing with feelings of depression in pregnancy. *Revista Brasileira de Saúde Materno Infantil* **2019**, *19*, pp. 581-590.
39. Dietary changes and the health transition in South Africa: implications for health policy. Available online: <http://www.fao.org/3/a0442e/a0442e0v.htm> (accessed on 14 December 2020).

40. Popkin, B.M. An overview on the nutrition transition and its health implications: the Bellagio meeting. *Public Health Nutr* **2002**, *5*, pp. 93-103.
41. Vorster, H.H.; Kruger, A.; Margetts, B.M. The nutrition transition in Africa: can it be steered into a more positive direction? *Nutrients* **2011**, *3*, pp. 429-441.
42. Black, R.E.; Allen, L.H.; Bhutta, Z.A.; Caulfield, L.E.; de Onis, M.; Ezzati, M.; Mathers, C.; Rivera, J. Maternal and child undernutrition: global and regional exposures and health consequences. *The Lancet* **2008**, *371*, pp. 243-260.
43. Symington, E.A.; Baumgartner, J.; Malan, L.; Zandberg, L.; Ricci, C.; Smuts, C.M. Nutrition during pregnancy and early development (NuPED) in urban South Africa: a study protocol for a prospective cohort. *BMC Pregnancy Childbirth* **2018**, *18*, pp. 308.
44. Shisana, O.; Rehle, T.; Simbayi, L.C.; Zuma, K.; Jooste, S.; Zungu, N.; Labadarios, D.; Onoya, D. *South African National HIV Prevalence, Incidence and Behaviour Survey, 2012.*, 1st ed ed.; HSRC Press: Cape Town, South Africa, 2014; pp. 1-153.
45. Tsai, A.C.; Scott, J.A.; Hung, K.J.; Zhu, J.Q.; Matthews, L.T.; Psaros, C.; Tomlinson, M. Reliability and validity of instruments for assessing perinatal depression in African settings: systematic review and meta-analysis. *PLoS One* **2013**, *8*, pp. 1-13.
46. MacIntyre, U.E.; Venter, C.S.; Vorster, H.H.; Steyn, H.S. A combination of statistical methods for the analysis of the relative validation data of the quantitative food frequency questionnaire used in the THUSA study. *Public Health Nutr* **2000**, *4*, pp. 45-51.
47. Wentzel-Viljoen, E.; Laubscher, R.; Kruger, A. Using difference approaches to assess the reproducibility of a culturally sensitive quantified food frequency questionnaire. *South Afr J Clin Nutr* **2011**, *23*, pp. 143-148.
48. SAFOODS. *SAMRC Food Quantities Manual for South Africa*, 3rd ed.; South African Medical Research Council: Cape Town, 2018.
49. SAFOODS. *SAMRC Food Composition Tables for South Africa*, 5th ed.; South African Medical Research Council: Cape Town, 2017.
50. Crozier, S.R.; Robinson, S.M.; Godfrey, K.M.; Cooper, C.; Inskip, H.M. Women's dietary patterns change little from before to during pregnancy. *The Journal of Nutrition* **2009**, *139*, pp. 1956-1963.
51. Field, A. *Discovery statistics using SPSS*, 3rd edition ed.; SAGE Publications Ltd: London, 2012.
52. Willett, W.C.; Howe, G.R.; Kushi, L.H. Adjustment for total energy intake in epidemiologic studies. *The American Journal of Clinical Nutrition* **1997**, *65*, pp. 1220S-1228S.
53. The SAARF Universal Living Standards Measure (SU-LSM™) 12 Years of Continuous Development. Available online: <http://www.saarf.co.za/LSM/lsm-article.asp> (accessed on 4 December 2020).
54. Stewart, A.; Marfell-Jones, M.; de Ridder, H. *International Standards for Anthropometric Assessment*; I. S. F. T. A. O.: Lower Hutt, New Zealand, 2011.
55. Hsieh, F.Y.; Bloch, D.A.; Larsen, M.D. A Simple Method of Sample Size Calculation for Linear and Logistic Regression. *Stat Med* **1998**, *17*, pp. 1623-1634.
56. Baskin, R.; Hill, B.; Jacka, F.N.; O'Neil, A.; Skouteris, H. Antenatal dietary patterns and depressive symptoms during pregnancy and early post-partum. *Matern Child Nutr* **2017**, *13*, pp.

57. Banti, S.; Mauri, M.; Oppo, A.; Borri, C.; Rambelli, C.; Ramacciotti, D.; Montagnani, M.S.; Camilleri, V.; Cortopassi, S.; Rucci, P., et al. From the third month of pregnancy to 1 year postpartum. Prevalence, incidence, recurrence, and new onset of depression. Results from the perinatal depression-research & screening unit study. *Compr Psychiatry* **2011**, *52*, pp. 343-351.
58. Bozoky, I.; Corwin, E.J. Fatigue as a Predictor of Postpartum Depression. *J Obstet Gynecol Neonatal Nurs* **2002**, *31*, pp. 436-443.
59. Tardy, A.L.; Pouteau, E.; Marquez, D.; Yilmaz, C.; Scholey, A. Vitamins and Minerals for Energy, Fatigue and Cognition: A Narrative Review of the Biochemical and Clinical Evidence. *Nutrients* **2020**, *12*, pp.
60. Huskisson, E.; Maggini, S.; Ruf, M. The Influence of Micronutrients on Cognitive Function and Performance. *The Journal of International Medical Research* **2007**, *35*, pp. 1-19.
61. Hannestad, U.; Theodorsson, E.; Evengard, B. beta-Alanine and gamma-aminobutyric acid in chronic fatigue syndrome. *Clin Chim Acta* **2007**, *376*, pp. 23-29.
62. Greig, A.J.; Patterson, A.J.; Collins, C.E.; Chalmers, K.A. Iron deficiency, cognition, mental health and fatigue in women of childbearing age: a systematic review. *Journal of Nutritional Science* **2013**, *2*, pp. 1-14.
63. Sanchez-Villegas, A.; Verberne, L.; De Irala, J.; Ruiz-Canela, M.; Toledo, E.; Serra-Majem, L.; Martinez-Gonzalez, M.A. Dietary fat intake and the risk of depression: the SUN Project. *PLoS One* **2011**, *6*, pp. e16268.
64. Melo, H.M.; Santos, L.E.; Ferreira, S.T. Diet-Derived Fatty Acids, Brain Inflammation, and Mental Health. *Front Neurosci* **2019**, *13*, pp. 265.
65. Dutheil, S.; Ota, K.T.; Wohleb, E.S.; Rasmussen, K.; Duman, R.S. High-Fat Diet Induced Anxiety and Anhedonia: Impact on Brain Homeostasis and Inflammation. *Neuropsychopharmacology* **2016**, *41*, pp. 1874-1887.
66. Goldstein, P.; Leshem, M. Dietary sodium, added salt, and serum sodium associations with growth and depression in the U.S. general population. *Appetite* **2014**, *79*, pp. 83-90.
67. Zhang, Y.; Yang, Y.; Xie, M.S.; Ding, X.; Li, H.; Liu, Z.C.; Peng, S.F. Is meat consumption associated with depression? A meta-analysis of observational studies. *BMC Psychiatry* **2017**, *17*, pp. 409.
68. Boston, P.F.; Dursun, S.M.; Reveley, M.A. Cholesterol and mental disorder. *Br J Psychiatry* **1996**, *169*, pp. 682-689.
69. Kaplan, J.R.; Shively, C.A.; Fontenot, M.B.; Morgan, T.M.; Howell, S.M.; Manuck, S.B.; Muldoon, M.F.; Mann, J.J. Demonstration of an association among dietary cholesterol, central serotonergic activity, and social behavior in monkeys. *Psychosom Med* **1994**, *56*, pp. 479-484.
70. Crozier, S.R.; Robinson, S.M.; Borland, S.E.; Godfrey, K.M.; Cooper, C.; Inskip, H.M.; Group, S.W.S.S. Do women change their health behaviours in pregnancy? Findings from the Southampton Women's Survey. *Paediatric and Perinatal Epidemiology* **2009**, *23*, pp. 446-453.
71. Crozier, S.R.; Inskip, H.M.; Godfrey, K.M.; Cooper, C.; Robinson, S.M.; Group, S.W.S.S. Nausea and vomiting in early pregnancy: Effects on food intake and diet quality. *Matern Child Nutr* **2017**, *13*, pp. 1-10.
72. Swardfager, W.; Herrmann, N.; Mazereeuw, G.; Goldberger, K.; Harimoto, T.; Lanctot, K.L. Zinc in depression: a meta-analysis. *Biol Psychiatry* **2013**, *74*, pp. 872-878.
73. Li, Z.; Wang, W.; Xin, X.; Song, X.; Zhang, D. Association of total zinc, iron, copper and selenium intakes with depression in the US adults. *J Affect Disord* **2018**, *228*, pp. 68-74.

74. Klainin, P.; Arthur, D.G. Postpartum depression in Asian cultures: a literature review. *Int J Nurs Stud* **2009**, *46*, pp. 1355-1373.
75. Miyake, Y.; Sasaki, S.; Tanaka, K.; Yokoyama, T.; Ohya, Y.; Fukushima, W.; Saito, K.; Ohfuji, S.; Kiyohara, C.; Hirota, Y., et al. Dietary folate and vitamins B12, B6, and B2 intake and the risk of postpartum depression in Japan: the Osaka Maternal and Child Health Study. *J Affect Disord* **2006**, *96*, pp. 133-138.
76. Mikkelsen, K.; Stojanovska, L.; Prakash, M.; Apostolopoulos, V. The effects of vitamin B on the immune/cytokine network and their involvement in depression. *Maturitas* **2017**, *96*, pp. 58-71.

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



© 2020 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).

CHAPTER 4: SUMMARY AND CONCLUSION

4.1 Summary

In low- and middle-income countries, perinatal depression is a greater problem than in high-income countries (Manikkam & Burns, 2012:940). There is a known bi-directional relationship between perinatal depression and fatigue (Giallo *et al.*, 2016:32; Kuo *et al.*, 2012:216). Also the relationship between diet and perinatal depression has been hypothesised to be bi-directional (Baskin *et al.*, 2015:46). The aim of this study was to assess the associations between dietary patterns and perinatal fatigue and depression. Women from urban Johannesburg were recruited (n = 250) and provided dietary data at early in pregnancy (< 18 weeks gestation). Participants were followed-up until 12 months postnatally and data on depression and fatigue were obtained three times during, and twice after pregnancy. We found that a “*Plant protein, iron, thiamine and folate*” nutrient pattern reduced the risk of perinatal fatigue early postnatally. An increased risk was found between perinatal depression early postnatally and an “*Animal protein, vitamin A, vitamin B₁₂ and copper*” nutrient pattern. A similar increase in risk was observed between a “*Fatty acids and sodium*” nutrient pattern. Finally, perinatal fatigue was found to be associated with perinatal depression throughout pregnancy, and up to six months postnatally.

4.2 Strengths and limitations

The prospective design of the larger NuPED study was a great strength of this study. This allowed the researchers to observe perinatal fatigue and depression across multiple time points during pregnancy and the postnatal period.

Another strength was the breadth of data (socio-economic and -demographic) that were gathered by the larger study. These data were valuable in terms of identifying potential confounding variables and adjusting for them in statistical models.

We used a lower EPDS cut-off than previous studies, as indicated by the literature (Tsai *et al.*, 2013:5). This allowed for greater sensitivity in terms of identifying women at risk for perinatal depression. Using the suggested cut-off for fatigue (Cheng *et al.*, 2015:66) was a strength in the sense that fatigue could be analysed statistically as a continuous as well as binary variable.

In terms of sample size, a strength was that the sample was large enough to determine nutrient patterns, and the prevalence of perinatal fatigue and depression. A limitation of the study was the low retention of participants to follow-up. A more complete data set would allow for greater statistical power.

4.3 Recommendations on future research

More research is needed on the dietary intake of pregnant women, as research on the topic is very limited. Research into the role of nutrition in perinatal fatigue should be continued as research in this specific area is limited (Cheng *et al.*, 2015:64). Although more literature exists on the role of nutrition in perinatal depression, more high quality studies are needed to fully explain the relationship (Silva *et al.*, 2019:12). The role of micronutrients and polyunsaturated fatty acids, especially omega-3 fatty acids, should be further investigated in order to identify underlying mechanisms or test current hypotheses.

Future researchers should consider the use of empirically derived dietary or nutrient patterns, as this may reduce bias introduced by the researcher in determining an *a priori* “healthy” dietary pattern (Newby & Tucker, 2004:177). Furthermore, the use of nutrient patterns over dietary patterns should be considered, as nutrient patterns are more universal to a certain extent (Moskal *et al.*, 2014:2).

Research into the role of antenatal depression in the aetiology of postnatal depression, specifically in low- and middle-income countries, needs to be investigated. This study found a higher prevalence of postnatal depression than antenatal depression, which is inconsistent with studies from high-income countries showing that the prevalence of antenatal depression is comparable, if not higher, than that of postnatal depression (Baskin *et al.*, 2017:1).

REFERENCES

- Baskin, R., Hill, B., Jacka, F.N., O'Neil, A. & Skouteris, H. 2017. Antenatal dietary patterns and depressive symptoms during pregnancy and early post-partum. *Maternal & Child Nutrition*, 13(1).
- Cheng, C.Y., Chou, Y.H., Wang, P., Tsai, J.M. & Liou, S.R. 2015. Survey of trend and factors in perinatal maternal fatigue. *Nursing & Health Sciences*, 17(1):64-70.
- Moskal, A., Pisa, P.T., Ferrari, P., Byrnes, G., Freisling, H., Boutron-Ruault, M.C., Cadeau, C., Nailler, L., Wendt, A., Kuhn, T., Boeing, H., Buijsse, B., Tjonneland, A., Halkjaer, J., Dahm, C.C., Chiuve, S.E., Quiros, J.R., Buckland, G., Molina-Montes, E., Amiano, P., Huerta Castano, J.M., Gurrea, A.B., Khaw, K.T., Lentjes, M.A., Key, T.J., Romaguera, D., Vergnaud, A.C., Trichopoulou, A., Bamia, C., Orfanos, P., Palli, D., Pala, V., Tumino, R., Sacerdote, C., de Magistris, M.S., Bueno-de-Mesquita, H.B., Ocke, M.C., Beulens, J.W., Ericson, U., Drake, I., Nilsson, L.M., Winkvist, A., Weiderpass, E., Hjartaker, A., Riboli, E. & Slimani, N. 2014. Nutrient patterns and their food sources in an International Study Setting: report from the EPIC study. *PloS One*, 9(6):e98647.
- Newby, P.K. & Tucker, K.L. 2004. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutrition Reviews*, 62(5):177-203.
- Silva, D.F.O., Cobucci, R.N., Gonçalves, A.K. & Lima, S.C.V.C. 2019. Systematic review of the association between dietary patterns and perinatal anxiety and depression. *BMC Pregnancy and Childbirth*, 19(1):1-13.
- Tsai, A.C., Scott, J.A., Hung, K.J., Zhu, J.Q., Matthews, L.T., Psaros, C. & Tomlinson, M. 2013. Reliability and validity of instruments for assessing perinatal depression in African settings: systematic review and meta-analysis. *PloS One*, 8(12):1-13.

APPENDIX 1: SOCIO-DEMOGRAPHIC QUESTIONNAIRE



NuPED

Nutrition during Pregnancy and Early Development

Socio-demographic questionnaire

Participant
nr:

Date:

Fieldworker:

1. Date of birth:								
	1	2	3	4	5			
2. How would you describe yourself in terms of population group?	Black	Coloured	Indian	White	Other. Specify:			
	1	2	3	4	5			
3. What is your home language?	English	Xhosa	Zulu	Sotho	Other. Specify:			
	1	2	3	4	5	6	7	
4. In which country were you born?	South Africa	Zimbabwe	Lesotho	Swaziland	Botswana	Namibia	Other. Specify:	
				1	2	3	4	
5. How long have you been staying in South Africa?				Less than 1 year	1 – 2 years	2 – 5 years	More than 5 years	
				1	2	3	4	5
6. What is your highest formal educational level?				None	Primary School	Std 6-8/ Gr 8-10	Std 9-10/ Gr 11&12	Tertiary Education
	1	2	3	4	5	6	7	8
7. What is your marital status?	Unmarried	Married	Divorced	Separated	Widowed	Living Together	Traditional Marriage	Other. Specify:
8. What is your employment status?								
	Unemployed	Homemaker by choice	Self-Employed	Wage-Earner	Self-employed Professional	Other. Specify:		

9. How many people live in your household most days of the week (including children and elderly)?

10. Do any members of the household receive any grants?

1	2	3	4	5	6
None	Child support	Social relief	Disability	Old age pension	Other. Specify

11. To determine your living standards measure, please indicate which of the following you currently have in your household:

X = Yes ; - = No

X	Metropolitan dweller (250 000+)		DVD Player / Blu Ray Player
	~~Living in a non-urban area~~		Refrigerator or combined fridge/freezer
	House / Cluster House / Town House		Electric Stove
	Tap water in house / on plot		Microwave oven
	Flush Toilet inside house		Deep Freezer - Free Standing
	Hot running water		Washing machine
	Built in Kitchen Sink		Tumble dryer
	No Domestic Workers or Gardeners		Dishwashing Machine
	Home security service		PayTV (M-net / DSTV / TopTV) Subscription
	2 Cell phones in Household		Home Theatre System
	3 or more Cell phones in Household		Vacuum Cleaner
	Zero or One Radio set in Household		Motor Vehicle
	Air conditioner (excl. fans)		Computer - Desktop / Laptop
	Have TV set(s)		Land line (excl. Cellphone)
	Swimming Pool		

APPENDIX 2: MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE



NuPED

Nutrition during Pregnancy and Early Development

Multidimensional Assessment of Fatigue (MAF) Scale

Fieldworker: _____

Participant nr:

Phase:

Date:

Instructions: These questions are about fatigue and the effect of fatigue on your activities.

Fatigue = physical or mental extreme tiredness, exhaustion or weariness

For each of the following questions, circle the number that most closely indicates how you have been feeling during the past week.

For example, suppose you really like to sleep late in the mornings. You would probably circle the number closer to the "a great deal" end of the line. This is where I put it:

Example: To what degree do you usually like to sleep late in the mornings?

12345678910
Not at all A great deal

Now please complete the following items based on the past week.

1. To what degree have you experienced fatigue?

12345678910
Not at all A great deal

If no fatigue, stop here.

2. How severe is the fatigue which you have been experiencing?

12345678910
Mild Severe

3. To what degree has fatigue caused you distress (discomfort, anxiety, concern or unhappiness)?

12345678910
No distress A great deal of distress

MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE (Continued)

Circle the number that most closely indicates to what degree fatigue has interfered with your ability to do the following activities in the past week. For activities you don't do, for reasons other than fatigue (e.g. you don't work because you are retired), check the box.

In the past week, to what degree has fatigue interfered with your ability to:

(NOTE: Check box to the left of each number if you don't do activity)

☐ 4. Do household chores/duties

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **5. Cook**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **6. Bathe or wash**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **7. Dress**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ 8. Work

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ 9. Visit or socialize with friends or family

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE (Continued)

(NOTE: Check box to the left of each number if you don't do activity)

☐ 10. Engage in sexual activity

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ 11. Engage in leisure and recreational activities

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ 12. Shop and do errands/buy groceries

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **13. Walk**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ 14. Exercise, other than walking

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

15. Over the past week, how often have you been fatigued?

4 Every day

3 Most, but not all days

2 Occasionally, but not most days

1 Hardly any days

16. To what degree has your fatigue changed during the past week?

4 Increased

3 Fatigue has gone up and down

2 Stayed the same

1 Decreased

APPENDIX 3: EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS-10)



NuPED

Nutrition during Pregnancy and Early Development

Edinburgh Postnatal Depression Scale (EPDS-10)

Participant nr:

--	--	--

 Fieldworker: _____
Phase:

--	--

 Date:

2	0	Y	Y	M	M	D	D
---	---	---	---	---	---	---	---

Your feelings now that you are pregnant/have had a baby.

As you are pregnant/have had a baby, we would like to know how you are feeling. The information you provide us will be kept private and confidential. There is a choice of four answers for each question. Please mark the one that comes closest to how you felt in the past seven days, not just how you feel today.

In the past seven days:

1. Have you been able to laugh and see the funny side of things?

- ☐ As much as you always could (0)
- ☐ Not quite so much now (1)
- ☐ Definitely not so much now (2)
- ☐ Not at all (3)

2. Have you looked forward with enjoyment to things?

- ☐ As much as you ever did (0)
- ☐ A little less than you used to (1)
- ☐ Much less than you used to (2)
- ☐ Hardly at all (3)

3. Have you blamed yourself when things went wrong, and it wasn't your fault?

- ☐ Yes, most of the time (3)
- ☐ Yes, some of the time (2)
- ☐ Not very much (1)
- ☐ No, never (0)

4. Have you been worried and you don't know why?

- ☐ No, not at all (0)
- ☐ Hardly ever (1)
- ☐ Yes, sometimes (2)
- ☐ Yes, very much (3)

5. Have you felt scared or panicky and you don't know why?

- ☐ Yes, quite a lot (3)
- ☐ Yes, sometimes (2)
- ☐ No, not much (1)
- ☐ No, not at all (0)

6. Have you had difficulty in coping with things?

- ☐ Yes, most of the time you haven't been managing at all (3)
- ☐ Yes, sometimes you haven't been managing as well as usual (2)
- ☐ No, most of the time you have managed quite well (1)
- ☐ No, you have been managing as well as ever (0)

7. Have you been so unhappy that you have had difficulty sleeping (not due to baby bump)?

- ☐ Yes, most of the time (3)
- ☐ Yes, sometimes (2)
- ☐ Not very much (1)
- ☐ No, not at all (0)

8. Have you felt sad or miserable?

- ☐ Yes, most of the time (3)
- ☐ Yes, quite a lot (2)
- ☐ Not very much (1)
- ☐ No, not at all (0)

9. Have you been so unhappy that you have been crying?

- ☐ Yes, most of the time (3)
- ☐ Yes, quite a lot (2)
- ☐ Only sometimes (1)
- ☐ No, never (0)

10. Have you thought of harming yourself or ending your life?

- ☐ Yes, quite a lot (3)*
- ☐ Sometimes (2)*
- ☐ Hardly ever (1)*
- ☐ Never (0)

Total Score:_____

- **If score ≥ 13 , please ask study coordinator to prepare referral letter to nearest mental health clinic**
- *** If score is > 0 for question 10, ask study coordinator to refer women IMMEDIATELY to the psychology department at RMMCH.**

For referrals only:

- ☐ Referral to nearest mental health clinic made
- ☐ Referral to psychology department at RMMCH made

Signature study coordinator issuing referral letter:_____