DIET QUALITY DURING PREGNANCY, ITS SOCIAL DETERMINANT FACTORS, AND ASSOCIATIONS WITH PERINATAL OUTCOMES AND OFFSPRING NEURODEVELOPMENT

Running Title:

Diet Quality during Pregnancy

Yamei Yu

Thesis Supervisors

Dr. Lise Dubois

Dr. William D. Fraser

Thesis Advisory Committee

Dr. Beth Potter

Dr. Julian Little

Dr. Tim Ramsay

Thesis submitted to the University of Ottawa in partial fulfillment of the requirements for the Doctorate in Philosophy degree in Epidemiology

School of Epidemiology and Public Health

University of Ottawa

TABLE OF CONTENTS

THESIS ABSTRACT

Proper nutrition during pregnancy provides fundamental building blocks to support both the health of the mother and the fetus. However, careful evaluation of diet quality during pregnancy based on high quality dietary data is scarce in Canada. The associations between diet quality and perinatal and offspring outcomes have not been established. Thus, this thesis has the following objectives: 1) to assess overall diet quality during pregnancy using high-quality nutrition data collected in a large birth cohort in Canada, including validating the tool for assessment of diet quality in pregnancy; 2) to identify the social factors that are associated with overall diet quality during pregnancy in this Canadian sample; 3) to synthesize the evidence on the association between overall diet quality and adverse perinatal outcomes; 4) to assess the relationships between maternal nutrition during pregnancy and offspring neurodevelopment. This thesis integrates three research manuscripts published or submitted for publication in scientific peer-reviewed journals. The first manuscript describes the distribution of diet quality during pregnancy with the finding that the diet of women in Canada still is suboptimal, especially regarding whole grains and 'greens and beans', where the majority of the women did not meet recommendations. Inequalities in diet quality were observed: pregnant women who were less educated, younger, overweight or obese before pregnancy, or parous have lower diet quality. The second manuscript, a systematic review and meta-analysis of 33 cohort studies demonstrated that good diet quality during pregnancy was associated with lower risks of adverse maternal and neonatal outcomes including gestational diabetes, hypertensive disorders of pregnancy, preterm birth, small for gestational age and low birth weight. The third manuscript

examined the associations between nutrition during pregnancy and indicators of offspring neurodevelopment. Statistically significant interactions between diet quality and multivitamin intake were found on the associations with cognitive and language development outcomes in the offspring at two years of age. The results indicated that adequate nutrition intake, through high quality diet or multivitamin use, is beneficial for children's neurodevelopment. This thesis helps fill gaps in knowledge in diet quality during pregnancy in Canada. The findings of this thesis are relevant to clinical and public health practice since diet quality can be used as a target for dietary interventions in pregnancy.

THESIS PREFACE

Ethical Standards Disclosure

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. Written informed consents were obtained from each participant in the 3D Cohort Study. Ethical approvals of 3D Cohort Study were obtained from the research ethics committee at Sainte-Justine's Hospital in Montreal and all other participating study sites. The Health Sciences and Science Research Ethics Board of the University of Ottawa granted approval for secondary data analyses, including those in this thesis (file number H-04-21-6908, Approval Date April/05/2021, Appendix 1).

Author Contributions

With the supervision from my thesis supervisors Dr. Lise Dubois and Dr. William D. Fraser, Yamei Yu (the Ph.D. Candidate) is the guarantor of this project, conducting and leading every step of this thesis: data application from the 3D Cohort Study committee, data coding, data cleaning, statistical analysis, creation of tables and figures, interpretation of the results, writing of manuscripts and the thesis, communication of the results and submission of the individual manuscripts and the thesis. For all three manuscripts in this thesis, Yamei Yu is the first author. Dr. Fraser and Dr. Dubois are the senior authors and share the role of corresponding authors for the publications.

Dr. Dubois and Dr. Fraser guided me in developing the topic of this thesis following several

episodes of discussion across the beginning one and a half years of my Ph.D. study. Before starting and during the first year of my Ph.D. study, I was actively involved in the Sino-Canada Healthy Life Trajectories Initiative (SHeLTI) project, which is a clustered randomized controlled trial (RCT) developed in partnership with the World Health Organization (WHO). It is one of four separate, but harmonized studies focused on developing and evaluating the effectiveness of a 'multifaceted, community-family-mother-child intervention' on childhood overweight and obesity and non-communicable diseases risks. The intervention starts from preconception, spans across pregnancy and into the postpartum period and early childhood[1]. I was involved in early setting up of the study, drafting the study protocol for the trial which is now published [1], and designing the nutrition component of the intervention during pregnancy. However, later we realized that data from SHeLTI study would not be available for use in my thesis in time for graduation, because it is a large trial that aims to recruit 4,500 families, with a 5-year follow-up period. Dr. Dubois and Dr. Fraser were very considerate and suggested that we change the strategy - to leverage already esiçxisting data from the 3D birth cohort for the thesis, while I continue to learn from collaboration in the SHeLTI project. In the end, the topic of the thesis focused on diet quality during pregnancy in the field of prenatal nutritional epidemiology, using data from the 3D birth cohort.

Dr. Dubois suggested professors to be assembled into the Thesis Advisory Committee (TAC): Dr. Beth Potter, Dr. Julian Little, and Dr. Tim Ramsay. The TAC members have been extremely helpful in the directions and the completeness of the thesis and provided strong methodological

support in our individual meetings and the TAC meetings. Also, Dr. Dubois invited Dr. Cindy Feng at Dalhousie University to serve as a consultant on statistics for my thesis. Dr. Feng contributed extensively whenever I need support for statistical expertise.

Dr. Fraser introduced me to Dr. Jean Seguin from University of Montreal, who is an expert in neurodevelopment. He provided strong support in the area of childhood neurodevelopment.

In the second paper of the thesis, Dr. Dean Fergusson provided guidance on the methodology of conducting a systematic review. Dr. Isabelle Hardy, a resident in Obstetrics and Gynecology from University of Sherbrooke was the co-first author for the second paper. She paired up with me for steps in the systematic review that need two persons to perform in parallel, including first and second round of screening, study quality assessment, and data extraction. Together with me, she was also involved in proof-reading of the paper. I was the guarantor of the project, conducted and lead each step of the systematic review and the paper.

Dr. Dubois and Dr. Fraser closely supervised and supported me in every step of the work involved in the thesis and the individual papers in regular meetings, from the beginning to the end.

ACKNOWLEDGEMENTS

Interestingly, this is the second time that I try to accomplish a Ph.D. study. For personal and family reasons, I had to give up my first attempt and graduated with an M.Sc. eight years ago. After four years, however, I was lucky enough to have the chance to start again in University of Ottawa. And this time, I am lucky to be able to finish and present my Ph.D. thesis, although during this process I realized that the pursuit of science and truth is a never-end journey even after Ph.D. training. This thesis would not have been possible without the people who had directly contributed greatly to it and who have beneficial influences on my academic and personal growth in the journey of my Ph.D. study.

I would like to express my sincere acknowledgement and gratefulness to my thesis supervisors Dr. Lise Dubois and Dr. William D. Fraser for their tremendous mentorship, guidance, and support throughout the journey of these 4 years of Ph.D. study. Dr. Dubois and Dr. Fraser have been guiding me from an academic perspective directly by guiding the development of research and indirectly by effectively linking me with experts in relevant areas: statisticians, nutritionists, epidemiologists, pediatricians, and peer students, with whom we were able to build collaborations and formulated the papers in this thesis. They are always strong advocates for me and ensure that I have access to the resources needed for the study and the thesis. They introduced and exposed me to other relevant projects for me to have the chance to learn and develop into an independent researcher in the future. They also have been standing with me and provided so much care and support with respect to my overall development in career and in my

life, which has turned into strong power for me to finish the thesis. Having them as my supervisors has been a huge privilege for me.

I want to acknowledge the members of my TAC, Dr. Tim Ramsay, Dr. Beth Potter and Dr. Julian Little for their time, assistance and guidance which were essential to the completion of this thesis. They have always been there ready to help the students with their methodological expertise and experiences in the way of pursuing an academic career.

I would like to thank statisticians Dr. Cindy Feng and Dr. Ramsay. They have always been so patient, open, and easy to access for discussing any questions or concerns that I had. Their support gave me courage to explore new methods in my research because I knew that I always had them at my back for a strong methodological support. And special thanks to Dr. Ramsay through whom I was exposed to different and very interesting perspectives and attitudes that have enlightened me every time I met him.

My sincere gratefulness to the co-authors who contributed to the manuscripts included in this thesis for their expertise and teamwork.

I would like to thank the professors and senior students in SEPH who had made this community feeling like home. The professors were always encouraging and supporting. Senior students shared their experiences with junior students in things including writing proposal, applying for scholarships, and career development. These have been so helpful for me as a junior student at that time.

I was lucky to be involved in the 3D Cohort Study. I learned a great deal regarding the analysis of high-quality data collected in a large birth cohort. I have witnessed the organisation and planning that led the establishment of excellent research, and the efforts from every team member that have made the implementation possible for the projects.

I would like to acknowledge the support from my family and friends without whom this experience would not have been possible. Thank my parents for always hoping for the best and believing the excellence in me. Thank my husband who is willing to explore and experience life together with me. Thanks to my child who shares innocent love with me. Thanks to my study partners who provided me a sense of collegiality.

FUNDING

I would like to acknowledge the financial support from the following sources, without which the thesis would not have been possible to complete:

1) Scholarship and funding for open-source publishing from Dr. Fraser's research project - Canadian Institutes of Health Research (CIHR) (Grant CRI 88413, MOP 133422 and HLT 151517) and the National Natural Sciences Foundation of China (NSFC) (Grant No. 81661128010).

2) The University of Ottawa Library funding for open-source publishing.

3) Queen Elizabeth II Graduate Scholarship in Science and Technology (QEII-GSST) for the academic year 2021-2022.

4) International scholarship from University of Ottawa for the academic years 2018-2020.

5) Excellence scholarship from University of Ottawa for the academic year 2021-2022.

LIST OF TABLES

Chapter 4

Chapter 5

Chapter 6

Chapter 7

LIST OF FIGURES

Chapter 7

Supplementary Figure 1 Directed acyclic graph (DAG) for determining the minimal sufficient adjustment sets for estimating the association between maternal nutrition and offspring neurodevelopment (‘total effect’).

LIST OF ABBREVIATIONS

aHEI, alternate Healthy Eating Index;

Bayley III, Bayley Scales of Infant and Toddler Development, 3rd edition;

BMI, Body Mass Index;

CI, Confidence Interval;

CIHR, Canadian Institutes of Health Research;

DAG, Directed Acyclic Graph;

FFQ, Food Frequency Questionnaires;

GDM, Gestational Diabetes Mellitus;

GWG, Gestational Weight Gain;

HDP, Hypertensive Disorders Of Pregnancy;

HEI, Healthy Eating Index;

HEI-C, Canadian adaptation of the Healthy Eating Index;

HeLTI, Healthy Life Trajectories Initiative;

LBW, Low Birth Weight;

LGA, Large for Gestational Age;

MCDI, MacArthur-Bates Communicative Development Inventories;

MD, Mediterranean Diet;

MML, Maternal Medication Logs;

MOOSE, Meta-analysis of Observational Studies in Epidemiology;

NAM, National Academy of Medicine;

NCDs, Non-Communicable Diseases;

NOS, Newcastle–Ottawa Scale;

NSFC, National Natural Sciences Foundation of China;

OR, Odds Ratios;

QEII-GSST, Queen Elizabeth II Graduate Scholarship in Science and Technology;

RCT, Randomized Controlled Trial

SD, Standard Deviations;

SGA, Small for Gestational Age;

TAC, Thesis Advisory Committee;

VIF, Variance Inflation Factor;

WHO, World Health Organization.

LIST OF APPENDICES

CHAPTER 1: THESIS INTRODUCTION

This thesis is written to fulfill the requirements for the Doctorate in Philosophy degree in Epidemiology. Epidemiology is the field of science that is defined by John M. Last in his book *A Dictionary of Epidemiology, 4th ed* as "the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems"[2]. In alignment with the definition, this thesis studied the distribution and determinants of diet quality during pregnancy, and the association between diet quality and perinatal and childhood neurodevelopment outcomes, for the purpose of applying the study results to support the improvement of diet quality during pregnancy and subsequently, the improvement of perinatal and childhood outcomes. The thesis is manuscript-based and is situated in the field of nutritional epidemiology in pregnancy. It includes a systematic review on the associations between diet quality during preconception or pregnancy and perinatal outcomes, and secondary data analysis of the 3D Cohort Study, a relatively large Canadian birth cohort which recruited 2366 pregnant women from 2010 to 2012 in Quebec. This pregnancy and birth cohort collected high quality nutrition and health status data during pregnancy and in childhood of the offspring and performed detailed neurodevelopmental assessments at two years of age. The goal of the thesis is to assess overall diet quality in pregnant women, to identify the social determinants of diet quality, and to estimate the relationships between diet quality, adverse perinatal outcomes and neurodevelopment in the offspring. This thesis includes ten sections:

thesis introduction, background, methods, three individual manuscripts, integrated discussion with conclusions, appendices and references.

1.1 Objectives of the Studies

This thesis focuses on the determinants and impacts of diet quality during pregnancy. Specifically, four objectives were identified:

1) To assess overall diet quality during pregnancy, including developing and validating the tool for assessment of diet quality.
2) To identify the social determinants that are associated with overall diet quality during pregnancy in a large birth cohort.
3) To synthesize the knowledge on the association between overall diet quality and adverse perinatal outcomes through a systematic review and meta-analysis.
4) To assess the relationships between maternal nutrition during pregnancy and offspring neurodevelopment.

1.2 Thesis Outline

This thesis is manuscript-based. The thesis includes three manuscripts that present the results which address the main study objectives. These three manuscripts were written and formatted following the requirements of the scientific journals that were selected for submission for

publication. Chapter 2 (Background) lays the foundation of the thesis and includes an introduction to the concepts, the rationale, the statement of problems, conceptual framework guiding the thesis, and a review of scientific knowledge related to the thesis. In Chapter 3 and Chapter 4, I present the details of the methodology for the 3D Cohort Study, and for generating and validating the diet quality index to the extent that I am not able to elaborate in detail in individual manuscripts, and for the purpose of providing the readers with a coherent flow of information. The subsequent three chapters present the three manuscripts which comprise the results sections of the thesis. Chapter 5 describes the distribution of diet quality during pregnancy and identifies the social factors associated with diet quality in Canada. Before doing the analysis, I selected the tool for assessing diet quality and validated it in the current cohort of pregnant women. Chapter 6 demonstrates that good diet quality during pregnancy was associated with lower risks of adverse maternal and neonatal outcomes including gestational diabetes, hypertensive disorders of pregnancy, preterm birth, small for gestational age and low birth weight, after synthesizing the evidence from prospective cohort studies using systematic review and meta-analysis. Chapter 7 examines the association between nutrition during pregnancy and offspring neurodevelopment. Statistically significant interactions between diet quality and multivitamin intake were found in association with cognitive and language development outcomes in the offspring at two years of age. In Chapter 8, I summarize the key findings of the thesis, discuss the implications of these findings, the strengths and limitations of the studies, and

finally, future research directions. Finally, Chapter 9 is the appendices and Chapter 10 is the references for the thesis except for those in the three individual manuscripts.

CHAPTER 2: BACKGROUND

This background section includes an introduction to the rationale, the statement of problems, conceptual framework guiding the thesis, concepts, and a review of scientific knowledge related to the thesis. I first discuss the importance of maternal diet during pregnancy. Then I introduce the concept of diet quality, i.e., adherence to evidence-based nutrition guidelines for maternal diet during pregnancy, and the use of diet quality indices to measure diet as a whole. Next, I present studies on the determinants of diet quality during pregnancy for women living in high-income economies. The remainder of the section outlines the evidence concerning the associations between diet quality during pregnancy, perinatal outcomes and indicators of childhood neurodevelopment. These elements contribute to the identification of knowledge gaps which underpin the research objectives in the three sections for individual manuscripts.

2.1 The Importance of Maternal Diet during Pregnancy

A child's experience in the first 1000 days, including the prenatal period, is a unique period to develop his or her ability to grow and prosper in society[3,4]. Malnutrition during pregnancy represents a major public health issue that affects not only the health of the women, but also the health of offspring, and contributes substantially to the global burden of disease and disability[5,6]. The Lancet defined malnutrition as "the coexistence of overnutrition (overweight and obesity) alongside undernutrition (stunting and wasting), at all levels of the population—country, city,

community, household, and individual"[7]. In line with this definition, the double burden of malnutrition during pregnancy could result from inadequate intake of healthy foods leading to energy and protein malnutrition, with related consequences including lower birth weight (LBW), stunting in childhood and non-communicable diseases (NCDs) in future life[8]. It may also result from over-consumption of nonnutritive energy and underconsumption of nutrient-dense foods leading to micronutrient malnutrition, obesity and NCDs for pregnant women and offspring[8]. While previous efforts have mainly focused on evaluating and solving the problem of either undernutrition or overnutrition separately, now it is advocated that malnutrition in all its forms should be addressed together leveraging the common drivers and resources[9,10]. However, research on the association between nutrition during pregnancy and related outcomes has been limited and has generated conflicting results due to the lack of high-quality diet information in pregnancy and due to the limited duration of follow-up and assessment of the children. Research in this area is of great public health relevance, in order to develop and provide evidence-based interventions during this critical period of life, for prevention of future NCDs and long-term development of the children at the individual level, and for the overall development and economic growth for the human at the population level[11].

2.2 Adherence to Prenatal Dietary Guidelines

Individuals may be considered as having good overall diet quality when they follow the recommendations from evidence-based dietary guidelines[12]. The Canadian government developed dietary guidelines to help pregnant women to understand the amount and type of food they need to support a healthy pregnancy[13]. Briefly, pregnant women are encouraged to follow Eating Well with Canada's Food Guide (CFG), developed by Health Canada, which describes the variety and amount of food to be consumed, in addition to daily supplementation of a multi-vitamin containing 0.4 mg of folic acid and 16 to 20 mg of iron[14]. As for the amount of food, the 2007 version of CFG[15] recommended women aged 19 to 50 to eat seven to eight servings of vegetables and fruit, six to seven servings of grain products, two servings of milk and alternatives, and two servings of meat and alternatives per day. Pregnant women were advised to include an additional two to three servings per day from any of the four food groups[16]. Women can choose foods from any food group based on personal preferences. The amount of food generally recommended during pregnancy is the equivalent of an extra snack or a small meal. It was not stated which food groups should be the source of the additional two to three servings recommended during pregnancy. However, the examples given by Health Canada are from three groups: milk and alternatives, vegetables and fruit, and grain products. In the 2019 version of CFG[17], no specific amounts for each of the food groups were specified. Only the relative amount

of food in a plate for daily consumption is presented with examples on recommended and non-recommended food.

Adherence to dietary guidelines remains low in high-income countries. For example, only 35% of pregnant women in a Canadian cohort met the recommendations for vegetables and fruits in 2002-2005, only 10% of pregnant women in Australia in 2013, and 25% in New Zealand in 2010 met the recommendations for vegetables[18-23]. Adherence to Canadian dietary guidelines has not been well assessed in Canada using rigorous dietary assessment methods. In a survey of 2313 pregnant women conducted in London, Ontario, pregnant women were found to have poor eating patterns compared to the CFG 2007, with only 3.5% of them consuming the recommended number of servings for all four food groups and 15.3% not consuming the minimum number of servings for any of the four food groups[18]. The limitation of this study is that it used a food frequency questionnaire (FFQ) to quantify the absolute dietary intakes, even though FFQ is best adapted to ranking people in a population, rather than quantifying absolute intakes. Also, the actual size of the portion consumed was not measured, not all available foods were included, and often a single question covered several foods. Furthermore, the conclusion that pregnant women were having inadequate dietary intakes might not provide a complete picture, because it contradicts the fact that more than 50% of the pregnant women are still gaining weight in excess of current recommendations[24]. One possible assumption to explain this could be that women were under-eating “healthy foods” identified in the four main good groups, but at the same time

eating excessive amounts of "unhealthy food" not included in the four main food groups, resulting in excessive weight gain. It was also possible that the FFQ used in the study did not cover some important items not included in the four main food groups. Finally, the study did not distinguish between 'recommended foods' and 'non-recommended foods' in the four food groups. Using a more rigorous nutritional assessment tool, such as a 3-day food record, will aid in quantifying the adherence to the recommendations and evaluate the overall diet quality for Canadian pregnant women.

2.3 Measuring Overall Diet Quality using Diet Quality Indices

Proper total energy intakes and not overeating in daily life are strong determinants of good health[25,26]. However, a good diet is not only related to total energy intake, but also to overall diet quality, more specifically, the combination of food consumption (what people habitually eat and avoid eating)[5]. Diet of good quality includes a variety of vegetables, fruits, whole grains, protein, low fat dairy, healthy oils, and limited intake of saturated and trans fats, added sugars, and sodium[12]. It was reported from the U.S. Nurses' Health Study (NHS), NHS II and Health Professionals Follow-up Study (HPFS) that poor diet quality, including consumption of potato chips, potatoes (including boiled or mashed potatoes and French fries), sugar-sweetened beverages, and both processed and unprocessed red meats, was positively associated with long

term weight gain, whereas good diet quality, including higher consumption of vegetables, whole grains, fruits, nuts, and yogurt, was negatively associated with long term weight gain[27].

Consuming a good-quality diet and decreasing consumption of poor-quality foods could be an effective strategy in helping individuals consume less total energy with minimal hunger experience, compared to only suggesting a reduction in energy intake. Decreased total energy intake, and biomarkers of the brain-adipose axis which are involved in appetite control could have mediating roles in the relationship between good diet quality and good health[27,28].

Moreover, focusing solely on total energy intake is not very informative for the public, since the general population does not have enough knowledge of efficient dietary choices to achieve a certain amount of total energy, and people's meal planning is generally based on varieties of food rather than energy content. Studies focusing on diet quality, which emphasise food combinations in the overall diet could have more practical applications in terms of conveying the dietary changes required to improve health status.

Diet quality is a relatively new concept in nutritional epidemiology compared to single nutrient study. Diet quality is mostly measured by diet quality indices, where the diet score is based on adherence to dietary guidelines or a specific pattern defined *a priori*[29]. Compared to single nutrient or single food group measures, diet quality indices enable research on overall diet using broader components of food groups, based on the best available knowledge concerning associations between diet and health. There are two main groups of diet quality indices based on the source of items used to score the overall diet. Firstly, some diet quality indices are based on

national dietary guidelines. For example, the Healthy Eating Index (HEI)[30,31] in the U.S. was developed in 2008 to assess the alignment of diet to Dietary Guidelines for Americans (DGA). Newer versions of the HEI (HEI–2010[32] and HEI–2015[12]) correspond to evolving versions of the DGAs. In Canada, HEI–2005 and HEI–2010 have been adapted to recommendations in CFG 2007 to create Canadian versions of HEIs[33,34]. Secondly, other diet quality indices evaluate adherence to certain healthy dietary patterns such as Mediterranean–style patterns[35], or Dietary Approaches to Stop Hypertension (DASH)–style patterns[36]. Systematic reviews identified a list of diet quality indices including the Diet Quality Index (DQI), Dietary Guideline Index (DGI), Dietary Diversity Score (DDS), Recommended Food Score (RFS)[29,37]. The diet quality indices usually have several groups of items each reflecting a distinct category of quality including adequacy, moderation, variety and balance in food intake. Adequacy is a measure of the sufficiency of intake of nutrients and foods; moderation is a measure of whether certain nutrients or foods are consumed in excess; variety is a measure of the diversity of food choices; and balance is a measure of the equilibrium of food intake[33]. Some researchers also calculate diet quality using nutrients only (instead of the conventional way of using food groups) by adding the points evaluating the adequacy of nutrient intakes compared to Dietary Reference Intakes (DRIs)[38].

The first version of diet quality indices in Canada was the Canadian adaption of HEI developed by Didier Garriguet in 2009[33]. Briefly, it was developed by adapting the American HEI–2005[30] to conform to recommendations in CFG 2007[39]. The total score is 100, with higher scores

indicating better diet quality. The Canadian adaption of HEI was evaluated using the 2004 Canadian Community Health Survey (CCHS) – Nutrition for the population aged two year and above. The average score was 58.8 points, with children aged 2 to 8 having the highest average scores (65 points). Average scores tended to fall in early adolescence, stabilizing at around 55 points from ages 14 to 30 and turning upwards to 60 points at age 71 or older. At all ages, women's scores exceeded those of men[33]. With the update of HEI version 2010, the Canadian adaption of HEI (HEI-C 2010) was developed in 2017 by Mahsa Jessri *et al.*[34]. The adaptions were still based on recommendations from the CFG 2007[39]. Compared to the 2009 version of Canadian HEI, HEI-C 2010 added "refined grains" in the moderation components of the scoring system and deleted "total grain products" from the adequate components. For fatty acids, total amount of unsaturated fat in the 2009 version was replaced by a ratio of (PUFA + MUFA)/SFA. Finally, HEI-C 2010 contains 8 components for foods that should be consumed in adequacy and 3 for moderation, with a total score remaining at 100. HEI-C 2010 was validated using data from CCHS Cycle 2.2 with 12,805 participants ≥18 years old[34]. The total mean error-corrected HEI-C 2010 score was 50.85 points out of 100. Lower adherence to the index recommendations was associated with higher likelihood of being obese. The two Canadian HEIs were not validated in pregnant women. However, the U.S. version of HEI was validated in pregnant women and was found to be inversely associated with body weight before pregnancy and gestational weight gain[40-42].

Although improving trends in healthy food consumption have been observed in recent years, diet in high-income countries is still jeopardized by unhealthy foods containing high saturated fat, refined grains, free sugars, and low fiber[43]. Diet quality (what people habitually eat and avoid eating) may be difficult to change due to barriers at individual, social-cultural and environmental levels[44]. However, pregnancy offers a window of opportunity for intervention, because pregnant women may be more willing to adopt healthier dietary habits during this period of life due to perceived benefits to the babies and themselves[45,46]. It was found in a Canadian study that pregnant women had slightly better diet quality than non-pregnant women of childbearing age matched on age and body mass index (BMI)[47]. A longitudinal study in the U.K., however, found that dietary patterns change little from the prepregnancy to the pregnancy period[48]. Across trimesters of pregnancy and from late pregnancy to the postpartum period, no variation in total HEI scores was observed[49,50]. Considering that children share dietary patterns with their parents[51], a good-quality diet during pregnancy is likely to be transmitted to the next generation and to have potential long–lasting positive health effects.

2.4 Determinants of Diet Quality during Pregnancy and Conceptual Framework

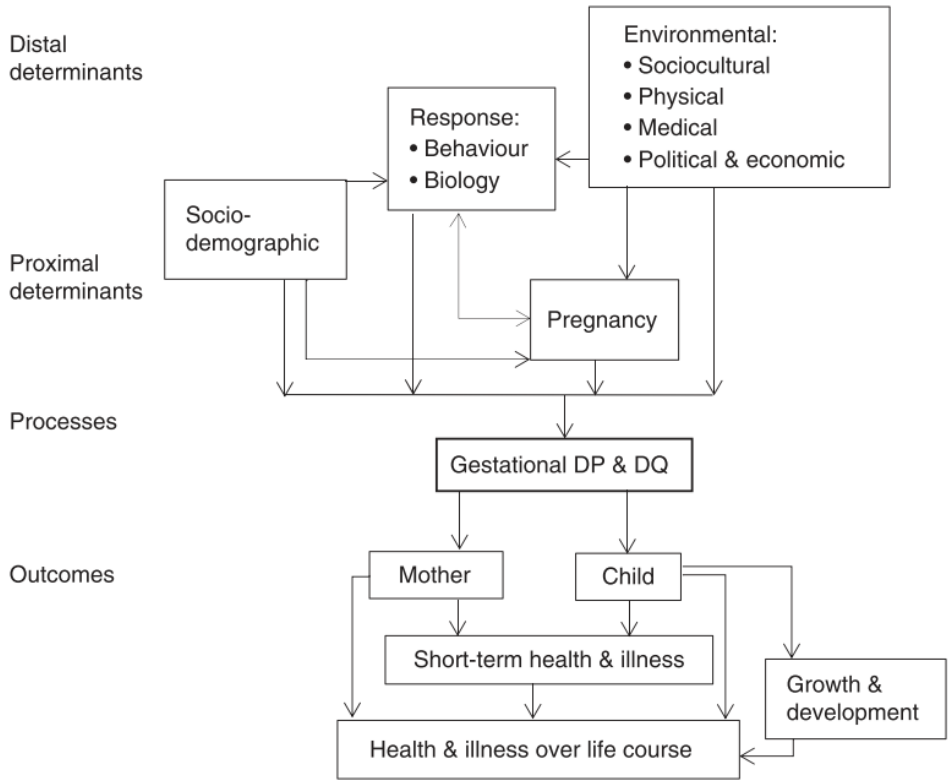
Health determinants are defined as ‘any factor, whether event, characteristic, or other definable entity, that brings about change in a health condition, or other defined characteristic’[52] (p. 37). The diet quality gap among nonpregnant individuals is not simply a matter of personal choice. It

is thought to be a consequence of many factors, including the access to and price of healthy foods, knowledge of a healthful diet, and pressing needs that may take priority over a healthful diet[53]. Empowering individuals and creating supportive environments by addressing the broader determinants of healthy eating is required. In a systematic review, Doyle *et al.* proposed a conceptual framework to study the determinants of dietary patterns and diet quality during pregnancy[54] (see Figure 1 below). Determinants were further divided into 4 categories in the framework: 1) sociodemographic factors (education, ethnicity/ birthplace/ nationality, income/ financial difficulty/ health insurance, food insecurity, marital status/ partnership/ cohabitation, occupation/employment), 2) environmental factors (food environment, social support, place of residence), 3) individual behavioral and biological factors (age, pre-pregnancy BMI, smoking, physical activity, alcohol and caffeine intake, depression and stress/ anxiety), and 4) pregnancy related factors (parity, nausea, pregnancy body image).

On the basis of a systematic review[54] it was concluded that women who were older, more educated, with higher income or other markers of affluence were more likely to follow a healthier dietary pattern or have a better diet quality. The finding was consistent across different populations and settings. However, because not all studies used multivariable models, it was not clear how these factors were confounded by each other. Findings regarding ethnicity and parity were less consistent and they could be acting as markers of age, education status and other sociodemographic factors. Healthy eating also aligned with other health behaviours before and during pregnancy including adequate physical activity, no smoking and lower prepregnancy

BMI. The authors commented that the relationship between diet quality and prepregnancy BMI was difficult to interpret. Instead of interpreting prepregnancy BMI as a determinant of diet quality during pregnancy, it could also be that diet tracking back to prepregnancy was a determinant of prepregnancy BMI. The finding from another study that dietary patterns changed little[48] from prepregnancy to pregnancy supports this hypothesis. Other determinants in the framework that were not well researched include food insecurity and pregnancy related factors. More research of sound methodology was called for by the authors in order to conclusively disentangle the interplay of the different determinants of diet quality during pregnancy.

Figure1: Conceptual multiple determinants life course framework of diet in pregnancy (DP, dietary pattern; DQ, dietary quality)[54]



In high-income countries such as the U.S. and Canada some population subgroups still have inadequate access to food to provide adequate nutrition. A food-insecure household, as defined by the U.S. Department of Agriculture (USDA), is one in which "access to adequate food is limited by a lack of money and other resources." Healthy food choices such as fresh fruit and vegetables are often more expensive than energy-dense, processed foods. Starting from before pregnancy, social inequalities exert their influences on different aspects of the maternity experience. Women of childbearing age living in food insecure households have been found to have nutrient inadequacies, including key nutrients for a healthy pregnancy[55]. Food insecurity has been found to be associated with poor maternal experiences, including prepregnancy obesity, higher gestational weight gain, non-normal birth weight, and GDM[55]. Socioeconomic disparities in birth weight have also been documented in Canada, Sweden, Denmark, the U.S., and these disparities are a persistent factor in the etiology of adverse birth outcomes[56] such as intrauterine growth retardation (IUGR)[57].

Main sources of social inequalities—income, education, ethnicity— have an established impact on diet quality in general populations in Canada[58-60]. Only two previous studies in Canada are available on a limited number of determinants, and the dietary assessment methods used were suboptimal, with one using 1-day food recall[61] and another using a FFQ[18]. The relationship between social inequality and diet quality during pregnancy, and the subsequent adverse pregnancy and infant growth outcomes in Canada, require more study.

2.5 Association between Diet Quality and Perinatal Outcomes

Although there are dietary guidelines for women in preconception and pregnancy to achieve a good quality of diet[62], little evidence was available on the benefits until the last few decades. The publication of findings from pregnancy and birth cohorts with high quality dietary data has improved the knowledge base regarding the health impacts of diet quality on perinatal adverse outcomes[63,64], including excessive/inadequate gestational weight gain, gestational diabetes (GDM), hypertensive disorders of pregnancy (HDP), cesarean delivery, preterm birth, and extremes of birthweight.[65-70]

Several systematic reviews reported the associations between maternal dietary patterns and rates of GDM, HDP, preterm birth and fetal growth.[71-75] However, the validity of these studies has been limited by the inclusion of a single publication database[73], lack of a meta-analysis[71-73], and reporting of only a few of the relevant perinatal outcomes[74]. These reviews are also limited by the absence of registered or published protocols, which hinders the evaluation of a potential reporting bias.[76] Most importantly, the inclusion of studies using *a posteriori* dietary patterns[71-75] limits the relevance of these results to guide dietary interventions as they are data-driven and vary greatly between studies. To date, no systematic review has evaluated the association between diet quality and adverse perinatal outcomes.

Gestational Weight Gain

In 2009[77], the Institute of Medicine (IOM; now known as the National Academy of Medicine) updated the gestational weight gain (GWG) guidelines[78] to provide specific recommendations regarding GWG. The new GWG guidelines incorporated World Health Organization (WHO) categories of maternal BMI and recommended less GWG women with overweight or obesity than for women who are normal and underweight. Briefly, the IOM recommended 12.5–18 kg of total GWG for singleton pregnancies with a prepregnancy BMI categorized as underweight (BMI <18.5), 11.5–16 kg for normal weight (BMI 18.5–24.9), 7–11.5 kg for overweight (BMI 25–29.9) and 5–9 kg for obese (BMI ≥30) women. Total GWG within the IOM recommendations was considered as "appropriate", above the recommendations was considered as "excessive" and below the recommendations was considered as "inadequate"[78].

Inappropriate, i.e. either excessive or inadequate GWG may be detrimental to perinatal health, independently from maternal prepregnancy BMI. A systematic review[79] found that excessive GWG is associated with an increased risk of large for gestational age (LGA) (odds ratio 1.85, 95% confidence interval 1.76 to 1.95), macrosomia (1.95, 1.79 to 2.11), and caesarean delivery (1.30, 1.25 to1.35). High maternal GWG is also associated with higher risks of gestational hypertensive disorders, pre–eclampsia, preterm birth and gestational diabetes (GDM)[80]. Low GWG is associated with increased risk of small for gestational age (SGA) (1.53, 1.44 to1.64) and preterm birth (1.70, 1.32 to 2.20).

Inappropriate GWG has become a global epidemic, with prevalence of excessive and inadequate GWG respectively reaching 50% and 20% across continents and ethnicities[81]. In 2010, Health

Canada adopted the 2009 IOM guidelines for gestational weight gain. Data from the 3D Cohort Study in Quebec indicated that excessive total gestational weight gain occurred in all pre-pregnancy BMI categories (27%, 44%, 75% and 68% of underweight, normal, overweight and obese women, respectively)[24]. Similar results were found in a birth cohort in Alberta (30%, 46%, 80% and 80% of underweight, normal, overweight and obese women, respectively)[82].

Existing studies on the association between diet quality and GWG demonstrated inconsistent results. Diet quality was found to be associated with lower rates of gestational weight gain in Norwegian Mother and Child Cohort Study (MoBa) [83] conducted in Norway and Infancia y Medio Ambiente (INMA) study[84] in Spain. In the Viva study[85] conducted in the U.S., however, the Dietary Approaches to Stop Hypertension (DASH) diet score measured at around 11 weeks of pregnancy was found to be positively associated with subsequent GWG among women who were obese before pregnancy, which was unexpected for the authors. On the other hand, the generation R study[86] conducted in the Netherlands, the Prospective New Hampshire Birth Cohort Study (NHBCS)[87] in the U.S. and the Growing Up in Singapore Towards healthy Outcomes (GUSTO) Study[88] in Singapore did not find statistically significant relationship between diet quality and gestational weight gain. Up to the time of initiating our systematic review, there had been no previous systematic reviews that evaluated the quality of the studies and synthesized the literature on the relationship between overall diet quality and gestational weight gain.

Adverse Maternal Outcomes

GDM is diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation[89]. Accumulating evidence indicates that there is an association between diet quality and GDM.

Preeclampsia together with gestational hypertension without proteinuria comprise hypertensive disorders of pregnancy. They significantly increase maternal and infant morbidity and are among the major contributors to maternal deaths, accounting for 10-15% worldwide[90]. Preeclampsia is a complication in pregnancy characterized by new-onset increased blood pressure with proteinuria or with significant end-organ dysfunction that usually occurs after 20 weeks of gestation[91]. It has been hypothesized that nutrition might play a role in the development of preeclampsia for many years[92]. However, evidence is insufficient to demonstrate the effectiveness of specific nutrients in prevention of hypertension. It is possible that the effect of individual nutrients is small or have been confounded by the overall diet quality. Some studies have explored the relationship between diet quality and hypertensive disorders of pregnancy[93-96]. However, no systematic review has been done to evaluate the study quality and to synthesize the results.

Birth Outcomes

Being born too large or too small are associated with neonatal mortality, morbidity, impaired development, and chronic diseases later in life[97]. Macrosomia is generally defined as a birth weight greater than 4000g or 4500g, irrespective of gestational age, while large for gestational age (LGA) is defined as a birth weight >90th percentile as per gestational age. Macrosomia and LGA increase the risk of labor abnormalities, shoulder dystocia, birth trauma, and permanent injury to the newborn[98]. Mothers giving birth to LGA babies are also at higher risk for postpartum hemorrhage. This problem has gained more attention in recent years as the proportion of high birth weight babies is increasing in parallel to the obesity epidemic. The increase is mainly related to a higher proportion of overweight/obese women becoming pregnant, women gaining more gestational weight—9 to 10 kg in the 1950s and 1960s vs 15 kg in 2000—and a reduction in smoking prevalence[57]. On the other hand, SGA, which is a measure used as a proxy indicator of IUGR, is also associated with higher perinatal mortality, morbidity, and long-term adverse consequences[97]. SGA refers to newborns with a low birth weight for gestational age (<10th percentile), according to the reference curve for normal fetal growth or birth weight for gestational age[99]. In a Swedish study, SGA was associated with an increased risk of death throughout the neonatal and childhood period, with the highest risk estimates for death from infection and neurologic disease[100]. Macrosomia affected 10% of pregnancies in a Canadian birth cohort[101], while 6.1% of Canadian newborns had low birth weight (birth weight <2500g) in 2009 to 2013[102,103]. LGA and SGA influenced 10.3%, and 8.9%, respectively, of Canadian newborns from 2009 to 2013[103]. Preterm birth is another relatively frequent pregnancy complication

defined as birth before 37 weeks of gestation. In 2017, it represented approximately 8.2% of the births in Canada[104]. It is one of the leading causes of neonatal mortality, and is associate with an increased risk of cognitive abnormalities, as well as metabolic and cardiovascular disease in the offspring [105-107].

It is well accepted that the quality of the fetal environment is essential for adequate fetal development[108]. Fetal growth in utero is related to maternal nutritional intake and the ability of the placenta to transfer nutrients to the fetus. Starvation during acute famine periods has been associated with subsequent abnormal birth weight[109]. Conversely, excessive weight gain in pregnancy is associated with LGA and macrosomia in offspring[79]. Although some studies reported the relationships between nutrients and child health[3,110], the relationships between overall diet quality and pregnancy and birth outcomes are not well established. A systematic review[74] found that healthy dietary patterns—characterized by high intakes of vegetables, fruits, whole grains, low-fat dairy, and lean protein foods—were associated with a weak trend towards a lower risk of small-for-gestational-age (OR: 0.86; 95% CI: 0.73, 1.01; I^2 = 34%); and unhealthy dietary patterns—characterized by high intakes of refined grains, processed meat, and foods high in saturated fat or sugar—were associated with lower birthweight (mean difference:−40 g; 95% CI:−61,−20 g; I^2 =0%). However, no systematic review has been conducted on the association between overall diet quality and birth outcomes.

2.6 Association between Diet Quality and Offspring Neurodevelopment

The first 1,000 days of life, which include pregnancy and two years postpartum, is a time when the brain forms and develops rapidly and lays the foundation of neurodevelopment. During this crucial early stage, proliferation, migration, aggregation, and myelination of the neurons forms the architecture of the brain and provide the foundation for cognitive, motor, and language functions later in life [111]. Particularly, throughout the third trimester, the structure of the brain changes from a smooth bilobed shape to a more complex one with gyrations and sulcations that resembles the adult brain[112,113]. The early period of neurodevelopment represents a time of great opportunity and vulnerability for future educational attainment and participation in community activities of the children at the individual level, and for the overall development and economic growth for the human at the population level[11].

Proper nutrition during pregnancy provides fundamental building blocks for the developing brain[3,114]. The brain is vulnerable to damage if the nutrients required to support its growth are insufficient[115]. Research from the great Dutch famine found smaller mean brain volumes and perfusion after several decades in those exposed to the famine in utero [116,117]. In addition to energy and macronutrients deficiency characterized in the famine, micronutrients, including zinc, iron, choline, B-vitamins and iodine, were also found to be essential for brain growth[118].

Despite increasing interest in the associations between maternal diet quality during pregnancy and childhood neurodevelopment, to date, there have been few studies quantifying this

association directly[119,120]. Most previous studies used components of a good quality diet, such as fish, seafood, fruit intake, certain nutrients, or data-driven dietary pattern as an approximate for diet quality [119]. One recent U.S. cohort study found that higher diet quality scores during pregnancy were associated with better cognition in the offspring[121]. On the other hand, interventional studies using multivitamin supplementation did not demonstrate positive effects in improving offspring neurodevelopment[120]. The discrepancy between these results and findings of the Dutch famine studies could possibly be explained by a modifying effect of diet quality on the association between multivitamin intake and neurodevelopment, since both diet and multivitamins provide nutrients during pregnancy. However, no studies have measured the potential interaction between the two exposures.

2.7 Knowledge Gaps, Objectives and Hypotheses

In summary, a good quality diet during pregnancy provides proper nutrition, the fundamental building blocks to support both the health of mothers and the fetus. However, through the literature review in this chapter, knowledge gaps were identified that limit the formulation of evidence-based interventions to improve diet quality in pregnancy. First, careful evaluation of diet quality during pregnancy based on high quality dietary data is scarce in Canada. The distribution of diet quality during pregnancy in Canada is unclear and the social inequality of diet quality is not well investigated. Due to limited evidence, it is difficult to estimate what aspects of

diet need to be improved and which sub-populations need to be targeted. In addition, the associations between diet quality and perinatal and offspring outcomes have not been established. Examining these relationships will strengthen arguments that the improvement of diet quality during pregnancy will overall health in both mothers and the offspring.

Thereby, the thesis is meant to provide evidence that will fill these knowledge gaps. Specifically, four objectives were identified: 1) To assess overall diet quality during pregnancy, including developing and validate the tool for assessment of diet quality. 2) To identify the social determinant factors that are associated with overall diet quality during pregnancy in a large birth cohort. 3) To synthesize the knowledge on the association between overall diet quality and adverse perinatal outcomes through a systematic review and meta-analysis. 4) To assess the relationships between maternal nutrition during pregnancy and offspring neurodevelopment.

The hypotheses of the thesis were: 1) Pregnant women have low compliance to the guidelines for some of the food groups which could jeopardize their diet quality. 2) Social factors are be associated with diet quality during pregnancy. 3) Better diet quality is associated with a lower probability of maternal and perinatal adverse outcomes, and with better neurodevelopment in the offspring.

CHAPTER 3. METHODS - THE 3D COHORT STUDY

A large part of the thesis was based on the comprehensive health measures of the 3D Cohort Study. In order to give the readers some background knowledge on the cohort before reading the results sections, this chapter presents a general description of this cohort and the details of sample recruitment, cohort follow-up and data collection,

3.1 General Description

The 3D Cohort Study is a pregnancy and birth cohort that involved recruitment of 2,366 pregnant women in Quebec from 2010 to 2012. It was established to improve knowledge about the links between various adverse exposures during pregnancy and birth and later health outcomes in children. This multi-institutional network and transdisciplinary research programme is represented through a network of researchers with various expertise, many of whom are national and international leaders. The 3D Cohort Study is based on the premise that pregnancy is the 'foundation period' for future health and development. The network brings together complementary expertise in nutrition, obstetrics, neonatology and pediatrics, developmental psychology and neurology, sociology, anthropology, ethics and knowledge translation. Through this transdisciplinary collaboration, critical knowledge gaps in perinatal health addressed with the goal of knowledge synthesis and translation to policy.

3.2 Sample and Recruitment

Pregnant women and their partners were recruited at routine prenatal visits during the first trimester of pregnancy (8 to < 14 weeks) from nine obstetric hospitals in Quebec (seven in Montreal and one each in Sherbrooke and in Quebec City) from May 25, 2010 to August 30, 2012[1]. Eligible women who were planning to deliver in the participating centers were invited to participate. They were between 18 and 47 years of age at the time of recruitment and able to communicate in French or English. Exclusion criteria included current intravenous drug use, severe illnesses or life-threatening conditions, and multiple gestation pregnancies. Of the 9864 women screened, 6348 (64%) met the eligibility criteria, and 2456 women (39%) agreed to participate (see Figure 1 below). Later, 47 women were determined to be ineligible and 43 withdrew completely from the study, asking that all their data and biospecimens be destroyed, leaving 2366 women to participate in the study (37% of eligible women). Among women in the 3D Cohort Study, 1721 of their partners (1704 biological fathers) agreed to participate (73%). The most common reason for ineligibility was not being within the gestational age window (25% of ineligible women). The study sample is on average both older and of lower parity than Canadian and Quebec births overall. In comparison with the Canadian population, the 3D Cohort Study participants were more likely to be born outside Canada (35% of participants compared to 27% for Canadians), to hold a university degree (62% compared to 35%), and to be married or living with a partner (94% compare to 60%). The household income level of

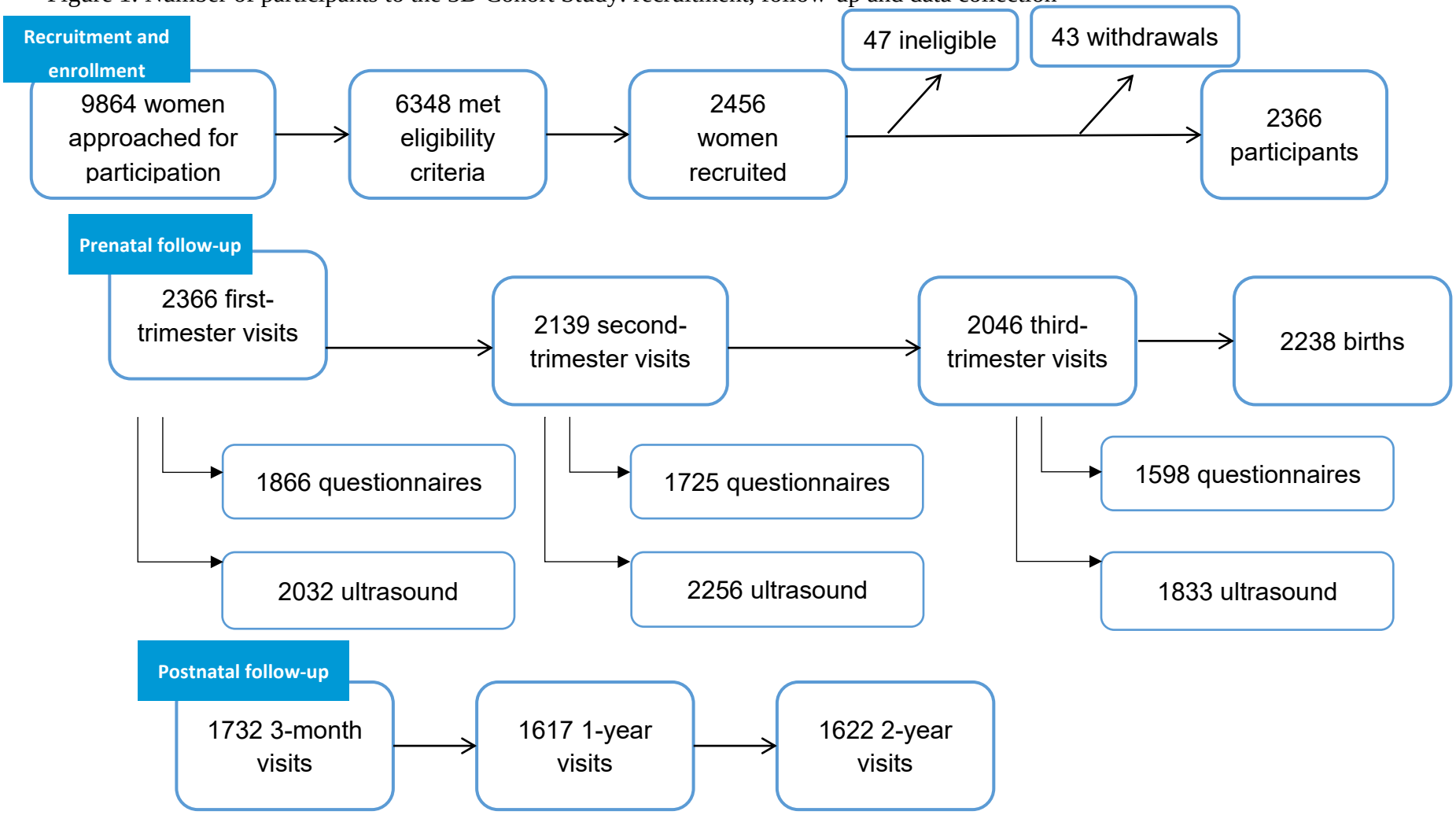
participants was also relatively high, with nearly half (48%) of the study sample reporting annual household income greater than $80,000 (compared to 30% of Canadians).

3.3 Cohort Follow-up and Data Collection

Data collection during pregnancy and among children during follow-up was conducted by trained research nurses and research assistants. Recruitment was done at the first trimester of pregnancy (8–14 weeks); participants were also met at mid (20–24 weeks) and late (32–35 weeks) pregnancy, and at delivery. In total, 2238 participants had a live singleton birth (94%). Postnatal visits were done when the child was aged 3 months, 1 year, and 2 years. The 3D Transition Study is continuing to follow the cohort children up to 10 years of age.

Self reported information about maternal sociodemographic characteristics, collected by interviewers, included maternal age, ethnicity, marital status, socio-economic status (education, family income, occupation), prepregnancy weight, pregnancy and medical history, family medical history, paternal ethnicity and age, maternal tobacco smoke, alcohol consumption and family food insecurity.

Figure 1: Number of participants to the 3D Cohort Study: recruitment, follow-up and data collection



CHAPTER 4. Generating and Validating a Diet Quality Indicator

To reach the objectives of the thesis, a diet quality indicator was needed to quantify diet quality in pregnancy. This chapter presents a detailed description on how I generated and validated HEI-C as an indicator for diet quality during pregnancy using raw data from the 3D Cohort Study. As described in the background part, diet quality is mostly measured by diet quality indices, where the diet score is based on adherence to dietary guidelines or a specific pattern defined *a priori*[29]. In Canada, HEI–2005 and HEI–2010 have been adapted to recommendations in CFG 2007 to create Canadian versions of HEIs[33,34]. I decided to use the Canadian adaption of HEI (HEI-C 2010) developed in 2017 by Mahsa Jessri *et al.* [34].

A large amount of work has been allocated to assigning food to the number of food group servings, which were not already available in the nutrition database of the 3D Cohort Study. Additionally, 'mixed dishes' (e.g., spaghetti with meat sauce) which account for 8% of the total energy intake, were broken down into food groups by manually matching to standard recipes in the Food Patterns Equivalents Database (FPED) developed by U.S. Department of Agriculture (USDA)[122]. This step further increases the quality of our data because in other studies and in CFG classifying system, mixed dishes were classified into a subgroup called 'recipes' without breaking down into the four main food groups, which leads to underestimation of the number of servings of some food groups.

Furthermore, HEI-C 2010 was not validated in the pregnant population, so I additionally did some validation using data from the 3D Cohort Study.

4.1 Completing the 3-day Food Records

A total of 1550 women (66% of the total participants) accepted to complete a 3-day food record at the second prenatal visit (20-24 weeks). The 3-day food record was used to record dietary intakes on 2 weekdays and 1 weekend day (See Appendix 3 - 3D Cohort Study Questionnaire 2C). Pregnant women were trained by the research nurses on how to complete the 3-day food record. They completed the food record at home and returned the food records by mail.

4.2 Generating Energy and Nutrients from the 3-day Food Records

The food items in the food records were coded by trained nutritionists into Food Processor software (ESHA Research, Inc., Salem), which was linked to the Canadian Nutrient File, to generate a complete database of energy, macronutrients and micronutrients intakes. Since the content of added sugars was not readily available in the Canadian Nutrient File, it was calculated following a published method[123].

4.3 Assigning food to number of food group servings

The food items were assigned to four major Canada's Food Guide (CFG) food groups, 30 sub-groups, and to Tiers 1-4 using the food Classification system developed by Health Canada[124] CFG encourages people to choose foods lower in fat, sugar and salt. Foods that exceed at least

two upper thresholds (total fat: >10 g/reference amount (RA), sugars: >19 g/RA, sodium: >360 mg/RA, saturated fat: > 2 g/RA) are classified into Tier 4. For 'milk and alternatives' and 'meat and alternatives' group, the upper threshold for saturated fat was not counted due to the fact that these food groups contain more inherent saturated fats than other food groups. Foods allocated to Tier 4 were excluded when counting the number of CFG servings of food in the four major food groups,, because they were classified as 'not in line with the guidance in CFG[124].

In the CFG classifying system, mixed dishes (e.g., spaghetti with meat sauce) were classified into a subgroup called 'recipes' without breaking down into the four main food groups. The energy intake from foods in the subgroup 'recipes' accounted for 8% of the total energy intake of this study population. Thus, an omission of the mixed dishes in counting the number of servings of the four main groups would lead to an underestimation of number of servings. For a more concise estimate, mixed dishes in the food records were decomposed to food groups and subgroup servings by linking to standard recipes in the Food Patterns Equivalents Database (FPED) developed by U.S. Department of Agriculture (USDA), which converts the foods and beverages to USDA Food Patterns components[122]. The matching was performed manually according to name and description, with a secondary aim being to minimize the energy density gap. When there were multiple possible matches, the one with the smallest gap in energy density per 100 grams was chosen. When an exact match was not found in FPED, the most similar item regarding components of the food groups was chosen. This process was performed by a student with a background in nutrition and reviewed by a nutritionist that was familiar with the foods

consumed locally. USDA Food Patterns components were then converted to the number of servings in the CFG.

4.4 Generating the Canadian adaption of Healthy Eating Index

Overall diet quality in pregnancy was calculated according to the Canadian adaption of Healthy Eating Index (HEI-C) 2010 developed in 2017 by Jessri *et al.*[34]. HEI-C contains eight components for foods that should be consumed in adequate amounts (total fruits and vegetables, whole fruit, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids) and three that should be consumed in moderate amounts (refined grains, sodium, empty calories), resulting in a total score of 100 (see supplementary table 1). At the time of data collection, people's diet was guided by age and sex-specific recommendations from CFG 2007, which were designed scientifically for the food intake pattern to meet the nutrient requirements and to avoid nutrient excess. So number of servings for 19 to 50 years old women in CFG 2007 were used in this study: i.e. eight servings of vegetables and fruits, six to seven servings of grain products, two servings of 'milk and alternatives', and two servings of 'meat and alternatives' per day[13-16]. Because pregnant women were advised to include an additional two to three servings per day from any of the four food groups,[16] the cut-offs for 'total vegetables and fruits', grain products and 'milk and alternatives' were set at eight, seven, and three, respectively, to align with the examples given by Health Canada[18]. The cut-offs for whole fruit and 'greens and beans' component were set at 21% of that for 'total vegetables and fruits', which

are 1.68 servings[33,34]. The cut-offs for whole grains were set at 50% of that for total grain products, which are 3.5 servings, according to CFG 2007 recommendations. Empty calories were defined as calories from saturated fats, alcohol and added sugars[34,123]. The detailed scoring standards for min and max of each of the HEI-C components used in this study is listed in table 1. Intermediate intakes were scored proportionately between minimum and maximum values. Total HEI-C score, adequacy sub-score, and moderation sub-score were sums of specific individual components.

Table 1. Scoring criteria for the Healthy Eating Index-Canada 2010 (HEI-C 2010) for pregnant women, adapted from Jessri *et al.* [34]

Component	**Max pts**	**Standard for max score**	**Standard for min score (0)**
Adequacy Sub-score	60		
Total fruits and vegetables[3]	10	8 servings	No servings
Whole fruit[4, 5]	5	1.68 servings	No servings
Greens and beans[5]	5	1.68 servings	No servings
Whole grains[6]	10	3.5 servings	No servings
Dairy	10	3 servings	No servings
Total protein foods	5	2 servings	No servings
Seafood and plant proteins[7]	5	0.64 servings	No servings
Fatty acids	10	(PUFA + MUFA)/SFA ≥ 2.5	(PUFA + MUFA)/SFA ≤ 1.2
Moderation Sub-score	40		
Refined grains[8]	10	<50% of grains refined	0% grains refined
Sodium[9]	10	<= 1500 mg	≥ 4600 mg
Empty calories[10]	20	≤ 19% of energy	≥ 50% of energy
Total HEI-C 2010 Score	100		

[1]Scoring criteria for the Healthy Eating Index-Canada 2010 was adapted to servings based on the age and sex-specific recommendations in Canadian Food Guide (CFG) 2007 for women 19 to 50 years old and pregnant women. [2]Scores between the maximum and minimum were assigned

proportionally. [3]Includes fruit juice. [4]Excludes fruit juice. [5]The standard for max scores of the "whole fruit" and "greens and beans" components represent 21% of the "vegetables and fruit" recommendation in CFG. [6]The standard for max score of the "whole grains" component is 50% of the "grain products" recommendation in CFG. [7]The standard for max score of the "seafood and plant proteins" component represents 32% of the "meat and alternatives" recommendation in CFG. [8]The maximum score standard for the refined grains component is <50% of grain products consumed as refined grains based on CFG recommendations. [9]Respondents scored 10 points if their sodium consumption was at or less than their adequate intake, 8 points if their sodium consumption was at their upper intake level and 0 points if their consumption was twice their upper intake level. [10]Includes calories from solid fats, alcohol and added sugars.[34]

4.5 Validation of HEI-C 2010 in 3D Cohort Study

HEI-C 2010 has not been validated for use in pregnant women. We performed validation analysis using data from the 3D Cohort Study and the methods used by Guenther et al. when validating the American HEI-2010[125] and by Jessri et al. when validating HEI-C 2010 in the general population[34]. To test the validity of the HEI-C score in the pregnancy population, Spearman correlations between the total HEI-C score and energy intake to test whether it measures diet quality independent of diet quantity[1]. Spearman correlations between the total score and component scores were used to estimate the reliability of the HEI-C score[1]. HEI-C scores were also divided into quartiles, to present the mean and SD of selected nutrients in each HEI-C quartile[2]. To compare diet quality among compliers, intermediate compliers, and poor compliers of CFG 2007, the scores for each HEI-C component were divided into quartiles. Those scoring in the top 25% were considered compliers for that component, those scoring in the bottom 25% were deemed poor compliers, and those scoring in the middle 50% were deemed intermediate compliers.

As shown in table 2, HEI-C score had a statistically significant but relatively small in magnitude correlation with energy intake during pregnancy ($r = 0.08$, $p = 0.001$). As expected, the HEI-C score was found to have low to medium correlations with individual component scores, but strong correlations with total moderation ($r = 0.76$, $p<0.0001$) and adequacy scores ($r = 0.91$, $p<0.0001$). Higher density of beneficial micronutrients from food including calcium, vitamin A,

folate, vitamin C, vitamin D, calcium, magnesium, iron, and zinc were found in higher quartiles of HEI-C (Table 3). Density of protein, fiber, polyunsaturated fatty acids, and monounsaturated fatty acids increased in higher quartiles of HEI-C, while density of total fat, saturated fat, added sugars, and sodium decreased. There was no significant trend for carbohydrate. Figure 2 shows the prevalence of compliers, intermediate compliers, and poor compliers for each component of HEI-C. Good compliance was observed most frequently for empty calories (87%) whole fruits (74%), and protein foods (74%), while poor compliance was observed most frequently whole grains (56%), refined grains (50%), fatty acids (49%).

These results indicate that HEI-C has validation results in the pregnant population that are comparable to the validation results obtained in the general population.

Table 2. Pearson correlation coefficients between HEI-C and its components.[a]

Components	Total score	Energy	Total adequacy score	Total moderation score	Total fruits and vegetables	Whole fruit	Greens and beans	Whole grains	Milk and alternatives	Total protein foods	Seafood, plant proteins	(PUFA+ MUFA)/ SFA	Refined grains	Sodium	Empty calories
Total score	1.00														
Energy	**0.08**	1.00													
Total adequacy	**0.91**	**0.38**	1.00												
Total moderation	**0.76**	**-0.41**	**0.41**	1.00											
Fruits and vegetables	**0.49**	**0.33**	**0.59**	**0.14**	1.00										
Whole fruit	**0.45**	**0.12**	**0.49**	**0.21**	**0.53**	1.00									
Greens and beans	**0.40**	**0.15**	**0.49**	**0.11**	**0.37**	**0.18**	1.00								
Whole grains	**0.67**	**0.15**	**0.55**	**0.58**	**0.11**	**0.09**	**0.12**	1.00							
Milk and alternatives	**0.19**	**0.41**	**0.34**	**-0.12**	**0.08**	**0.05**	**0.08**	**0.12**	1.00						
Total protein foods	**0.34**	**0.23**	**0.42**	**0.07**	**0.12**	**0.11**	**0.12**	**0.10**	0.04	1.00					
Seafood, plant proteins	**0.46**	**0.19**	**0.56**	**0.12**	**0.17**	**0.19**	**0.15**	**0.15**	**0.08**	**0.46**	1.00				
(PUFA+ MUFA)/SFA	**0.48**	-0.03	**0.48**	**0.28**	**0.16**	**0.12**	**0.12**	**0.09**	**-0.26**	**0.19**	**0.25**	1.00			
Refined grains	**0.69**	0.00	**0.52**	**0.69**	**0.11**	**0.11**	**0.13**	**0.92**	**0.10**	**0.08**	**0.14**	**0.09**	1.00		
Sodium	**0.19**	**-0.63**	**-0.12**	**0.60**	**-0.10**	**0.09**	**-0.05**	**-0.06**	**-0.29**	**-0.10**	-0.04	**0.09**	**0.05**	1.00	
Empty calories	**0.49**	**-0.22**	**0.31**	**0.58**	**0.26**	**0.22**	**0.12**	**0.07**	**-0.09**	**0.15**	**0.11**	**0.40**	**0.07**	**0.15**	1.00

[a] Statistically significant ($p < 0.05$) correlations were shown in bold font.

Table 3. Mean daily intakes of macro- and micronutrients by quartiles of the HEI-C.[a]

	HEI-C 2010 Quartile (mean±SD)				p-trend [d]
	1 (Unhealthy)	2	3	4 (Healthiest)	
HEI-C range	28.8-55.2	55.2-62.7	62.7-70.6	70.6-95.6	-
Energy intake, kcal/day	2135.9±480.8	2198.2±460	2185.3±463.8	2261.7±435.7	<0.001
Carbohydrate, % energy	51.4±6.2	51.7±6	52.4±5.9	51.9±5.7	0.096
Total fat, % energy	34.1±5.5	33.6±5.2	32.8±5.4	33.1±5.3	0.002
Protein, % energy	15.9±2.8	16.5±2.6	16.8±2.6	17.5±2.5	<0.001
Fiber density, g/1000 kcal	8.6±2.1	10.2±2.7	11.4±2.9	12.9±2.9	<0.001
Added sugar, % energy	11.2±4.4	9.5±3.8	8.5±3.3	8.1±3.1	<0.001
Saturated fat, % energy	13.2±2.8	12.2±2.6	11.4±2.5	10.4±2.4	<0.001
Monounsaturated fatty acids, % energy	11.8±2.5	12±2.6	12.1±2.8	12.7±3.1	<0.001
Polyunsaturated fatty acids, % energy	5.5±1.7	5.8±1.7	5.8±1.7	6.4±1.8	<0.001
Alcohol, g	0.3±1.2	0.3±1.3	0.2±0.8	0.2±0.9	0.133
Cholesterol density, mg/1000 kcal	130.8±49.1	129.9±46.5	125.1±45.5	122.4±44.7	0.005
Calcium density, mg/1000 kcal	510.9±152.8	548.2±146.3	560.8±134.3	566.1±135.9	<0.001
Vitamin A density in RAE, µg/1000 kcal	364±175.8	408.1±302.3	430.7±151	453.1±332.8	<0.001
Vitamin D density, µg/1000 kcal	2.2±1.1	2.4±1.2	2.6±1.2	2.8±1.4	<0.001
Vitamin C density, mg/1000 kcal	60.4±33.1	75.2±34.8	84.1±37.6	88±33.5	<0.001
Sodium density, mg/1000 kcal	1436.3±324.6	1311.9±263.9	1261.3±285.4	1187.3±281.9	<0.001
Naturally-occurring folate density, µg/1000 kcal [b]	218.7±65.7	260.6±79	278±81.4	326.3±96	<0.001
Folacin density from food sources, µg/1000 kcal [c]	361.8±92.8	384.2±104.4	388.1±108	411.6±112.5	<0.001
Phosphorus density, mg/1000 kcal	643.8±114.6	684.6±114.1	713.2±116.7	743.4±114	<0.001
Magnesium density, mg/1000 kcal	142.2±23.6	160.7±28.4	175.6±29	194.3±31.7	<0.001
Iron density, mg/1000 kcal	6.8±1.2	6.9±1.3	7.1±1.4	7.1±1.3	<0.001
Zinc density, mg/1000 kcal	5.2±1.1	5.3±1.1	5.4±1.1	5.7±1	<0.001
Potassium density, mg/1000 kcal	1348.9±235	1504.5±248.7	1618.8±261.3	1714.4±249.8	<0.001

[a] Estimates are mean±SD unless otherwise specified.

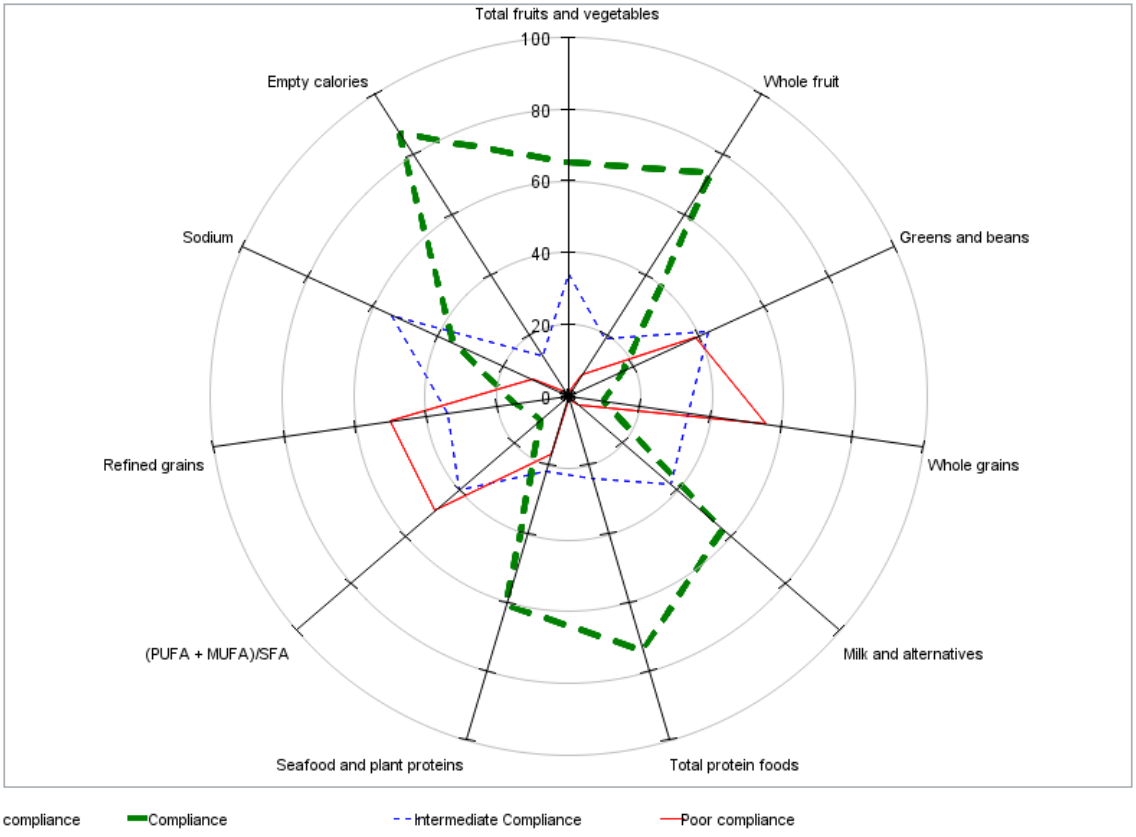
[b] Naturally-occurring folate includes various forms of folate found naturally in foods. 6

[c] Sum of quantities of naturally occurring folate in addition to folic acid without considering their differing bioavailability.

[d] p-trend was estimated by entering quartiles of HEI-C as a continuous variable. A p-trend < 0.05 was considered statistically significant.

HEI-C: Canadian Healthy Eating Index; SD: standard deviation; RAE: retinol activity equivalents.

Figure 2. Percentage of compliers (in green), intermediate compliers (in blue), and poor compliers (in red) for each component of the Healthy Eating Index-Canada (HEI-C) among pregnant women. Each spoke represents an individual HEI-C component. The outermost circle represents 100% prevalence, while the center of the circle represents 0% prevalence.



CHAPTER 5. MANUSCRIPT 1 - DIET QUALITY DURING PREGNANCY AND ITS ASSOCIATION WITH SOCIAL FACTORS: 3D COHORT STUDY (DESIGN, DEVELOP, DISCOVER)

Article Preface

This manuscript described the distribution of diet quality during pregnancy and studied the association between social factors and diet quality during pregnancy based on 1,535 pregnant women who provided dietary information in the 3D Cohort Study in Quebec, Canada. Therefore, it addressed the first two objectives of this thesis: 1) To assess overall diet quality during pregnancy; and 2) To identify the social determinant factors that are associated with overall diet quality during pregnancy in a large birth cohort. YY is the guarantor of the paper. YY, WF and LD contributed to the conception of the research question. YY and CF contributed to the statistical analyses. YY, BB and LD contributed to the dietary data coding. YY, CF, BB, LD, and WF contributed to drafting and reviewing of the paper and provided approval for the version submitted for publishing. Written informed consents were obtained from each participant in the 3D Cohort Study. Ethical approvals of 3D Cohort Study were obtained from the research ethics committee at Sainte-Justine's Hospital in Montreal and all other participating study sites. The Health Sciences and Science Research Ethics Board of the University of Ottawa granted approval for secondary data analyses, including those in this manuscript (file number H-04-21-6908, Approval Date April/05/2021, Appendix 1).

This manuscript was formatted for submission as an original research article to the journal *Maternal and Child Nutrition*. This article has been published and can be found in the following link: **https://onlinelibrary.wiley.com/doi/10.1111/mcn.13403?af=R**. The

published manuscript could also be found in Appendix 2.

How to cite this article:

Yu, Y., Feng, C., Bédard, B., Fraser, W., & Dubois, L. (2022). Diet quality during pregnancy and its association with social factors: 3D Cohort Study (Design, Develop, Discover). Maternal & Child Nutrition, e13403. https://doi.org/10.1111/mcn.13403

I additionally provided details of the 3D Cohort Study setting and the validation of the healthy eating index in our population in chapter 3 - method.

Title Page

Diet quality during pregnancy and its association with social factors: 3D Cohort Study (Design, Develop, Discover)

Authorship

Yu, Yamei[1]

Feng, Cindy[1,2]

Bédard, Brigitte[1]

*Fraser, William D.[3]

*Dubois, Lise[1]

*These two authors contributed equally.

Author affiliations

1. School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ontario, Canada
2. Department of Community Health and Epidemiology, Dalhousie University, Halifax, Canada
3. Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, and the Centre de Recherche du Centre hospitalier Universitaire de Sherbrooke (CRCHUS)

Corresponding authors

Dubois, Lise

ldubois@uottawa.ca

School of Epidemiology and Public Health, Faculty of Medicine

University of Ottawa

Fraser, William

William.Fraser@usherbrooke.ca

+1 819 821-8000 poste 12873

Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, and the Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke (CRCHUS)

Ethical Statement: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Health Sciences and Science Research Ethics Board of the University of Ottawa, research ethics committee at Sainte-Justine's Hospital in Montreal, and all other participating study sites. Written informed consent was obtained from all subjects/patients.

Contributor Statement: YY is the guarantor of the paper. YY, WF and LD contributed to the conception of the research question. YY and CF contributed to the statistical analyses. YY, BB and LD contributed to the dietary data coding. YY, CF, BB, LD, and WF

contributed to drafting and reviewing of the paper and provided approval for the version submitted for publishing.

Conflict of Interest Statement: All authors declare no conflict of interest in conducting this work.

Acknowledgements: The authors would like to acknowledge all the participants and the study team members who had great contribution to this study.

Financial Support: This research project is sponsored jointly by the Canadian Institutes of Health Research (CIHR) (Grant CRI 88413, MOP 133422 and HLT 151517) and the National Natural Sciences Foundation of China (NSFC) (Grant No. 81661128010).

Data availability statement: Data available on request due to privacy/ethical restrictions.

Abstract

Good diet quality during pregnancy provides adequate nutrition to support both the mothers and the fetus. The objective of this study is to describe the distribution of diet quality during pregnancy and study the association between social factors and diet quality during pregnancy in a Canadian population. This study was based on 1,535 pregnant women who provided dietary information in the 3D Cohort Study in Quebec, Canada. A 3-day food record was used to collect dietary intake in the second trimester of pregnancy. A Canadian adaption of the Healthy Eating Index (HEI-C) 2010 was used to quantify diet quality. Univariate and multiple linear regression models were used to calculate unadjusted and adjusted effect estimates and confidence intervals (CIs) for the association between social factors and HEI-C. The mean HEI-C 2010 score in this study was 62.9 (SD:11.2). Only 4.5% and 8.3% of the pregnant women consumed the recommended amounts of whole grains and 'greens and beans', respectively. Diet quality was lower in some sub-groups of pregnant women. After multivariable adjustment, lower diet quality was observed in participants who were less educated, younger, overweight or obese before pregnancy, or parous. There was an interaction between ethnicity and immigration status on diet quality in pregnancy. These findings could be useful for health practitioners and policy makers in developing strategies to improve the diet quality of pregnant women.

KEYWORDS

Diet, Healthy; Pregnancy; Cohort Studies; Educational Status; Obesity, Maternal; Parity

KEY MESSAGES

- The diet of the women in Canada still needs improvement, especially regarding whole grains and ‘greens and beans’, where the majority of the women did not meet the recommendations.
- Pregnant women who were less educated, younger, overweight or obese before pregnancy, or parous should be targeted for improving diet quality in Canada.
- There was an interaction between ethnicity and immigration status on diet quality during pregnancy.

Introduction

The first 1000 days, including the prenatal period, is a unique period for children to develop their ability to grow and prosper in society(Koletzko et al., 2017; Schwarzenberg, Georgieff, & Committee On Nutrition, 2018). Malnutrition during pregnancy represents a major public health issue that affects maternal health and offspring development, and contributes substantially to the global burden of disease and disability(Hanson et al., 2015; Lim, Vos, & Flaxman, 2013). Good diet quality during pregnancy provides adequate nutrition to support both the mothers and the fetus, and is an important contributor to the children's physical and intellectual development(Fleming et al., 2018; Hanson et al., 2015; Stephenson et al., 2018).

A diet of good quality includes a variety of vegetables, fruits, whole grains, protein, low fat dairy, healthy oils, and a limited intake of saturated and trans fats, added sugars, and sodium(Krebs-Smith et al., 2018). Individuals may be considered as having good overall diet quality when they follow the recommendations from dietary guidelines(Krebs-Smith et al., 2018). However, the proportion of pregnant women following the recommendations remains low in high-income countries(Bodnar & Siega-Riz, 2002; Crozier et al., 2009; Fowler, Evers, & Campbell, 2012; Malek, Umberger, Makrides, & Zhou, 2016; Morton et al., 2014; Pick, Edwards, Moreau, & Ryan, 2005). For example, only 35% of pregnant women in a Canadian cohort met the recommendations for vegetables and fruits in 2002-2005(Fowler et al., 2012), and only 10% of pregnant women in an Australia study met the recommendations for vegetables in 2013(Malek et al., 2016). What people habitually eat and avoid eating is not simply a matter of personal choices. Changes in diet quality may be difficult due to barriers at the individual, social-

cultural and environmental levels(Mozaffarian, Angell, Lang, & Rivera, 2018; Sugiyama & Shapiro, 2014). However, pregnancy offers a window of opportunity for intervention, because pregnant women may be more willing to adopt healthier dietary habits during this period of life due to perceived benefits to the babies and themselves(Gardner et al., 2012; Vanstone, Kandasamy, Giacomini, DeJean, & McDonald, 2017).

Starting from before pregnancy, social inequalities exert their influences on different aspects of the women's experience. Even in high-income countries such as the U.S. and Canada, some subgroups of the population still have limited access to high quality foods to provide adequate nutrition(Ivers & Cullen, 2011). It is thus vital to study social factors associated with diet quality in order to develop effective public health interventions. A systematic review(Doyle, Borrmann, Grosser, Razum, & Spallek, 2017) found that women who were older, more educated, with higher income or other markers of affluence were more likely to follow a healthier dietary pattern or have a better diet quality. The finding was consistent across different populations and settings. However, not all studies used multivariable models, so it was not clear how these factors were confounded by each other. Findings regarding ethnicity and parity were less consistent and they could be acting as markers of age, education status and other sociodemographic factors.

Thus, the objective of this paper is to characterize diet quality during pregnancy and identify social factors associated with diet quality of pregnant women that could inform the targeting of interventions designed to reduce the inequities in diet quality.

Methods

The 3D Cohort Study

The 3D Cohort Study is a pregnancy and birth cohort that recruited 2,366 pregnant women who were at 8–14 weeks of gestation and planning to deliver in urban clinical centers in three of the four largest metropolitan areas in Quebec, Canada from 2010 to 2012. Detailed information of the cohort has been described elsewhere(Fraser et al., 2016). Briefly, inclusion criteria included age 18 and 47 years at recruitment and able to communicate in French or English. Exclusion criteria included current intravenous drug use, severe illnesses or life-threatening conditions, and multiple gestation. Structured interviews were conducted at recruitment, mid, late pregnancy, and postpartum by research nurses and research assistants. Written informed consents were obtained from each participant. Ethical approvals were obtained from the Health Sciences and Science Research Ethics Board of the University of Ottawa, research ethics committee at Sainte-Justine's Hospital in Montreal, and all other participating study sites.

Exposures

Information about maternal characteristics were collected by interviewers at recruitment (8–14 weeks of gestation). Characteristics used in this study included maternal age (<25, 25–<35, ≥35), ethnicity (white, non-white), marital status (married, live with common law/partner, single), education (secondary school diploma or less, college, undergraduate degree, graduate degree), household income in Canadian dollars (<30 000, 30,000–59,999, 60,000–79,999, 80,000–99,999, ≥100,000), parity (0, ≥1), and self-reported prepregnancy weight. Height was measured by trained research nurses. Pre-pregnancy BMI (kg/m^2) was calculated using self-reported prepregnancy weight in kilograms

divided by height in meters squared. Social support was considered but not included into the model because this information was not collected in the study.

Outcome: Diet Quality in Pregnancy

1. Generating energy and nutrients from 3-day food record

Details of dietary data collection and processing have been described elsewhere(Dubois et al., 2018; Morisset, Dubois, Colapinto, Luo, & Fraser, 2017). Briefly, a 3-day food record was provided to the participants at the second prenatal visit (20-24 weeks) to record dietary intakes on 2 weekdays and 1 weekend day. Pregnant women were trained by the research nurses on how to complete the 3-day food record. They completed the food record at home and returned the food records by mail. The food items in the food records were coded by trained nutritionists into Food Processor software (ESHA Research, Inc., Salem), which was linked to the Canadian Nutrient File, to generate a complete database of energy, macronutrients and micronutrients intakes. Since the content of added sugars was not readily available in the Canadian Nutrient File, it was calculated following a published method(Brisbois, Marsden, Anderson, & Sievenpiper, 2014).

2. Assigning food to number of food group servings

The food items were assigned to four major Canada's Food Guide (CFG) food groups, 30 sub-groups, and to Tiers 1-4 using the food Classification system developed by Health Canada(Elvidge Munene et al., 2015) CFG encourages people to choose foods lower in fat, sugar and salt. Foods that exceed at least two upper thresholds (total fat: >10 g/reference amount (RA), sugars: >19 g/RA, sodium: >360 mg/RA, saturated fat: > 2

g/RA) will be classified into Tier 4. For ‘milk and alternatives’ and ‘meat and alternatives’ group, the upper threshold for saturated fat was not counted due to the fact that these food groups contain more inherent saturated fats than other food groups. Foods allocated to Tier 4 were excluded when counting the number of CFG servings of food in the four major food groups, because they were classified as ‘not in line with the guidance in CFG(Elvidge Munene et al., 2015).

In CFG classifying system, mixed dishes (e.g., spaghetti with meat sauce) were classified into a subgroup called ‘recipes’ without breaking down into the four main food groups. The energy intake from foods in the subgroup ‘recipes’ accounted for 8% of the total energy intake of this study population. Thus, an omission of the mixed dishes in counting the number of servings of the four main groups would lead to an underestimation of number of servings. For a more concise estimate, mixed dishes in the food records were decomposed to food group and subgroup servings by linking to standard recipes in the Food Patterns Equivalents Database (FPED) developed by U.S. Department of Agriculture (USDA), which converts the foods and beverages to USDA Food Patterns components(USDA). The matching was performed manually according to name and description, with a secondary aim at minimizing the energy density gap. When there were multiple possible matches, the one with the smallest gap in energy density per 100 grams was chosen. When an exact match was not found in FPED, the most similar item regarding components of the food groups was chosen. This process was performed by a student with a background in nutrition and reviewed by a nutritionist that was familiar with the foods consumed locally. USDA Food Patterns components were then converted to the number of servings in the CFG.

3. Generating diet quality

Overall diet quality in pregnancy was calculated according to the Canadian adaption of Healthy Eating Index (HEI-C) 2010 developed in 2017 by Jessri *et al.*(Jessri, Ng, & L'Abbe, 2017). HEI-C contains eight components for foods that should be consumed in adequate amounts (total fruits and vegetables, whole fruit, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids) and three that should be consumed in moderate amounts (refined grains, sodium, empty calories), resulting in a total score of 100 (see supplementary table 1). At the time of data collection, people's diet was guided by age and sex-specific recommendations from CFG 2007, which were designed scientifically for the food intake pattern to meet the nutrient requirements and to avoid nutrient excess. So number of servings for 19 to 50 years old women in CFG 2007 were used in this study: i.e. eight servings of vegetables and fruits, six to seven servings of grain products, two servings of 'milk and alternatives', and two servings of 'meat and alternatives' per day("Eating Well with Canada's Food Guide 2007," 2007; Health Canada, 2010; "Healthy eating and pregnancy," 2019; "Prenatal Nutrition Guidelines for Health Professionals - Background on Canada's Food Guide," 2009). Because pregnant women were advised to include an additional two to three servings per day from any of the four food groups,("Prenatal Nutrition Guidelines for Health Professionals - Background on Canada's Food Guide," 2009) the cut-offs for 'total vegetables and fruits', grain products and 'milk and alternatives' were set at eight, seven, and three, respectively, to align with the examples given by Health Canada(Fowler et al., 2012). The cut-offs for whole fruit and 'greens and beans' component were set at 21% of that for 'total vegetables and fruits', which are 1.68 servings(Garriguet, 2009; Jessri et al.,

2017). The cut-offs for whole grains were set at 50% of that for total grain products, which are 3.5 servings, according to CFG 2007 recommendations. Empty calories were defined as calories from saturated fats, alcohol and added sugars(Brisbois et al., 2014; Jessri et al., 2017). The detailed scoring standards for min and max of each of the HEI-C components used in this study was listed in supplementary table 1. Intermediate intakes were scored proportionately between min and max. Total HEI-C score, adequacy sub-score, and moderation sub-score were sums of specific individual components.

Statistical Analyses

A flow chart for the study samples is presented in figure1. Proportions were used to display the characteristics of the 3D Cohort Study sample, sample with reliable diet information, and complete case sample (participants with no missing values on any of the variables included in the multiple linear regression model). Mean and SD of the intakes for each component of the HEI-C were calculated in the sample with reliable diet information. Mean, SD, range, and the proportion reaching the maximum scores were calculated for the total HEI-C score and the components. To validate that higher HEI-C was associated with higher beneficial nutrients supply, HEI-C scores were divided into quartiles, to present the mean and SD of selected nutrients in each HEI-C quartile (Jessri et al., 2017). Univariate and multiple linear regression models were used to calculate unadjusted and adjusted effect estimates and confidence intervals (CIs) for the association between maternal characteristics and HEI-C. Multiple linear regression was performed on complete case sample. Residual plots were used to visually check for homoscedasticity and normality assumptions of the multiple linear regression models.

Since the assumptions of the models were roughly met, no transformations of the variables were performed. Interactions between pairs of the social factors were tested by adding the product interaction term to the multiple regression model. All statistical analyses were performed using Statistical Analysis System software version 9.4 (SAS v9.4; SAS Institute Inc., Cary, NC, USA). A two-sided $p < 0.05$ was set as the level of statistical significance.

Results

A total of 1,535 pregnant women (65% of the 3D Cohort Study sample) who provided complete and reliable information for the 3-day food record were included in this study. (Figure 1) Mean age at enrollment was 31.5 (SD:4.3) years. Mean prepregnancy BMI was 23.8 kg/m² (SD:5.1). Mean gestational age at food record completion was 23.0 weeks (SD: 2.9). As shown in Table 1, only a small proportion had less than or equal to secondary school education (6.2%) or had annual household incomes below 30,000 Canadian dollars (7.8%). 30.6% were overweight or obese before pregnancy. More than half (58.0%) were nulliparous. Most were born in Canada (71.7%), classified themselves as white (80.1%), and were married or living with a partner (95.8%). Compared with the total 3D Cohort Study sample, participants included in this study were on average older, with higher income and education level, more likely to be white and born in Canada, and less likely to be overweight or obese before pregnancy.

As shown in Table 2, the mean HEI-C 2010 score was 62.9 (SD:11.2). The proportion of women reaching the recommended servings for whole grains were 4.5%. Similarly, only 8.3% reached the recommended servings of 'greens and beans'. About half consumed the recommended servings of protein foods (49.4%) and 'seafood and plant proteins' (52.1%). The majority (62.5%) of the participants consumed the recommended servings of whole fruits.

Higher density of beneficial micronutrients from food including calcium, vitamin A, folate, vitamin C, vitamin D, calcium, magnesium, iron, and zinc was found in higher quartiles of HEI-C (supplementary Table 2). Density of protein, fiber, polyunsaturated fatty acids, and monounsaturated fatty acids increased in higher quartiles of HEI-C, while

the density of total fat, saturated fat, added sugars, and sodium decreased. There was no significant trend for carbohydrate.

Table 3 showed unadjusted and multivariable adjusted analysis for the social factors in association with HEI-C score. In univariate analysis, women who were <25 years of age, single, overweight or obese before pregnancy, or parous had lower HEI-C scores than the reference group. Women who had an undergraduate degree, attended graduate studies, or with household income above 100,000 Canadian dollars had higher HEI-C scores than the reference group. In multivariable analysis, participants who attended graduate studies (Mean difference: 4.0 [95% CI: 1.2 to 6.9]) had higher HEI-C scores compared to secondary school or less. Participants who were <25 years of age (Mean difference: -4.9 [95% CI: -7.6 to -2.2] compared to 25–35 years of age), overweight (Mean difference: -2.8 [95% CI: -4.4 to -1.3] compared to normal BMI), obese (Mean difference: -3.1 [95% CI: -4.9 to -1.3] compared to normal BMI), parous (Mean difference: -2.7 [95% CI: -3.9 to -1.5] compared to nulliparous) had lower HEI-C scores. Household income and marital status no longer had a statistically significant association with HEI-C after adjustment.

There was an interaction between ethnicity and immigration status on HEI-C. As shown in table 4, for women who were born in Canada, visible minority women had lower HEI-C scores than white women (Mean difference: -5.9 [95%CI: -9.5 to -2.3], P=0.001). On the contrary, for women who were not born in Canada, visible minority women had higher HEI-C scores than white women (Mean difference: 3.9 [95%CI: 1.6 to 6.2], P=0.001). For white women, those who were not born in Canada had lower HEI-C than those who were born in Canada (Mean difference: -3.6 [95%CI: -5.5 to -1.6], P<0.001). However, for non-white women, those who were not born in Canada had higher HEI-C

than those who were born in Canada (Mean difference: 6.2 [95%CI: 2.4 to 10.0], P=0.001).

Discussion

This study demonstrated that diet quality of pregnant women still needs improvement, especially with respect to the intake of whole grains and 'greens and beans'. Diet quality among pregnant women was associated with social factors. After multivariable adjustment, diet quality was lower in some sub-groups of pregnant women, including those who were less educated, younger, overweight or obese before pregnancy, or parous.

Pregnant women in this study were having better diet quality than that reported in the general population(Jessri et al., 2017) (mean HEI-C: 62.9 v.s. 50.9). However, cautious interpretation of this comparison is needed because pregnant women in this study has higher social economic status than the general pregnant women and general population in Canada. Still, the compliance in specific subgroups of food was low. In this study, only 4.5% of the pregnant women met the recommended number of servings for whole grains, only 8.3% for greens and beans and only about 1 in 3 for 'milk and alternatives'. The results were consistent with findings from other high-income countries indicating that a large portion of pregnant women were not meeting the dietary guidelines(Bodnar & Siega-Riz, 2002; Crozier et al., 2009; Malek et al., 2016; Morton et al., 2014; Pick et al., 2005). Because CFG 2007 was designed for meeting nutritional requirements, the results in this study indicated that women might have some difficulties meeting the dietary guidelines, thus could have inadequate nutrition supplies. Indeed, previous research from our group found that intake of iron, folate and vitamin D from food sources were below recommended values for a vast majority of pregnant women (Dubois et al., 2017). For women having difficulties meeting the guidelines, other sources of nutrients, such as

nutritional supplements and exposure to sunshine, could be recommended as appropriate to meet the needs for adequacy of nutrients supply.

Consistent with our findings, higher education, older age, and lower prepregnancy BMI were found to be associated with higher diet quality(Bodnar & Siega-Riz, 2002; Kritsotakis et al., 2015; Rifas-Shiman, Rich-Edwards, Kleinman, Oken, & Gillman, 2009; Savard et al., 2019; Shin, Lee, & Song, 2016), including in low-income settings.(Fowles et al., 2011) The interpretation of the lower diet quality in women with overweight and obesity before pregnancy requires comment. In addition to interpreting prepregnancy BMI as a determinant of diet quality during pregnancy, it could also be interpreted that diet tracking back to prepregnancy was a determinant of prepregnancy BMI. The finding from previous studies that diet quality changed little(Savard et al., 2019) from prepregnancy to pregnancy supports this hypothesis.

Interestingly, in our study, although income was positively associated with diet quality in univariable analysis, the association was no longer statistically significant after multivariable adjustment, mainly due to the confounding effect of age and education. This result was in line with an urban pregnancy cohort in the U.S.(Deierlein et al., 2021). Similar to our findings, parity has been found to be inversely associated with diet quality in two U.S. cohorts, and inversely associated with a 'health conscious' dietary pattern in a population-based cohort study in U.K. (Bodnar & Siega-Riz, 2002; Northstone, Emmett, & Rogers, 2008; Rifas-Shiman et al., 2009). Some possible mechanisms for this association could be that parous women are more likely to rely on their own past knowledge or assumptions for healthy behaviors during pregnancy, rather than seeking out information, compared to nulliparous women(Declercq, Sakala, Corry, &

Applebaum, 2007; Grenier et al., 2021). Parous women also reported a larger number of 'very stressful' days one year before birth than nulliparous women, which might influence their ability to maintain a healthy diet (Public Health Agency of Canada, 2009). Our results indicate that parous women need more attention from care providers or social support to improve diet quality compared with nulliparous women. Only one previous study found the opposite direction of this association that parity was positively associated with diet quality (Nash, Gilliland, Evers, Wilk, & Campbell, 2013), possibly because age was not adjusted in the analysis. It has been shown from previous studies that higher parity was associated with older age, and age has been consistently reported to be positively associated with diet quality (Bodnar & Siega-Riz, 2002; Kritsotakis et al., 2015; Rifas-Shiman et al., 2009; Savard et al., 2019).

To our knowledge, our study is the first to report the interaction between ethnicity and immigration status (born in Canada) on diet quality during pregnancy. Validation of this finding in other studies is needed due to the limitation that this study sample was not a representative sample of the Canadian pregnant population. While 'the healthy immigrant effect' indicates that immigrants are generally healthier than the native-born population(Vang, Sigouin, Flenon, & Gagnon, 2017), this result indicates that ethnicity needs to be considered when studying the association between immigration and diet, or other diet related health outcomes.

Our study has some limitations. The distributions of the 3D Cohort Study sample and our study sample that have reliable dietary information were toward that of a high socio-economic status, and thus not a representative sample of the population of Canadian pregnant women. Because higher education is associated with higher diet quality, the true

estimates of HEI-C in the general population could be lower than estimates in this study. The results of the study might not be generalized to populations with a lower socio-economic status. Additionally, causality could not be concluded due to the nature of the study design. Furthermore, our study only captures diet in the second/third trimester of pregnancy. However, although diet quality might change in the first trimester due to nausea or food aversions, studies have shown that diet quality changes little across trimesters(Lebrun et al., 2019; Savard et al., 2019). Our study also had several strengths, including a large sample size, a large set of covariates and the 3-day food records dietary assessment method used, which is less prone to memory bias and is recognized as one of the most accurate tools for dietary assessment(Bingham et al., 1995; Kolar et al., 2005).

Conclusion

Social factors are associated with diet quality during pregnancy in Canada. Women who were less educated, younger, parous, or with a higher BMI had lower diet quality in pregnancy. These findings could be useful for health practitioners and policy makers in developing strategies to improve the diet quality of pregnant women.

References

Bingham, S. A., Cassidy, A., Cole, T. J., Welch, A., Runswick, S. A., Black, A. E., . . . et al. (1995). Validation of weighed records and other methods of dietary assessment using the 24 h urine nitrogen technique and other biological markers. *Br J Nutr, 73*(4), 531-550. doi:10.1079/bjn19950057

Bodnar, L. M., & Siega-Riz, A. M. (2002). A Diet Quality Index for Pregnancy detects variation in diet and differences by sociodemographic factors. *Public Health Nutr, 5*(6), 801-809. doi:10.1079/PHN2002348

Brisbois, T. D., Marsden, S. L., Anderson, G. H., & Sievenpiper, J. L. (2014). Estimated intakes and sources of total and added sugars in the Canadian diet. *Nutrients, 6*(5), 1899-1912. doi:10.3390/nu6051899

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. *Paediatr Perinat Epidemiol, 23*(5), 446-453. doi:10.1111/j.1365-3016.2009.01036.x

Declercq, E. R., Sakala, C., Corry, M. P., & Applebaum, S. (2007). Listening to Mothers II: Report of the Second National U.S. Survey of Women's Childbearing Experiences: Conducted January-February 2006 for Childbirth Connection by Harris Interactive(R) in partnership with Lamaze International. *J Perinat Educ, 16*(4), 9-14. doi:10.1624/105812407X244769

Deierlein, A. L., Ghassabian, A., Kahn, L. G., Afanasyeva, Y., Mehta-Lee, S. S., Brubaker, S. G., & Trasande, L. (2021). Dietary Quality and Sociodemographic and Health Behavior Characteristics Among Pregnant Women Participating in the New York University Children's Health and Environment Study. *Front Nutr, 8*, 639425. doi:10.3389/fnut.2021.639425

Doyle, I. M., Borrmann, B., Grosser, A., Razum, O., & Spallek, J. (2017). Determinants of dietary patterns and diet quality during pregnancy: a systematic review with narrative synthesis. *Public Health Nutr, 20*(6), 1009-1028. doi:10.1017/S1368980016002937

Dubois, L., Diasparra, M., Bedard, B., Colapinto, C. K., Fontaine-Bisson, B., Morisset, A. S., . . . Fraser, W. D. (2017). Adequacy of nutritional intake from food and supplements in a cohort of pregnant women in Quebec, Canada: the 3D Cohort Study (Design, Develop, Discover). *Am J Clin Nutr, 106*(2), 541-548. doi:10.3945/ajcn.117.155499

Dubois, L., Diasparra, M., Bedard, B., Colapinto, C. K., Fontaine-Bisson, B., Tremblay, R. E., & Fraser, W. D. (2018). Adequacy of nutritional intake during pregnancy in relation to prepregnancy BMI: results from the 3D Cohort Study. *Br J Nutr, 120*(3), 335-344. doi:10.1017/S0007114518001393

Eating Well with Canada's Food Guide 2007. (2007). Retrieved from https://www.canada.ca/en/health-canada/services/canada-food-guide/about/history-food-guide/eating-well-with-canada-food-guide-2007.html

Elvidge Munene, L. A., Dumais, L., Esslinger, K., Jones-Mclean, E., Mansfield, E., Verreault, M. F., . . . St-Pierre, S. (2015). A surveillance tool to assess diets according to Eating Well with Canada's Food Guide. *Health Rep, 26*(11), 12-20. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/26583693

Fleming, T. P., Watkins, A. J., Velazquez, M. A., Mathers, J. C., Prentice, A. M., Stephenson, J., . . . Godfrey, K. M. (2018). Origins of lifetime health around the time of conception: causes and consequences. *Lancet, 391*(10132), 1842-1852. doi:10.1016/S0140-6736(18)30312-X

Fowler, J. K., Evers, S. E., & Campbell, M. K. (2012). Inadequate dietary intakes among pregnant women. *Can J Diet Pract Res, 73*(2), 72-77. doi:10.3148/73.2.2012.72

Fowles, E. R., Bryant, M., Kim, S., Walker, L. O., Ruiz, R. J., Timmerman, G. M., & Brown, A. (2011). Predictors of dietary quality in low-income pregnant women: a path analysis. *Nurs Res, 60*(5), 286-294. doi:10.1097/NNR.0b013e3182266461

Fraser, W. D., Shapiro, G. D., Audibert, F., Dubois, L., Pasquier, J. C., Julien, P., . . . Group, D. S. (2016). 3D Cohort Study: The Integrated Research Network in Perinatology of Quebec and Eastern Ontario. *Paediatr Perinat Epidemiol, 30*(6), 623-632. doi:10.1111/ppe.12320

Gardner, B., Croker, H., Barr, S., Briley, A., Poston, L., Wardle, J., & Trial, U. (2012). Psychological predictors of dietary intentions in pregnancy. *J Hum Nutr Diet, 25*(4), 345-353. doi:10.1111/j.1365-277X.2012.01239.x

Garriguet, D. (2009). Diet quality in Canada. *Health Rep, 20*(3), 41-52. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19813438

Grenier, L. N., Atkinson, S. A., Mottola, M. F., Wahoush, O., Thabane, L., Xie, F., . . . Murray-Davis, B. (2021). Be Healthy in Pregnancy: Exploring factors that impact pregnant women's nutrition and exercise behaviours. *Matern Child Nutr, 17*(1), e13068. doi:10.1111/mcn.13068

Hanson, M. A., Bardsley, A., De-Regil, L. M., Moore, S. E., Oken, E., Poston, L., . . . Morris, J. L. (2015). The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". *Int J Gynaecol Obstet, 131 Suppl 4*, S213-253. doi:10.1016/S0020-7292(15)30034-5

Health Canada. (2010, 2019-09-05). Prenatal Nutrition Guidelines for Health Professionals. Retrieved from https://www.canada.ca/en/health-canada/services/canada-food-guide/resources/prenatal-nutrition/eating-well-being-active-towards-healthy-weight-gain-pregnancy-2010.html

Healthy eating and pregnancy. (2019). Retrieved from https://www.canada.ca/en/public-health/services/pregnancy/healthy-eating-pregnancy.html

Ivers, L. C., & Cullen, K. A. (2011). Food insecurity: special considerations for women. *Am J Clin Nutr, 94*(6), 1740S-1744S. doi:10.3945/ajcn.111.012617

Jessri, M., Ng, A. P., & L'Abbe, M. R. (2017). Adapting the Healthy Eating Index 2010 for the Canadian Population: Evidence from the Canadian National Nutrition Survey. *Nutrients, 9*(8). doi:10.3390/nu9080910

Kolar, A. S., Patterson, R. E., White, E., Neuhouser, M. L., Frank, L. L., Standley, J., . . . Kristal, A. R. (2005). A practical method for collecting 3-day food records in a large cohort. *Epidemiology, 16*(4), 579-583. doi:10.1097/01.ede.0000165363.27323.ac

Koletzko, B., Brands, B., Grote, V., Kirchberg, F. F., Prell, C., Rzehak, P., . . . Early Nutrition Programming, P. (2017). Long-Term Health Impact of Early Nutrition: The Power of Programming. *Ann Nutr Metab, 70*(3), 161-169. doi:10.1159/000477781

Krebs-Smith, S. M., Pannucci, T. E., Subar, A. F., Kirkpatrick, S. I., Lerman, J. L., Tooze, J. A., . . . Reedy, J. (2018). Update of the Healthy Eating Index: HEI-2015. *J Acad Nutr Diet, 118*(9), 1591-1602. doi:10.1016/j.jand.2018.05.021

Kritsotakis, G., Chatzi, L., Vassilaki, M., Georgiou, V., Kogevinas, M., Philalithis, A. E., & Koutis, A. (2015). Social capital, tolerance of diversity and adherence to Mediterranean diet: the Rhea Mother-Child Cohort in Crete, Greece. *Public Health Nutr, 18*(7), 1300-1307. doi:10.1017/S136898001400144X

Lebrun, A., Plante, A. S., Savard, C., Dugas, C., Fontaine-Bisson, B., Lemieux, S., . . . Morisset, A. S. (2019). Tracking of Dietary Intake and Diet Quality from Late Pregnancy to the Postpartum Period. *Nutrients, 11*(9). doi:10.3390/nu11092080

Lim, S. S., Vos, T., & Flaxman, A. D. (2013). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010 (vol 380, pg 2224, 2012). *Lancet, 381*(9874), 1276-1276. Retrieved from <Go to ISI>://WOS:000317351000028

Malek, L., Umberger, W., Makrides, M., & Zhou, S. J. (2016). Adherence to the Australian dietary guidelines during pregnancy: evidence from a national study. *Public Health Nutr, 19*(7), 1155-1163. doi:10.1017/S1368980015002232

Morisset, A. S., Dubois, L., Colapinto, C. K., Luo, Z. C., & Fraser, W. D. (2017). Prepregnancy Body Mass Index as a Significant Predictor of Total Gestational Weight Gain and Birth Weight. *Can J Diet Pract Res, 78*(2), 66-73. doi:10.3148/cjdpr-2016-035

Morton, S. M., Grant, C. C., Wall, C. R., Atatoan Carr, P. E., Bandara, D. K., Schmidt, J. M., . . . Camargo, C. A., Jr. (2014). Adherence to nutritional guidelines in pregnancy: evidence from the Growing Up in New Zealand birth cohort study. *Public Health Nutr, 17*(9), 1919-1929. doi:10.1017/S1368980014000482

Mozaffarian, D., Angell, S. Y., Lang, T., & Rivera, J. A. (2018). Role of government policy in nutrition-barriers to and opportunities for healthier eating. *BMJ, 361*, k2426. doi:10.1136/bmj.k2426

Nash, D. M., Gilliland, J. A., Evers, S. E., Wilk, P., & Campbell, M. K. (2013). Determinants of diet quality in pregnancy: sociodemographic, pregnancy-specific, and food environment influences. *J Nutr Educ Behav, 45*(6), 627-634. doi:10.1016/j.jneb.2013.04.268

Northstone, K., Emmett, P., & Rogers, I. (2008). Dietary patterns in pregnancy and associations with socio-demographic and lifestyle factors. *Eur J Clin Nutr, 62*(4), 471-479. doi:10.1038/sj.ejcn.1602741

Pick, M. E., Edwards, M., Moreau, D., & Ryan, E. A. (2005). Assessment of diet quality in pregnant women using the Healthy Eating Index. *J Am Diet Assoc, 105*(2), 240-246. doi:10.1016/j.jada.2004.11.028

Prenatal Nutrition Guidelines for Health Professionals - Background on Canada's Food Guide. (2009). Retrieved from https://www.canada.ca/en/health-canada/services/publications/food-nutrition/prenatal-nutrition-guidelines-health-professionals-background-canada-food-guide-2009.html

Public Health Agency of Canada. (2009). What Mothers Say: The Canadian Maternity Experiences Survey. Retrieved from https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/rhs-ssg/pdf/survey-eng.pdf

Rifas-Shiman, S. L., Rich-Edwards, J. W., Kleinman, K. P., Oken, E., & Gillman, M. W. (2009). Dietary quality during pregnancy varies by maternal characteristics in Project Viva: a US cohort. *J Am Diet Assoc, 109*(6), 1004-1011. doi:10.1016/j.jada.2009.03.001

Savard, C., Lemieux, S., Carbonneau, E., Provencher, V., Gagnon, C., Robitaille, J., & Morisset, A. S. (2019). Trimester-Specific Assessment of Diet Quality in a Sample of Canadian Pregnant Women. *Int J Environ Res Public Health, 16*(3). doi:10.3390/ijerph16030311

Schwarzenberg, S. J., Georgieff, M. K., & Committee On Nutrition. (2018). Advocacy for Improving Nutrition in the First 1000 Days to Support Childhood Development and Adult Health. *Pediatrics, 141*(2). doi:10.1542/peds.2017-3716

Shin, D., Lee, K. W., & Song, W. O. (2016). Pre-Pregnancy Weight Status Is Associated with Diet Quality and Nutritional Biomarkers during Pregnancy. *Nutrients, 8*(3), 162. doi:10.3390/nu8030162

Stephenson, J., Heslehurst, N., Hall, J., Schoenaker, D., Hutchinson, J., Cade, J. E., . . . Mishra, G. D. (2018). Before the beginning: nutrition and lifestyle in the preconception period and its

importance for future health. *Lancet, 391*(10132), 1830-1841. doi:10.1016/S0140-6736(18)30311-8

Sugiyama, T., & Shapiro, M. F. (2014). The growing socioeconomic disparity in dietary quality: mind the gap. *JAMA Intern Med, 174*(10), 1595-1596. doi:10.1001/jamainternmed.2014.3048

USDA. Food Patterns Equivalents Database. Retrieved from https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/docs/fped-overview/

Vang, Z. M., Sigouin, J., Flenon, A., & Gagnon, A. (2017). Are immigrants healthier than native-born Canadians? A systematic review of the healthy immigrant effect in Canada. *Ethn Health, 22*(3), 209-241. doi:10.1080/13557858.2016.1246518

Vanstone, M., Kandasamy, S., Giacomini, M., DeJean, D., & McDonald, S. D. (2017). Pregnant women's perceptions of gestational weight gain: A systematic review and meta-synthesis of qualitative research. *Matern Child Nutr, 13*(4). doi:10.1111/mcn.12374

Tables and Figures

Figure 1. Flow diagram for the study samples.

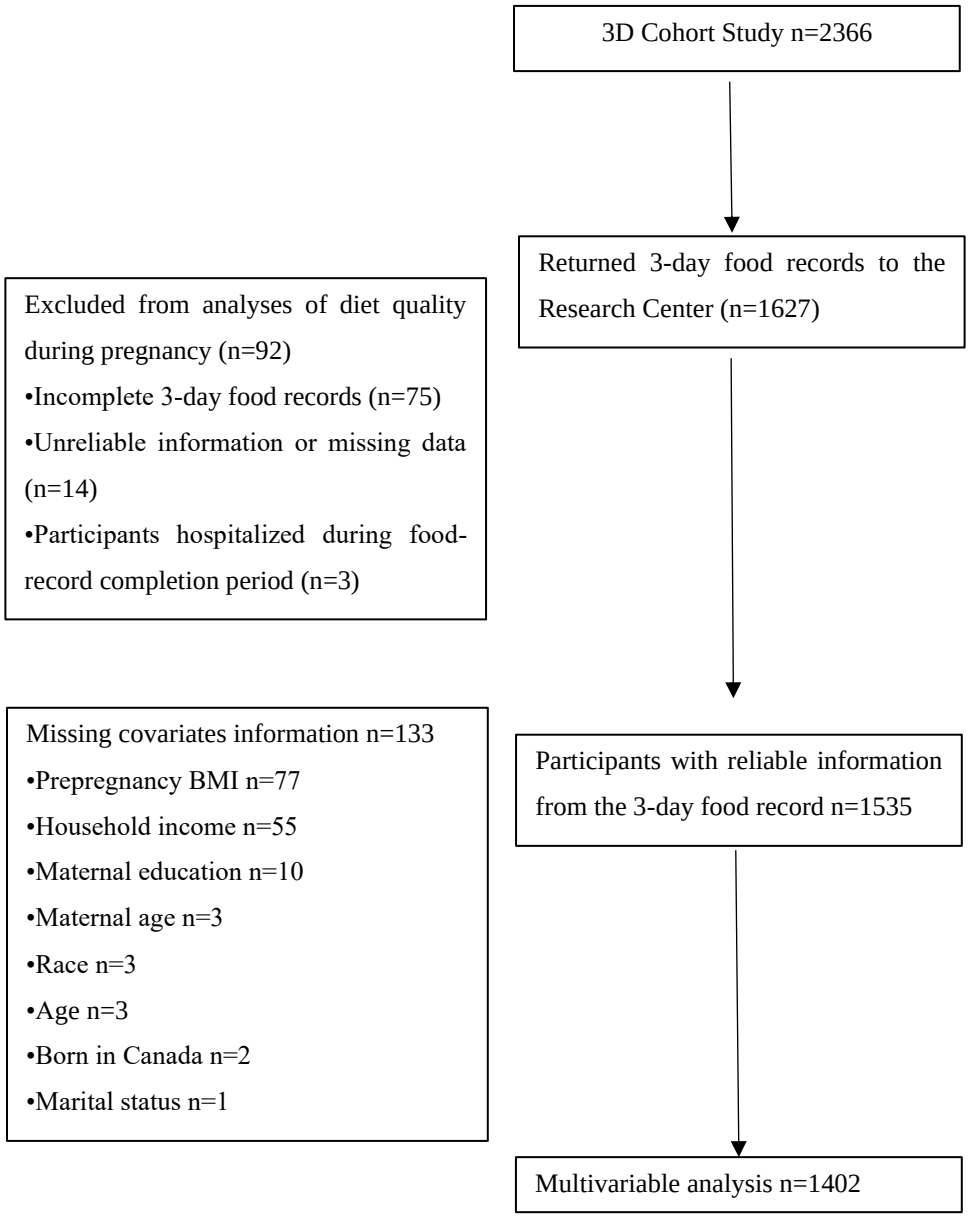


Table 1. Characteristics of the study sample.

Characteristics	3D sample	Sample with reliable diet information	Complete case sample #
n	2366	1535	1402
Mother's age (%)			
<25	7.3	5.5	5.4
25–<35	70.7	73.7	74.0
≥35	22.0	20.8	20.7
Maternal education (%)			
Secondary school or less	9.5	6.2	5.7
College	28.2	25.6	25.2
Undergraduate degree or above	62.3	68.2	69.1
Household income (CAD) (%)			
<30 000	10.8	7.8	7.4
30,000–59,999	19.1	17.2	17.1
60,000–79,999	17.2	17.8	18.1
80,000–99,999	18.9	22.4	22.4
≥100 000	29.1	34.8	35.0
Married/Common law/partner (%)	94.5	95.8	95.9
Prepregnancy BMI (%)			
underweight < 18.5	6.0	6.2	6.2
nomral weight 18.5 - 24.9	63.3	65.4	65.6
overweight 25 -29.9	18.4	16.8	16.4
obese >30	12.3	11.7	11.8
Nulliparous (%)	54.2	58.0	58.2
Mother born in Canada (%)	65.1	71.7	73.0
Mother white (%)	72.2	80.1	81.1

*Sample with no missing value in diet and covariates in multivariate analysis.

Table 2. Mean food and nutrient intakes and scores of components of Canadian Healthy Eating Index (HEI-C) for 1,535 women participating in the 3D Cohort Study.

Component	Intake	Scores		Proportion reaching max score (%)
	Mean ± SD	Mean ± SD	Range	
Total fruits and vegetables, servings/d	7.4±2.8	8.1±2.1	0.4-10	36.5
Whole fruit, servings/d	2.4±1.6	4.2±1.3	0-10	62.5
Greens and beans, servings/d	0.7±0.7	2.0±1.6	7.7-20	8.3
Whole grains, servings/d	1.0±1.1	2.8±2.9	0-5	4.5
Milk and alternatives (servings/d)	2.6±1.3	7.6±2.6	0-5	33.6
Total protein foods (servings/d)	2.1±0.9	4.3±1.0	0-10	49.4
Seafood and plant proteins (servings/d)	0.8±0.7	3.6±1.8	0-10	52.1
(PUFA + MUFA)/SFA (no unit)	1.6±0.5	3.2±2.9	0.1-5	4.5
Refined grains (% of total grains)	82.6±18.8	3.3±3.3	0-5	7.6
Sodium (mg)	2841±848	6.0±2.6	0-10	3.5
Empty calories (% of energy)	21.3±4.7	17.9±2.4	0-10	33.1
Total adequacy score		**35.7±8.0**	**10.7-57.4**	**0.0**
Total moderation score		**27.2±5.2**	**11.4-40**	**0.4**
Total HEI-C score		**62.9±11.2**	**28.8-95.6**	**0.0**

Table 3. Unadjusted and multivariable adjusted analyses for the social factors in association with Canadian Healthy Eating Index (HEI-C).

Characteristics	n	HEI-C scores	Regression estimates (95% CI)	
		Mean ± SD	Unadjusted	Multivariable[a]
Total	1,535	62.9±11.2		
Age (y)				
<25	85	56.3±10.5	**-6.2(-8.8,-3.6)**	**-4.9(-7.6,-2.2)**
25–<35	1129	63.1±11.3	Reference	Reference
≥35	318	64.2±10.5	0.9(-0.6,2.3)	1.2(-0.2,2.6)
Missing	3	59.9±8.1		
Education				
Secondary school or less	94	57.5±11	Reference	Reference
College	391	60.3±11.2	2.1(-0.6,4.7)	0.3(-2.4,2.9)
Undergraduate degree	628	63.9±11.3	**5.6(3.0,8.1)**	2.7(0,5.4)
Graduate degree	412	65.2±10.2	**6.8(4.1,9.4)**	**4.0(1.2,6.9)**
Missing	10	59.9±8.6		
Household income (CAD)				
<30 000	116	60.3±11.1	Reference	Reference
30,000–59,999	254	61.9±11.5	1.5(-1.1,4.0)	1.4(-1.2,3.9)
60,000–79,999	263	61.6±10.7	1.2(-1.3,3.7)	0.3(-2.4,2.9)
80,000–99,999	332	62.6±10.7	1.9(-0.6,4.4)	0.2(-2.5,2.8)
≥100,000	515	65±11.2	**4.5(2.1,6.8)**	1.9(-0.7,4.5)
Missing	55	62.3±11.4		
Marital status				
Married	614	63.1±10.7	Reference	Reference
Common law/partner	856	63.1±11.4	0.3(-1.0,1.5)	0.1(-1.3,1.4)
Single	64	58.7±12.7	**-4.3(-7.4,-1.3)**	-3.1(-6.3,0)
Missing	1	57.1±0		
Prepregnancy BMI				

Underweight (BMI< 18.5)	90	64.8±11.6	1.2(-1.2,3.6)	1.7(-0.6,4.1)
Normal weight (BMI 18.5 - 24.9)	953	64±11.1	Reference	Reference
Overweight (BMI 25.0 -29.9)	245	60.8±10.8	**-3.1(-4.7,-1.5)**	**-2.8(-4.4,-1.3)**
Obese (BMI ≥30.0)	170	59.4±10.7	**-4.5(-6.3,-2.7)**	**-3.1(-4.9,-1.3)**
Missing	77	62.8±11.5		
Parity				
0	891	64±10.9	Reference	Reference
≥1	644	61.4±11.4	**-2.5(-3.7,-1.4)**	**-2.7(-3.9,-1.5)**
Born in Canada				
No	434	62.8±10.9	-0.2(-1.5,1.1)	**-5.9(-9.5,-2.3)**
Yes	1099	63±11.3	Reference	Reference
Missing	2	55.6±2.2		
White				
No	305	63.1±10.8	0(-1.5,1.5)	**-3.6(-5.5,-1.6)**
Yes	1227	62.9±11.3	Reference	Reference
Missing	3	59.7±5.3		
Born in Canada * White (P for interaction)				P<0.001

CI: confidence interval; SD: standard deviation.

[a] adjusted for all characteristics simultaneously using complete case sample(n=1402).

Table 4. Interaction between ethnicity and immigration status on Canadian Healthy Eating Index (HEI-C).*

	Ethnicity White	Ethnicity Non-white	β(95% CI) for ethnicity within strata of immigration status	P for interaction
	β(95% CI), P	β(95% CI), P		
Born in Canada				<0.001
Yes	Reference	**-5.9(-9.5,-2.3), P=0.001**	**-5.9(-9.5,-2.3), P=0.001**	
No	**-3.6(-5.5,-1.6), P<0.001**	0.3(-1.6,2.2), P=0.75	**3.9(1.6,6.2), P=0.001**	
β(95% CI) for immigration status within strata of ethnicity	**-3.6(-5.5,-1.6), P<0.001**	**6.2(2.4,10.0), P=0.001**		

*Adjusted for age, education, household income, marital status, prepregnancy BMI and parity.

Supplementary Materials

Supplementary Table 1. Scoring criteria for the Healthy Eating Index-Canada 2010 (HEI-C 2010) for pregnant women, adapted from Jessri *et al.*. (Jessri, Ng, & L'Abbe, 2017)

Component	**Max pts**	**Standard for max score**	**Standard for min score (0)**
Adequacy Sub-score	60		
Total fruits and vegetables[3]	10	8 servings	No servings
Whole fruit[4, 5]	5	1.68 servings	No servings
Greens and beans[5]	5	1.68 servings	No servings
Whole grains[6]	10	3.5 servings	No servings
Dairy	10	3 servings	No servings
Total protein foods	5	2 servings	No servings
Seafood and plant proteins[7]	5	0.64 servings	No servings
Fatty acids	10	(PUFA + MUFA)/SFA ≥ 2.5	(PUFA + MUFA)/SFA ≤ 1.2
Moderation Sub-score	40		
Refined grains[8]	10	<50% of grains refined	0% grains refined
Sodium[9]	10	<= 1500 mg	≥ 4600 mg
Empty calories[10]	20	≤ 19% of energy	≥ 50% of energy
Total HEI-C 2010 Score	100		

[1]Scoring criteria for the Healthy Eating Index-Canada 2010 was adapted to servings based on the age and sex-specific recommendations in Canadian Food Guide (CFG) 2007 for women 19 to 50 years old and pregnant women. [2]Scores between the maximum and minimum were assigned proportionally. [3]Includes fruit juice. [4]Excludes fruit juice. [5]The standard for max scores of the "whole fruit" and "greens and beans" components

represent 21% of the "vegetables and fruit" recommendation in CFG. [6]The standard for max score of the "whole grains" component is 50% of the "grain products" recommendation in CFG. [7]The standard for max score of the "seafood and plant proteins" component represents 32% of the "meat and alternatives" recommendation in CFG. [8]The maximum score standard for the refined grains component is <50% of grain products consumed as refined grains based on CFG recommendations. [9]Respondents scored 10 points if their sodium consumption was at or less than their adequate intake, 8 points if their sodium consumption was at their upper intake level and 0 points if their consumption was twice their upper intake level. [10]Includes calories from solid fats, alcohol and added sugars.[34]

Reference:

Jessri, M., Ng, A. P., & L'Abbe, M. R. (2017). Adapting the Healthy Eating Index 2010 for the Canadian Population: Evidence from the Canadian National Nutrition Survey. Nutrients, 9(8). doi:10.3390/nu9080910

Supplementary Table 2. Mean daily dietary intakes of macro- and micronutrients by quartiles of the Canadian Healthy Eating Index (HEI-C).

	HEI-C 2010 Quartile (mean±SD)			
	1(worse diet quality)	2	3	4 (better diet quality)
HEI-C range	28.8-55.2	55.2-62.7	62.7-70.6	70.6-95.6
Energy intake, kcal/day	2135.9±480.8	2198.2±460	2185.3±463.8	2261.7±435.7
Carbohydrates, % energy	51.4±6.2	51.7±6	52.4±5.9	51.9±5.7
Total fat, % energy	34.1±5.5	33.6±5.2	32.8±5.4	33.1±5.3
Protein, % energy	15.9±2.8	16.5±2.6	16.8±2.6	17.5±2.5
Fiber density, g/1000 kcal	8.6±2.1	10.2±2.7	11.4±2.9	12.9±2.9
Added sugar, % energy	11.2±4.4	9.5±3.8	8.5±3.3	8.1±3.1
Saturated fat, % energy	13.2±2.8	12.2±2.6	11.4±2.5	10.4±2.4
Monounsaturated fatty acids, % energy	11.8±2.5	12±2.6	12.1±2.8	12.7±3.1
Polyunsaturated fatty acids, % energy	5.5±1.7	5.8±1.7	5.8±1.7	6.4±1.8
Cholesterol density, mg/1000 kcal	130.8±49.1	129.9±46.5	125.1±45.5	122.4±44.7
Calcium density, mg/1000 kcal	510.9±152.8	548.2±146.3	560.8±134.3	566.1±135.9
Vitamin A density in RAE, µg/1000 kcal	364±175.8	408.1±302.3	430.7±151	453.1±332.8
Folate density, µg/1000 kcal b	218.7±65.7	260.6±79	278±81.4	326.3±96
Vitamin C density, mg/1000 kcal	60.4±33.1	75.2±34.8	84.1±37.6	88±33.5
Vitamin D density, µg/1000 kcal	2.2±1.1	2.4±1.2	2.6±1.2	2.8±1.4
Sodium density, mg/1000 kcal	1436.3±324.6	1311.9±263.9	1261.3±285.4	1187.3±281.9
Magnesium density, mg/1000 kcal	142.2±23.6	160.7±28.4	175.6±29	194.3±31.7
Iron density, mg/1000 kcal	6.8±1.2	6.9±1.3	7.1±1.4	7.1±1.3
Zinc density, mg/1000 kcal	5.2±1.1	5.3±1.1	5.4±1.1	5.7±1

SD: standard deviation; RAE: retinol activity equivalents.

CHAPTER 6. MANUSCRIPT 2 – ASSOCIATION BETWEEN DIET QUALITY DURING PRECONCEPTION OR PREGNANCY AND PERINATAL OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Article Preface

This manuscript addressed the third objective of this thesis: 3) To synthesize the knowledge on the association between overall diet quality and adverse perinatal outcomes using systematic review and meta-analysis. YY was the guarantor of the review. YY, WS, OF, IM, WF and LD contributed to the conception of the research question. YY, IH, WS, CF and DAF contributed to the development of search strategies, eligibility criteria and methodology for data synthesis. YY, IH and YZ worked in duplicate to screen the articles, extracting information and assessing risk of bias. YY analyzed the data and drafted the results. YY, IH, WS, LD, WF, OF, IM, CF, YZ and DAF contributed to drafting of the paper and provided approval for the version submitted for publishing. Detailed methodology of this systematic review was published as a research protocol in the journal *BMJ Open* and could be reached through the following link - https://bmjopen.bmj.com/content/10/2/e033130. A published version of the protocol could also be found in Appendix 4.

This manuscript was formatted for submission as an original research article to the journal *Plos One*. The confirmation for the submission could be found in Appendix 5.

Additionally, I presented the results from the 3D Cohort Study on the associations between diet

quality during pregnancy and perinatal outcomes in Appendix 6, to compare with the meta-analysis results generated from the systematic review.

Title Page

Association Between Diet Quality During Preconception or Pregnancy and Perinatal Outcomes: a Systematic Review and Meta-Analysis

Running Title: Diet Quality and Perinatal Outcomes

Yamei Yu †[1], Isabelle S Hardy†[2], Wenguang Sun[3], Dean Fergusson[1,4], Yulai Zhou[3], Cindy Feng[1,5], Fengxiu Ouyang[6], Isabelle Marc[7], William D Fraser[2¶*], Lise Dubois[1¶*].

†These authors have contributed equally to this work and share first authorship.

¶ These authors have contributed equally to this work and share senior authorship.

[1] School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ontario, Canada.

[2]Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Québec, Canada.

[3]The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.

[4]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ontario, Canada.

[5]Department of Community Health and Epidemiology, Dalhousie University, Halifax, Canada

[6]Ministry of Education - Shanghai Key Laboratory of Children's Environmental Health. Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

[7]Department of Pediatrics and Centre de recherche du CHU de Quebec, Université Laval, Quebec, Canada.

*** Corresponding authors:**

William Fraser: william.fraser@usherbrooke.ca +1 819 346-1110 x12911

Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, and the Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke (CRCHUS).

3001 12e avenue Nord, Sherbrooke, Québec, Canada, J1H 5N4.

Lise Dubois : ldubois@uottawa.ca School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa.

Conflict of Interest Statements

Yamei Yu: no conflicts of interest. Isabelle S Hardy: no conflicts of interest. Wenguang Sun: no conflicts of interest. Dean Fergusson: no conflicts of interest. Yulai Zhou: no conflicts of interest. Cindy Feng: no conflicts of interest. Fengxiu Ouyang: no conflicts of interest. Isabelle Marc: no conflicts of interest. William D Fraser: no conflicts of interest. Lise Dubois: no conflicts of interest.

Funding

This research project is sponsored jointly by the Canadian Institutes of Health Research (CIHR) (Grant HLT 151517) and the National Natural Sciences Foundation of China (NSFC) (Grant No. 81661128010).

Author Contributions

YY was the guarantor of the review. YY, WS, OF, IM, WF and LD contributed to the conception of the research question. YY, IH, WS, CF and DAF contributed to the development of search strategies, eligibility criteria and methodology for data synthesis. YY, IH and YZ worked in duplicate to screen the articles, extracting informations and assessing risk of bias. YY analyzed the data and drafted the results. YY, IH, WS, LD, WF, OF, IM, CF, YZ and DAF contributed to drafting of the paper and provided approval for the version submitted for publishing.

Data Availability Statement

The datasets for this study will be made available upon request.

Supplementary Material

MOOSE Checklist for Meta-analyses of Observational Studies.

Acknowledgments

The authors would like to thank Lindsey Sikora (librarian) for counselling in developing the searching strategies. We also thank Dr Jean-Patrice Baillargeon and Dr Zhuoyu Wang for critical reviews and suggestions in formulating the systematic review.

Manuscript word count: 3434.

Number of tables: 7.

Number of figures: 12.

Abbreviations:

aHEI : alternate Healthy Eating Index

FFQ: food frequency questionnaires

GDM: gestational diabetes mellitus

GWG: gestational weight gain

HDP: hypertensive disorders of pregnancy

HEI: Healthy Eating Index

LGA: Large for Gestational Age

LBW: Low Birth Weight

MD: Mediterranean Diet

MOOSE: Meta-analysis of Observational Studies in Epidemiology

NAM: National Academy of Medicine

NOS: Newcastle–Ottawa Scale

OR: odds ratios

SGA: Small for Gestational Age

Abstract

Background: Although dietary guidelines are routinely used for the counselling of women in preconception and pregnancy, the correlation between good diet quality and perinatal outcomes has not been established.

Methods: The databases Medline, Embase, Food Science and Technology Abstracts and CINAHL were searched from inception up to 5th March 2020. Two authors independently screened and selected prospective cohort studies reporting risk estimates of the association between diet quality scores during preconception or pregnancy and perinatal outcomes. Data were independently coded by two authors. Odd ratios and mean differences from individual studies were pooled using random-effects models. The protocol of this meta-analysis was submitted to be registered on PROSPERO March 15th, 2019 (CRD42019128732).

Results: Thirty-three prospective cohort studies (315,431 participants) were included in the meta-analysis. No association was found between diet quality and excessive (OR: 0.91; 95 CI: 0.76, 1.10; I^2 = 59%) or inadequate (OR: 0.90; 95 CI: 0.70, 1.17; I^2 = 80%) gestational weight gain. Women in the top tertile of diet quality scores had a lower risk of gestational diabetes (OR: 0.77; 95 CI: 0.65, 0.90; I^2 = 72%), hypertensive disorders of pregnancy (OR: 0.87; 95 CI: 0.83, 0.92; I^2 = 0%), preterm birth (OR: 0.77; 95 CI: 0.66, 0.89; I^2 = 16%), small for gestational age (OR: 0.88; 95 CI: 0.79, 0.99; I^2 = 5%) and low birth weight (OR: 0.60; 95 CI: 0.37, 0.99; I^2 = 23%) compared to those in the bottom tertile. The pooled results for the association between diet

quality and large for gestational age and macrosomia were not statistically significant. No studies were found for the association between diet quality and delivery mode.

Conclusion: Data from prospective cohort studies demonstrate that good diet quality during pregnancy is associated with lower risk of adverse maternal and neonatal outcomes.

Keywords: Diet, Food, and Nutrition, pregnancy, preconception care, pregnancy complications.

Abstract word count: 295.

Introduction

The first 1000 days of life, including the prenatal period, offers a unique opportunity for the children and future generations to develop their ability to grow and prosper in society[1-3]. Mounting evidence from human and animal studies have shown that the maternal environment regulates embryonic epigenetic modulation and can predispose to later development of diseases[4,5]. Maternal nutrition in particular appears to be a key driver of epigenetic programming[3,5,6].

Although women in preconception and pregnancy have been advised to achieve a good quality of diet[7], little evidence was available on the benefits until the last few decades. The publication of the results of pregnancy and birth cohorts with high quality dietary data has facilitated the research on the health impacts of diet quality on perinatal adverse outcomes[8,9], including excessive/inadequate gestational weight gain, gestational diabetes (GDM), hypertensive disorders of pregnancy (HDP), cesarean delivery, preterm birth, and extremes of birthweight.[10-15]

Several systematic reviews reported the associations between maternal dietary patterns and rates of GDM, HDP, preterm birth and fetal growth.[16-20] However, the validity of these studies has been limited by the inclusion of a single publication database[18], lack of a meta-analysis[16-18], and reporting of only a few of the relevant perinatal outcomes[19]. These reviews are also limited by the absence of registered or published protocols, which hinders the evaluation of a potential reporting bias.[21] Most importantly, the inclusion of studies using *a posteriori* dietary patterns[16-20] limits the relevance of these results to guide dietary interventions. *A posteriori* dietary patterns

are generated from data-driven methods such as actor analysis, principal components analysis or cluster analysis. They are population specific, vary greatly between studies and thus not comparable across populations.

Diet quality, a relatively new concept, can be measured by scoring diet in terms of '*a priori*' defined adherence to dietary guidelines or a specific pattern.[22,23] To date, no systematic review has evaluated the association between diet quality and adverse perinatal outcomes. The objective of this study is to synthesize the evidence and quantify the association between diet quality in preconception or pregnancy and perinatal adverse outcomes in prospective cohort studies.

Methods

This systematic review and meta-analysis was conducted following the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines[24]. A detailed description of the methodology has been published previously[25].

Search strategy

Four databases of published literature (MEDLINE ALL (Ovid), Embase (Ovid), Food Science and Technology Abstracts (Ovid) and CINAHL (EBSCOHost)) were searched from database creation to the cut-off date of March 5th2020. Both medical subject headings and text keywords were used to develop a comprehensive search strategy with inputs from the whole research team including the health science librarian (LS)[26]. Two groups of keywords were used: 'preconception

or pregnancy', and 'diet quality' (See Table S1 for detailed search terms used in OVID Medline). The reference lists of included studies and relevant review articles were screened to identify any additional studies. When eligible abstracts were identified, the title and authors were searched to determine if full-text articles had been published. Eligibility was limited to full-text articles published in scholarly peer-reviewed journals in English[27].

Study Selection

The primary outcome of this systematic review is excessive or inadequate gestational weight gain according to the NAM recommendations, and secondary outcomes include GDM, pre-eclampsia, preterm birth, delivery mode and birth weight. Studies were included if they met the following criteria: 1) Prospective cohort studies of women in the preconception period or pregnancy recruited from the general population. 2) Diet quality measured with pre-specified scoring scales and validated dietary assessment methods. 3) Assessment of the association between diet quality score and any of the systematic review outcomes. The publications identified with the search process were uploaded to the Covidence software. YY and IH independently screened the titles and abstracts. All references that met the inclusion criteria or those for which eligibility was uncertain were selected for full-text screening. Reasons for exclusion at the time of full-text screening were recorded. Any disagreements arising during the selection process were resolved by discussion with a third reviewer (LD). The process of study selection is reported using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram[28].

Data Management

YY, IH and YZ independently extracted information from the included studies using a predefined data coding sheet. Authors were contacted to obtain more information if related data was ambiguous or not included in the publications. In cohorts reporting different diet quality scores, the results based on the largest sample size were included in the meta-analysis to avoid sample overrepresentation. When diet quality measures were provided on equal sample sizes, results for the diet quality score with the most items were included. In cohorts where diet quality was reported at different time points in pregnancy, second trimester measures were selected. For each of these decisions, sensitivity analyses were then performed using other reported results from the same cohort to test the robustness of the findings. For each study, results from the model adjusting for the most confounding variables were selected.

YY and IH independently assessed the quality and risk of bias of each included study with the Newcastle–Ottawa Scale (NOS)[29]. The sum of points was used to categorize overall study quality as either high (7-9), moderate (4–6) or low (0-3).

Statistical Analysis

Meta-analyses using random-effects models were conducted for each outcome. Adjusted mean differences (MD) and odds ratios (OR) were pooled for continuous and categorical outcomes, respectively. Different scales of reporting diet quality across studies, including one absolute unit increase, one SD increase, tertiles, quartiles, quintiles were transformed to calculate

the effect size in the top tertile of diet quality scores compared with the bottom tertile using methodology reported in previous studies[19,30,31]. There are two assumptions for this method: 1) diet quality scores are normally distributed and 2) the associations with the outcomes are log-linear. In a normal distribution, the means of the top and bottom tertiles, quartiles, quintiles of are 2.18, 2.54, 2.80 SD apart, respectively. Log ORs and SEs were multiplied by 2.18/SD, 2.18, 2.18/2.54, 2.18/2.80 for the transformation from 1 unit, 1 SD, quartile, quntile, respectively, to estimates in tertile. Heterogeneity was assessed using the I^2 statistic, Cochran's Q test (P-heterogeneity) and by visual inspection of the forest plots. Sources of heterogeneity were assessed by conducting subgroup analyses when there was a substantial amount of heterogeneity ($I^2 \geq 75\%$ or P-heterogeneity<0.05).

Sensitivity analyses were performed by excluding one study at a time to evaluate the influence of any individual study on the pooled estimate. The robustness of the estimates was also examined with sensitivity analyses excluding moderate- and low-quality studies. Publication bias was assessed by visual inspection of a funnel plot and Egger's test when at least 10 studies were included in the meta-analyses[32].

Data analyses were performed using R version 4.0.3 (R Project for Statistical Computing). Two-tailed P values were used and $P < .05$ was considered statistically significant.

Results

Study selection, Characteristics, and Quality

The study selection process is shown in Figure 1. We identified 6113 unique publications from the databases and one from other sources. After title and abstract assessment, 98 publications were selected for full-text screening. A total of 34 articles met our eligibility and were included in this review, and 33 were included in meta-analyses.

As shown in Table S2, only two studies[33,34] were of moderate quality (NOS = 6) and all other studies were of high quality (NOS 7-9). The detailed characteristics of included studies are presented in Table S3. The sample sizes and study periods of the cohorts ranged from 41 to 72,072, and 1991 to 2017 respectively. All studies but one were conducted in pregnant women from the general population, with variable exclusion criteria related to maternal prepregnancy BMI, history of preterm birth, and maternal comorbidities. One study was conducted in pregnant women with obesity or history of GDM[35]. Four cohorts were conducted in Singapore[36], Malaysia[33], Mexico[37], and a French Caribbean island[38]. The other cohorts were conducted in high-income countries located in Europe, North America, and Oceania. Six studies used at least one self-reported outcome, while all other studies used valid assessments including medical records or standardized measurements. For dietary assessment, four[33,37,39,40] studies used dietary recalls, one[36] used both dietary recalls and food diaries, three[35,41,42] used non-validated FFQ, and the remainder of studies used a validated FFQ. Studies varied as to the timepoint and period of dietary assessment. Four studies[43-46] assessed diet in prepregnancy and other studies assessed diet during pregnancy. Diet quality was assessed using 22 different scores, with versions of aHEI,

HEI and MD scores most frequently assessed (Table S4). There was large variability of potential confounders included in the multivariable models across studies (Table S5).

Maternal Outcomes

Gestational Weight Gain

Six studies reported gestational weight gain according to NAM guideline as an outcome.[33,47-51] Pooled results demonstrated no statistically significant association between diet quality and excessive (OR: 0.91; 95 CI: 0.76, 1.10; I^2 = 59%; P-heterogeneity = 0.03; Figure 2) or inadequate gestational weight gain (OR: 0.90; 95 CI: 0.70, 1.17; I^2 = 80%; P-heterogeneity < 0.01; Figure S1). Results were consistent in the sensitivity analysis where the moderate quality study[33] was excluded (Table S6). Due to small number of studies, we were unable to detect the covariate that could explain the observed heterogeneity (Table S7).

Three studies reported gestational weight gain as a continuous outcome.[40,52,53] A Meta-analysis could not be performed because effect estimates were not available for one of the studies[52]. Rohatgi *et al.* found a strong association between HEI-2010 and GWG (p=0.0011), but no detailed effect estimates were reported[52]. Fulay *et al.* found that in women who were obese before pregnancy, each one-unit increment in the DASH diet score was associated with 0.19 (95% CI: 0.05, 0.34) kg higher GWG from the time of dietary assessment to delivery[53]. In a

small study of 41 women, Grandy et al. did not find a statistically significant association between HEI-2010 and GWG[40].

GDM

Seven studies reported GDM as an outcome[34,35,43,44,47,54,55]. When results were pooled, pregnant women in the top tertile of diet quality scores had a lower risk of GDM compared with those in the bottom tertile (OR: 0.77; 95 CI: 0.65, 0.90; I^2 = 72%; P-heterogeneity <0.01; Figure 3). The results were consistent when the moderate-quality study[34] was excluded (Table S6). Subgroup analysis suggested that the association is stronger in studies with adjustment for education level (n=4, OR: 0.64; 95 CI: 0.56, 0.73; I^2 =0) than in those without adjustment for education level (n=3, OR: 0.91; 95 CI: 0.83, 0.99; I^2 =0). No heterogeneity between studies in each subgroup requiring further exploration was identified (Table S7).

HDP

Five studies reported HDP as an outcome [44,45,47,56,57]. When results were pooled, pregnant women in the top tertile of diet quality scores had a lower risk of HDP compared to those in the bottom tertile (OR: 0.87; 95 CI: 0.83, 0.92; I^2 = 0%; P-heterogeneity = 0.67; Figure 4). All studies were of high quality (NOS score ≥7). (Table S2)

Delivery Mode

No studies evaluated the association between diet quality and delivery mode.

Infant Birth Outcomes

Preterm Birth

Eight studies reported preterm birth as an outcome [36,38,42,46,53,56,58,59]. When results were pooled, pregnant women in the top tertile of diet quality scores had a lower risk of preterm birth compared to those in the bottom tertile (OR: 0.77; 95 CI: 0.66, 0.89; I^2 = 16%; P-heterogeneity = 0.30; Figure 5). All studies were of high quality (NOS score ≥ 7) (Table S2). In the study of Saunders et al.[38], prepregnancy BMI was found to be a strong effect modifier and the protective effect of good diet quality on preterm birth was stronger in overweight/obese women.

Birth Weight Extremes

SGA and LBW

Six[47,48,60-63] and five[37,46,59,61,62] studies reported SGA and LBW as outcomes, respectively. When results were pooled, women in the top tertile of diet quality scores had a lower risk of SGA (OR: 0.88; 95 CI: 0.79, 0.99; I^2 = 5%; P-heterogeneity = 0.39; Figure S2) and LBW (OR: 0.60; 95 CI: 0.37, 0.99; I^2 = 23%; P-heterogeneity = 0.27; Figure S3) compared to those in the bottom tertile. All studies were of high quality (NOS score ≥7) (Table S2).

LGA and Macrosomia

Six[47,48,60-63] and three[59,61,62] studies reported LGA and Macrosomia as outcomes, respectively. Pooled results for the association between diet quality and LGA or Macrosomia were not statistically significant (Women in the top tertile as compared to bottom tertile. For LGA, OR: 0.90; 95 CI: 0.71, 1.15; I^2 = 59%; P-heterogeneity =0.03; Figure S4. For Macrosomia, OR: 1.12; 95 CI: 0.69, 1.81; I^2 = 33%; P-heterogeneity =0.22; Figure S5.). All studies were of high quality (NOS score ≥7) (Table S2).

Birth Weight as a Continuous Variable and Birth Weight for Gestational Age Z-score

Nine[36,39-41,61,63-66] and three[60,62,63] studies reported birth weight as a continuous variable and birth weight for gestational age z-score as outcome measures, respectively. Pooled results for the associations were not statistically significant (women in the top tertile compared with the bottom tertile. For birth weight, beta: -7.8; 95 CI: -56.0, 40.5; I^2 = 79%; P-heterogeneity <0.01; Figure S6. For birth weight for gestational age z-score, beta: 0.0; 95 CI: -0.1, 0.2; I^2 = 74%; P-heterogeneity =0.02; Figure S7.). All studies were of high quality (NOS score ≥7) (Table S2).

Sensitivity Analyses

The pooled estimates were similar with the omission of one study at a time, or with the inclusion of different dietary scores from the same cohort (Table S6).

Discussion

Main Findings

This review identified 34 prospective cohort studies reporting the association between maternal diet quality and adverse perinatal outcomes, 33 of which were included in the meta-analyses.

Interpretation

The results of this study are consistent with the association of healthy dietary patterns in pregnancy with lower odds of GDM[17,20], HDP[17,20], preterm birth[16,19,20] and SGA[19] reported in previous systematic reviews. These results highlight the potential benefits of a healthy diet on the regulation of glycaemia and systemic inflammation through the consumption of low glycemic-index foods and micronutrients[3,67]. We found no significant association between diet quality and excessive/inadequate gestational weight gain, LGA/macrosomia, and birthweight as a continuous variable. These results concord with previous research suggesting that energy intake, rather than diet quality, is the main driver of gestational weight gain and fetal growth[67]. No study evaluating the association of diet quality with delivery mode was identified. Only two cohorts (four studies) included measures of dietary quality in prepregnancy, which limited our ability to draw conclusions on subgroup analyses in prepregnancy. Studies were all of moderate or good quality and sensitivity analyses revealed consistent findings with the exclusion of moderate quality studies.

Strengths and Limitations

This is the first systematic review evaluating and synthesizing the associations between maternal diet quality and adverse perinatal outcomes. The rigorous search and screening strategies employed, as well as the prospective registration and publication of our protocol limit the possibility of reporting bias. This review has several limitations. The exclusion of non-English publications, of abstracts, and of other grey literature could lead to publication bias. Publication bias could not be formerly assessed due to the limited number of studies reporting each specific outcome (less than 10 for any outcome). Some of the included studies reported diet quality measured with different tools and/or at different timepoints. A single measure had to be selected to conduct the meta-analysis which could influence the results of the analysis. However, this is unlikely as sensitivity analyses conducted using other measures from the same cohorts provided similar estimates. These results are derived from observational studies and therefore no conclusions can be made on causal inference. The interpretation of these results is also limited by the variability in study populations, dietary scores, reported outcomes, and adjustment of confounding factors across studies. The vast majority of cohorts were conducted in high-income countries and therefore these results cannot be applied to middle and low-income countries. Twenty-two different dietary scores were used in the identified studies. The components of each diet quality score vary according to the underlying dietary recommendations, but they included similar adequacy components (vegetables, fruit, fish, nuts and unsaturated fats), and moderation items (added sugars and saturated fats). The robustness of the meta-analysis results in the sensitivity analyses including different diet quality scores measured in the same population is also reassuring as to the comparability of these scores. In the majority of studies, diet was

appraised using an FFQ. While the use of FFQs has been associated with recall bias and classification errors, this is likely to bias results towards the null hypothesis. Studies reported variable outcome sets, which limited the number of results available for each outcome. While most studies used validated measurements or medical registration for outcome measurements, others relied on self-reporting. Misclassification related to self-reporting could have diminished the strength of the associations. In studies reporting GDM as an outcome, diet before 24 weeks of pregnancy was measured in six studies[35,43,44,47,54,55], but the timing of dietary assessment and recall period were not reported in the last study[34]. While we cannot exclude reverse causation due to measure of diet after implementation of dietary interventions in the last study, this would be expected to bias results towards the null hypothesis. While the results accounting for the most confounders were used in the meta-analysis, adjusted factors varied greatly between studies, and we cannot exclude the possibility of unaccounted confounding factors.

Conclusion

The results of this systematic review and meta-analysis demonstrate that good diet quality in pregnancy is associated with lower odds of GDM, HDP, preterm birth, and SGA/LBW. These findings support the potential of interventions based on dietary guidelines in preconception and pregnancy to prevent perinatal complications. Long term follow-up of these cohort studies will be critical to establish the correlation between maternal diet quality and cardiometabolic complications in women and children.

Identified knowledge gaps include studies in middle and low-income countries, the association of maternal diet quality in preconception with perinatal outcomes, and the association of maternal diet quality with delivery mode.

The use of standardized diet quality scores and core outcome sets in future studies would improve the quality of the evidence generated through systematic reviews and meta-analyses.

References

1. Schwarzenberg SJ, Georgieff MK, Committee On N. Advocacy for Improving Nutrition in the First 1000 Days to Support Childhood Development and Adult Health. *Pediatrics.* 2018;141(2).

2. Koletzko B, Brands B, Grote V, et al. Long-Term Health Impact of Early Nutrition: The Power of Programming. *Ann Nutr Metab.* 2017;70(3):161-169.

3. Hanson MA, Bardsley A, De-Regil LM, et al. The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". *Int J Gynaecol Obstet.* 2015;131 Suppl 4:S213-253.

4. Godfrey KM, Gluckman PD, Hanson MA. Developmental origins of metabolic disease: life course and intergenerational perspectives. *Trends Endocrinol Metab.* 2010;21(4):199-205.

5. Fleming TP, Watkins AJ, Velazquez MA, et al. Origins of lifetime health around the time of conception: causes and consequences. *Lancet.* 2018;391(10132):1842-1852.

6. Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *Lancet.* 2018;391(10132):1830-1841.

7. Jahns L, Davis-Shaw W, Lichtenstein AH, Murphy SP, Conrad Z, Nielsen F. The History and Future of Dietary Guidance in America. *Adv Nutr.* 2018;9(2):136-147.

8. Lawlor DA, Andersen AM, Batty GD. Birth cohort studies: past, present and future. *Int J Epidemiol.* 2009;38(4):897-902.

9. De-Regil LM, Harding KB, Roche ML. Preconceptional Nutrition Interventions for Adolescent Girls and Adult Women: Global Guidelines and Gaps in Evidence and Policy with Emphasis on Micronutrients. *J Nutr.* 2016;146(7):1461S-1470S.

10. Larque E, Labayen I, Flodmark CE, et al. From conception to infancy - early risk factors for childhood obesity. *Nat Rev Endocrinol.* 2019;15(8):456-478.

11. Patro Golab B, Santos S, Voerman E, et al. Influence of maternal obesity on the association between common pregnancy complications and risk of childhood obesity: an individual participant data meta-analysis. *Lancet Child Adolesc Health.* 2018;2(11):812-821.

12. Voerman E, Santos S, Patro Golab B, et al. Maternal body mass index, gestational weight gain, and the risk of overweight and obesity across childhood: An individual participant data meta-analysis. *PLoS Med.* 2019;16(2):e1002744.

13. Hu Z, Tylavsky FA, Han JC, et al. Maternal metabolic factors during pregnancy predict early childhood growth trajectories and obesity risk: the CANDLE Study. *Int J Obes (Lond).* 2019;43(10):1914-1922.

14. Liao XP, Yu Y, Marc I, et al. Prenatal determinants of childhood obesity: a review of risk factors (1). *Can J Physiol Pharmacol.* 2019;97(3):147-154.

15. Woo Baidal JA, Locks LM, Cheng ER, Blake-Lamb TL, Perkins ME, Taveras EM. Risk Factors for Childhood Obesity in the First 1,000 Days: A Systematic Review. *Am J Prev Med.* 2016;50(6):761-779.

16. Raghavan R, Dreibelbis C, Kingshipp BL, et al. Dietary patterns before and during pregnancy and birth outcomes: a systematic review. *Am J Clin Nutr.* 2019;109(Suppl_7):729S-756S.

17. Raghavan R, Dreibelbis C, Kingshipp BL, et al. Dietary patterns before and during pregnancy and maternal outcomes: a systematic review. *Am J Clin Nutr.* 2019;109(Suppl_7):705S-728S.

18. Sanchez-Villegas A, Brito N, Doreste-Alonso J, et al. Methodological aspects of the study of dietary patterns during pregnancy and maternal and infant health outcomes. A systematic review. *Matern Child Nutr.* 2010;6 Suppl 2:100-111.

19. Chia AR, Chen LW, Lai JS, et al. Maternal Dietary Patterns and Birth Outcomes: A Systematic Review and Meta-Analysis. *Adv Nutr.* 2019;10(4):685-695.

20. Kibret KT, Chojenta C, Gresham E, Tegegne TK, Loxton D. Maternal dietary patterns and risk of adverse pregnancy (hypertensive disorders of pregnancy and gestational diabetes mellitus) and birth (preterm birth and low birth weight) outcomes: a systematic review and meta-analysis. *Public Health Nutr.* 2018:1-15.

21. Kirkham JJ, Altman DG, Williamson PR. Bias due to changes in specified outcomes during the systematic review process. *PLoS One.* 2010;5(3):e9810.

22. Asghari G, Mirmiran P, Yuzbashian E, Azizi F. A systematic review of diet quality indices in relation to obesity. *Br J Nutr.* 2017;117(8):1055-1065.

23. Wirt A, Collins CE. Diet quality--what is it and does it matter? *Public Health Nutr.* 2009;12(12):2473-2492.

24. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA.* 2000;283(15):2008-2012.

25. Yu Y, Hardy I, Sun W, Fergusson DA, Fraser W, Dubois L. Diet quality during preconception or pregnancy and gestational weight gain: protocol for a systematic review and meta-analysis. *BMJ Open.* 2020;10(2):e033130.

26. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol.* 2016;75:40-46.

27. Fergusson D, Laupacis A, Salmi LR, McAlister FA, Huet C. What should be included in meta-analyses? An exploration of methodological issues using the ISPOT meta-analyses. *Int J Technol Assess Health Care.* 2000;16(4):1109-1119.

28. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ.* 2009;339:b2535.

29. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Published 2011. Accessed.

30. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. *JAMA.* 1998;279(18):1477-1482.

31. Araujo AB, Dixon JM, Suarez EA, Murad MH, Guey LT, Wittert GA. Clinical review: Endogenous testosterone and mortality in men: a systematic review and meta-analysis. *J Clin Endocrinol Metab.* 2011;96(10):3007-3019.

32. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. The Cochrane Collaboration.

33. Yong HY, Mohd Shariff Z, Mohd Yusof BN, et al. Pre-Pregnancy BMI Influences the Association of Dietary Quality and Gestational Weight Gain: The SECOST Study. *International Journal of Environmental Research & Public Health [Electronic Resource]*. 2019;16(19):04.

34. Anand SS, Gupta M, Teo KK, et al. Causes and consequences of gestational diabetes in South Asians living in Canada: results from a prospective cohort study. *CMAJ open.* 2017;5(3):E604-E611.

35. Meinila J, Valkama A, Koivusalo SB, et al. Association between diet quality measured by the Healthy Food Intake Index and later risk of gestational diabetes-a secondary analysis of the RADIEL trial. *European Journal of Clinical Nutrition.* 2017;71(4):555-557.

36. Chia AR, Tint MT, Han CY, et al. Adherence to a healthy eating index for pregnant women is associated with lower neonatal adiposity in a multiethnic Asian cohort: the Growing Up in Singapore Towards healthy Outcomes (GUSTO) Study. *American Journal of Clinical Nutrition.* 2018;107(1):71-79.

37. Ancira-Moreno M, O'Neill MS, Rivera-Dommarco JA, et al. Dietary patterns and diet quality during pregnancy and low birthweight: The PRINCESA cohort. *Maternal and Child Nutrition.* 2020;(no pagination).

38. Saunders L, Guldner L, Costet N, et al. Effect of a Mediterranean Diet during Pregnancy on Fetal Growth and Preterm Delivery: Results From a French Caribbean Mother-Child Cohort Study (TIMOUN). *Paediatric & Perinatal Epidemiology.* 2014;28(3):235-244.

39. Shapiro AL, Kaar JL, Crume TL, et al. Maternal diet quality in pregnancy and neonatal adiposity: the Healthy Start Study. *Int J Obes (Lond).* 2016;40(7):1056-1062.

40. Grandy M, Snowden JM, Boone-Heinonen J, Purnell JQ, Thornburg KL, Marshall NE. Poorer maternal diet quality and increased birth weight. *J Matern-Fetal Neo M.* 2018;31(12):1613-1619.

41. Chatzi L, Mendez M, Garcia R, et al. Mediterranean diet adherence during pregnancy and fetal growth: INMA (Spain) and RHEA (Greece) mother-child cohort studies. *Brit J Nutr.* 2012;107(1):135-145.

42. Martin CL, Sotres-Alvarez D, Siega-Riz AM. Maternal Dietary Patterns during the Second Trimester Are Associated with Preterm Birth. *Journal of Nutrition.* 2015;145(8):1857-1864.

43. Tobias DK, Zhang C, Chavarro J, et al. Prepregnancy adherence to dietary patterns and lower risk of gestational diabetes mellitus. *Am J Clin Nutr.* 2012;96(2):289-295.

44. Schoenaker DA, Soedamah-Muthu SS, Mishra GD. Quantifying the mediating effect of body mass index on the relation between a Mediterranean diet and development of maternal pregnancy complications: the Australian Longitudinal Study on Women's Health. *American Journal of Clinical Nutrition.* 2016;104(3):638-645.

45. Gicevic S, Gaskins AJ, Fung TT, et al. Evaluating pre-pregnancy dietary diversity vs. dietary quality scores as predictors of gestational diabetes and hypertensive disorders of pregnancy. *PLoS ONE.* 2018;13(4):e0195103.

46. Gresham E, Collins CE, Gita DM, Byles JE, Hure AJ. Diet quality before or during pregnancy and the relationship with pregnancy and birth outcomes: the Australian Longitudinal Study on Women's Health. *Public Health Nutrition.* 2016;19(16):2975-2983.

47. Rifas-Shiman SL, Rich-Edwards JW, Kleinman KP, Oken E, Gillman MW. Dietary quality during pregnancy varies by maternal characteristics in Project Viva: a US cohort. *Journal of the American Dietetic Association.* 2009;109(6):1004-1011.

48. Hillesund ER, Bere E, Haugen M, Overby NC. Development of a New Nordic Diet score and its association with gestational weight gain and fetal growth - a study performed in the Norwegian Mother and Child Cohort Study (MoBa). *Public health nutrition.* 2014;17(9):1909-1918.

49. Tielemans MJ, Erler NS, Leermakers ETM, et al. A Priori and a Posteriori Dietary Patterns during Pregnancy and Gestational Weight Gain: The Generation R Study. *Nutrients.* 2015;7(11):9383-9399.

50. Ancira-Moreno M, Vadillo-Ortega F, Rivera-Dommarco JA, et al. Gestational weight gain trajectories over pregnancy and their association with maternal diet quality: results from the PRINCESA cohort. *Nutrition.* 2019;65:158-166.

51. Augustin H, Winkvist A, Barebring L. Poor Dietary Quality is Associated with Low Adherence to Gestational Weight Gain Recommendations among Women in Sweden. *Nutrients.* 2020;12(2).

52. Rohatgi KW, Tinius RA, Cade WT, Steele EM, Cahill AG, Parra DC. Relationships between consumption of ultra-processed foods, gestational weight gain and neonatal outcomes in a sample of US pregnant women. *PeerJ.* 2017;5:e4091.

53. Fulay AP, Rifas-Shiman SL, Oken E, Wei P. Associations of the dietary approaches to stop hypertension (DASH) diet with pregnancy complications in Project Viva. *European Journal of Clinical Nutrition.* 2018;72(10):1385-1395.

54. Karamanos B, Thanopoulou A, Anastasiou E, et al. Relation of the Mediterranean diet with the incidence of gestational diabetes. *European Journal of Clinical Nutrition.* 2014;68(1):8-13.

55. Badon SE, Enquobahrie DA, Wartko PD, et al. Healthy Lifestyle During Early Pregnancy and Risk of Gestational Diabetes Mellitus. *American Journal of Epidemiology.* 2017;186(3):326-333.

56. Hillesund ER, Overby NC, Engel SM, et al. Associations of adherence to the New Nordic Diet with risk of preeclampsia and preterm delivery in the Norwegian Mother and Child Cohort Study (MoBa). *Eur J Epidemiol.* 2014;29(10):753-765.

57. Arvizu M, Bjerregaard AA, Madsen MTB, et al. Sodium Intake during Pregnancy, but Not Other Diet Recommendations Aimed at Preventing Cardiovascular Disease, Is Positively Related to Risk of Hypertensive Disorders of Pregnancy. *Journal of Nutrition.* 2020;150(1):159-166.

58. Mikkelsen TB, Osterdal ML, Knudsen VK, et al. Association between a Mediterranean-type diet and risk of preterm birth among Danish women: a prospective cohort study. *Acta Obstet Gynecol Scand.* 2008;87(3):325-330.

59. Navarro P, Mehegan J, Murrin CM, Kelleher CC, Phillips CM. Adherence to the Healthy Eating Index-2015 across Generations Is Associated with Birth Outcomes and Weight Status at Age 5 in the Lifeways Cross-Generation Cohort Study. *Nutrients.* 2019;11(4).

60. Poon AK, Yeung E, Boghossian N, Albert PS, Zhang C. Maternal Dietary Patterns during Third Trimester in Association with Birthweight Characteristics and Early Infant Growth. *Scientifica.* 2013;2013:786409.

61. Emond JA, Karagas MR, Baker ER, Gilbert-Diamond D. Better diet quality during pregnancy is associated with a reduced likelihood of an infant born small for gestational age: An analysis of the prospective New Hampshire birth cohort study. *Journal of Nutrition.* 2018;148(1):22-30.

62. Gonzalez-Nahm S, Hoyo C, Ostbye T, Neelon B, Allen C, Benjamin-Neelon SE. Associations of maternal diet with infant adiposity at birth, 6 months and 12 months. *BMJ Open.* 2019;9(9):e030186.

63. Zhu Y, Hedderson MM, Sridhar S, Xu F, Feng J, Ferrara A. Poor diet quality in pregnancy is associated with increased risk of excess fetal growth: a prospective multi-racial/ethnic cohort study. *International Journal of Epidemiology.* 2019;48(2):423-432.

64. Rodriguez-Bernal CL, Rebagliato M, Iniguez C, et al. Diet quality in early pregnancy and its effects on fetal growth outcomes: The infancia y medio ambiente (childhood and environment) mother and child cohort study in Spain. *American Journal of Clinical Nutrition.* 2010;91(6):1659-1666.

65. Badon SE, Miller RS, Qiu C, Sorensen TK, Williams MA, Enquobahrie DA. Maternal healthy lifestyle during early pregnancy and offspring birthweight: differences by offspring sex. *Journal of Maternal-Fetal and Neonatal Medicine.* 2018;31(9):1111-1117.

66. Kennedy RAK, Turner MJ. Development of a novel Periconceptual Nutrition Score (PENS) to examine the relationship between maternal dietary quality and fetal growth. *Early Human Development.* 2019;132:6-12.

67. Mousa A, Naqash A, Lim S. Macronutrient and Micronutrient Intake during Pregnancy: An Overview of Recent Evidence. *Nutrients.* 2019;11(2).

Tables and Figures

Figure 1. Flowchart of study selection.

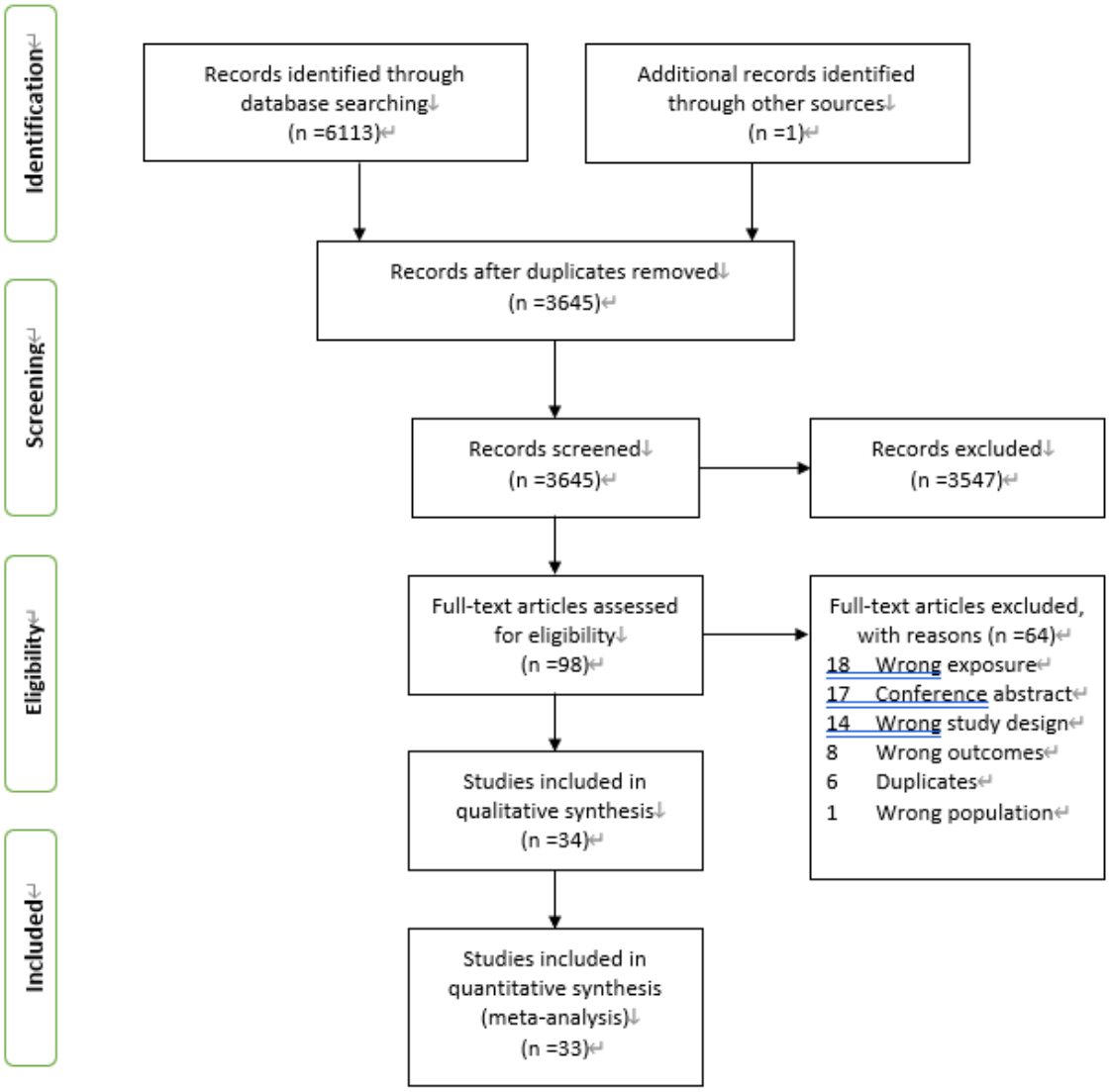


Figure 2. Associations between maternal diet quality and the risk of excessive gestational weight gain.

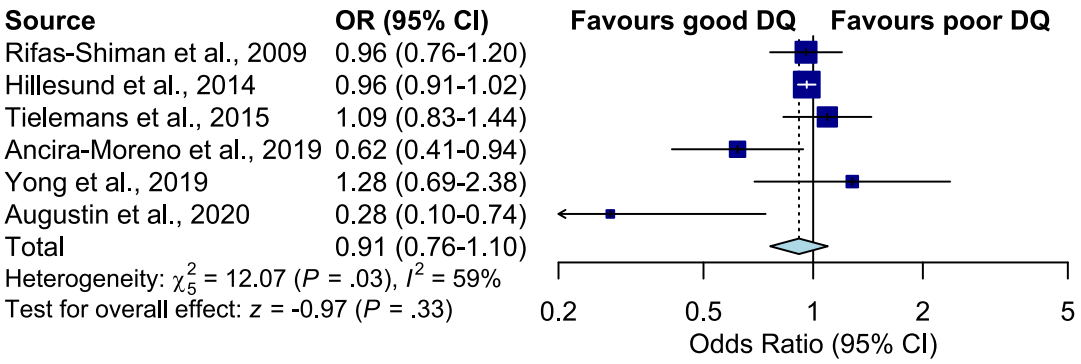


Figure 3. Associations between maternal diet quality and the risk of gestational diabetes (GDM).

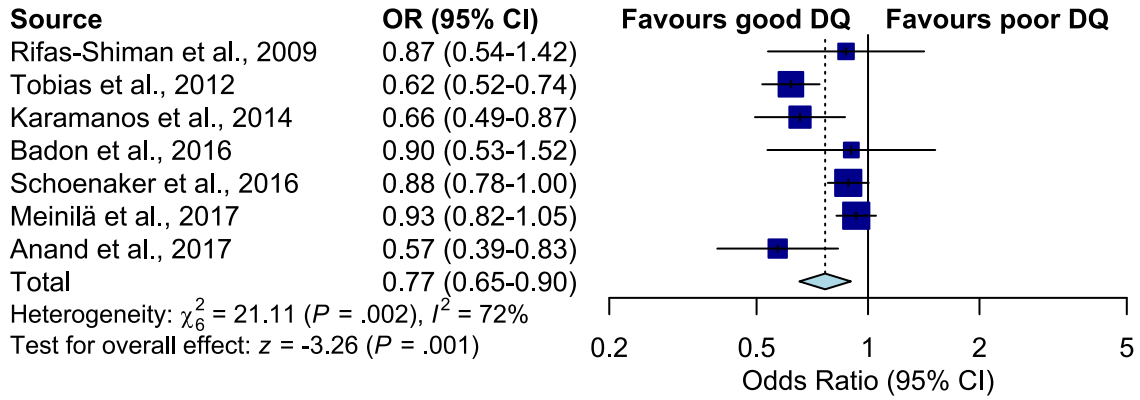


Figure 4. Associations between maternal diet quality and the risk of hypertensive disorders of pregnancy (HDP).

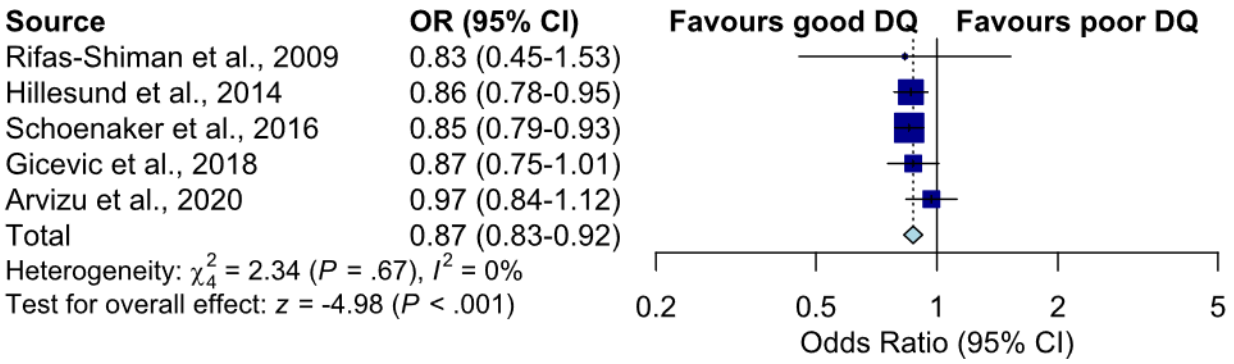
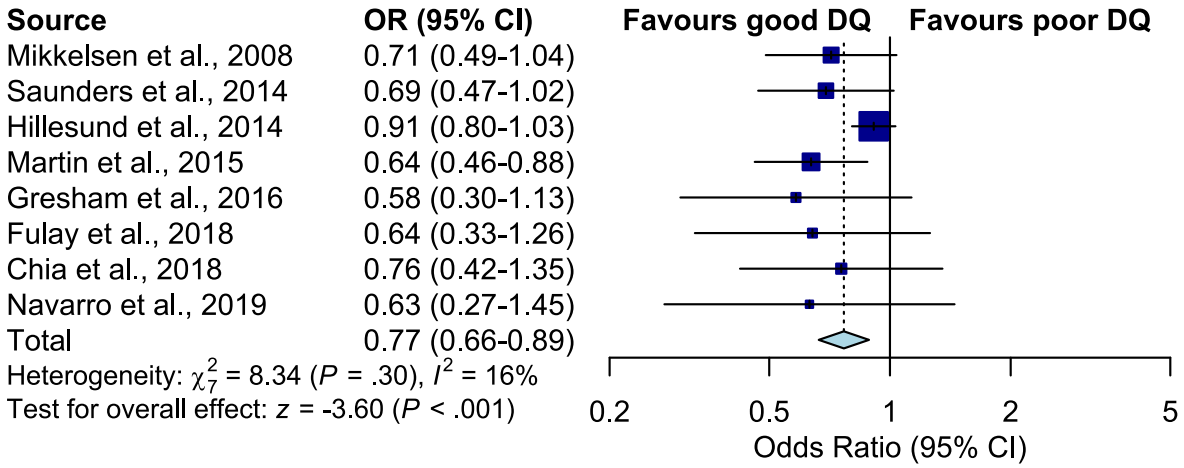


Figure 5. Associations between maternal diet quality and the risk of preterm birth.



Online-only supplement

Table S1. Search terms in OVID Medline.

1	healthy eating index.ti,ab. (1112)
2	recommended food score.ti,ab. (72)
3	Diet, Mediterranean/ (2862)

4	((mediterranean* adj3 diet) or Mediterranean adequacy index).ti,ab. (4127)
5	Dietary Approaches To Stop Hypertension/ (61)
6	dietary approach* to stop hypertension.ti,ab. (675)
7	Diet Quality Index.ti,ab. (294)
8	Dietary Guidelines for Americans Index.ti,ab. (2)
9	Dietary Guideline Index.ti,ab. (29)
10	Framingham Nutritional Risk Score.ti,ab. (3)
11	(French Program* National Nutrition Sante-Guideline Score or PNNS-GS).ti,ab. (18)
12	Dietary Quality Score.ti,ab. (19)
13	Food Variety Score.ti,ab. (35)
14	Australian Recommended Food Score.ti,ab. (33)
15	Dietary Diversity Score.ti,ab. (232)
16	Healthy Food Index.ti,ab. (5)
17	(Healthy Food and Nutrient Index).ti,ab. (1)
18	Diet quality index.ti,ab. (294)
19	Dietary quality.ti,ab. (1155)
20	(diet* adj3 (pattern* or quality)).ti,ab. (14978)
21	((adherence or compliance or score* or index* or indice*) adj3 (guideline* or recommendation* or healthy or pyramid) adj3 (diet* or food or nutrition*)).ti,ab. (1210)

22	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (19684)
23	((child adj3 bearing) or childbearing).ti,ab. (14960)
24	(pregnan* or gestat* or matern* or perinatal or gravidit*).ti,ab. (726572)
25	(pre-pregnan* or prepregnan* or preconception* or pre-conception*).ti,ab. (11222)
26	exp Pregnancy/ (859642)
27	Pregnant Women/ (7403)
28	23 or 24 or 25 or 26 or 27 (1125180)
29	22 and 28 (1451)

Table S2. The quality of studies assessed by Newcastle-Ottawa Scale for each outcome.[a]

Study for each outcome	Representativeness of the exposed cohort [b]	Selection of the non-exposed cohort	Ascertainment of exposure [c]	Outcome does not present at start	Controls for prepregnancy BMI	Controls for ethnicity or socioeconomic background or education	Assessment of outcome	Follow-up long enough	Adequacy of follow up of cohorts [d]	**TOTAL SCORE**
GWG according to IOM guideline										
Rifas-Shiman et al., 2009	1	1	1	1	1	1	0	1	1	8
Hillesund et al., 2014	0	1	1	1	1	1	0	1	1	7
Tielemans et al., 2015	0	1	1	1	1	1	0	1	1	7
Yong et al., 2019	1	1	0	1	1	1	0	1	0	6
Ancira-Moreno et al., 2020	1	1	0	1	1	1	1	1	0	7
Augustin et al., 2020	0	1	1	1	1	1	1	1	1	8
GDM										
Rifas-Shiman et al., 2009	1	1	1	1	1	1	1	1	1	9
Tobias et al., 2012	0	1	1	1	1	1	0	1	1	7
Karamanos et al., 2014	1	1	1	1	1	0	1	1	1	8
Badon et al., 2016	1	1	1	0	1	1	1	1	1	8
Schoenaker et al., 2016	1	1	1	1	1	1	0	1	0	7

Meinilä et al., 2017	0	1	0	1	1	1	1	1	1	7
Anand et al., 2017	0	1	0	0	1	1	1	1	1	6
HDP										
Rifas-Shiman et al., 2009	1	1	1	1	1	1	1	1	1	9
Hillesund et al., 2014	1	1	1	1	1	1	1	1	1	9
Schoenaker et al., 2016	1	1	1	1	1	1	0	1	0	7
Gicevic et al., 2018	1	1	1	1	1	1	0	1	1	8
Arvizu et al., 2020	1	1	1	1	1	1	1	1	1	9
Preterm birth										
Mikkelsen et al., 2008	1	1	0	1	1	1	1	1	1	8
Hillesund et al., 2014	1	1	1	1	1	1	1	1	1	9
Saunders et al., 2014	1	1	1	0	1	1	1	1	1	8
Martin et al., 2015	1	1	1	1	1	1	1	1	0	8
Gresham et al., 2016	1	1	1	1	0	1	0	1	1	7
Fulay et al., 2018	1	1	1	1	1	1	1	1	1	9
Chia et al., 2018	1	1	1	1	1	1	1	1	1	9
Navarro et al., 2019	1	1	1	1	1	1	1	1	1	9
SGA										
Rifas-Shiman et al., 2009	1	1	1	1	1	1	1	1	1	9

Poon et al., 2013	0	1	1	1	1	1	1	1	1	8
Hillesund et al., 2014	0	1	1	1	1	1	1	1	1	8
Zhu et al., 2019	1	1	1	1	1	1	1	1	1	9
Emond et al., 2018	1	1	1	1	1	1	1	1	1	9
Gonzalez-Nahm et al., 2019	1	1	1	1	1	1	1	1	0	8
LBW										
Gresham et al., 2016	1	1	1	1	0	1	0	1	1	7
Emond et al., 2018	1	1	1	1	1	1	1	1	1	9
Gonzalez-Nahm et al., 2019	1	1	1	1	1	1	1	1	0	8
Navarro et al., 2019	1	1	1	1	1	1	1	1	1	9
Ancira-Moreno et al., 2020	1	1	0	1	1	1	1	1	0	7
LGA										
Rifas-Shiman et al., 2009	1	1	1	1	1	1	1	1	1	9
Hillesund et al., 2014	0	1	1	1	1	1	1	1	1	8
Poon et al., 2013	1	1	1	1	1	1	1	1	1	9
Emond et al., 2018	1	1	1	1	1	1	1	1	1	9
Zhu et al., 2019	1	1	1	1	1	1	1	1	1	9
Gonzalez-Nahm et al., 2019	1	1	1	1	1	1	1	1	0	8
Macrosomia										

Emond et al., 2018	1	1	1	1	1	1	1	1	1	9
Gonzalez-Nahm et al., 2019	1	1	1	1	1	1	1	1	0	8
Navarro et al., 2019	1	1	1	1	1	1	1	1	1	9
Birth weight continuous										
Rodrıguez-Bernal et al., 2010	1	1	1	1	1	1	1	1	1	9
Chatzi et al., 2012	1	1	1	1	1	1	1	1	1	9
Shapiro et al., 2016	1	1	1	1	1	1	1	1	0	8
Badon et al., 2016	1	1	1	1	1	1	1	1	1	9
Chia et al., 2018	1	1	1	1	1	1	1	1	1	9
Emond et al., 2018	1	1	1	1	1	1	1	1	1	9
Grandy et al., 2018	0	1	1	0	1	0	1	1	1	6
Kennedy et al., 2019	1	1	0	1	1	1	1	1	1	8
Zhu et al., 2019	1	1	1	1	1	1	1	1	1	9
Birth weight z-score										
Poon et al., 2013	1	1	1	1	1	1	1	1	1	9
Gonzalez-Nahm et al., 2019	1	1	1	1	1	1	1	1	0	8
Zhu et al., 2019	1	1	1	1	1	1	1	1	1	9

[a] A study can be awarded one or zero score for each criteria, with "1" denotes for meeting the criteria and "0" for not meeting the criteria or no information provided.

[b] One score assigned if cohort was truly or somewhat representative of the average pregnant women in community/population.

[c] One score assigned where diets were assessed using validated food frequency questionnaire, multiple 24-h recalls, or multiple-day food record, and diet quality score was validated.

[d] One score assigned where the follow-up rate was ≥80%. Follow-up rate was defined as a ratio of those in analysis divided by those with plausible dietary data in the cohort.

Table S3. Characteristics of studies included for each outcome.

Study	Cohort	Country	Study Period	Population	n	Mean age, y	BMI, kg/m^2	Diet quality index	Dietary assessment tool	Diet period	Time for dietary assessment	Outcome assessment	% or Mean
GWG													
Rifas-Shiman et al., 2009	Project Viva	U.S.A.	1999-2002	General	1,777	32.4	24.6	aHEI-P	166-item validated FFQ	Early pregnancy	Early pregnancy	Last weight in medical record minus self-reported prepregnancy weight	50% for excessive GWG
Hillesund et al., 2014	Norwegian Mother and Child Cohort Study (MoBa)	Norway	1999–2008	General: exclude delivery <37wk, pre-pregnancy diabetes	66,597	30.1	24.0	New Nordic Diet (NND) Score	255-item validated FFQ	Conception until mid-pregnancy	Around week 22	Self-reported weight at birth minus prepregnancy weight	47% for excessive, 19% for inadequate

Tielemans et al., 2015	Generation R Study	Netherlands	2002-2006	General: underweight excluded	3,374	31.5	23.1	Dutch Healthy Diet Index	293-item validated FFQ	Previous three months	Median 13.4 weeks	Self-report maximum weight minus prepregnancy weight	43% for excessive, 14 % for inadequate
Ancira-Moreno et al., 2019	PRINCESA cohort	Mexico	2009-2014	General, exclude GDM, preeclampsia	660	25.1	25.7	Maternal Diet Quality Score	Multiple-step 24-h dietary recall	Previous day	First, second and third trimester	Measured weight, rate of GWG	41% for excessive, 30% for inadequate
Yong et al., 2019	SECOST (Seremban Cohort Study)	Malaysia	2013-2016	General: underweight excluded	480	30.2	24.1	HEI for Malaysians	One day 24-hour dietary recall	Previous 24 hours	Second trimester	Weight reported in medical records for 37±2 weeks minus week ≤14	23% for excessive, 38% for inadequate
Augustin et al., 2020	GraviD cohort	Sweden	2013-2014	General: >34wk	1,113	31.9	24.1	Dietary quality index	174-item validated FFQ	Past two months	Third trimester	Weight in medical record, 37±2 weeks minus weight ≤14	40% for excessive, 25% for inadequate
GDM													

Rifas-Shiman et al., 2009	Project Viva	U.S.A.	1999-2002	General	1,777	32.4	24.6	aHEI-P	166-item validated FFQ	Early pregnancy	Early pregnancy	Routinely tested	5.0%
Tobias et al., 2012	Nurses' Health Study II	U.S.A.	1991-2001	General, exclude history of GDM, diabetes and cancers	21,376	>30	<25	aHEI, aMED, DASH	61-item validated FFQ	Prepregnancy	Prepregnancy	Self-reported of physician diagnosis	4.1%
Karamanos et al., 2014	Gestational Diabetes in the Mediterranean Region Study	10 Mediterranean countries	2010-2011	General, exclude history of diabetes	1,003	30.2	24.7	Mediterranean diet score	78-item validated FFQ	Prior to the OGTT	N.A.	Measured	29.0%
Badon et al., 2016	Omega Study	U.S.A.	1996-2008	General	3,005	33.0	23.0	aHEI-2010	122-item validated FFQ	Past 3 months	Average 15 weeks	Measured	4.7%
Schoenaker et al., 2016	Australian Longitudinal Study on Women's Health	Australia	2003-2012	General	3,378	<30	23.7	Mediterranean diet score	101-item validated FFQ	Past 12 months	Prepregnancy	Self-reported of diagnosis or treatment	7.1%
Meinilä et al., 2017	RADIEL trial	Finland	2008-2014	Specific: obese and/or history of GDM	137	32.0	32.2	Healthy Food Intake Index	Non-validated FFQ	N.A.	First trimester	Measured	21.2%

Anand et al., 2017	South Asian Birth Cohort (START)	Canada	2011-2015	Specific: South Asian women in Ontario	1,006	30.2	23.8	No specific name	164-item validated FFQ	N.A.	N.A.	Measured	36.3%
HDP													
Rifas-Shiman et al., 2009	Project Viva	U.S.A.	1999-2002	General	1,777	32.4	24.6	aHEI-P	140-item validated FFQ	Early pregnancy	Early pregnancy	Clinical records	3.4%
Hillesund et al., 2014	Norwegian Mother and Child Cohort Study (MoBa)	Norway	1999–2008	General	72,072	30.1	24.0	New Nordic Diet (NND) Score	255-item validated FFQ	Conception until mid-pregnancy	Around week 22	Medical record	4.0%
Schoenaker et al., 2016	Australian Longitudinal Study on Women's Health	Australia	2003-2012	General	3,167	<30	23.7	Mediterranean diet score	101-item validated FFQ	Past 12 months	Prepregnancy	Self-reported of diagnosis or treatment	8.6%
Gicevic et al., 2018	Nurses' Health Study II	U.S.A.	1991-2001	General, exclude chronic disease, GDM and HDP	14,339	>30	<25	aHEI	131-item validated FFQ	Past year	Prepregnancy	Self-reported of physician diagnosis	9.9%
Arvizu et al., 2020	Danish National Birth Cohort	Denmark	1996-2002	General	66,651	30.0	24.0	AHA primary AHA secondary	360-item validated FFQ	Past 4 weeks	Around 20 weeks	From registry	2.0%

								DASH					
Preterm birth													
Mikkelsen et al., 2008	Danish National Birth Cohort	Denmark	1996-2000	General, normal BMI (19-32)	35,530	29.7	22.3	Mediterranean-type diet	360-item validated FFQ	Past 4 weeks	25 weeks	National registries, birth before 37 weeks	4.3%
Hillesund et al., 2014	Norwegian Mother and Child Cohort Study (MoBa)	Norway	1999–2008	General	72,072	30.1	24.0	New Nordic Diet (NND) Score	255-item validated FFQ	Conception until mid-pregnancy	Around week 22	Spontaneous preterm delivery only	5.2%
Saunders et al., 2014	A French Caribbean Mother–Child Cohort Study (TIMOUN)	Guadeloupe, Caribbean, African descent	2004-2007	General	728	31.0	<25	Adapted version of the MD score	214-item validated FFQ	During pregnancy	Shortly after delivery	Medical record, birth before 37 weeks	14.7%
Martin et al., 2015	PIN (Pregnancy, Infection, and Nutrition) study	U.S.A.	2001-2005	General	3,143	<30	<25	DASH	84-item non-validated FFQ	Previous 3-mo	26–29 wk of gestation	Medical record, birth before 37 weeks	11.6%
Gresham et al., 2016	Australian Longitudinal Study on Women's Health (ALSWH)	Australia	1996-2012	General	1,897	20.8	N.A.	Australian Recommended Food Score	74-item validated FFQ	Past 12 months	Prepregnancy and pregnancy	Self-reported	6.4%

Fulay et al., 2018	Project Viva	U.S.A.	1999-2002	General	1,760	32.2	<25	DASH and DASH OMNI	140-item validated FFQ	Early pregnancy	Before 22 weeks	Medical record, birth before 37 weeks	7.2%
Chia et al., 2018	Growing Up in Singapore Towards healthy Outcomes (GUSTO)	Singapore	2009-2010	General	1,051	30.5	<25	HEI-SGP	24h-recalls and 3-day food diaries	26–28 wk	26–28 wk of gestation	Medical record, birth before 37 weeks	7.2%
Navarro et al., 2019	Lifeways cross-generation cohort study	Ireland	2001-2003	General	958	30.1	23.8	HEI-2015	149-item validated FFQ	12-16 weeks	First trimester of pregnancy	Medical record, birth before 37 weeks	5.6%
SGA													
Rifas-Shiman et al., 2009	Project Viva	U.S.A.	1999-2002	General	1,777	32.4	24.6	aHEI-P	166-item validated FFQ	Early pregnancy	Early pregnancy	Medical record	5.5%
Poon et al., 2013	Infant Feeding Practices Study II	U.S.A.	2005-2007	General: >35wk, 5 pounds, no medical condition	893	29.1	26.1	aHEI-P	124-item validated FFQ	Past month	28-36 weeks	birth screener	8.0%

Hillesund et al., 2014	Norwegian Mother and Child Cohort Study (MoBa)	Norway	1999–2008	General: excluded delivery at <37, pre-pregnancy diabetes	66,597	30.1	24.0	New Nordic Diet (NND) Score	255-item validated FFQ	Conception until mid-pregnancy	Around week 22	Registration	10.4%
Zhu et al., 2019	Pregnancy and Environment Lifestyle Study (PETALS)	U.S.A.	2014-2017	General	2,269	N.A.	N.A.	HEI-2010	110-item validated FFQ	Past three months	10-13 weeks	Registration	10.2%
Emond et al., 2018	New Hampshire Birth Cohort Study (NHBCS)	U.S.A.	2009-2017	General, exclude underweight	862	31.2	N.A.	aHEI-2010	61-item validated FFQ	Diet in pregnancy	24-28 weeks	Medical records	4.6%
Gonzalez-Nahm et al., 2019	Nurture study	U.S.A.	2013-2015	General	817	27.4	30.1	AHEI-2010	110-item validated FFQ	Past 30 days	20-36 weeks	Medical record	8.6%
LBW													
Gresham et al., 2016	Australian Longitudinal Study on Women's Health (ALSWH)	Australia	1996-2012	General	1,897	20.8	N.A.	Australian Recommended Food Score	74-item validated FFQ	Past 12 months	Prepregnancy and pregnancy	Self-reported	3.0%

Emond et al., 2018	New Hampshire Birth Cohort Study (NHBCS)	U.S.A.	2009-2017	General	862	31.2	N.A.	HEI-2010	61-item validated FFQ	Diet in pregnancy	24-28 weeks	Medical records	3.4%
Gonzalez-Nahm et al., 2019	Nurture study	U.S.A.	2013-2015	General	817	27.4	30.1	AHEI-2010	110-item validated FFQ	Past 30 days	20-36 weeks	Medical record	8.7%
Navarro et al., 2019	Lifeways cross-generation cohort study	Ireland	2001-2003	General	958	30.1	23.8	HEI-2015	149-item validated FFQ	12-16 weeks	First trimester of pregnancy	Medical record, birth before 37 weeks	4.9%
Ancira-Moreno et al., 2020	PRINCESA cohort	Mexico	2009-2014	General	660	25.1	25.7	Maternal Diet Quality Score	multiple-step 24-h dietary recall	Previous day	First, second and third trimester	Medical records	7.4%
LGA													
Rifas-Shiman et al., 2009	Project Viva	U.S.A.	1999-2002	General	1,777	32.4	24.6	aHEI-P	166-item validated FFQ	Early pregnancy	Early pregnancy	Medical record	13.3%
Poon et al., 2013	Infant Feeding Practices Study II	U.S.A.	2005-2007	General: >35wk, 5 pounds, no medical condition	893	29.1	26.1	aHEI-P	124-item validated FFQ	Past month	28-36 weeks	birth screener	9.1%

Hillesund et al., 2014	Norwegian Mother and Child Cohort Study (MoBa)	Norway	1999–2008	General: excluded delivery at <37	66,597	30.1	24.0	New Nordic Diet (NND) Score	255-item validated FFQ	Conception until mid-pregnancy	Around week 22	Registration	11.2%
Emond et al., 2018	New Hampshire Birth Cohort Study (NHBCS)	U.S.A.	2009-2017	General	862	31.2	N.A.	aHEI-2010	61-item validated FFQ	Diet in pregnancy	24-28 weeks	Medical records	8.7%
Zhu et al., 2019	Pregnancy and Environment Lifestyle Study (PETALS)	U.S.A.	2014-2017	General, no pre-existing disease (diabetes, cancer, etc.)	2,269	N.A.	N.A.	HEI-2010	110-item validated FFQ	Past three months	10-13 weeks	Registration	8.2%
Gonzalez-Nahm et al., 2019	Nurture study	U.S.A.	2013-2015	General	817	27.4	30.1	AHEI-2010	110-item validated FFQ	Past 30 days	20-36 weeks	Medical record	13.1%
Macrosomia													
Emond et al., 2018	New Hampshire Birth Cohort Study (NHBCS)	U.S.A.	2009-2017	General	862	31.2	N.A.	aHEI-2010	61-item validated FFQ	Diet in pregnancy	24-28 weeks	Medical records	8.7%

Gonzalez-Nahm et al., 2019	Nurture study	U.S.A.	2013-2015	General	817	27.4	30.1	AHEI-2010	110-item validated FFQ	Past 30 days	20-36 weeks	Medical record	13.1%
Navarro et al., 2019	Lifeways cross-generation cohort study	Ireland	2001-2003	General	958	30.1	23.8	HEI-2015	149-item validated FFQ	12-16 weeks	First trimester of pregnancy	Medical record, birth before 37 weeks	17.9%
Birth weight as a continuous variable													
Rodriguez-Bernal et al., 2010	Valencia Birth Cohort	Spain	2004-2005	General	782	N.A.	<25	AHEI-P	100-item validated FFQ	First trimester	10-13 weeks	Medical records	3324
Chatzi et al., 2012	INMA-Atlantic	Spain	2004-2008	General	1,074	31.4	23.3	Mediterranean diet score	100-item validated FFQ	First trimester	Mean 13.8 weeks	Medical records	3283
Chatzi et al., 2012	INMA-Mediterranean	Spain	2004-2008	General	1,386	30.0	23.7	Mediterranean diet score	100-item validated FFQ	First trimester	Mean 13.8 weeks	Medical records	3233

Chatzi et al., 2012	RHEA	Greece	2004-2008	General	824	29.5	24.3	Mediterranean diet score	250-item non-validated FFQ	First trimester	14th–18th week	Medical records	3206
Shapiro et al., 2016	Healthy Start Study	U.S.A.	2010-2014	General:exclude current multiples, GDM and <32 wks, history of diabetes, premature and other diseases	1,079	27.8	N.A.	HEI-2010	Self-Administered 24h recall	Monthly, average 2 recalls	Monthly from 8 - 24 weeks to delivery	Measured	3254
Grandy et al., 2018	N.A.	U.S.A.	2012-2013	General: healthy women without gestational diabetes and delivered term	41	30.9	29.7	HEI-2010	3*24-hour food recalls	3 weeks following the study visit	37–38 weeks	Measured	3500
Emond et al., 2018	New Hampshire Birth Cohort Study (NHBCS)	U.S.A.	2009-2017	General	862	31.2	N.A.	aHEI-2010	61-item validated FFQ	Diet in pregnancy	24-28 weeks	Medical records	3449

Badon et al., 2016	Omega Study	U.S.A.	1996-2008	General	3,005	33.0	23.0	aHEI-2010	122-item validated FFQ	Past 3 months	Average 15 weeks	Measured	3446
Chia et al., 2018	Growing Up in Singapore Towards healthy Outcomes (GUSTO)	Singapore	2009-2010	General, exclude twin, IVF	1,051	30.5	<25	HEI-SGP	24h recalls and 3-day food diaries	26–28 wk	26–28 wk of gestation	Medical record, birth before 37 weeks	3090
Kennedy et al., 2019	N.A.	Ireland	N.A.	General	202	32.2	26.2	Periconceptual Nutrition Score	Four-day diet history	<=18 weeks	<=18 weeks	Measured	3524
Zhu et al., 2019	Pregnancy and Environment Lifestyle Study (PETALS)	U.S.A.	2014-2017	General	2,269	N.A.	N.A.	HEI-2010	110-item validated FFQ	Past three months	10-13 weeks	Registration	N.A.
Birth weight z-score													
Poon et al., 2013	Infant Feeding Practices Study II	U.S.A.	2005-2007	General: >35wk, 5 pounds, no medical condition	893	29.1	26.1	aHEI-P	124-item validated FFQ	Past month	28-36 weeks	birth screener	

Gonzalez-Nahm et al., 2019	Nurture study	U.S.A.	2013-2015	General	817	27.4	30.1	AHEI-2010	110-item validated FFQ	Past 30 days	20-36 weeks	Medical record
Zhu et al., 2019	Pregnancy and Environment Lifestyle Study (PETALS)	U.S.A.	2014-2017	General	2,269	N.A.	N.A.	HEI-2010	110-item validated FFQ	Past three months	10-13 weeks	Registration

Table S4. Characteristics of diet quality scores.

			Adequacy							Moderation					
DQ scores	Study	Total score (number of components)	Fruits and/or vegetables	Whole grains, cereals, fiber, potatoes	Nuts, Legumes, Soy,	Protein foods, diary	Fatty acids	Supplements	Others [4]	Trans Fat	Red/processed meat, meat, poultry	Sodium	Refined grains	Empty calories, snacks	Others [5]
aHEI	Tobias et al., 2012	2.5 - 87.5 (9)	0 - 20	0 - 10	0 - 10	0 - 10	0 - 10	2.5 - 7.5	0 - 10	0 - 10					
aHEI-2010	Badon et al., 2016 Emond et al., 2018 Gicevic et al., 2018 Gonzalez-Nahm et al., 2019	0 - 100 (10)	0 - 20	0 - 10	0 - 10		0 - 20			0 - 10	0 - 10	0 - 10		0 - 10	
aHEI-P	Rifas-Shiman et al., 2009	0 - 90 (9)	0 - 20	0 - 10		0 - 10	0 - 10	0 - 30		0 - 10					
	Rodrıguez-Bernal et al., 2010	0 - 100 (10)	0 - 20	0 - 10	0 - 10	0 - 10	0 - 10	0 - 30		0 - 10					

	Poon et al., 2013	0 - 130 (13)	0 - 20	0 - 10	0 - 10		0 - 20	0 - 30		0 - 10	0 - 10	0 - 10		0 - 10	
HEI -2010 [1]	Shapiro et al., 2016	0 - 100 (12)	0 - 20	0 - 10		0 - 20	0 - 10					0 - 10	0 - 10	0 - 20	
	Grandy et al., 2018														
	Zhu et al., 2019														
HEI- 2015 [1]	Navarro et al., 2019	0 - 100 (13)	0 - 20	0 - 10		0 - 20	0 - 10					0 - 10	0 - 10	0 - 20	
HEI-SGP [1]	Chia et al., 2018	0 - 100 (12)	0 - 20	0 - 20		0 - 20		0 - 10						0 - 10	0 - 10
HEI for Malaysians [3]	Yong et al., 2019	0 - 100 (9)	0 - 20	0 - 10	0 - 10	0 - 30						0 - 10			0 - 10
MD score	Mikkelsen et al., 2008	0 - 5 (5)	0 - 1			0 - 2	0 - 1		0 - 1						
	Chatzi et al., 2012	0 - 8 (8)	0 - 2	0 - 1	0 - 1	0 - 2	0 - 1				0 - 1				
	Karamanos et al., 2014	0 - 12 (12)	0 - 2	0 - 3	0 - 1	0 - 1	0 - 1				0 - 1				0-3
	Schoenaker et al., 2016	0 - 10 (10)	0 - 2	0 - 1	0 - 1	0 - 1	0 - 1				0 - 2				0 - 2
Alternate MD (aMED)	Poon et al., 2013	0 - 8 (8)	0 - 2	0 - 1	0 - 1	0 - 1	0 - 1				0 - 1				
Adapted MD score	Saunders et al., 2014	0 - 9 (9)	0 - 2	0 - 1	0 - 1	0 - 1	0 - 1				0 - 2				0 - 1
DASH	Martin et al., 2015	8 - 40 (8)	2 - 10	1 - 5	1 - 5	1 - 5					1 - 5	1 - 5		1 - 5	
	Fulay et al., 2018														
	Arvizu et al., 2020														
DASH OMNI	Fulay et al., 2018	9 - 45 (9)	2 - 10	1 - 5	1 - 5	1 - 5	1 - 5				1 - 5	1 - 5		1 - 5	
AHA primary	Arvizu et al., 2020	0 - 50 (5)	0 - 10	0 - 10		0 - 10						0 - 10		0 - 10	
AHA secondary	Arvizu et al., 2020	0 - 80 (8)	0 - 10	0 - 10	0 - 10	0 - 10					0 - 10	0 - 10		0 - 20	

New Nordic Diet (NND) Score	Hillesund et al., 2014	0 - 10 (10)	0 - 1	0 - 3		0 - 1		0 - 2					
Dutch Healthy Diet Index	Tielemans et al., 2015	0 - 60 (6)	0 - 20	0 - 10		0 - 10				0 - 10		0 - 10	
Australian Recommended Food Score [2]	Gresham et al., 2016	0 - 72 (72)											
Healthy Food Intake Index	Meinilä et al., 2017	0 - 17 (11)	0 - 3	0 - 3	0 - 1	0 - 4	0-4					0 - 3	0 - 1
No specific name	Anand et al., 2017	0 - 6 (6)	0 - 4						0 - 1				0 - 1
Periconceptual Nutrition Score [2]	Kennedy et al., 2019	0 - 23 (23)	0 - 2			0 - 1							
Maternal Diet Quality Score	Ancira-Moreno et al., 2020	0 - 7 (7)	0 - 1		0 - 1	0 - 1	0 - 1		0 - 1			0 - 2	
Dietary quality index [2]	Augustin et al., 2020	0 -12 (12)											

[1] Scored per 1000 kcal

[2] Not clearly described or able to be summarized in the table. Specifically, Periconceptual Nutrition Score used only nutrients for scoring.

[3] Yong et al. 2019 gave a range to each group, so each group were evaluated both as adequacy and moderation

[4] Others include: meal pattern, coffee, water, moderate alcohol

[5] Others include: Total fat, fried food, fast food, high-fat diary, alcohol, diary, eggs, cheese

Table S5-1. Adjusted covariates for GDM.

Adjusted for	Rifas-Shiman et al., 2009	Tobias et al., 2012	Karamanos et al., 2014	Badon et al., 2016	Schoenaker et al., 2016	Meinilä et al., 2017	Anand et al., 2017
Reasons for selecting covariates[a]			2			3	2
prepregnancy BMI	Y	Y	Y	Y		Y	Y
weight							Y
age	Y	Y	Y	Y		Y	Y
gravidity	Y	Y			Y		
education	Y				Y	Y	
sedentary time		Y					
area of residence							
race	Y			Y			
total energy intake		Y	Y		Y		
smoking status		Y		Y			
physical activity		Y		Y	Y		
family history of type 2 diabetes		Y	Y				Y
stress				Y			
weight gain during pregnancy			Y				
GDM history		excluded				Y	

polycystic ovary syndrome					Y		

[a] Reasons for selecting covariates: 1 denotes for change in the effect estimates by removing from the multivariable model. 2 denotes for univariate p value. 3 denotes for previous literature. 4 denotes for directed acyclic graphs.

Table S5-2. Adjusted covariates for HDP.

Adjusted for	Rifas-Shiman et al., 2009	Hillesund et al., 2014	Schoenaker et al., 2016	Gicevic et al., 2018	Arvizu et al., 2020
Reasons for selecting covariates[a]					4
prepregnancy BMI	Y	Y		Y	Y
height					Y
age	Y	Y		Y	Y
gravidity	Y	Y	Y	Y	Y
education	Y	Y	Y		Y
area of residence					Y
race	Y			Y	
total energy intake		Y	Y	Y	Y
smoking status		Y		Y	Y
physical activity			Y	Y	
sedentary time				Y	
family history of hypertension				Y	
GDM history				Y	
GDM in the current pregnancy				Y	Y

diabetes		Y			
chronic hypertension		Y			
multivitamin use				Y	
vitamin C and vitamin E intake					Y

[a] Reasons for selecting covariates: 1 denotes for change in the effect estimates by removing from the multivariable model. 2 denotes for univariate p value. 3 denotes for previous literature. 4 denotes for directed acyclic graphs.

Table S5-3. Adjusted covariates for preterm birth.

Adjusted for	Mikkelsen et al., 2008	Hillesund et al., 2014	Saunders et al., 2014	Martin et al., 2015	Gresham et al., 2016	Fulay et al., 2018	Chia et al., 2018	Navarro et al., 2019
Reasons for selecting covariates[a]		1			3			
prepregnancy BMI	Y	Y	Y	Y		Y	Y	Y
weight					Y			
height							Y	
age	Y	Y		Y	Y	Y	Y	Y
gravidity	Y	Y		Y	Y		Y	
education	Y	Y	Y	Y	Y	Y	Y	Y
income				Y			Y	Y
socio-economic status								Y
area of residence			Y		Y			
race				Y		Y		
marital status			Y	Y				Y
infant sex							Y	Y
total energy intake		Y	Y	Y		Y	Y	Y
smoking status	Excluded	Y	Y		Y	Y	Y	Y

alcohol use							Y	Y
physical activity	Y				Y		Y	
other dietary patterns						Y		
diabetes		Y						
chronic hypertension		Y						
weight gain during pregnancy			Y			Y	Y	

[a] Reasons for selecting covariates: 1 denotes for change in the effect estimates by removing from the multivariable model. 2 denotes for univariate p value. 3 denotes for previous literature. 4 denotes for directed acyclic graphs.

Table S5-4. Adjusted covariates for birth weight.

	Rifas-Shiman et al., 2009	Poon et al., 2013	Hillesund et al., 2014	Emond et al., 2018	Zhu et al., 2019	Gonzalez-Nahm et al., 2019	Gresham et al., 2016	Navarro et al., 2019	Ancira-Moreno et al., 2020	Rodriguez-Bernal et al., 2010	Chatzi et al., 2012	Shapiro et al., 2016	Badon et al., 2016	Chia et al., 2018	Grandy et al., 2018	Kennedy et al., 2019
Reasons for selecting covariates[a]		3	2,3		1						2	3				3
prepregnancy BMI	Y	Y	Y	Y	Y	Y		Y	Y	Y			Y	Y	Y	Y
weight							Y									
maternal/paternal height			Y						Y	Y				Y		
age	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	Y	Y	Y
gravidity	Y		Y	Y	Y	Y	Y		Y	Y	Y		Y	Y	Y	Y
education	Y	Y	Y	Y		Y	Y	Y	Y		Y			Y		Y
income								Y				Y		Y		Y
socio-economic status		Y						Y			Y					
area of residence							Y									
race	Y	Y			Y	Y						Y	Y	Y		
country of origin																

marital status								Y	Y							
infant sex								Y	Y		Y	Y	Y	Y		Y
gestational age at delivery					Y					Y	Y	Y	Y			Y
preterm birth									Y	Y						
total energy intake		Y	Y	Y	Y	Y		Y	Y		Y	Y		Y	Y	
average energy expenditure												Y				
smoking status		Y	Y	Y		Y	Y	Y		Y	Y	Y	Y	Y		Y
alcohol use		Y						Y						Y		
physical activity			Y	Y	Y		Y						Y	Y		
stress													Y			
quality of life																Y
planned pregnancy																Y
GDM in the current pregnancy			Y									Exclude			Exclude	
gestational hypertension and preeclampsia												Y				
chronic hypertension					Y							Y				
weight gain during pregnancy				Y					Y	Y				Y		

maternal urinary arsenic				Y												
prenatal supplement use					Y											
prepregnancy folic acid																Y

[a] Reasons for selecting covariates: 1 denotes for change in the effect estimates by removing from the multivariable model. 2 denotes for univariate p value. 3 denotes for previous literature. 4 denotes for directed acyclic graphs.

Table S5-5. Adjusted covariates for GWG.

Adjusted for	Rifas-Shiman et al., 2009	Hillesund et al., 2014	Tielemans et al., 2015	Ancira-Moreno et al., 2020	Yong et al., 2019	Augustin et al., 2020
Reasons for selecting covariates[a]		2,3	1,3			
prepregnancy BMI	Y	Y	Y	Y	Y	Y
weight						
age	Y	Y	Y	Y	Y	
age square		Y				
gravidity	Y	Y	Y	Y	Y	Y
income			Y			
education	Y	Y	Y	Y	Y	Y
race	Y					
gestational age at registration						Y
gestational age at follow-up			Y			
gestational age at delivery		Y				Y
marital status				Y		
infant sex			Y	Y		
total energy intake		Y		Y		

smoking status		Y	Y			Y
alcohol use			Y			
physical activity		Y		Y	Y	
sedentary time						
stress			Y			
preexisting medical disorders						Y

[a] Reasons for selecting covariates: 1 denotes for change in the effect estimates by removing from the multivariable model. 2 denotes for univariate p value. 3 denotes for previous literature. 4 denotes for directed acyclic graphs.

Table S6. Results for sensitivity analyses.

Excessive gestational weight gain	
Overall estimate	0.91 (0.76, 1.10)
Only include high quality studies	0.89 (0.72, 1.08)
Omit one study at a time	ranged from 0.84 (0.61, 1.17) to 0.97 (0.82, 1.14)
Inadequate gestational weight gain	
Overall estimate	0.90 (0.69, 1.18)
Only include high quality studies	0.99 (0.76, 1.29)
Omit one study at a time	ranged from 0.83 (0.64, 1.07) to 0.99 (0.76, 1.29)
GDM	
Overall estimate	0.77 (0.65, 0.90)
Only include high quality studies	0.79 (0.67, 0.93)
Omit one study at a time	ranged from 0.73 (0.60, 0.88) to 0.82 (0.71, 0.94)
HDP	
Overall estimate	0.87 (0.83, 0.92)
Omit one study at a time	ranged from 0.86 (0.81, 0.91) to 0.89 (0.83, 0.95)
Preterm birth	
Overall estimate	0.77 (0.67, 0.89)

Omit one study at a time	ranged from 0.67 (0.56, 0.80) to 0.85 (0.76, 0.94)
SGA	
Overall estimate	0.88 (0.79, 0.99)
Omit one study at a time	ranged from 0.82 (0.62, 1.09) to 0.90 (0.80, 1.00)
Alternately include similar dietary patterns from the same cohort	0.89 (0.82, 0.97)
LBW	
Overall estimate	0.60 (0.37, 0.99)
Omit one study at a time	ranged from 0.53 (0.32, 0.89) to 0.69 (0.44, 1.07)
LGA	
Overall estimate	0.90 (0.71, 1.15)
Omit one study at a time	ranged from 0.81 (0.64, 1.03) to 0.99 (0.82, 1.21)
Alternately include similar dietary patterns from the same cohort	0.84 (0.61, 1.16)
Birth weight as a continuous variable	
Overall estimate	-7.8 (-56.0, 40.5)
Omit one study at a time	ranged from -19.8 (-64.5, 24.8) to 5.8 (-35.8, 47.4)

Table S7-1. Results for subgroup analyses for gestational weight gain.

Characteristics	Excessive gestational weight gain				Inadequate gestational weight gain			
	N	OR (95% CI)	I^2,%	P[a]	N	OR (95% CI)	I^2,%	P[a]
All studies	6	0.91 (0.76, 1.10)	59%		6			
Population				0.75				<0.01
≥1000	4	0.95 (0.80-1.14)	57		4	1.08 (0.83-1.41)	69	
<1000	2	0.83 (0.37-1.86)	76		2	0.60 (0.48-0.75)	0	
Mean age, y				0.04				0.07
≥30	5	0.97 (0.82-1.14)	49		5	0.96 (0.73-1.28)	82	
<30	1	0.56 (0.34-0.93)	-		1	0.57 (0.35-0.94)	-	
Prepregnancy BMI, kg/m2				0.27				0.01
<25	5	0.89 (0.72-1.08)	65		5	0.99 (0.76-1.29)	72	
≥25	1	1.28 (0.69-2.38)	-		1	0.61 (0.47-0.78)	-	
Dietary assessment time				0.61				0.50
1st trimester	1	0.96 (0.76-1.20)	-		1	0.79 (0.57-1.11)	-	
2nd trimester	5	0.87 (0.66-1.15)	67		5	0.93 (0.68-1.28)	84	
Dietary assessment tool				0.75				<0.01
Validated FFQ	4	0.95 (0.80-1.14)	57		4	1.08 (0.83-1.41)	69	

Recall	2	0.83 (0.37-1.86)	76		2	0.60 (0.48-0.75)	0	
Validated diet quality score				0.75				<0.01
Yes	4	0.95 (0.80-1.14)	57		4	1.08 (0.83-1.41)	69	
No	2	0.83 (0.37-1.86)	76		2	0.60 (0.48-0.75)	0	
Adjustment for confounders								
BMI								
Yes	6				6			
No	0				0			
Age				0.01				<0.01
Yes	5	0.96 (0.84-1.09)	34		5	0.83 (0.64-1.07)	79	
No	1	0.28 (0.10-0.74)	-		1	2.22 (1.12-4.43)	-	
Energy				0.54				0.47
Yes	2	0.78 (0.47-1.30)	77		2	0.79 (0.48-1.29)	76	
No	4	0.94 (0.68-1.31)	61		4	1.01 (0.63-1.61)	86	
Parity								
Yes	0				0			
No	6				6			
Education								

Yes	6				6			
No	0				0			
Income				0.19				0.06
Yes	1	1.09 (0.83-1.44)	-		1	1.27 (0.93-1.73)	-	
No	5	0.86 (0.67-1.09)	65		5	0.84 (0.62-1.14)	81	
Smoking				0.9				<0.01
Yes	3	0.90 (0.66-1.24)	71		3	1.23 (0.86-1.76)	76	
No	3	0.88 (0.59-1.30)	59		3	0.66 (0.54-0.79)	0	
Physical activity				0.94				0.10
Yes	3	0.88 (0.62-1.27)	62		3	0.72 (0.49-1.06)	86	
No	3	0.87 (0.58-1.29)	71		3	1.22 (0.75-1.98)	77	

[a] P values for differences between groups

Table S7-1. Results for subgroup analyses for GDM, LGA and birth weight as a continuous outcome.

Characteristics	GDM				LGA				Birth weight as a continuous outcome			
	N	OR (95% CI)	I^2,%	P[a]	N	OR (95% CI)	I^2,%	P[a]	N	OR (95% CI)	I^2,%	P[a]
All studies	7	0.77 (0.65-0.90)	72		6	0.90 (0.71, 1.15)	59		11	-7.8 (-56.0, 40.5)	79	
Study population				>0.99								
Gerneral	5	0.75 (0.62-0.92)	67									
Specific	2	0.75 (0.47-1.21)	83									
n				0.03				0.53				0.79
≥1000	6	0.73 (0.60-0.88)	66		3	0.85 (0.60-1.20)	80		5	-0.5 (-122.4-121.4)	87	
<1000	1	0.93 (0.82-1.05)	-		3	1.00 (0.69-1.46)	2		6	-17.7 (-60.0- 24.6)	66	
Mean age, y				0.15				0.12				0.8
≥30	6	0.74 (0.59-0.91)	74		3	0.94 (0.72-1.23)	59		7	-11.0 (-85.5- 63.6)	83	
<30	1	0.88 (0.78-1.00)	-		2	1.14 (0.72-1.79)	2		2	-29.7 (-79.8- 20.4)	0	
Unknown					1	0.62 (0.40-0.94)			2	15.8 (-123.5-155.0)	91	
Prepregnancy BMI, kg/m2				0.03				0.11				0.28
<25	6	0.73 (0.60-0.88)	66		2	0.97 (0.71-1.31)	74		6	9.8 (-39.9- 59.5)	71	
≥25	1	0.93 (0.82-1.05)	-		2	1.14 (0.72-1.79)	2		2	-68.8 (-757.9-620.2)	96	
Unknown					2	0.65 (0.45-0.93)	0		3	-38.9 (-73.2- -4.6)	0	

Dietary assessment time				0.02				0.06				
Prepregnancy	2	0.74 (0.52-1.06)	90									<0.01
1st trimester	2	0.93 (0.82-1.04)	0		2	0.73 (0.57-0.93)	0		2	15.8 (-123.5- 155.0)	91	
2nd trimester	3	0.66 (0.54-0.81)	0		2	1.05 (0.84-1.32)	16		8	3.2 (-42.2- 48.6)	68	
3rd trimester					2	1.14 (0.72-1.79)	2		1	-422.9 (-634.4- -211.5)	-	
Dietary assessment tool				0.03								
Non-validated FFQ	1	0.93 (0.82-1.05)	-									0.69
Validated FFQ	6	0.73 (0.60-0.88)	66						7	-1.1 (-47.8- 45.7)	73	
Recall									4	-32.7 (-179.8-114.4)	88	
Validated diet quality score				>0.99								<0.01
Yes	5	0.75 (0.62-0.92)	67						10	-19.8 (-64.5- 24.8)	76	
No	2	0.75 (0.47-1.21)	83						1	280.2 (103.6-456.8)	-	
Self-reported outcome				0.84								
Yes	2	0.74 (0.52-1.06)	90		0							
No	5	0.78 (0.62-0.97)	59		6							
Adjustment for confounders												
BMI				0.15								0.96
Yes	6	0.74 (0.59-0.91)	74						7	-7.2 (-76.4-62.1)	84	

No	1	0.88 (0.78-1.00)	-						4	-9.4 (-79.8-60.8)	74	
Age				0.15								
Yes	6	0.74 (0.59-0.91)	74									
No	1	0.88 (0.78-1.00)										
Energy				0.47				0.46				0.08
Yes	3	0.72 (0.56-0.93)	83		5	0.93 (0.70-1.25)	56		8	-34.4 (-86.2- 17.4)	76	
No	4	0.82 (0.64-1.04)	48		1	0.79 (0.59-1.08)			3	89.2 (-40.4-218.7)	87	
Parity				0.94				0.94				0.45
Yes	3	0.77 (0.58-1.02)	81		5	0.90 (0.68-1.18)	67		10	-4.8 (-58.3-48.7)	81	
No	4	0.76 (0.58-0.98)	69		1	0.92 (0.50-1.69)			1	-37.2 (-102.6-28.2)	-	
Education				<0.01				0.04				0.03
Yes	3	0.91 (0.83-0.99)	0		5	0.99 (0.82-1.20)	33		7	31.0 (-26.4-88.5)	74	
No	4	0.64 (0.56-0.73)	0		1	0.62 (0.40-0.94)			4	-72.7 (-145.0--0.4)	77	
Income												
Yes	0				0				0			
No	7				7				11			
Smoking				0.38				<0.01				0.29
Yes	2	0.69 (0.49-0.96)	44		4	1.09 (0.99-1.19)	0		8	3.2 (-42.2-48.6)	68	

No	5	0.81 (0.69-0.94)	60		2	0.73 (0.57-0.93)	0		3	-91.4 (-262.1-79.4)	92	
Physical activity				0.91				0.7				0.56
Yes	3	0.77 (0.58-1.03)	81		3	0.84 (0.54-1.29)	75		4	-28.0 (-56.0--0.1)	0	
No	4	0.76 (0.59-0.98)	69		3	0.93 (0.67-1.29)	26		7	-0.7 (-87.7-86.2)	86	

[a] P values for differences between groups

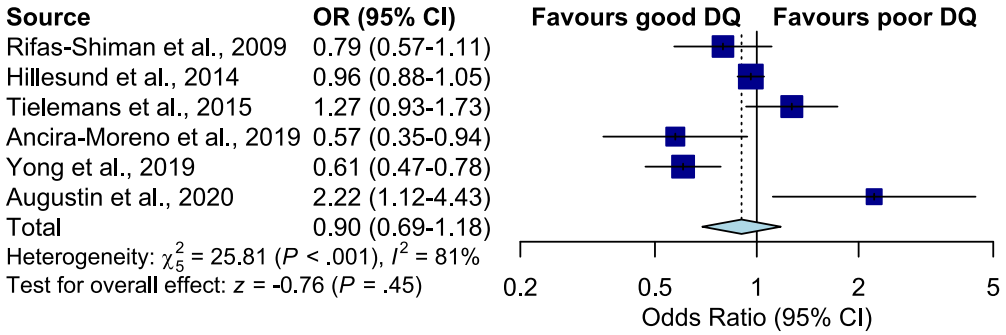


Figure S1. Associations between maternal diet quality and the risk of inadequate gestational weight gain (GWG).

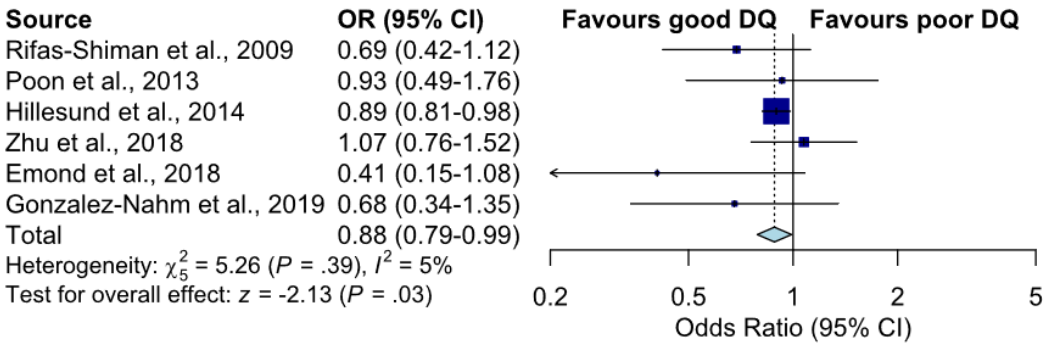


Figure S2. Associations between maternal diet quality and the risk of small for gestational age (SGA).

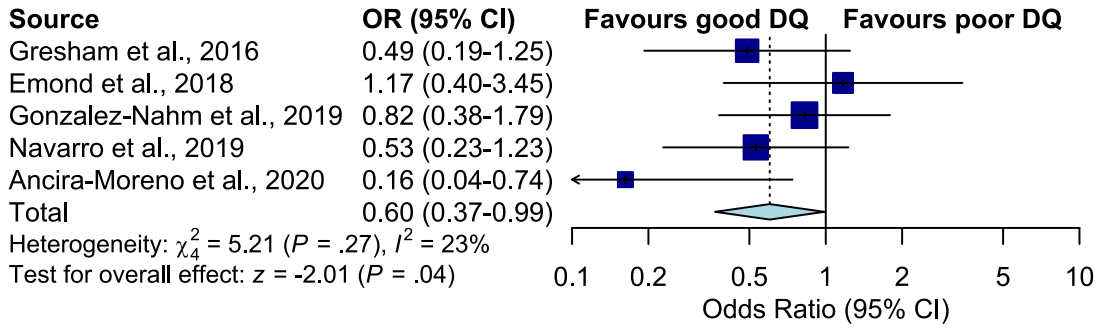


Figure S3. Associations between maternal diet quality and the risk of low birth weight (LBW).

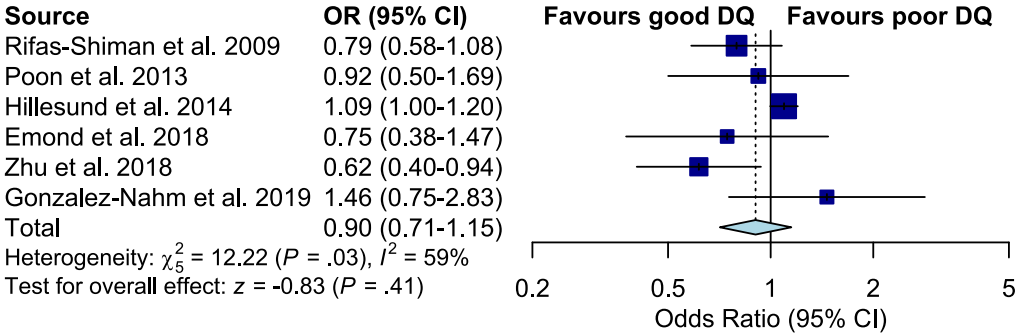


Figure S4. Associations between maternal diet quality and the risk of large for gestational age (LGA).

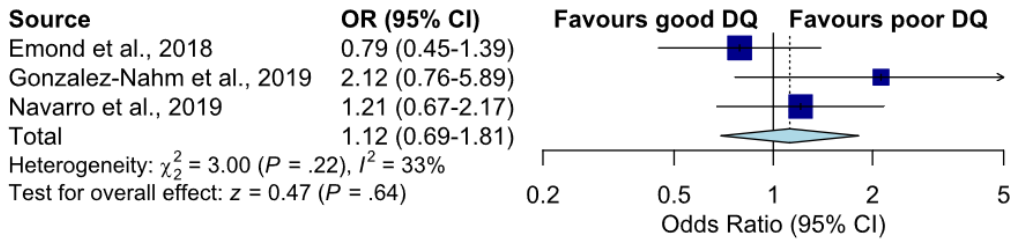


Figure S5. Associations between maternal diet quality and the risk of macrosomia.

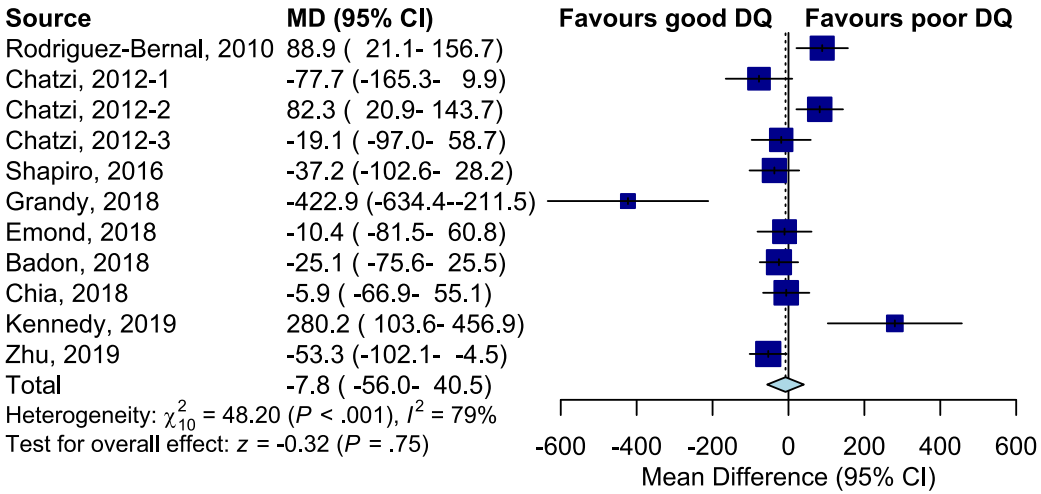


Figure S6. Associations between maternal diet quality and birth weight.

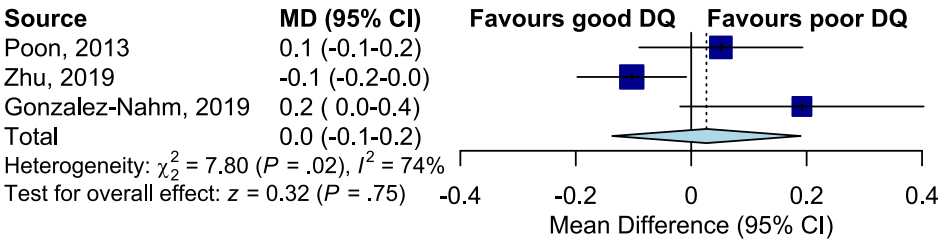


Figure S7. Associations between maternal diet quality and birth weight for gestational age z-score.

CHAPTER 7. MANUSCRIPT 3 - INTERACTION BETWEEN MATERNAL DIET QUALITY AND MULTIVITAMIN INTAKE DURING PREGNANCY ON OFFSPRING NEURODEVELOPMENT AT 2 YEARS OF AGE

Article preface

This manuscript showed that there were statistically significant interactions between diet quality and multivitamin intake in association with cognitive and language development outcomes in the offspring. Therefore, it addressed the fourth objectives of this thesis: 4) To assess the relationships between maternal nutrition during pregnancy and offspring neurodevelopment. YY is the guarantor of the paper. YY, WF and LD designed research; YY, WF, LD, JS, MS, GM, and AM conducted research; YY, CF, WS, and HL analyzed data; YY, JS, HL and IH wrote the paper. YY, WF and LD had primary responsibility for final content. All authors read and approved the final manuscript. Written informed consents were obtained from each participant in the 3D Cohort Study. Ethical approvals of 3D Cohort Study were obtained from the research ethics committee at Sainte-Justine's Hospital in Montreal and all other participating study sites. The Health Sciences and Science Research Ethics Board of the University of Ottawa granted approval for secondary data analyses, including those in this manuscript (file number H-04-21-6908, Approval Date April/05/2021, Appendix 1). The STROBE-nut reporting checklist could be found in Appendix 7.

This manuscript was formatted for submission as an original research article to the journal

American Journal of Clinical Nutrition. The proof for the submission could be found in Appendix 8.

Title Page

Maternal Diet Quality and Multivitamin Intake During Pregnancy Interact in the Association with Offspring Neurodevelopment at 2 Years of Age

Authors and Affiliations

Yamei Yu [1]

Cindy Feng [1,2]

Jean R Seguin [3]

Isabelle S Hardy [4]

Wenguang Sun [5]

Tim Ramsay [1]

Julian Little [1]

Beth Potter [1]

Han Liu [5]

Marie-Noëlle Simard [6]

Gina Muckle [7]

Andrea MacLeod [8]

*William D Fraser [4]

*Lise Dubois [1]

*These two authors contributed equally.

4. School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ontario, Canada
5. Department of Community Health and Epidemiology, Dalhousie University, Halifax, Canada
6. Department of Psychiatry and Addictology, University of Montreal, Montreal, Canada
7. Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Canada
8. The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
9. School of Rehabilitation, University of Montreal, Montreal, Canada
10. School of Psychology, Laval University, Canada
11. Department of Communication Sciences & Disorders, University of Alberta, Edmonton, Canada

Corresponding authors

Dubois, Lise

ldubois@uottawa.ca

School of Epidemiology and Public Health, Faculty of Medicine

University of Ottawa

Fraser, William

William.Fraser@usherbrooke.ca

+1 819 821-8000 poste 12873

Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, and the Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke (CRCHUS)

Financial Support: This research project is sponsored jointly by the Canadian Institutes of Health Research (CIHR) (Grant CRI 88413, MOP 133422 and HLT 151517) and the National Natural Sciences Foundation of China (NSFC) (Grant No. 81661128010). The sponsors had no role in the design, execution, interpretation, or writing of the study.

Acknowledgements: The authors would like to acknowledge all the participants and the study team members who contributed to this study.

Data Sharing: Data is available from the 3D Cohort Study committee upon request and approvement.

Conflict of Interest: All authors declare no conflict of interest in conducting this work.

Running title: Maternal nutrition and offspring neurodevelopment

Abbreviations:

Bayley III, Bayley Scales of Infant and Toddler Development, 3rd edition;

BMI, Body mass index;

CI, confidence interval;

DAG, directed acyclic graph;

HEI-C, Canadian adaptation of the Healthy Eating Index;

MCDI, MacArthur-Bates Communicative Development Inventories;

MML, maternal medication logs;

RCT, randomized controlled trial

SD, standard deviations;

VIF, Variance inflation factor;

WHO, World Health Organization.

Abstract

Background

Nutrition during pregnancy is associated with neurodevelopmental outcomes in the offspring, but few studies have investigated the potential interaction between diet quality and multivitamin intake.

Objectives

To evaluate the interaction between diet quality and multivitamin intake during pregnancy on offspring neurodevelopment.

Methods

This analysis included 1534 mother-child dyads from the 3D Cohort Study (Quebec, Canada). Dietary information was collected using a 3-day food record in the second trimester of pregnancy. Diet quality was measured with the Canadian adaptation of the Healthy Eating Index (HEI-C) 2010 and was categorized as low or high compared to the median. Multivitamin intake in pregnancy was recorded as a dichotomous outcome based on the maternal medication log. At 24 months, children's cognitive, motor and language development were measured using validated assessments. Multiple linear regressions were used for the analysis.

Results

There were statistically significant interactions between diet quality and multivitamin intake in association with cognitive and language development outcomes in the offspring (p for interactions = 0.018 and 0.023, respectively). The cognitive and language scores were lowest in the children born to the group of women who did not take multivitamins and had a low diet quality. Among

women who did not take multivitamins, high diet quality was associated with better offspring cognitive and language scores (mean difference [95% CI] = 4.2 [0.1, 8.2], p=0.04; and 11.3 [3.1, 19.5], p=0.01, respectively). Among women who took multivitamins, no such associations were found. On the other hand, taking multivitamins was associated with 3.0 (95% CI: 0.3 to 5.8, p=0.03) points higher cognitive composite scores in participants who had a low diet quality, but not in those with a high diet quality.

Conclusions

Adequate nutrition supply, through high quality diet or multivitamin use, are key contributors to the healthy neurodevelopment of children.

Keywords: birth cohort; maternal diet during pregnancy; early-life nutrition; prenatal nutrition; multivitamins; Healthy Eating Index; childhood cognition; cognitive development; early development; language development; neurodevelopment

Introduction

The first 1,000 days of life, which include pregnancy and two years postpartum, is a time when the brain forms and develops rapidly and lays the foundation of neurodevelopment. During this crucial early stage, proliferation, migration, aggregation, and myelination of the neurons forms the architecture of the brain and provide the foundation for cognitive, motor, and language functions later in life [1]. Particularly, throughout the third trimester, the structure of the brain changes from a smooth bilobed shape to a more complex one with gyrations and sulcations that resembles the adult brain [2,3]. The early period of neurodevelopment represents a time of great opportunity and vulnerability for future educational attainment and participation in community activities of the children at the individual level, and for the overall development and economic growth for the human at the population level [4].

Proper nutrition during pregnancy provides fundamental building blocks for the developing brain [5,6]. The brain is vulnerable to damage if the nutrients required to support its growth are insufficient [7]. Research from the great Dutch famine found smaller brain volume and perfusion after several decades in those exposed to the famine in utero [8,9]. In addition to energy and macronutrients deficiency characterized in the famine, micronutrients, including zinc, iron, choline, B-vitamins and iodine, were also found to be essential for brain growth [10].

Pregnant women generally get essential nutrients through a good quality diet or multivitamin supplements when the supply from diet is not optimal [11,12]. Diet quality can be assessed by measuring compliance with dietary guidelines [13,14]. Despite increasing interest in the associations

between maternal diet quality during pregnancy and childhood neurodevelopment, to date, there were few studies quantifying this association directly [15,16]. Most previous studies used components of a good quality diet, such as fish, seafood, fruit intake, certain nutrients, or data-driven dietary pattern as an approximate for diet quality [15]. One recent U.S. cohort study found that higher diet quality scores during pregnancy were associated with better cognition in the offspring [17]. On the other hand, interventional studies using multivitamin supplementation did not demonstrate positive effects in improving offspring neurodevelopment [16]. The discrepancy between these results and findings of the Dutch famine studies could possibly be explained by a modifying effect of diet quality on the association between multivitamin intake and neurodevelopment, since both diet and multivitamins provide nutrients during pregnancy. However, no studies have measured the potential interaction between the two exposures.

The objective of this paper is to evaluate diet quality and multivitamin intake during pregnancy, and their interactions, in relation to neurodevelopment outcomes in the offspring.

Methods

Design, Setting, and Participants

This study included 1534 pregnant women enrolled in the 3D Prospective Cohort Study in Quebec, Canada, for which information on dietary intake and use of multivitamins in pregnancy was available. The protocol of this study and the methods used for dietary data collection and processing have been described in detail elsewhere[18-20]. Between 2010 and 2012, 2366 pregnant women from the province of Quebec were recruited in the first trimester of pregnancy. Extensive interviews were conducted in the first, second, and third trimester of pregnancy, and postpartum at 3 months, 1 year, and 2 years. All participants signed written informed consents. The Health Sciences and Science Research Ethics Board of the University of Ottawa, and the research ethics committee at Sainte-Justine Hospital in Montreal and all other participating study sites provided ethical approvals for this study.

Exposures and Measurements

Women were asked to complete a 3-day food record between 20 and 24 weeks of gestation. Using the dietary information obtained from the 3-day food records, a Canadian adaptation of the Healthy Eating Index (HEI-C) 2010 was used to quantify diet quality. The HEI-C measures compliance with the Canadian Food Guide recommendations[21] by scoring intakes of eight foods that should be consumed in adequate amounts, and three that should be consumed in moderate amounts, resulting in a total (maximum) score of 100 [14]. This Index has been validated for use in the general adult population[14] and in the pregnant women of this study (data not shown). Details

of the methods used to code data and food groups for the nutritional analysis of the 3D Cohort Study has been described elsewhere [22]. Briefly, the energy, macronutrients, and micronutrients of each food item were compiled by trained nutritionists using the Food Processor software (ESHA Research, Inc., Salem), which was linked to the Canadian Nutrient File [23]. Food items were also classified into four food groups and 30 sub-groups using the food Classification system developed by Health Canada [24]. Mixed dishes were decomposed into food group servings according to the Food Patterns Equivalents Database developed by U.S. Department of Agriculture [25]. This information was used to calculate the scores for each component of the HEI-C, which were compiled to obtain the total HEI-C sore. The total HEI-C score was further dichotomized into low and high diet quality by median split.

Multivitamin supplement intake was captured using the maternal medication logs (MML) administered by research nurses during study visits in each trimester of pregnancy and at delivery. The nutritional information of each multivitamin was confirmed by trained nutritionists using Health Canada's Licensed Natural Health Products Database[26] and each companies' product label and website. For this study, use of multivitamins in pregnancy was considered as a dichotomous variable based on the information stated in the MML of either "did not take multivitamins" or "took multivitamins".

Outcomes and Measurements

Neurodevelopmental assessments were performed on the children at around two years of age by trained research personnel who were unaware of the exposures of this study and covariate

information. Cognitive and motor (fine and gross) scales of childhood development were assessed using the Bayley Scales of Infant and Toddler Development, 3rd edition (Bayley III scale). The Bayley III is a validated and standardized developmental assessment for children aged 1–42 months with established test–retest reliability, internal consistency as well as convergent and divergent validity [27,28]. Each scale consists of a series of developmental play tasks. The cognitive scale assesses cognitive processes like memory, exploration, manipulation, and sensorimotor development. The motor scale evaluates the quality of movement, sensory integration, perceptual–motor integration, prehension, and other milestones. Scale-specific raw scores were converted to scaled scores and to composite scores according to the score distribution in normally developed children of the same age. For the fine and gross motor subtests, only scaled scores were available. Means were set at 10 and 100 with a standard deviation of 3 and 15 for the scaled scores (fine and gross motor) and the composite scores (cognitive, motor), respectively.

To measure language abilities, this study focused on early word production via a standard parent-report task. Specifically, the toddler short-form versions of MacArthur-Bates Communicative Development Inventories (MCDI) questionnaire administered either in English or French were used [29,30]. This questionnaire is a 100-word checklist that focuses on words commonly used in the lives of young children. Parents were asked to identify the words on the list that their child says, even if the pronunciation does not match the adult target. The English MacArthur-Bates toddler short form has established reliability as well as content and concurrent validity. A French

version of the short form has been adapted for French-speaking children in Québec using the approach described by Fenson et al [29,31].

Statistical Analyses

Means and standard deviations (SD) of the neurodevelopment scores were calculated. Univariate and multiple linear regression models were used to calculate crude and adjusted effect estimates and confidence intervals (CIs). Interaction on an additive scale was assessed by adding a product term to the linear regression model [32]. Variance inflation factors (VIFs) were used to test for multicollinearity in multiple linear regression models. No multicollinearity was observed in the models using a cut-off VIF value of 10. A directed acyclic graph (DAG, Supplementary Figure 1) was used to select potential confounding variables in the adjusted model to estimate the association between maternal nutrition during pregnancy and neurodevelopment outcomes of the children ('total effect') [33]. As a sensitivity analysis, multiple imputation according to the Markov chain Monte Carlo method was used to imputing missing information in covariates and outcomes by creating and pooling 20 imputed data sets for analyses based on "missing at random" assumption [34].

All statistical analyses were performed using Statistical Analysis System software version 9.4 (SAS v9.4; SAS Institute Inc., Cary, NC, USA). A two-sided $p < 0.05$ was set as the level of statistical significance. For interaction terms statistically significance, an alpha level of 0.10 was considered.

Results

Out of 2366 participants enrolled in the 3D Cohort Study, 1535 women completed the 3-day food record and were eligible for study inclusion. One additional participant was excluded due to missing information on multivitamin consumption in pregnancy, leaving 1534 mothers for inclusion in analysis (full sample). Compared with participants with low diet quality, participants with high diet quality were older, more likely to have completed university studies, and had higher household income. They were also less likely to be overweight or obese and to smoke. Participants who took multivitamins and those who did not had comparable characteristics, with the exception of tobacco use. The proportion of participants who reported smoking in pregnancy was higher in participants not taking multivitamins (20.5% vs 12.5%) (Table 1).

Table 1. Participant characteristics according to diet quality and multivitamins intake. (n=1534)

Characteristics	Low diet quality	High diet quality	Not taking multivitamins	Taking multivitamins
	n (%)	n (%)	n (%)	n (%)
Total	767	767	161	1373
Mother's age				
<25	61 (8)	24 (3.1)	11 (6.8)	74 (5.4)
25–<35	563 (73.6)	565 (73.8)	116 (72)	1012 (73.9)
≥35	141 (18.4)	177 (23.1)	34 (21.1)	284 (20.7)
Maternal education				
Secondary school or less	65 (8.5)	29 (3.8)	12 (7.5)	82 (6)
College	231 (30.4)	159 (20.8)	37 (23)	353 (25.9)
Undergraduate university degree	298 (39.2)	330 (43.3)	69 (42.9)	559 (41)
Graduate university studies	167 (21.9)	245 (32.1)	43 (26.7)	369 (27.1)
Household income (CAD)				
<30 000	65 (8.8)	51 (6.9)	14 (9)	102 (7.7)
30,000–59,999	141 (19)	113 (15.3)	38 (24.4)	216 (16.3)
60,000–79,999	150 (20.2)	112 (15.2)	24 (15.4)	238 (18)
80,000–99,999	167 (22.5)	165 (22.4)	31 (19.9)	301 (22.8)
≥100 000	219 (29.5)	296 (40.2)	49 (31.4)	466 (35.2)
Marital status				
Married	306 (39.9)	308 (40.2)	65 (40.4)	549 (40)
Common law/partner	420 (54.8)	435 (56.7)	90 (55.9)	765 (55.8)
Others	40 (5.2)	24 (3.1)	6 (3.7)	58 (4.2)
Prepregnancy BMI				
underweight < 18.5	36 (4.9)	54 (7.4)	10 (6.5)	80 (6.1)
nomral weight 18.5 - 24.9	442 (60.5)	511 (70.4)	98 (63.6)	855 (65.6)

overweight 25 -29.9	143 (19.6)	102 (14)	30 (19.5)	215 (16.5)
obese ≥30	110 (15)	59 (8.1)	16 (10.4)	153 (11.7)
Parity				
0	408 (53.2)	482 (62.8)	89 (55.3)	801 (58.3)
≥1	359 (46.8)	285 (37.2)	72 (44.7)	572 (41.7)
Mother born in Canada				
No	217 (28.4)	217 (28.3)	53 (32.9)	381 (27.8)
Yes	548 (71.6)	550 (71.7)	108 (67.1)	990 (72.2)
Mother white				
No	152 (19.9)	153 (20)	30 (18.8)	275 (20.1)
Yes	613 (80.1)	613 (80)	130 (81.3)	1096 (79.9)
Smoking during pregnancy				
No	646 (84.3)	681 (89)	128 (79.5)	1199 (87.5)
Yes	120 (15.7)	84 (11)	33 (20.5)	171 (12.5)
Sex of the child				
Female	391 (51.4)	368 (48)	77 (48.4)	682 (49.9)
Male	369 (48.6)	398 (52)	82 (51.6)	685 (50.1)

Cognitive, motor, and language development scores at 2 years of age were available for 1182, 1134 and 1108 children, respectively. After excluding participants with missing data on covariates, 1066, 1040, and 981 remained respectively for complete case analysis. (Figure 1) The characteristics of participants for complete case analysis were very similar to those in the full sample (Supplementary Table 1).

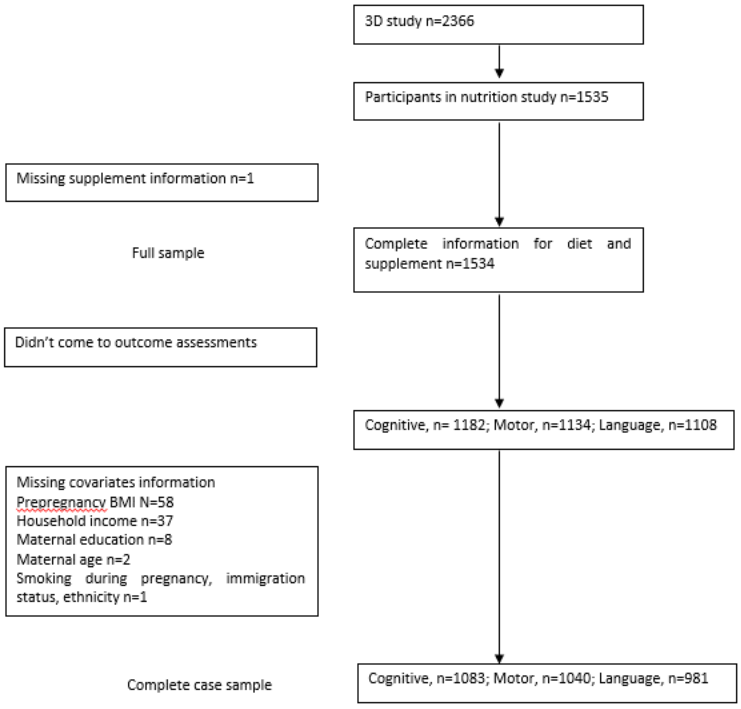


Figure 1. Flow chart for study participants.

As shown in Table 2, there were statistically significant interactions between diet quality and multivitamin intake during pregnancy for the outcome of cognitive development of children at 2 years of age measured by Bayley III (P for interaction = 0.007 and 0.018, respectively, in unadjusted and adjusted models). In the unadjusted model, the lowest cognitive composite scores (mean[SD] = 96.9[11.4]) were found in the group with low diet quality and no intake of multivitamins. It is lower than that in the other three groups: the group with high diet quality and no intake of multivitamins (mean[SD] = 102.8(11.4); mean difference [95% CI] = 5.9 [1.7,10.1], P=0.01), the group with low diet quality and intake of multivitamins (mean[SD] = 102.8[11.4]; mean difference [95% CI] = 4.0 [1.2,6.9], P=0.01), and the group with high diet quality with intake of multivitamins (mean[SD] = 100.6[11.4]; mean difference [95% CI] = 3.7 [0.9,6.6], P=0.01). Having a high diet quality during pregnancy was significantly associated with higher cognitive composite scores in the offspring among women who did not take multivitamins during pregnancy (mean difference [95% CI] = 5.9 [1.7,10.1], P=0.01), but not among women who took multivitamins (mean difference [95% CI] = 0.3 [-1.1,1.7], P=0.70). Similarly, taking multivitamins during pregnancy was associated with higher cognitive composite scores in the offspring among women who had a low diet quality during pregnancy (mean difference [95% CI] = 4 [1.2,6.9], P=0.01), but not in those who had a high diet quality during pregnancy (mean difference [95% CI] =-2.1 [-5.5,1.3], P=0.22). These associations persisted after adjusting for multiple potential confounding variables including maternal characteristics including age, energy intake, prepregnancy body mass index (BMI), education, smoking, marital status, immigration status, ethnicity, parity, family income, and children's characteristics including biological sex

and age at neurodevelopment measurement. However, the mean differences became slightly smaller. In adjusted models, the mean difference of cognitive composite scores between those with high vs. low diet quality was 4.2 (95% CI, 0.1, 8.2; P=0.04) for participants who did not take multivitamins during pregnancy. The mean difference of cognitive composite scores between those who took multivitamins vs. who did not take multivitamins was 3.0 (95% CI, 0.3, 5.8; P=0.03) for participants with a low diet quality during pregnancy.

Similarly, there were statistically significant interactions between diet quality and multivitamin intake during pregnancy for the outcome of language development of children at 2 years of age (P for interaction = 0.008 and 0.023, respectively, in unadjusted and adjusted models). In adjusted models, among women who did not take multivitamins during pregnancy, the MacArthur-Bates language score was 11.3 points (95% CI, 3.1,19.5; P=0.01) higher in the children of women with a high diet quality in pregnancy, compared with the children of women with a low diet quality. Among women who had a low diet quality during pregnancy, the difference in MacArthur-Bates language scores of offspring between those who took multivitamins vs. who did not take multivitamins was no longer statistically significant after adjustment.

Table 2. Interaction between diet quality and multivitamins intake during pregnancy on cognitive and language development of children at 2 years of age.

	Not taking multivitamins		Taking multivitamins		MD(95% CI) for multivitamins within strata of diet quality	p for interaction
	Mean(SD), n	MD(95% CI), p	Mean(SD), n	MD(95% CI), p		
Cognitive, unadjusted						0.007
Low diet quality	96.9(11.4), 69	Reference	100.9(11.4), 476	**4(1.2,6.9), P=0.01**	**4(1.2,6.9), P=0.01**	
High diet quality	102.8(11.4), 47	**5.9(1.7,10.1), P=0.01**	100.6(11.4), 491	**3.7(0.9,6.6), P=0.01**	-2.1(-5.5,1.3), P=0.22	
MD (95% CI) for diet quality within strata of multivitamins		**5.9(1.7,10.1), P=0.01**		0.3(-1.1,1.7), P=0.7		
Cognitive, adjusted [1]						0.018
Low diet quality	94.9(13.3), 69	Reference	97.9(22.3), 476	**3(0.3,5.8), P=0.03**	**3(0.3,5.8), P=0.03**	
High diet quality	99(12.5), 47	**4.2(0.1,8.2), P=0.04**	96.9(23.8), 491	2(-0.7,4.8), P=0.15	-2.1(-5.4,1.1), P=0.19	
MD (95% CI) for diet quality within strata of multivitamins		**4.2(0.1,8.2), P=0.04**		-1(-2.4,0.4), P=0.16		
Language, unadjusted						0.008
Low diet quality	47.3(23.2), 64	Reference	54.6(23.2), 434	**7.3(1.2,13.4), P=0.02**	**7.3(1.2,13.4), P=0.02**	
High diet quality	61.9(23.2), 42	**14.6(5.6,23.6), P=0**	56.2(23.2), 441	**8.9(2.8,15), P=0**	**-5.7(-13,1.6), P=0.02**	
MD (95% CI) for diet quality within strata of multivitamins		**14.6(5.6,23.6), P=0**		1.6(-1.5,4.7), P=0.31		
Language, adjusted [1]						0.023
Low diet quality	43.9(26.1), 64	Reference	48.8(45), 434	4.9(-0.7,10.4), P=0.09	4.9(-0.7,10.4), P=0.09	

High diet quality	55.2(24.8), 42	**11.3(3.1,19.5), P=0.01**	50(47.8), 441	**6.1(0.5,11.7), P=0.03**	-5.2(-11.9,1.5), P=0.13
MD (95% CI) for diet quality within strata of multivitamins		**11.3(3.1,19.5), P=0.01**		1.2(-1.6,4.1), P=0.39	

MD: Mean difference, denoting for the regression coefficient in the linear regression model.

[1] Adjusted for maternal characteristics including age, energy intake, prepregnancy body mass index (BMI), education, smoking, marital status, immigration status, ethnicity, parity, family income, and children's characteristics including biological sex and age at neurodevelopment measurement.

As shown in table 3, after adjustment, there were no statistically significant interactions between diet quality and multivitamin intake during pregnancy on motor development outcomes of children at 2 years of age.

Table 3. Interaction between diet quality and multivitamins intake during pregnancy on motor development of children at 2 years of age.

	No multivitamins		Took multivitamins		MD(95% CI) for multivitamins within strata of diet quality	P for interaction
	Mean(SD), n	MD(95% CI), P	Mean(SD), n	MD(95% CI), P		
Fine motor, unadjusted						0.04
Low diet quality	11.3(2.6), 65	Reference	11.6(2.6), 464	0.3(-0.4,1), P=0.34	0.3(-0.4,1), P=0.34	
High diet quality	12.3(2.6), 44	1(-0.1,2), P=0.06	11.5(2.6), 467	0.2(-0.5,0.9), P=0.63	-0.8(-1.6,0), P=0.06	
MD(95% CI) for diet quality within strata of multivitamins		1(-0.1,2), P=0.06		-0.2(-0.5,0.2), P=0.34		
Fine motor, adjusted [1]						0.17
Low diet quality	11.2(3.2), 65	Reference	11.3(5.4), 464	0.2(-0.5,0.8), P=0.62	0.2(-0.5,0.8), P=0.62	
High diet quality	11.7(3), 44	0.5(-0.5,1.5), P=0.31	11.1(5.7), 467	-0.1(-0.7,0.6), P=0.88	-0.6(-1.4,0.2), P=0.17	
MD(95% CI) for diet quality within strata of multivitamins		0.5(-0.5,1.5), P=0.31		-0.2(-0.6,0.1), P=0.2		
Gros motor, unadjusted						0.112
Low diet quality	9(2.3), 65	Reference	8.9(2.3), 464	-0.2(-0.7,0.4), P=0.6	-0.2(-0.7,0.4), P=0.6	
High diet quality	9.8(2.3), 44	0.7(-0.1,1.6), P=0.09	8.9(2.3), 467	0.7(-0.2,1.7), P=0.11	**-0.9(-1.6,-0.2), P=0.01**	
MD(95% CI) for diet quality within strata of multivitamins		0.7(-0.1,1.6), P=0.09		0(-0.3,0.3), P=0.98		
Gros motor, adjusted [1]						0.163
Low diet quality	9(2.8), 65	Reference	8.8(4.7), 464	-0.2(-0.8,0.4), P=0.43	-0.2(-0.8,0.4), P=0.43	
High diet quality	9.7(2.6), 44	0.7(-0.2,1.5), P=0.13	8.8(4.9), 467	-0.2(-0.8,0.4), P=0.49	-0.9(-1.6,-0.2), P=0.01	

MD(95% CI) for diet quality within strata of multivitamins	**0.7(-0.2,1.5), P=0.13**	0(-0.3,0.3), P=0.87

MD: Mean difference, denoting for the regression coefficient in the linear regression model.

[1] Adjusted for maternal characteristics including age, energy intake, prepregnancy body mass index (BMI), education, smoking, marital status, immigration status, ethnicity, parity, family income, and children's characteristics including biological sex and age at neurodevelopment measurement.

In the sensitivity analyses imputing for missing values in covariates and neurodevelopment outcomes, we found similar trends. (P for interaction = 0.025 and 0.019, respectively, in unadjusted and adjusted models for cognitive development; P for interaction = 0.028 and 0.063, respectively, in unadjusted and adjusted models for language development)

Discussion

The results of this study demonstrate that there is a significant interaction between diet quality and multivitamin intake in pregnancy in the association with the cognitive and language development of children at 2 years of age. High diet quality during pregnancy was associated with better cognitive and language development in the offspring among women who did not take multivitamins. No such associations were found in those who took multivitamins. Similarly, taking multivitamins during pregnancy was associated with better cognitive development in the offspring among women with low diet quality. No such associations were found among those with a higher diet quality. The lowest cognitive and language development were observed in the group of children whose mother ate a lower quality diet and did not take multivitamins during pregnancy. This group of women were lacking in the quality of nutrition supply from food and supplement sources compared to those in the other three groups (Supplementary Table 2). To our knowledge, no previous studies have reported this interaction.

Assuming a causal relationship, several mechanisms could explain the association between early nutrition and children's neurodevelopment ('total effect'). First, high quality nutrition directly provides nutrients that work as fundamental building blocks for brain growth and development ('direct effect') [5,6]. Animal studies have shown that maternal diets deficient in micronutrients could lead to hippocampal learning deficits [35], which can adversely impact several abilities

(which would include cognition and language in human) [36]. Second, the relationship between the quality of nutrition during pregnancy and offspring neurodevelopment could be mediated by birth weight, preterm birth or by children's diet ('indirect effect', see Supplementary Figure1). Indeed, micronutrient supplementation in pregnancy has been associated with a small reduction of the rates of preterm birth, small for gestational age, and low birth weight [37]. Maternal diet quality is correlated with the diet quality of their children [38]. A combination of improved perinatal outcomes and better diet quality during childhood could also partly explain the association between adequate nutrition during pregnancy and improved offspring neurodevelopment [39]. A mediation analysis could help to determine the contribution of each pathway in a potential causal relationship [40]. However, insufficient power precluded us from performing mediation analysis in the study sample due to the small portion of pregnant women who did not take multivitamins. Therefore, this study only provides estimates of the global association between prenatal nutrition and offspring neurodevelopment ('total effect').

The results of this study suggest that providing multivitamin supplementation or improving diet quality in women with a good nutritional status, might not impact neurodevelopment outcomes. This concurs with the results from a multivitamin supplementation study in Indonesia[41]. Although there were no effects in the overall study population, among undernourished women, children in the multivitamin group showed better cognitive abilities than in the control group. In

a double-blind, randomized, controlled trial in rural China, multivitamin supplementation led to a 1.2 point increase in the mental development scales of the BSID (2nd version) of children reported at 1 year of age[42]. A very limited number of studies have evaluated the effect of multivitamin supplementation and diet quality interventions in pregnancy on offspring neurodevelopment thus far [16]. More studies on this question are needed and should include an evaluation of the baseline nutrition status of the population.

The World Health Organization (WHO) currently recommends iron and folic acid supplementation for women during pregnancy as part of routine antenatal care. However, multivitamin supplementation has not been recommended. Despite Health Canada's recommendation of daily multivitamins supplements and the provision of free multivitamins for low-income pregnant women as part of the OLO program in the province of Quebec, 10.5% of the women in this cohort did not take any multivitamins during pregnancy. This is particularly concerning as our study showed that taking multivitamins might mitigate the potential harm of nutrient deficiency on offspring neurodevelopment in women with a poor diet. Future studies evaluating the barriers to multivitamin use in pregnancy are needed to inform targeted interventions in women with low diet quality at the start of pregnancy.

Our study has several strengths. Most previous studies on this topic evaluated exposure to single nutrients including zinc, iron, choline, B-vitamins and iodine [10,43]. It is worth noting that nutrient deficiencies rarely occur individually during pregnancy [44], and most RCTs of single nutrient supplementation did not identify beneficial effects [16]. The use of the Healthy Eating Index as a measurement of overall diet quality in this study makes it more relevant for the design of public health interventions than studies that measure single nutrient. Although the percentage of women not taking multivitamins in this study is low, the high quality and large sample of the cohort provided sufficient power to conduct analyses with a large set of covariates. Furthermore, the 3-day food records dietary assessment method used in this study is recognized as one of the most accurate tools for dietary assessment and is less prone to memory biases than food frequency questionnaires or 24-hour recalls [45,46].

Our study also has several limitations. Although we identified potential confounding variables using DAG, causal relationship cannot be established in an observational study. Further interventional studies such as RCTs are needed to strengthen the argument for causality. Participants with missing information in the covariates were excluded in the main analysis, which could possibly lead to selection bias. However, our sensitivity analysis using multiple imputation generated similar trends, indicating that the risk of selection bias is low. Although the exposures and outcomes were measured with validated tools, misclassification remains possible

owing to the difficulty of measuring diet and neurodevelopment. Research personnel who conducted the measurements of neurodevelopment were blinded to the exposure or other background information of the children and family. As a result, the misclassification is more likely to be nondifferential across exposure groups and would bias effect estimates towards the null hypothesis [47]. The distribution of our study population was skewed towards that of an older high socio-economic status group and is not a representative sample of the population of Canadian pregnant women [18,22]. However, a previous study showed that the effect of selection bias due to the higher socioeconomic status on exposure–outcome associations could be limited [48]. Lastly, our study only captures diet in the second/third trimester of the pregnancy. However, other studies have shown that diet quality changes little across trimesters[49,50].

Conclusion

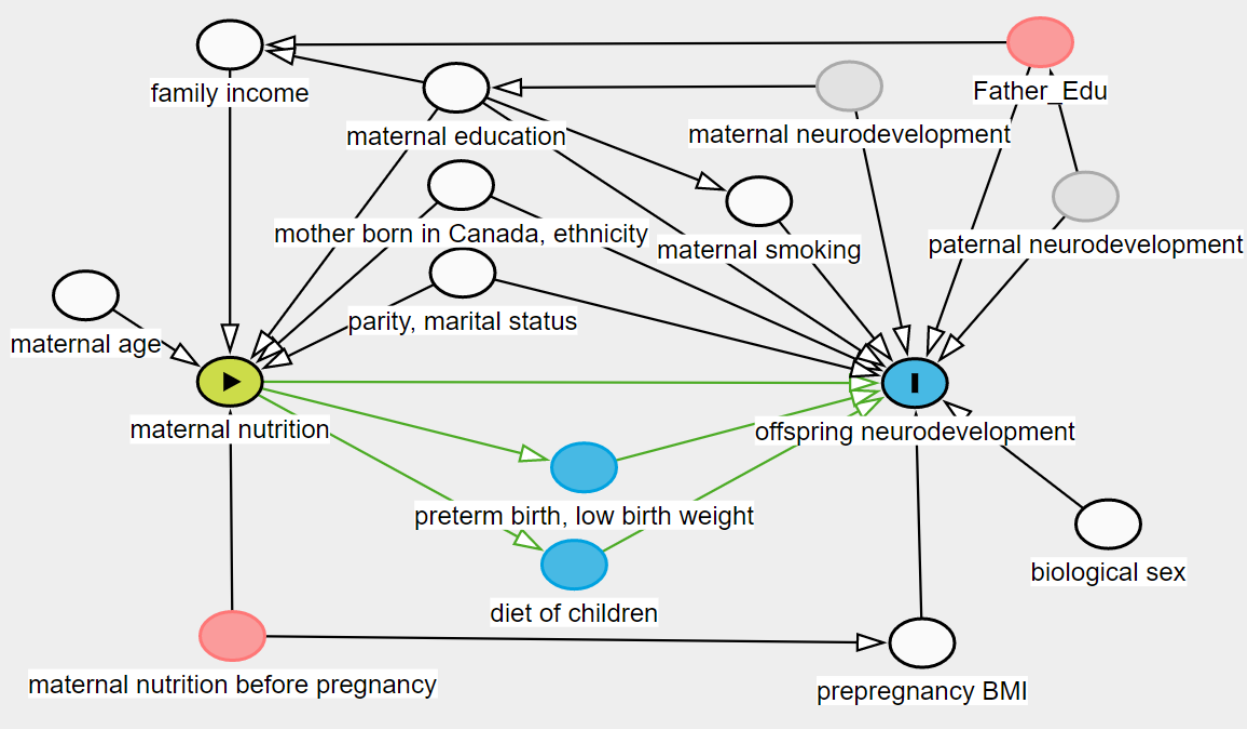
There is a statistically significant interaction between diet quality and multivitamins intake during pregnancy in association with cognitive and language development of children at 2 years of age. The efforts to improve offspring neurodevelopment outcomes through nutritional intervention should specifically target women with poor diet quality and not taking multivitamins.

Supplementary Materials

Interaction between maternal diet quality and multivitamin intake during pregnancy on offspring neurodevelopment at 2 years of age

Yamei Yu et al.

Supplementary Figure 1 Directed acyclic graph (DAG) used to determine minimal sufficient adjustment sets to estimate the association between maternal nutrition and offspring neurodevelopment ('total effect').



Legend: = exposure; = outcome; = ancestor of outcome; = ancestor of exposure and outcome; = adjusted variables; = unobserved variables; = causal path. Minimal sufficient adjustment sets used to estimate the total effect of maternal nutrition on offspring neurodevelopment include biological sex, family income, maternal age, maternal education, maternal smoking, mother born in Canada, ethnicity, parity, marital status, and

prepregnancy BMI . The relationship between proper nutrition during pregnancy and offspring neurodevelopment could be mediated by birth weight, preterm birth or by children's diet ('indirect effect').

Supplementary Table 1. Participant characteristics in the full sample [1] and in complete case sample [2] for cognitive and motor development [1].

	Complete case sample [1]	Full sample
Characteristics	n (%)	n (%)
Total	1083	1534
Mother's age		
<25	54 (5)	85 (5.6)
25–<35	812 (75)	1128 (73.7)
≥35	217 (20)	318 (20.8)
Maternal education		
Secondary school or less	54 (5)	94 (6.2)
College	260 (24)	390 (25.6)
Undergraduate university degree	467 (43.1)	628 (41.2)
Graduate university studies	302 (27.9)	412 (27)
Household income (CAD)		
<30 000	67 (6.2)	116 (7.8)
30,000–59,999	174 (16.1)	254 (17.2)
60,000–79,999	189 (17.5)	262 (17.7)
80,000–99,999	254 (23.5)	332 (22.4)
≥100 000	399 (36.8)	515 (34.8)
Marital status		
Married	418 (38.6)	614 (40.1)
Common law/partner	626 (57.8)	855 (55.8)
Others	39 (3.6)	64 (4.2)
Prepregnancy BMI		
underweight < 18.5	64 (5.9)	90 (6.2)
nomral weight 18.5 - 24.9	707 (65.3)	953 (65.4)
overweight 25 -29.9	189 (17.5)	245 (16.8)
obese ≥30	123 (11.4)	169 (11.6)
Parity		
0	634 (58.5)	890 (58)
≥1	449 (41.5)	644 (42)
Mother born in Canada		
No	260 (24)	434 (28.3)
Yes	823 (76)	1098 (71.7)
Mother white		
No	177 (16.3)	305 (19.9)
Yes	906 (83.7)	1226 (80.1)

Smoking during pregnancy		
No	947 (87.4)	1327 (86.7)
Yes	136 (12.6)	204 (13.3)
Sex of the child		
Female	543 (50.1)	759 (49.7)
Male	540 (49.9)	767 (50.3)

[1] Full sample is the sample with information on diet and supplement.

[2] Complete case sample is the sample with complete data on diet quality, supplement intake, cognitive and motor scores and all the covariates.

Supplementary Table 2. Mean (SD) intake of selected nutrients for the participants from food and supplement sources.

	Mean(SD)			
Nutrients	Lower HEI, no multivitamins	Higher HEI, no multivitamins	Lower HEI, took multivitamins	Higher HEI, took multivitamins
N	94	67	673	700
Iron (mg)	18.41 (17.52)	26.39 (30.48)	45.77 (22.28)	48.46 (24.16)
Zinc (mg)	11.07 (3.37)	11.61 (2.65)	19.81 (5.01)	21.2 (5.23)
Vitamin A in RAE(μg) [1]	776.76 (292.67)	984.8 (921.11)	1756.51 (732.27)	1893.13 (574.66)
Vitamin B1 (mg)	1.88 (0.67)	3.33 (12.22)	3.76 (3.17)	3.78 (2.21)
Vitamin B2 (mg)	2.27 (0.67)	2.19 (0.52)	4.19 (3.16)	4.28 (2.28)
Vitamin B3 (mg)	20.99 (5.88)	22.07 (4.76)	38.59 (7.65)	40.67 (7.83)
Vitamin B6 (mg)	3.48 (12.8)	1.98 (0.45)	5.69 (6.11)	6.17 (5.13)
Vitamin B12 (μg)	8.78 (29.75)	5.77 (4.03)	12.64 (49.86)	11.48 (19.58)
Folate (μg)	1185.47 (1470.29)	1283.24 (1341.53)	1783.52 (1343.87)	1900.39 (1397.05)
Vitamin C (mg)	147.02 (132.39)	198.73 (82.57)	236.13 (117.12)	279.5 (94.85)
Vitamin D (μg)	5.87 (5.17)	6.2 (3.41)	13.94 (4.99)	15.34 (9.1)
Choline (mg)	177.33 (54.5)	200.22 (63.89)	182.93 (62.29)	207.3 (61.68)

[1] RAE: Retinol Activity Equivalent

SD: standard deviation.

CHAPTER 8. INTEGRATED DISCUSSION WITH CONCLUSIONS

8.1 Summary of thesis findings

To fulfill the requirement of a Doctor of Philosophy degree in epidemiology, this thesis studied the distribution and determinants of diet quality during pregnancy and examined the association between diet quality and perinatal and childhood neurodevelopment outcomes, in order to provide evidence to support future interventions to improve diet quality during pregnancy. The results indicate that the diet of the women in Canada still needs improvement, especially regarding whole grains and 'greens and beans'. Only 4.5% of the pregnant women met the recommended number of servings for whole grains, only 8.3% for greens and beans and only about 1 in 3 for 'milk and alternatives'. Inequalities in diet quality were observed: pregnant women who were less educated, younger, overweight or obese before pregnancy, or parous have lower diet quality in Canada. (Manuscript 1) By synthesizing the evidence from 33 prospective cohort studies (315,431 participants) using systematic review and meta-analysis, we found that women in the top tertile of diet quality scores had a lower risk of gestational diabetes (OR: 0.77; 95 CI: 0.65, 0.90; I2 = 72%), hypertensive disorders of pregnancy (OR: 0.87; 95 CI: 0.83, 0.92; I2 = 0%), preterm birth (OR: 0.77; 95 CI: 0.66, 0.89; I2 = 16%), small for gestational age (OR: 0.88; 95 CI: 0.79, 0.99; I2 = 5%) and low birth weight (OR: 0.60; 95 CI: 0.37, 0.99; I2 = 23%) compared to those in the bottom tertile. No associations were found between diet quality and excessive or inadequate gestational weight gain, large for gestational age and macrosomia. No studies were found for the association

between diet quality and delivery mode. (Manuscript 2) This study provided the evidence from prospective cohort studies that good diet quality during pregnancy is associated with lower odds of adverse perinatal outcomes. We observed similar results for preeclampsia in the 3D Cohort Study. From our literature review, we found that there is a research gap regarding the relationship between diet during pregnancy and neurodevelopment outcomes in the offspring, which the 3D Cohort Study could add value. In the process of doing the analysis using data from the 3D Cohort Study, interactions between diet quality and multivitamin intake were found on association with cognitive and language development outcomes in the offspring at two years of age (p for interactions = 0.018 and 0.023, respectively). The cognitive and language scores were lowest in the group of women who did not take multivitamins and had a low diet quality. Among women who did not take multivitamins, high diet quality was associated with better offspring cognitive and language scores (mean difference [95% CI] = 4.2 [0.1, 8.2], p=0.04; and 11.3 [3.1, 19.5], p=0.01, respectively). Among women who took multivitamins, no such associations were found. On the other hand, taking multivitamins was associated with 3.0 (95% CI: 0.3 to 5.8, p=0.03) points higher cognitive composite scores in participants who had a low diet quality, but not in those with a high diet quality. The results support the provision of adequate nutrition supply, through high quality diet or multivitamin use, for proper neurodevelopment of children. (Manuscript 3)

8.2 Public health and clinical relevance of the findings

Malnutrition during pregnancy represents a major public health issue that affects not only the health of the women, but also the health of offspring, and contributes substantially to the global burden of disease and disability[5,6].

This thesis helps to fill knowledge gaps in diet quality during pregnancy in Canada. The findings of this thesis are relevant to clinical and public health practice since diet quality measures provide a potential target for dietary interventions through implementation of dietary guidelines, and also because pregnancy offers a window of opportunity for intervention[45,46].

As previously mentioned, high quality dietary intake information during pregnancy is lacking in Canada. As a result, few previous studies have examined the quality of diet in Canada, which makes evidence-based interventions difficult. Our study provided a clear picture to the public health and clinical practitioners concerning which food groups should be targeted for improving diet quality during pregnancy, and on the other hand, the social factors associated with low diet quality, which could be used to identify target populations with low diet quality and to reduce social inequality in diet quality during pregnancy in Canada.

Previous research on the relationship between diet quality and perinatal outcomes generated inconsistent results, and the quality of the studies was unclear. The systematic review searched four databases, evaluated quality of the studies, and synthesized the results, which made the evidence from research more accessible to public health and clinical practitioners for decision making. The

findings consistently showed that women in the top tertile of diet quality scores have lower risk of adverse perinatal outcomes, including 22% lower risk of gestational diabetes, 13% lower risk of hypertensive disorders of pregnancy, 23% lower risk of preterm birth, 12% lower risk of small for gestational age, and 40% lower risk of low birth weight compared to those in the bottom tertile of diet quality scores. The thesis also makes a significant contribution to the evidence on the association between nutrition during pregnancy and childhood neurodevelopment. Despite increasing interest in the associations on this association, there were few studies quantifying this association directly [119,120]. Only one recent study in the U.S. reported the association between diet quality and childhood neurodevelopment, and no studies have investigated the interaction between diet quality and multivitamins. Our results indicated that adequate nutritional intake, through high quality diet or multivitamin use, is essential for the neurodevelopment of children. The efforts to improve offspring neurodevelopment through nutritional intervention should specifically target women with poor diet quality and not taking multivitamins. The World Health Organization (WHO) currently recommends iron and folic acid supplementation for women during pregnancy as part of routine antenatal care. However, multivitamin supplementation has not been recommended. Despite Health Canada's recommendation of daily multivitamins supplements and the provision of free multivitamins for low-income pregnant women as part of the OLO program in the province of Quebec, 10.5% of the women in this cohort did not take any multivitamins during pregnancy. This is particularly concerning as our study showed that taking multivitamins might mitigate the potential harm of nutrient deficiency on offspring neurodevelopment in women with a poor diet. Future studies

evaluating the barriers to multivitamin use in pregnancy are needed to inform targeted interventions in women with low diet quality at the start of pregnancy.

8.3 Limitations and Strengths of the studies

Studies in this thesis have some limitations that the readers should consider before interpretations of the results.

External validity (generalization) and selection bias due to high socioeconomic status of the sample

The distributions of the 3D Cohort Study sample and our study sample that have reliable dietary information were towards that of a high socioeconomic status, and thus not a representative sample of the population of Canadian pregnant women[126,127]. This could be particularly relevant to the estimates of the absolute intakes of some food groups and absolute HEI-C scores. As the results showed, higher education is associated with higher diet quality. As a result, the true estimates of HEI-C in the general population could be lower than the estimates in this study, and these absolute estimates of diet quality may not be generalized to a population with a lower socioeconomic status.

However, the influence of a slightly higher social economic status of the sample on the estimates of associations (selection bias) included in the studies might be moderate. A previous study from

the Danish National Birth Cohort that tried to quantify selection bias showed that the effect of potential selection bias due to the higher socioeconomic status on exposure–outcome associations could be limited [128]. This is in line with results from our sensitivity analysis included in the third paper. Participants with missing information in the covariates or outcomes were excluded in the main analysis, which could possibly lead to selection bias. However, our sensitivity analysis using multiple imputation generated similar results, indicating that the risk of selection bias is low.

Causality

Causal relationship cannot be established in the associations detected in the thesis because they are based on data from observational studies, and causal reasoning in observational studies might be jeopardized by residual confounding, reverse causality, and other biases. Further interventional studies such as RCTs are needed to strengthen the argument for causality.

Residual confounding, which refers to the 'the distortion that remains after controlling for confounding in the design and/or analysis of a study'[129], is one of the most stubborn biases in observational studies. Even advanced methods such as propensity scores and instrumental variables could not totally eliminate the effect of residual confounding[130]. Residual confounding could arise if there are unmeasured or undetected confounding, or the adjusted confounding variables were measured imperfectly. Possibilities of residual confounding could not be ruled out

because all the results in the thesis are based on data from observational studies. For the association between maternal nutrition and childhood neurodevelopment, although we identified potential confounding variables using DAG, there could be possibility that we are not aware of some potential confounding variables and did not include them in the DAG, such as social support. It is also possible that the adjusted variables were not measured perfectly to the extent that could completely remove the effect of the confounding variable. For the association between maternal nutrition and childhood neurodevelopment, reverse causation seems unlikely though, because we are certain that the exposure happens before the outcome of interest.

Misclassifications

Although the exposures and outcomes were measured with validated tools, misclassification remains possible owing to the difficulty of measuring diet and neurodevelopment. People with lower social economic status tend to report a better diet quality than what they actually consume [131]. Lower social economic status is also associated with lower neurodevelopment. This would bias the estimates on the association between diet quality and neurodevelopmental towards the null hypothesis. Research personnel who conducted the measurements of neurodevelopment were blinded to the exposure or other background information of the children and family. Neurodevelopment outcomes were treated as continuous variables. As a result, the potential

misclassifications of neurodevelopment are more likely to be nondifferential across exposure groups and would yield an expectation of no bias [132,133].

Other Limitations

Furthermore, the 3D Cohort Study only captures diet in the second/third trimester of pregnancy. However, although diet quality might change in the first trimester due to nausea or food aversions, studies have shown that diet quality changes little across trimesters[49,50].

Strengths

We used 3-day food records dietary assessment method, which is less prone to memory biases compared to other dietary assessment tools and is recognized as one of the most accurate tools for dietary assessment [134-136]. Most previous studies evaluated exposure to single nutrients including zinc, iron, choline, B-vitamins and iodine [118,137]. It is worth noting that nutrient deficiencies rarely occur individually during pregnancy [138]. The use of the healthy eating index as a measurement of overall diet quality in this thesis is more relevant for public health interventions than single nutrient studies.

8.4 Implications for future research

Considering the fact that the majority of the women did not meet the recommendations for whole grains and 'greens and beans', studies on the barriers of meeting these specific guidelines are needed to enlighten health practitioners and policy makers in developing strategies to improve the diet quality of pregnant women. Future studies are also needed on how to minimize the social inequality in diet quality during pregnancy.

In the process of the systematic review, knowledge gaps were identified for studies in middle and low-income countries on diet quality during pregnancy to test whether the results found in high-income countries could be generalized to middle and low-income countries. Few studies on the association of maternal diet quality in preconception with perinatal outcomes, and the association of maternal diet quality with delivery mode were found. Diet quality was assessed using 22 different scores in the studies included in the systematic review. This highlighted the need of advancing the development and use of harmonized and standardized diet quality scores across countries in future studies that would facilitate the process of comparison between studies and synthesizing evidence to form a stronger recommendation.

Maternal diet quality and multivitamin intake during pregnancy interact in the association with offspring neurodevelopment. Future research trying to establish the causality of this association is needed. Future research should consider the baseline nutrition status because the results of this study suggest that providing multivitamin supplementation or improving diet quality in women

with a good nutritional status might not impact neurodevelopment outcomes. The lowest cognitive and language development were observed in the group of children whose mother ate a lower quality diet and did not take multivitamins during pregnancy. This group of women were lacking in the quality of nutrition supply from food and supplement sources compared to those in the other three groups. Future studies evaluating the barriers to multivitamin use in pregnancy are needed to inform targeted interventions in women with low diet quality at the start of pregnancy. Research also needed to be done to replicate the results observed from our study, ideally in a population with lower diet quality or lower prevalence of multivitamin intake, where larger effects could potentially be detected.

8.5 Conclusions

Studies in this thesis fills a research gap in diet quality of pregnant women in Canada and adds value to the evidence of associations between maternal diet quality and perinatal and childhood outcomes, thus supporting the importance of diet quality during pregnancy. Even in high-income countries like Canada, the diet of the women still needs improvement, and particularly in certain vulnerable populations. Evidence from out systematic review of cohort studies demonstrates that good diet quality during pregnancy is associated with a lower risk of adverse maternal and neonatal outcomes. Maternal diet quality and multivitamin intake during pregnancy interact in the association with offspring neurodevelopment. Results from these associations identified from

the thesis can support the design of studies aiming to strengthen the hypothesis of the causality of these associations and promote the improvement in the care of women both before and during pregnancy.

CHAPTER 9. APPENDICES

Appendix 1. University of Ottawa Ethics Approval

04/05/2021

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-04-21-6908
Titre du projet / Project Title	Determinants of overall diet quality during pregnancy and associations with gestational weight gain, children's birth weight, body weight trajectories and development
Type de projet / Project Type	Thèse de doctorat / Doctoral thesis
Statut du projet / Project Status	Approuvé / Approved
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	04/05/2021
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	03/05/2022

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Yamei YU	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Chercheur Principal / Principal Investigator
Lise DUBOIS	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments

550, rue Cumberland, pièce 154 Ottawa (Ontario) K1N 6N5 Canada
550 Cumberland Street, Room 154 Ottawa, Ontario K1N 6N5 Canada

613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

04/05/2021

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

Le Comité d'éthique de la recherche (CÉR) de l'Université d'Ottawa, opérant conformément à l'*Énoncé de politique des Trois conseils* (2014) et toutes autres lois et tous règlements applicables, a examiné et approuvé la demande d'éthique du projet de recherche ci-nommé.

L'approbation est valide pour la durée indiquée plus haut et est sujette aux conditions énumérées dans la section intitulée "Conditions Spéciales ou Commentaires". Le formulaire « Renouvellement ou Fermeture de Projet » doit être complété quatre semaines avant la date d'échéance indiquée ci-haut afin de demander un renouvellement de cette approbation éthique ou afin de fermer le dossier.

Toutes modifications apportées au projet doivent être approuvées par le CÉR avant leur mise en place, sauf si le participant doit être retiré en raison d'un danger immédiat ou s'il s'agit d'un changement ayant trait à des éléments administratifs ou logistiques du projet. Les chercheurs doivent aviser le CÉR dans les plus brefs délais de tout changement pouvant augmenter le niveau de risque aux participants ou pouvant affecter considérablement le déroulement du projet, rapporter tout évènement imprévu ou indésirable et soumettre toute nouvelle information pouvant nuire à la conduite du projet ou à la sécurité des participants.

The University of Ottawa Research Ethics Board, which operates in accordance with the *Tri-Council Policy Statement* (2014) and other applicable laws and regulations, has examined and approved the ethics application for the above-named research project.

Ethics approval is valid for the period indicated above and is subject to the conditions listed in the section entitled "Special Conditions or Comments". The "Renewal/Project Closure" form must be completedfour weeks before the above-referenced expiry date to request a renewal of this ethics approval or closure of the file.

Any changes made to the project must be approved by the REB before being implemented, except when necessary to remove participants from immediate endangerment or when the modification(s) only pertain to administrative or logistical components of the project. Investigators must also promptly alert the REB of any changes that increase the risk to participant(s), any changes that considerably affect the conduct of the project, all unanticipated and harmful events that occur, and new information that may negatively affect the conduct of the project or the safety of the participant(s).

Riana MARCOTTE
Responsable d'éthique en recherche / Protocol Officer
Pour/For **Daniel LAGAREC** Président(e) du/ Chair of the **Comité d'éthique de la recherche en sciences de la santé et sciences / Health Sciences and Sciences Research Ethics Board**

550, rue Cumberland, pièce 154 550 Cumberland Street, Room 154
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada

613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

Appendix 2. Published Version of Manuscript 1

Received: 14 September 2021 | Revised: 15 June 2022 | Accepted: 21 June 2022

DOI: 10.1111/mcn.13403

ORIGINAL ARTICLE

Maternal & Child Nutrition WILEY

Diet quality during pregnancy and its association with social factors: 3D Cohort Study (Design, Develop, Discover)

Yamei Yu[1] | Cindy Feng[1,2] | Brigitte Bédard[1] | William Fraser[3] | Lise Dubois[1]

[1]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

[2]Department of Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada

[3]Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, and the Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke (CRCHUS), Sherbrooke, Quebec, Canada

Correspondence
William Fraser, Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, and the Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke (CRCHUS), Sherbrooke, Quebec, Canada.
Email: William.Fraser@usherbrooke.ca

Lise Dubois and Yamei Yu, School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, 600 Peter Morand (3158), Ottawa, Canada K1G5Z3.
Email: ldubois@uottawa.ca

Funding Information
Canadian Institutes of Health Research, Grant/Award Numbers: CRI 88413, HLT 151517, MOP 133422; National Natural Science Foundation of China, Grant/Award Number: 81661128010

Abstract

Good diet quality during pregnancy provides adequate nutrition to support both the mothers and the fetus. The objective of this study is to describe the distribution of diet quality during pregnancy and to study the association between social factors and diet quality during pregnancy in a Canadian population. This study was based on 1535 pregnant women who provided dietary information in the 3D Cohort Study in Quebec, Canada. A 3-day food record was used to collect dietary intake in the second trimester of pregnancy. A Canadian adaption of the Healthy Eating Index (HEI-C) 2010 was used to quantify diet quality. Univariate and multiple linear regression models were used to calculate unadjusted and adjusted effect estimates and confidence intervals for the association between social factors and HEI-C. The mean HEI-C 2010 score in this study was 62.9 (SD: 11.2). Only 4.5% and 8.3% of the pregnant women consumed the recommended amounts of whole grains and 'greens and beans', respectively. Diet quality was lower in some subgroups of pregnant women. After multivariable adjustment, lower diet quality was observed in participants who were less educated, younger, overweight or obese before pregnancy, or parous. There was an interaction between ethnicity and immigration status on diet quality in pregnancy. These findings could be useful for health practitioners and policymakers in developing strategies to improve the diet quality of pregnant women.

KEYWORDS
Cohort Studies, diet, educational status, healthy, maternal, obesity, parity, pregnancy

William Fraser and Lise Dubois contributed equally to this study.

1 | INTRODUCTION

The first 1000 days, including the prenatal period, is a unique period for children to develop their ability to grow and prosper in society (Koletzko et al., 2017; Schwarzenberg et al., 2018). Malnutrition during pregnancy represents a major public health issue that affects maternal health and offspring development and contributes substantially to the global burden of disease and disability (Hanson et al., 2015; Lim et al., 2013). Good diet quality during pregnancy provides adequate nutrition to support both the mothers and the fetus and is an important contributor to the children's physical and intellectual development (Fleming et al., 2018; Hanson et al., 2015; Stephenson et al., 2018).

A diet of good quality includes a variety of vegetables, fruits, whole grains, protein, low-fat dairy, healthy oils and a limited intake of saturated and trans fats, added sugars and sodium (Krebs-Smith et al., 2018). Individuals may be considered as having good overall diet quality when they follow the recommendations from dietary guidelines (Krebs-Smith et al., 2018). However, the proportion of pregnant women following the recommendations remains low in high-income countries (Bodnar & Siega-Riz, 2002; Crozier et al., 2009; Fowler et al., 2012; Malek et al., 2016; Morton et al., 2014; Pick et al., 2005). For example, only 35% of pregnant women in a Canadian cohort met the recommendations for vegetables and fruits in 2002–2005 (Fowler et al., 2012), and only 10% of pregnant women in an Australia study met the recommendations for vegetables in 2013 (Malek et al., 2016). What people habitually eat and avoid eating is not simply a matter of personal choices. Changes in diet quality may be difficult due to barriers at the individual, social-cultural and environmental levels (Mozaffarian et al., 2018; Sugiyama & Shapiro, 2014). However, pregnancy offers a window of opportunity for intervention, because pregnant women may be more willing to adopt healthier dietary habits during this period of life due to perceived benefits to the babies and themselves (Gardner et al., 2012; Vanstone et al., 2017).

Starting from before pregnancy, social inequalities exert their influence on different aspects of the women's experience. Even in high-income countries such as the United States and Canada, some subgroups of the population still have limited access to high-quality foods to provide adequate nutrition (Ivers & Cullen, 2011). It is thus vital to study social factors associated with diet quality to develop effective public health interventions. A systematic review (Doyle et al., 2017) found that women who were older, more educated, with higher income or other markers of affluence were more likely to follow a healthier dietary pattern or have a better diet quality. The finding was consistent across different populations and settings. However, not all studies used multivariable models, so it was not clear how these factors were confounded by each other. Findings regarding ethnicity and parity were less consistent and they could be acting as markers of age, education status and other sociodemographic factors.

Thus, the objective of this paper is to characterize diet quality during pregnancy and identify social factors associated with the diet quality of pregnant women that could inform the targeting of interventions designed to reduce the inequities in diet quality.

Key message

- The diet of the women in Canada still needs improvement, especially regarding whole grains and 'greens and beans', where the majority of the women did not meet the recommendations.
- Pregnant women who were less educated, younger, overweight or obese before pregnancy, or parous should be targeted for improving diet quality in Canada.
- There was an interaction between ethnicity and immigration status on diet quality during pregnancy.

2 | METHODS

2.1 | The 3D Cohort Study

The 3D Cohort Study is a pregnancy and birth cohort that recruited 2366 pregnant women who were at 8–14 weeks of gestation and planning to deliver in urban clinical centres in three of the four largest metropolitan areas in Quebec, Canada from 2010 to 2012. Detailed information on the cohort has been described elsewhere (Fraser et al., 2016). Briefly, inclusion criteria included age 18 and 47 years at recruitment and ability to communicate in French or English. Exclusion criteria included current intravenous drug use, severe illnesses or life-threatening conditions, and multiple gestations. Structured interviews were conducted at recruitment, mid, late pregnancy and post-partum by research nurses and research assistants. Written informed consents were obtained from each participant. Ethical approvals were obtained from the Health Sciences and Science Research Ethics Board of the University of Ottawa, the research ethics committee at Sainte-Justine's Hospital in Montreal and all other participating study cites.

2.2 | Exposures

Information about maternal characteristics was collected by interviewers at recruitment (8–14 weeks of gestation). Characteristics used in this study included maternal age (<25, 25–<35, ≥35), ethnicity (White, non-White), marital status (married, live with common law/partner, single), education (secondary school diploma or less, college, undergraduate degree, graduate degree), household income in Canadian dollars (<30,000, 30,000–59,999, 60,000–79,999, 80,000–99,999, ≥100,000), parity (0, ≥1) and self-reported prepregnancy weight. Height was measured by trained research nurses. Prepregnancy body mass index (BMI)

(kg/m^2) was calculated using self-reported prepregnancy weight in kilograms divided by height in metres squared. Social support was considered but not included in the model due to a lack of information.

2.3 | Outcome: Diet quality in pregnancy

2.3.1 | Generating energy and nutrients from a 3-day food record

Details of dietary data collection and processing have been described elsewhere (Dubois et al., 2018; Morisset et al., 2017). Briefly, a 3-day food record was provided to the participants at the second prenatal visit (20–24 weeks) to record dietary intakes on 2 weekdays and 1 weekend day. Pregnant women were trained by the research nurses on how to complete the 3-day food record. They completed the food record at home and returned the food records by mail. The food items in the food records were coded by trained nutritionists into Food Processor software (ESHA Research, Inc.), which was linked to the Canadian Nutrient File, to generate a complete database of energy and macronutrient and micronutrient intakes. As the content of added sugars was not readily available in the Canadian Nutrient File, it was calculated following a published method (Brisbois et al., 2014).

2.3.2 | Assigning food to a number of food group servings

The food items were assigned to four major Canada's Food Guide (CFG) food groups, 30 subgroups and to Tiers 1–4 using the food classification system developed by Health Canada (Elvidge Munene et al., 2015). CFG encourages people to choose foods lower in fat, sugar and salt. Foods that exceed at least two upper thresholds (total fat: >10 g/reference amount (RA); sugars: >19 g/RA; sodium: >360 mg/RA; saturated fat: >2 g/RA) will be classified into Tier 4. For 'milk and alternatives' and 'meat and alternatives' group, the upper threshold for saturated fat was not counted due to the fact that these food groups contain more inherent saturated fats than other food groups. Foods allocated to Tier 4 were excluded when counting the number of CFG servings of food in the four major food groups because they were classified as 'not in line with the guidance in CFG' (Elvidge Munene et al., 2015).

In CFG classifying system, mixed dishes (e.g., spaghetti with meat sauce) were classified into a subgroup called 'recipes' without breaking down into the four main food groups. The energy intake from foods in the subgroup 'recipes' accounted for 8% of the total energy intake of this study population. Thus, an omission of the mixed dishes in counting the number of servings of the four main groups would lead to an underestimation of the number of servings. For a more concise estimate, mixed dishes in the food records were decomposed into food group and subgroup servings by linking to standard recipes in the Food Patterns Equivalents Database (FPED) developed by the US Department of Agriculture (USDA), which converts the foods and beverages to USDA Food Patterns components (USDA). The matching was performed manually according to name and description, with a secondary aim of minimizing the energy density gap. When there were multiple possible matches, the one with the smallest gap in energy density per 100 g was chosen. When an exact match was not found in FPED, the most similar item regarding components of the food groups was chosen. This process was performed by a student with a background in nutrition and reviewed by a nutritionist who was familiar with the foods consumed locally. USDA Food Patterns components were then converted to the number of servings in the CFG.

2.3.3 | Generating diet quality

Overall diet quality in pregnancy was calculated according to the Canadian adaption of Healthy Eating Index (HEI-C) 2010 developed in 2017 (Jessri et al., 2017). HEI-C contains eight components for foods that should be consumed in adequate amounts (total fruits and vegetables, whole fruit, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids) and three that should be consumed in moderate amounts (refined grains, sodium, empty calories), resulting in a total score of 100 (see Supporting Information: Table 1). At the time of data collection, people's diet was guided by age- and sex-specific recommendations from CFG 2007, which were designed scientifically for the food intake pattern to meet the nutrient requirements and to avoid nutrient excess. Thus, the number of servings for 19–50-year-old women in CFG 2007 were used in this study: that is, eight servings of vegetables and fruits, six to seven servings of grain products, two servings of 'milk and alternatives' and two servings of 'meat and alternatives' per day (Health Canada, 2007, 2009, 2010, 2019-). Because pregnant women were advised to include an additional two to three servings per day from any of the four food groups (Health Canada, 2009), the cut-offs for 'total vegetables and fruits', grain products and 'milk and alternatives' were set at eight, seven, and three, respectively, to align with the examples given by Health Canada (Fowler et al., 2012). The cut-offs for whole fruit and 'greens and beans' component were set at 21% of that for 'total vegetables and fruits', which are 1.68 servings (Garriguet, 2009; Jessri et al., 2017). The cut-offs for whole grains were set at 50% of that for total grain products, which are 3.5 servings, according to CFG 2007 recommendations. Empty calories were defined as calories from saturated fats, alcohol and added sugars (Brisbois et al., 2014; Jessri et al., 2017). The detailed scoring standards for min and max of each of the HEI-C components used in this study were listed in Supporting Information: Table 1. Intermediate intakes were scored proportionately between min and max. Total HEI-C score, adequacy subscore and moderation subscore were sums of specific individual components.

2.4 | Statistical analyses

A flowchart for the study samples was presented in Figure 1. Proportions were used to display the characteristics of the 3D study sample, a sample with reliable diet information and a complete case sample (participants with no missing values on any of the variables included in the multiple linear regression model). The mean and SD of the intakes for each component of the HEI-C were calculated in the sample with reliable diet information. Mean, SD, range and the proportion reaching the maximum scores were calculated for the total HEI-C score and the components. To validate that higher HEI-C was associated with higher beneficial nutrient supply, HEI-C scores were divided into quartiles, to present the mean and SD of selected nutrients in each HEI-C quartile (Jessri et al., 2017). Univariate and multiple linear regression models were used to calculate unadjusted and adjusted effect estimates and confidence intervals (CIs) for the association between maternal characteristics and HEI-C. Multiple linear regression was performed on the complete case sample. Residual plots were used to visually check for homoscedasticity and normality assumptions of the multiple linear regression models. As the assumptions of the models were roughly met, no transformations of the variables were performed. Interactions between pairs of the social factors were tested by adding the product interaction term to the multiple regression model. All statistical analyses were performed using Statistical Analysis System software version 9.4 (SAS v9.4; SAS Institute Inc.). A two-sided $p < 0.05$ was set as the level of statistical significance.

3 | RESULTS

A total of 1535 pregnant women (65% of the 3D Cohort Study sample) who provided complete and reliable information for the 3-day food record were included in this study (Figure 1). The mean age at enrolment was 31.5 (SD: 4.3) years. Mean prepregnancy BMI was 23.8 kg/m^2 (SD: 5.1). The mean gestational age at food record completion was 23.0 weeks (SD: 2.9). As shown in Table 1, only a small proportion had less than or equal to secondary school education (6.2%) or had annual household incomes below 30,000 Canadian dollars (7.8%); 30.6% were overweight or obese before pregnancy. More than half (58.0%) were nulliparous. Most were born in Canada (71.7%), classified themselves as White (80.1%), and were married or living with a partner (95.8%). Compared with the total 3D study sample, participants included in this study were on average older, with higher income and education level, more likely to be White and born in Canada and less likely to be overweight or obese before pregnancy.

As shown in Table 2, the mean HEI-C 2010 score was 62.9 (SD: 11.2). The proportion of women reaching the recommended

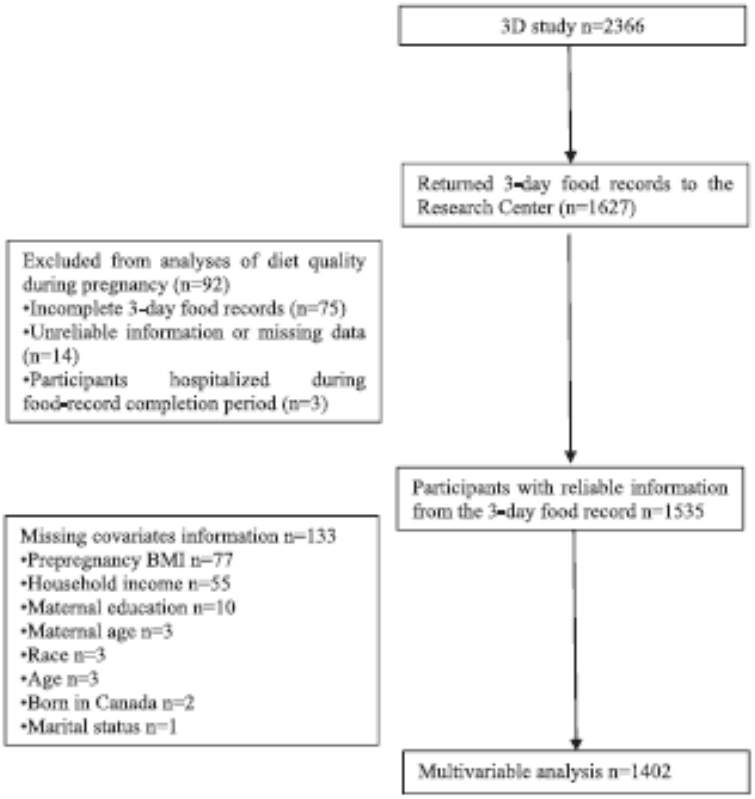


FIGURE 1 Flow diagram for the study samples

TABLE 1 Characteristics of the study samples

Characteristics	3D sample	Sample with reliable diet information	Complete case sample[a]
n	2366	1535	1402
Mother's age (%)			
<25	7.3	5.5	5.4
25–<35	70.7	73.7	74.0
≥35	22.0	20.8	20.7
Maternal education (%)			
Secondary school or less	9.5	6.2	5.7
College	28.2	25.6	25.2
Undergraduate degree or above	62.3	68.2	69.1
Household income (CAD) (%)			
<30,000	10.8	7.8	7.4
30,000–59,999	19.1	17.2	17.1
60,000–79,999	17.2	17.8	18.1
80,000–99,999	18.9	22.4	22.4
≥100,000	29.1	34.8	35.0
Married/common law/partner (%)	94.5	95.8	95.9
Prepregnancy BMI (%)			
Underweight < 18.5	6.0	6.2	6.2
Normal weight 18.5–24.9	63.3	65.4	65.6
Overweight 25–29.9	18.4	16.8	16.4
Obese > 30	12.3	11.7	11.8
Nulliparous (%)	54.2	58.0	58.2
Mother born in Canada (%)	65.1	71.7	73.0
Mother White (%)	72.2	80.1	81.1

Abbreviations: BMI, body mass index; CAD, Canadian dollars.
[a]Sample with no missing value in diet and covariates in multivariate analysis.

servings for whole grains was 4.5%. Similarly, only 8.3% reached the recommended servings of 'greens and beans'. About half consumed the recommended servings of protein foods (49.4%) and 'seafood and plant proteins' (52.1%). The majority (62.5%) of the participants consumed the recommended servings of whole fruits.

A higher density of beneficial micronutrients from food including calcium, vitamin A, folate, vitamin C, vitamin D, calcium, magnesium, iron, and zinc was found in higher quartiles of HEI-C (Supporting Information: Table 2). The density of protein, fibre, polyunsaturated fatty acids and monounsaturated fatty acids increased in higher quartiles of HEI-C, whereas the density of total fat, saturated fat, added sugars and sodium decreased. There was no significant trend for carbohydrates.

Table 3 showed unadjusted and multivariable-adjusted analyses for the social factors in association with the HEI-C score. In univariate analysis, women who were <25 years of age, single, overweight or obese before pregnancy, or parous had lower HEI-C scores than the reference group. Women who had an undergraduate degree, attended graduate studies or with household income above 100,000 Canadian dollars had higher HEI-C scores than the reference group. In multivariable analysis, participants who attended graduate studies (mean difference: 4.0 [95% CI: 1.2–6.9]) had higher HEI-C scores compared with secondary school or less. Participants who were <25 years of age (mean difference: −4.9 [95% CI: −7.6 to −2.2] compared with 25–35 years of age), overweight (mean difference: −2.8 [95% CI: −4.4 to −1.3] compared with normal BMI), obese (mean difference: −3.1 [95% CI: −4.9 to −1.3] compared with normal BMI), parous (mean difference: −2.7 [95% CI: −3.9 to −1.5] compared with nulliparous) had lower HEI-C scores. Household income and marital status no longer had a statistically significant association with HEI-C after adjustment.

There was an interaction between ethnicity and immigration status on HEI-C. As shown in Table 4, for women who were born in Canada, visible minority women had lower HEI-C scores than White women (mean difference: −5.9 [95% CI: −9.5 to −2.3], $p = 0.001$). On the contrary, for women who were not born in Canada, visible minority women had higher HEI-C scores than White women (mean difference: 3.9 [95% CI: 1.6–6.2], $p = 0.001$). For White women, those who were not born in Canada had lower HEI-C than those who were born in Canada (mean difference: −3.6 [95% CI: −5.5 to −1.6], $p < 0.001$). However, for non-White women, those who were not born in Canada had higher HEI-C than those who were born in Canada (mean difference: 6.2 [95% CI: 2.4–10.0], $p = 0.001$).

4 | DISCUSSION

This study demonstrated that the diet quality of pregnant women still needs improvement, especially with respect to the intake of whole grains and 'greens and beans'. Diet quality among pregnant women was associated with social factors. After multivariable adjustment, diet quality was lower in some subgroups of pregnant women, including those who were less educated, younger, overweight or obese before pregnancy, or parous.

Pregnant women in this study were having better diet quality than that reported in the general population (Jessri et al., 2017) (mean HEI-C: 62.9 vs. 50.9). However, a cautious interpretation of this comparison is needed because pregnant women in this study have higher socioeconomic status than the general pregnant women and general population in Canada. Still, the compliance in specific subgroups of food was low. In this study, only 4.5% of the pregnant women met the recommended number of servings for whole grains, only 8.3% for greens and beans and only about 1 in 3 for 'milk and

TABLE 2 Mean food and nutrient intakes and scores of components of HEI-C for 1535 women participating in the 3D Cohort Study

Component	Intake Mean ± SD	Scores Mean ± SD	Range	Proportion reaching max score (%)
Total fruits and vegetables, servings/day	7.4 ± 2.8	8.1 ± 2.1	0.4–10	36.5
Whole fruit, servings/day	2.4 ± 1.6	4.2 ± 1.3	0–10	62.5
Greens and beans, servings/day	0.7 ± 0.7	2.0 ± 1.6	7.7–20	8.3
Whole grains, servings/day	1.0 ± 1.1	2.8 ± 2.9	0–5	4.5
Milk and alternatives (servings/day)	2.6 ± 1.3	7.6 ± 2.6	0–5	33.6
Total protein foods (servings/day)	2.1 ± 0.9	4.3 ± 1.0	0–10	49.4
Seafood and plant proteins (servings/day)	0.8 ± 0.7	3.6 ± 1.8	0–10	52.1
(PUFA + MUFA)/SFA (no unit)	1.6 ± 0.5	3.2 ± 2.9	0.1–5	4.5
Refined grains (% of total grains)	82.6 ± 18.8	3.3 ± 3.3	0–5	7.6
Sodium (mg)	2841 ± 848	6.0 ± 2.6	0–10	3.5
Empty calories (% of energy)	21.3 ± 4.7	17.9 ± 2.4	0–10	33.1
Total adequacy score		35.7 ± 8.0	10.7–57.4	0.0
Total moderation score		27.2 ± 5.2	11.4–40	0.4
Total HEI-C score		62.9 ± 11.2	28.8–95.6	0.0

Abbreviations: HEI-C, Canadian Healthy Eating Index; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

alternatives'. The results were consistent with findings from other high-income countries, indicating that a large portion of pregnant women was not meeting the dietary guidelines (Bodnar & Siega-Riz, 2002; Crozier et al., 2009; Malek et al., 2016; Morton et al., 2014; Pick et al., 2005). Because CFG 2007 was designed for meeting nutritional requirements, the results in this study indicated that women might have some difficulties meeting the dietary guidelines, and thus could have inadequate nutrition supplies. Indeed, previous research from our group found that intake of iron, folate and vitamin D from food sources was below recommended values for a vast majority of pregnant women (Dubois et al., 2017). For women having difficulties meeting the guidelines, other sources of nutrients, such as nutritional supplements and exposure to sunshine, could be recommended as appropriate to meet the needs for adequacy of nutrients supply.

Consistent with our findings, higher education, older age, and lower prepregnancy BMI were found to be associated with higher diet quality (Bodnar & Siega-Riz, 2002; Kritsotakis et al., 2015; Rifas-Shiman et al., 2009; Savard et al., 2019; Shin et al., 2016), including in low-income settings (Fowles et al., 2011). The interpretation of the lower diet quality in women with overweight and obesity before pregnancy requires comment. In addition to interpreting prepregnancy BMI as a determinant of diet quality during pregnancy, it could also be interpreted that diet tracking back to prepregnancy was a determinant of prepregnancy BMI. The finding from previous studies that diet quality changed little (Savard et al., 2019) from prepregnancy to pregnancy supports this hypothesis.

Interestingly, in our study, although income was positively associated with diet quality in univariable analysis, the association was no longer statistically significant after multivariable adjustment, mainly due to the confounding effect of age and education. This result was in line with an urban pregnancy cohort in the United States (Deierlein et al., 2021). Similar to our findings, parity has been found to be inversely associated with diet quality in two US cohorts, and inversely associated with a 'health conscious' dietary pattern in a population-based cohort study in the United Kingdom (Bodnar & Siega-Riz, 2002; Northstone et al., 2008; Rifas-Shiman et al., 2009). Some possible mechanisms for this association could be that parous women are more likely to rely on their own past knowledge or assumptions for healthy behaviours during pregnancy, rather than seeking out information, compared with nulliparous women (Declercq et al., 2007; Grenier et al., 2021). Parous women also reported a larger number of 'very stressful' days 1 year before birth than nulliparous women, which might influence their ability to maintain a healthy diet (Public Health Agency of Canada, 2009). Our results indicate that parous women need more attention from care providers or social support to improve diet quality compared with nulliparous women. Only one previous study found the opposite direction of this association that parity was positively associated with diet quality (Nash et al., 2013), possibly because age was not adjusted in the analysis. It has been shown from previous studies that higher parity was associated with older age, and age has been consistently reported to be positively associated with diet quality (Bodnar & Siega-Riz, 2002; Kritsotakis et al., 2015; Rifas-Shiman et al., 2009; Savard et al., 2019).

To our knowledge, our study is the first to report the interaction between ethnicity and immigration status (born in Canada) on diet quality during pregnancy. Validation of this finding in other studies is needed due to the limitation that this study sample was not a representative sample of the Canadian pregnancy population. While

TABLE 3 Unadjusted and multivariable-adjusted analyses for the social factors in association with HEI-C

Characteristics	n	HEI-C scores, mean ± SD	Regression estimates (95% CI)[b]	
			Unadjusted	Multivariable[a]
Total	1535	62.9 ± 11.2		
Age (years)				
<25	85	56.3 ± 10.5	−6.2 (−8.8,−3.6)	−4.9 (−7.6,−2.2)
25–<35	1129	63.1 ± 11.3	Reference	Reference
≥35	318	64.2 ± 10.5	0.9 (−0.6,2.3)	1.2 (−0.2,2.6)
Missing	3	59.9 ± 8.1		
Education				
Secondary school or less	94	57.5 ± 11	Reference	Reference
College	391	60.3 ± 11.2	2.1 (−0.6,4.7)	0.3 (−2.4,2.9)
Undergraduate degree	628	63.9 ± 11.3	5.6 (3.0,8.1)	2.7 (0,5.4)
Graduate degree	412	65.2 ± 10.2	6.8 (4.1,9.4)	4.0 (1.2,6.9)
Missing	10	59.9 ± 8.6		
Household income (CAD)				
<30,000	116	60.3 ± 11.1	Reference	Reference
30,000–59,999	254	61.9 ± 11.5	1.5 (−1.1,4.0)	1.4 (−1.2,3.9)
60,000–79,999	263	61.6 ± 10.7	1.2 (−1.3,3.7)	0.3 (−2.4,2.9)
80,000–99,999	332	62.6 ± 10.7	1.9 (−0.6,4.4)	0.2 (−2.5,2.8)
≥100,000	515	65 ± 11.2	4.5 (2.1,6.8)	1.9 (−0.7,4.5)
Missing	55	62.3 ± 11.4		
Marital status				
Married	614	63.1 ± 10.7	Reference	Reference
Common law/partner	856	63.1 ± 11.4	0.3 (−1.0,1.5)	0.1 (−1.3,1.4)
Single	64	58.7 ± 12.7	−4.3 (−7.4,−1.3)	−3.1 (−6.3,0)
Missing	1	57.1 ± 0		
Prepregnancy BMI				
Underweight (BMI < 18.5)	90	64.8 ± 11.6	1.2 (−1.2,3.6)	1.7 (−0.6,4.1)
Normal weight (BMI: 18.5–24.9)	953	64 ± 11.1	Reference	Reference
Overweight (BMI: 25.0–29.9)	245	60.8 ± 10.8	−3.1 (−4.7,−1.5)	−2.8 (−4.4,−1.3)
Obese (BMI ≥ 30.0)	170	59.4 ± 10.7	−4.5 (−6.3,−2.7)	−3.1 (−4.9,−1.3)
Missing	77	62.8 ± 11.5		
Parity				
0	891	64 ± 10.9	Reference	Reference
≥1	644	61.4 ± 11.4	−2.5 (−3.7,−1.4)	−2.7 (−3.9,−1.5)
Born in Canada				
No	434	62.8 ± 10.9	−0.2 (−1.5,1.1)	−5.9 (−9.5,−2.3)
Yes	1099	63 ± 11.3	Reference	Reference
Missing	2	55.6 ± 2.2		

(Continues)

TABLE 3 (Continued)

Characteristics	n	HEI-C scores, mean ± SD	Regression estimates (95% CI)[b] Unadjusted	Multivariable[a]
White				
No	305	63.1 ± 10.8	0 (−1.5,1.5)	**−3.6 (−5.5,−1.6)**
Yes	1227	62.9 ± 11.3	Reference	Reference
Missing	3	59.7 ± 5.3		
Born in Canada × White (*p* for interaction)				**p < 0.001**

Abbreviations: BMI, body mass index; CAD, Canadian dollars; CI, confidence interval; HEI-C, Canadian Healthy Eating Index; SD, standard deviation.

[a]Adjusted for all characteristics simultaneously using a complete case sample (*n* = 1402).

[b]Stastistical significant values (*p* <0.05) were highlighted in bold.

TABLE 4 Interaction between ethnicity and immigration status on Canadian Healthy Eating Index (HEI-C)[a]

	Ethnicity White, β (95% CI), *p*	Ethnicity non-White, β (95% CI), *p*	β (95% CI) for ethnicity within strata of immigration status	*p* for interaction
Born in Canada				**<0.001**
Yes	Reference	**−5.9 (−9.5,−2.3), p = 0.001**	**−5.9 (−9.5,−2.3), p = 0.001**	
No	**−3.6 (−5.5,−1.6), p < 0.001**	0.3 (−1.6,2.2), p = 0.75	**3.9 (1.6,6.2), p = 0.001**	
β (95% CI) for immigration status within strata of ethnicity	**−3.6 (−5.5,−1.6), p < 0.001**	**6.2 (2.4,10.0), p = 0.001**		

[a]Adjusted for age, education, household income, marital status, prepregnancy BMI and parity.

'the healthy immigrant effect' indicates that immigrants are generally healthier than the native-born population (Vang et al., 2017), this result indicates that ethnicity needs to be considered when studying the association between immigration and diet, or other diet-related health outcomes.

Our study has some limitations. The distributions of the 3D study sample and our study sample that have reliable dietary information were towards that of a high socioeconomic status, and thus not a representative sample of the population of Canadian pregnant women. Because higher education is associated with higher diet quality, the true estimates of HEI-C in the general population could be lower than the estimates in this study. The results of the study might not be generalized to a population with a lower socioeconomic status. Additionally, causality could not be concluded due to the nature of the study design. Furthermore, our study only captures diet in the second/third trimester of pregnancy. However, although diet quality might change in the first trimester due to nausea or food aversions, studies have shown that diet quality changes little across trimesters (Lebrun et al., 2019; Savard et al., 2019). Our study also had several strengths, including a large sample size, a large set of covariates and the 3D food records dietary assessment method used, which is less prone to memory biases and is recognized as one of the most accurate tools for dietary assessment (Bingham et al., 1995; Kolar et al., 2005).

5 | CONCLUSION

Social factors are associated with diet quality during pregnancy in Canada. Women who were less educated, younger, parous or with a higher BMI had lower diet quality in pregnancy. These findings could be useful for health practitioners and policymakers in developing strategies to improve the diet quality of pregnant women.

AUTHOR CONTRIBUTIONS

Yamei Yu is the guarantor of the paper. Yamei Yu, William Fraser and Lise Dubois contributed to the conception of the research question. Yamei Yu and Cindy Feng contributed to the statistical analyses. Yamei Yu, Brigitte Bédard and Lise Dubois contributed to the dietary data coding. Yamei Yu, Cindy Feng, Brigitte Bédard, Lise Dubois and William Fraser contributed to the drafting and reviewing of the paper and provided approval for the version submitted for publishing.

ACKNOWLEDGEMENTS

The authors would like to acknowledge all the participants and the study team members who had made a great contribution to this study. This research project is sponsored jointly by the Canadian Institutes of Health Research (CIHR) (Grant Nos. CRI 88413, MOP 133422 and HLT 151517) and the National Natural Sciences Foundation of China (NSFC) (Grant No. 81661128010).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data are available on request due to privacy/ethical restrictions.

ETHICS STATEMENT

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Health Sciences and Science Research Ethics Board of the University of Ottawa, the research ethics committee at Sainte-Justine's Hospital in Montreal, and all other participating study cites. Written informed consent was obtained from all subjects/patients.

ORCID

Yamei Yu http://orcid.org/0000-0002-5151-3397

REFERENCES

Bingham, S. A., Cassidy, A., Cole, T. J., Welch, A., Runswick, S. A., Black, A. E., Thurnham, D., Bates, C., Khaw, K. T., Key, T. J. A., & Day, N. E. (1995). Validation of weighed records and other methods of dietary assessment using the 24 h urine nitrogen technique and other biological markers. *British Journal of Nutrition*, *73*(4), 531–550. https://doi.org/10.1079/bjn19950057

Bodnar, L. M., & Siega-Riz, A. M. (2002). A Diet Quality Index for pregnancy detects variation in diet and differences by socio-demographic factors. *Public Health Nutrition*, *5*(6), 801–809. https://doi.org/10.1079/PHN2002348

Brisbois, T. D., Marsden, S. L., Anderson, G. H., & Sievenpiper, J. L. (2014). Estimated intakes and sources of total and added sugars in the Canadian diet. *Nutrients*, *6*(5), 1899–1912. https://doi.org/10.3390/nu6051899

Crozier, S. R., Robinson, S. M., Borland, S. E., Godfrey, K. M., Cooper, C., & Inskip, H. M., the SWS Group. (2009). Do women change their health behaviours in pregnancy? Findings from the Southampton Women's Survey. *Paediatric and Perinatal Epidemiology*, *23*(5), 446–453. https://doi.org/10.1111/j.1365-3016.2009.01036.x

Declercq, E. R., Sakala, C., Corry, M. P., & Applebaum, S. (2007). Listening to mothers II: Report of the Second National U.S. Survey of Women's Childbearing Experiences: Conducted January–February 2006 for Childbirth Connection by Harris Interactive(R) in partnership with Lamaze International. *The Journal of Perinatal Education*, *16*(4), 9–14. https://doi.org/10.1624/105812407X244769

Deierlein, A. L., Ghassabian, A., Kahn, L. G., Afanasyeva, Y., Mehta-Lee, S. S., Brubaker, S. G., & Trasande, L. (2021). Dietary quality and socio-demographic and health behavior characteristics among pregnant women participating in the New York University Children's Health and Environment Study. *Frontiers in Nutrition*, *8*, 639425. https://doi.org/10.3389/fnut.2021.639425

Doyle, I. M., Borrmann, B., Grosser, A., Razum, O., & Spallek, J. (2017). Determinants of dietary patterns and diet quality during pregnancy: A systematic review with narrative synthesis. *Public Health Nutrition*, *20*(6), 1009–1028. https://doi.org/10.1017/S1368980016002937

Dubois, L., Diasparra, M., Bédard, B., Colapinto, C. K., Fontaine-Bisson, B., Morisset, A. S., Tremblay, R. E., & Fraser, W. D. (2017). Adequacy of nutritional intake from food and supplements in a cohort of pregnant women in Quebec, Canada: The 3D Cohort Study (Design, Develop, Discover). *American Journal of Clinical Nutrition*, *106*(2), 541–548. https://doi.org/10.3945/ajcn.117.155499

Dubois, L., Diasparra, M., Bedard, B., Colapinto, C. K., Fontaine-Bisson, B., Tremblay, R. E., & Fraser, W. D. (2018). Adequacy of nutritional intake during pregnancy in relation to prepregnancy BMI: Results from the 3D Cohort Study. *British Journal of Nutrition*, *120*(3), 335–344. https://doi.org/10.1017/S0007114518001393

Elvidge Munene, L. A., Dumais, L., Esslinger, K., Jones-Mclean, E., Mansfield, E., Verreault, M. F., Villeneuve, M., Miller, D., & St-Pierre, S. (2015). A surveillance tool to assess diets according to Eating Well with Canada's Food Guide. *Health Reports*, *26*(11), 12–20. https://www.ncbi.nlm.nih.gov/pubmed/26583693

Fleming, T. P., Watkins, A. J., Velazquez, M. A., Mathers, J. C., Prentice, A. M., Stephenson, J., Barker, M., Saffery, R., Yajnik, C. S., Eckert, J. J., Hanson, M. A., Forrester, T., Gluckman, P. D., & Godfrey, K. M. (2018). Origins of lifetime health around the time of conception: Causes and consequences. *Lancet*, *391*(10132), 1842–1852. https://doi.org/10.1016/S0140-6736(18)30312-X

Fowler, J. K., Evers, S. E., & Campbell, M. K. (2012). Inadequate dietary intakes among pregnant women. *Canadian Journal of Dietetic Practice and Research*, *73*(2), 72–77. https://doi.org/10.3148/73.2.2012.72

Fowles, E. R., Bryant, M., Kim, S., Walker, L. O., Ruiz, R. J., Timmerman, G. M., & Brown, A. (2011). Predictors of dietary quality in low-income pregnant women: A path analysis. *Nursing Research*, *60*(5), 286–294. https://doi.org/10.1097/NNR.0b013e3182266461

Fraser, W. D., Shapiro, G. D., Audibert, F., Dubois, L., Pasquier, J. C., Julien, P., Bérard, A., Muckle, G., Trasler, J., Tremblay, R. E., Abenhaim, H., Welt, M., Bédard, M. J., Bissonnette, F., Bujold, E., Gagnon, R., Michaud, J. L., Girard, I., Moutquin, J. M., … Luo, Z. C. (2016). 3D Cohort Study: The Integrated Research Network in Perinatology of Quebec and Eastern Ontario. *Paediatric and Perinatal Epidemiology*, *30*(6), 623–632. https://doi.org/10.1111/ppe.12320

Gardner, B., Croker, H., Barr, S., Briley, A., Poston, L., Wardle, J., & Trial, U. (2012). Psychological predictors of dietary intentions in pregnancy. *Journal of Human Nutrition & Dietetics*, *25*(4), 345–353. https://doi.org/10.1111/j.1365-277X.2012.01239.x

Garriguet, D. (2009). Diet quality in Canada. *Health Reports*, *20*(3), 41–52. https://www.ncbi.nlm.nih.gov/pubmed/19813438

Grenier, L. N., Atkinson, S. A., Mottola, M. F., Wahoush, O., Thabane, L., Xie, F., Vickers-Manzin, J., Moore, C., Hutton, E. K., & Murray-Davis, B. (2021). Be healthy in pregnancy: Exploring factors that impact pregnant women's nutrition and exercise behaviours. *Maternal & Child Nutrition*, *17*(1), e13068. https://doi.org/10.1111/mcn.13068

Hanson, M. A., Bardsley, A., De-Regil, L. M., Moore, S. E., Oken, E., Poston, L., Ma, R. C., McAuliffe, F. M., Maleta, K., Purandare, C. N., Yajnik, C. S., Rushwan, H., & Morris, J. L. (2015). The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". *International Journal of Gynaecology and Obstetrics*, *131*(Suppl 4), S213–S253. https://doi.org/10.1016/S0020-7292(15)30034-5

Health Canada. (2007). Eating well with Canada's food guide 2007. https://www.canada.ca/en/health-canada/services/canada-food-guide/about/history-food-guide/eating-well-with-canada-food-guide-2007.html

Health Canada. (2009). Prenatal nutrition guidelines for health professionals—Background on Canada's food guide. https://www.canada.ca/en/health-canada/services/publications/food-nutrition/prenatal-nutrition-guidelines-health-professionals-background-canada-food-guide-2009.html

Health Canada. (2010). Prenatal nutrition guidelines for health professionals. Retrieved September 5, 2019, from https://www.canada.ca/en/health-canada/services/canada-food-guide/resources/prenatal-nutrition/eating-well-being-active-towards-healthy-weight-gain-pregnancy-2010.html

Health Canada. (2019). Healthy eating and pregnancy. https://www.canada.ca/en/public-health/services/pregnancy/healthy-eating-pregnancy.html

Ivers, L. C., & Cullen, K. A. (2011). Food insecurity: Special considerations for women. *American Journal of Clinical Nutrition*, *94*(6), 1740S–1744S. https://doi.org/10.3945/ajcn.111.012617

Jessri, M., Ng, A. P., & L'Abbe, M. R. (2017). Adapting the Healthy Eating Index 2010 for the Canadian population: Evidence from the Canadian National Nutrition Survey. *Nutrients*, *9*(8):910. https://doi.org/10.3390/nu9080910

Kolar, A. S., Patterson, R. E., White, E., Neuhouser, M. L., Frank, L. L., Standley, J., Potter, J. D., & Kristal, A. R. (2005). A practical method for collecting 3-day food records in a large cohort. *Epidemiology*, *16*(4), 579–583. https://doi.org/10.1097/01.ede.0000165363.27323.ac

Koletzko, B., Brands, B., Grote, V., Kirchberg, F. F., Prell, C., Rzehak, P., Uhl, O., Weber, M., & Early Nutrition Programming, P. (2017). Long-term health impact of early nutrition: The power of programming. *Annals of Nutrition and Metabolism*, *70*(3), 161–169. https://doi.org/10.1159/000477781

Krebs-Smith, S. M., Pannucci, T. E., Subar, A. F., Kirkpatrick, S. I., Lerman, J. L., Tooze, J. A., Wilson, M. M., & Reedy, J. (2018). Update of the Healthy Eating Index: HEI-2015. *Journal of the Academy of Nutrition and Dietetics*, *118*(9), 1591–1602. https://doi.org/10.1016/j.jand.2018.05.021

Kritsotakis, G., Chatzi, L., Vassilaki, M., Georgiou, V., Kogevinas, M., Philalithis, A. E., & Koutis, A. (2015). Social capital, tolerance of diversity and adherence to Mediterranean diet: The Rhea Mother–Child Cohort in Crete, Greece. *Public Health Nutrition*, *18*(7), 1300–1307. https://doi.org/10.1017/S136898001400144X

Lebrun, A., Plante, A. S., Savard, C., Dugas, C., Fontaine-Bisson, B., Lemieux, S., Robitaille, J., & Morisset, A. S. (2019). Tracking of dietary intake and diet quality from late pregnancy to the postpartum period. *Nutrients*, *11*(9), 2080. https://doi.org/10.3390/nu11092080

Lim, S. S., Vos, T., & Flaxman, A. D. (2013). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010 (vol 380, pg 2224, 2012). *Lancet*, *381*(9874), 1276–1276.

Malek, L., Umberger, W., Makrides, M., & Zhou, S. J. (2016). Adherence to the Australian dietary guidelines during pregnancy: Evidence from a national study. *Public Health Nutrition*, *19*(7), 1155–1163. https://doi.org/10.1017/S1368980015002232

Morisset, A. S., Dubois, L., Colapinto, C. K., Luo, Z. C., & Fraser, W. D. (2017). Prepregnancy body mass index as a significant predictor of total gestational weight gain and birth weight. *Canadian Journal of Dietetic Practice and Research*, *78*(2), 66–73. https://doi.org/10.3148/cjdpr-2016-035

Morton, S. M., Grant, C. C., Wall, C. R., Atatoa Carr, P. E., Bandara, D. K., Schmidt, J. M., Ivory, V., Inskip, H. M., & Camargo C. A. Jr. (2014). Adherence to nutritional guidelines in pregnancy: Evidence from the growing up in New Zealand birth cohort study. *Public Health Nutrition*, *17*(9), 1919–1929. https://doi.org/10.1017/S1368980014000482

Mozaffarian, D., Angell, S. Y., Lang, T., & Rivera, J. A. (2018). Role of government policy in nutrition-barriers to and opportunities for healthier eating. *BMJ*, *361*, k2426. https://doi.org/10.1136/bmj.k2426

Nash, D. M., Gilliland, J. A., Evers, S. E., Wilk, P., & Campbell, M. K. (2013). Determinants of diet quality in pregnancy: Sociodemographic, pregnancy-specific, and food environment influences. *Journal of Nutrition Education and Behavior*, *45*(6), 627–634. https://doi.org/10.1016/j.jneb.2013.04.268

Northstone, K., Emmett, P., & Rogers, I. (2008). Dietary patterns in pregnancy and associations with socio-demographic and lifestyle factors. *European Journal of Clinical Nutrition*, *62*(4), 471–479. https://doi.org/10.1038/sj.ejcn.1602741

Pick, M. E., Edwards, M., Moreau, D., & Ryan, E. A. (2005). Assessment of diet quality in pregnant women using the Healthy Eating Index. *Journal of the American Dietetic Association*, *105*(2), 240–246. https://doi.org/10.1016/j.jada.2004.11.028

Public Health Agency of Canada. (2009). What mothers say: The Canadian Maternity Experiences Survey. https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/rhs-ssg/pdf/survey-eng.pdf

Rifas-Shiman, S. L., Rich-Edwards, J. W., Kleinman, K. P., Oken, E., & Gillman, M. W. (2009). Dietary quality during pregnancy varies by maternal characteristics in Project Viva: A US cohort. *Journal of the American Dietetic Association*, *109*(6), 1004–1011. https://doi.org/10.1016/j.jada.2009.03.001

Savard, C., Lemieux, S., Carbonneau, E., Provencher, V., Gagnon, C., Robitaille, J., & Morisset, A. S. (2019). Trimester-specific assessment of diet quality in a sample of Canadian pregnant women. *International Journal of Environmental Research and Public Health*, *16*(3):311. https://doi.org/10.3390/ijerph16030311

Schwarzenberg, S. J., & Georgieff, M. K., Committee On Nutrition. (2018). Advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. *Pediatrics*, *141*(2):e20173716. https://doi.org/10.1542/peds.2017-3716

Shin, D., Lee, K. W., & Song, W. O. (2016). Pre-pregnancy weight status is associated with diet quality and nutritional biomarkers during pregnancy. *Nutrients*, *8*(3), 162. https://doi.org/10.3390/nu8030162

Stephenson, J., Heslehurst, N., Hall, J., Schoenaker, D., Hutchinson, J., Cade, J. E., Poston, L., Barrett, G., Crozier, S. R., Barker, M., Kumaran, K., Yajnik, C. S., Baird, J., & Mishra, G. D. (2018). Before the beginning: Nutrition and lifestyle in the preconception period and its importance for future health. *Lancet*, *391*(10132), 1830–1841. https://doi.org/10.1016/S0140-6736(18)30311-8

Sugiyama, T., & Shapiro, M. F. (2014). The growing socioeconomic disparity in dietary quality: mind the gap. *JAMA Internal Medicine*, *174*(10), 1595–1596. https://doi.org/10.1001/jamainternmed.2014.3048

USDA. Food patterns equivalents database. https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/docs/fped-overview/

Vang, Z. M., Sigouin, J., Flenon, A., & Gagnon, A. (2017). Are immigrants healthier than native-born Canadians? A systematic review of the healthy immigrant effect in Canada. *Ethnicity & Health*, *22*(3), 209–241. https://doi.org/10.1080/13557858.2016.1246518

Vanstone, M., Kandasamy, S., Giacomini, M., DeJean, D., & McDonald, S. D. (2017). Pregnant women's perceptions of gestational weight gain: A systematic review and meta-synthesis of qualitative research. *Maternal & Child Nutrition*, *13*(4):e12374. https://doi.org/10.1111/mcn.12374

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Yu, Y., Feng, C., Bédard, B., Fraser, W., & Dubois, L. (2022). Diet quality during pregnancy and its association with social factors: 3D Cohort Study (Design, Develop, Discover). *Maternal & Child Nutrition*, e13403. https://doi.org/10.1111/mcn.13403

Appendix 3. 3D Cohort Study Questionnaire 2C- Food Diary

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*
QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center | ID | Monogram | Day | Month | Year

Food Diary
Third trimester of pregnancy

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*
QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center | ID | Monogram

Thank you for your continuing participation in this study!

We are interested in knowing what kinds of food you are eating during the second trimester of your pregnancy. This Food diary will allow you to record all the food and beverages you has consumed for **three consecutive days** (each day corresponding to a 24 hour period), over the course of the next week. Please record all foods and beverages (including water) consumed, both day and night, in this diary.

Before I forget, I need to ask that you **precisely measure and record** all the meals and snacks you consume right after eating, rather than waiting until the end of the day. During the three days that you are recording your food intake, it is **very important** that you maintain typical eating habits. Continue a normal eating regime, and take note of all irregularities.

Return both this food diary, the ***Corresponding Questionnaire and the Food Frequency Questionnaire***, to the research nurse at your next appointment

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ☐☐ ID ☐☐☐ Monogram ☐☐☐

Instructions for completing this Food Diary

Each day, is divided into 7 sections, starting from, and ending at midnight.

1. ***Time,*** Indicate the precise time you ate or drank something
2. ***Meal or Snack***, indicate if the consumed food was a meal or a snack.
3. ***Place***, Record the place where you ate your meal or snack, according to the following options:
   - House – H, Restaurant – R, Cafeteria - C, or Other – O (Specify)
4. ***Description of food and drinks***, record all food and beverages you consumed at this time. Taking care to specify certain important details like:
   - The name of food or drink.
   - The type and brand of the product, if it is known (*IE.* minestrone soup: vegetarian pizza).
   - Method of cooking, if applicable (*IE.* microwaves, toasted, oven-heated, re-heated)
   - Condiments and seasonings (*IE.* fats or oils, sugar/sweeteners, sauces, salt, pepper, ketchup and other condiments).
5. ***Consumed Portion***, It is important to record the quantities you consumed, using appropriate measurements [*IE.* Table spoon (Tbsp.), teaspoon (tsp), cup (c)], the weight or volume indicated on packaged products (*IE.* a 200 ml juice container, one quarter of a quiche of 550g). Number of units (*IE.* 1 average size apple, 1 chicken leg, 2 slices of bread) and/or the dimension of the food (*IE.*10 cm long piece banana, 1 miniature carrot). **N.B. If you do not finish your meal or snack, take care to subtract the portion of the food not eaten.**

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ☐☐ ID ☐☐☐ Monogram ☐☐☐

6. If the food consume is **homemade**, describe in the space provided, the ingredients, quantity and the method of cooking. If the food was prepared by another person (a friend, Take-Out), and you don't know the recipe, describe as best you can the ingredients in the dish in question (*IE.* a tomato sauce with mushrooms, spinach and celery)
7. ***Food supplements***, indicate if you took supplements during the day (*IE.* Multivitamins, vitamin D supplement, Iron supplements, omega 3, etc.). Record the complete name of the product, the brand, along with the quantity and the time each supplement was taken.

At the end of the three-day, please fill-out the ***Corresponding Questionnaire,*** highlighting important nutritional details about the meals and snacks you had last week.

Helpful tips

- To help you, **an example** of a completed diary entry for one day, is provided on the **next page**.
- At the end of the food diary, a **MEMORY AID** is provided to help you describe relevant information required for recording the various types of food you have consume.
- For any questions concerning the recording of information in the Food Diary, and corresponding questionnaire please contact your research nurse:_____, phone_____

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ID Monogram

DAY 1 Date: 24 September 2008 (Wednesday) ***EXAMPLE***

Time	Meal or Snack	Place[1]	Description of food and beverages	Portion consumed
			From midnight to 6:00	
04h00	*Snack*	*Home (H)*	*Tap water*	*¼ cup*
			Between 6:00 and 9:00	
08h15	*Meal*	*H*	*Country Harvest 7 grain bread, toasted (45 g / slice)* *With Bécel olive oil margarine* *Nutella hazelnut spread* *and raw banana (average)* *Mini Wheat Cereals (original)* *With Natrel 2% M.G milk with omega 3* *And dried cranberries* *Minute Maid orange juice, frozen concentrated, diluted with water 1:3.5*	*1 slice* *1 tsp.* *1 Tbsp* *½* *½ cup* *½ cup* *1 soup spoon* *200 ml*
			Between 9:00 and 12:00 (noon)	
10h00	*Snack*	*R*	*Muffin, dates and nuts, Tim Horton* *Decaffeinate coffee* *With cream* *And sugar*	*½ portion* *1 medium size* *2 pre-measured 15 ml* *1 sachet*

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ID Monogram

Time	Meal or Snack	Place[1]	Description of food and beverages	Portion consumed
			Between 12:00 and 14:00	
12h15	*Meal*	*H*	*Oven cooked chicken leg with bone and skin, carrots and onions* *Served with of St-Hubert BBQ sauce dry (made according to instructions)* *Uncle's Ben (original) long grain white rice, cooked according to directions with half water, half chicken stock and semi-salt butter* *V8 vegetable juice*	*meat + skin : 1 piece 3.5 in. X 2 in. X 1 in.* *2 Tbsp* *¾ cup* *1 can 156 ml.*
			Between 14:00 and 17:00	
15h20	*Snack.*	*Other Friend*	*Activia yogurt - strawberry and kiwi*	*1x 100 g container*
16h30	*Snack.*	*H*	*Brandon crackers, 50% less salt* *P'tit Québec cheddar cheese, light (22% M.F.)* *Naya bottled water*	*3* *1 piece: 1 in. X 3 in. X 2 in.* *¾, of a 500 ml bottle*

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ID Monogram

Time	Meal or Snack	Place[1]	Description of food and beverages	Portion consumed
			Between 17:00 and 20:00	
18h30	*Meal*	*H*	*Macaroni and Cheese (see recipe)* *English cucumber, with peel, raw, salt and pepper* *raw mini carrots* *with Vegetable Ranch dressing, Philadelphia (Kraft)* *Québon skim milk* *Unsweetened apple sauce, Home*	*1 ½ cup* *3 slices, 1 cm thick.* *5* *1 Tbsp.* *200 ml* *½ cup*
			Between 20:00 and 23:59	
20h30	*Snack.*	*H*	*Egg sandwich – for 1 sandwich:* *2 slices of bread (same as breakfast)* *1 hard boiled egg* *1 tbs. de Miracle Whip light salad dressing* *1 romaine lettuce leaf* *White cake (prepared as per packet instructions: add 1 egg and 2% milk)* *With a thin layer of ready made Betty Crocker chocolate frosting*	*¼ of the sandwich* *1 piece = 6 cm X 4 cm X 3.5 cm*

[1]Place of Meal/Snack: M= Home; R = Restaurant; C= Cafeteria; A = Other (Specify)

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ID Monogram

PLEASE record recipes or the ingredients of prepared meals made, if not already described.

Macaroni and cheese
2 cups – dry Catelli macaroni (boiled in water with salt and oil)
Cheese sauce:
2 ½ cups – skim milk
3 Tbsp. – all purpose whole grain flour
3 Tbsp. – butter semi-salt
¾ tsp. – prepared yellow mustard
¾ tsp.– Worcestershire sauce
2 ml – pepper
2 cups – mozzarella cheese partially skimmed (16 % M.F.), grated
Garnish:
1 cup – breadcrumbs
¼ cup parmesan cheese grated

Did you consume any nutritional supplements (IE. vitamins and minerals, omega 3, etc.) in the past 24 hours Yes X
If yes, please indicate the name of the product, the brad, the quantity and time the supplement was taken. No ___

Complete Name and Brand of the supplement *record the DIN or NPN identification number inscribed on the label (if any)	Quantity (Tablets, capsules, tsp, etc.)	At what time?
Centrum Forte –Multivitamin and mineral formula– complete from A to Z *DIN 02246361*	*1 tablet* *1 tablet*	*07h00* *12h00*

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ☐☐ ID ☐☐☐ Monogram ☐☐☐

Corresponding Questionnaire

Finally, please answer the following questions concerning the meals and snacks you have consumed over the course of the last week.

1. Over the course of the last week, what type of milk did you mainly use?
Whole milk (3.25% M.F.) ___ 2% M.F. milk partially skimmed ___ 1% M.F milk partially skimmed ___ Skimmed milk___
Soya drinks ___ Other(s) ___ Specify_____

2. Over the course of the last week, did you add sugar and milk or cream in your tea or coffee?
Coffee: Milk___ Cream ___ Sugar____ None___ I did not have coffee in the last week ___
If yes, how much?_____
Tea: Milk___ Cream ___ Sugar ____ None___ I did not have tea in the last week ___
If yes, how much?_____

3. Over the course of the last week, what kind of water did you drink?
Tap water___ Well water_____ Filtered water___ Bottled water _____

4. Over the course of the last week, what type(s) of bread did you eat?
White ___ Fibre enriched white ___ Whole wheat___ Multigrain___ Other(s) ___ Specify_____
Specify the complete product name and brand, ideally, indicate the weight by portion (at the top of table of food value on packing):
_____
_____
_____

5. If you ate meat during the last week, did you eat meat that had visible fat?
Yes___ No ___ A little ___ I did not eat any meat last week ___

6. If you ate poultry during the last week did you eat the skin?
Yes ___ No___ A little___ I did not eat any last week poultry last week ___

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ☐☐ ID ☐☐☐ Monogram ☐☐☐

7. Over the course of the last week, what type of cooking oils did you use to cook with?
Specify the **complete name** of the product and the **brand** and **other particularities** (*IE. Mazola corn oil, butter semi salt, Bécel soft margarine, reduced saturated fats, Fleischmann corn and canola hard margarine, lard, shortening*) :
_____
_____
_____

8. Over the course of the last week, what types of butters or margarines did you use for spreading? (*IE.* on bread, toast, crackers)?
Specify the **complete name** of the product and the **brand** and **other particularities:**
_____
_____
_____

9. Over the course of the last week, what type of vinaigrettes, mayonnaise and salad dressings did you use?
Specify the **complete name** of the product and the **brand** and **other particularities:** (*IE. Kraft low calorie Cesar Vinaigrette; Miracle Whip salad dressing*)
_____
_____
_____

10. Over the course of the last week, did you add extra salt to your food at the table?
Rarely ___ Occasionally___ Often___ Never____ (*Go to question 12*)

11. If you added extra salt, what type of salt did you use?
Ordinary salt __ Salt substitute___ Other ___ Specify_____

12. Over the course of the last week, when you cooked, did you add salt to your cooking?
Rarely ___ Occasionally___ Often___ Never____

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ☐☐ ID ☐☐☐ Monogram ☐☐☐

13. Over the course of the last week, did you eat fruit and or vegetables with the skin (including potatoes)?

List the fruits and vegetables you ate that had skin:_____

List the fruits and vegetables you ate that have skin removed:_____

14. Over the course of the last week, did you follow a special diet (IE. vegetarian, to reduce cholesterol, weight control.)?

Yes____ No ___ *Please specify*_____

PLEASE add any other information that you consider important regarding your food intake in the last week

_____

_____

_____

_____

_____

Thank you for your cooperation!

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ☐☐ ID ☐☐☐ Monogram ☐☐☐

Memory Aid

BREAD, CEREALS, PASTA AND RICE	• **Bread** : Type of flour (IE. whole grain, white, rye bread), type (IE. slices, Kaiser, hamburger bun, hot-dog bun), brand and other packaging details (IE. grams per slice) • **Cereals** – Kind (complete name on the package), brand, with or without milk • **Pasta** - Type (IE. spaghetti, macaroni), flavour (IE. With spinach, extra protein, whole wheat, egg pasta, vegetable pasta), brand, method of cooking (IE. added, salt, oil…) • **Rice** - Type (IE. white, brown, basmati, instant), brand, method of cooking (IE. Follow directions or not, made with water, chicken or vegetable stock, added fat, added vegetables)
OTHERS BAKED GOODS	• Complete name (IE. chocolate chip cookies, angle food cake, carrot muffin, cinnamon brioche), and brand, state (IE. frozen, fresh and refrigerated, commercial mix, homemade). Others characteristics (IE. type of decorations or frosting, nuts, dried fruits) • If home made, list the ingredients that were used, rather than the package directions or recipe
FRUITS AND VEGTABLES	• Name (IE. Green grapes, apple, orange, spaghetti squash, red or green cabbage, green or yellow beans) • State (IE. fresh, dried, preserved (jams etc.), frozen) • Preparation (IE. Peeled or not, sliced, diced, mashed, grated) • Eaten raw or cooked, with or without peel • Cooking method (IE. heated, boiled, steamed, micro-waved, baked, fried), added ingredients (IE. sugar, flour, cream, type of milk, butter sauce) • Topping added right before serving (IE. sauce, garnish, cream, ice cream, sour cream, butter)

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ID Monogram

MILK AND MILK PRODUCTS	• Type of milk products (IE. milk, cheese, cream, evaporated milk, sweetened condensed milk, ice cream, ice milk, yogurt), brand, % milk fat (%M.F.) • Sort of milk product (IE. cheddar cheese, gouda, cottage; chocolate milk, vanilla ice cream, Suisse strawberry yoghurt) and others additives (IE. milk with omega 3, fibre, calcium added)
MEAT AND POULTRY	• Type (IE. beef, pork, lamb, poultry, turkey, duck) • Cut or eaten portion (IE. interior round, filleted, cross roast, leg, breast, wings, thigh) • Method of cooking (IE. braised, grilled, roasted, sauté, boiled, stewed, fried), whole or butchered meat, poultry with or without skin. Added cooking ingredients (IE. sauces, marinades), if fat was used, please indicate the type of fat used (if the fat is consumed, specify the quantity) • Mention if visible fat on the meat was eaten or not • If weight is indicated, specify if recorded weight is before or after cooking
COLD-CUTS	• Type of cold-cut (turkey Bologna, pork and beef sausage, all beef hot dogs) • Form (IE. Sliced , section, whole) and others characteristics (IE. regular, "reduced", or low in fat) • If cooked, mode of cooking
FISH	• Fish species and state (IE. fresh, canned or frozen, dried, salted or smoked) • Description (IE. filet, slice, finger-stick), breaded or battered • Cooking method (IE. grilled, baked, poached), if fat was used, please indicate the type of fat used (specify the quantity consumed) • If a weight is indicated, specify if recorded weight is before or after cooking

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center ID Monogram

EGGS, BEANS, NUTS AND GRAINS	• **Eggs**: defining characteristics (IE. with omega 3), cooking method (IE. scrambled, fried, soft or hard boiled, omelette) if fat was used, please indicate the type of fat used, additional ingredients (IE. milk, vegetables, salt and pepper) • **Beans**: type (IE. kidney beans, lentils, chick peas), form (IE. dried, canned) • **Nuts and grains**: type (IE. walnuts, pumpkin seeds, almonds), form (IE. whole, chopped, flaked), processing (IE. roasted, dried, salted)
SOUP AND BEVERAGES	• **Carbonated beverages** - brand, size of the container, type (IE. regular or diet, with or without caffeine), with or without ice (with ice, estimate the proportion of the quantity of noted beverage) • **Pure fruit juice and fruit flavoured drinks** -- type (apple juice, nectar, fruit punch, etc.), form (fresh, refrigerated, frozen concentrate, out of a can or bottle), brand, 100% pure juice or not, sweetened or unsweetened, with or without added vitamin C (see information on packing) percent dilution if product is a frozen concentrate (IE. 1 part juice container with 3 parts water) and the type of water used (tap water, well water, filtered water, bottled water) • **Chocolate milk flavouring** –form (IE. chocolate powder, cocoa, chocolate syrup), preparation (water, milk % M.F.), additional ingredients (IE. sugar or sweetener, marsh mallows) • **Soya or rice drinks** –product name, brand, flavour, enriched with vitamins and minerals, or not. (see information on packing) • **Soup** – form (IE. canned, ready to eat or concentrated, (dehydrated) powdered soup mix) brand, characteristics (IE. low sodium content, low in fat), liquid used for dilution (IE. water, milk or cream and % M.F.) as well as the percent of dilution if it differs from directions • **Water**– type (tap water, well water, filtered water, bottled water, mineral water), brand
SNACK FOOD	• Type (IE. potatoes chips, nachos, popcorn, chocolate bar, soft candy bars, crackers), brand, and flavour (IE. BBQ, salt and vinegar, cheese flavoured, caramel), others characteristics (IE. regular, light, calorie or salt reduced) • Additional flavouring (IE. seasonings, butter)

IRNPQEO *Integrated Research Network in Perinatology of Quebec and East Ontario*

QUESTIONNAIRE 2C – Food Diary *(between 20-24 weeks)*

Center | ID | Monogram

FATS AND OIL	• Type (IE. margarine, butter, oil, vinaigrette, shortening, bacon), brand, characteristics (IE. regular, light, calories reduced, none salted, half-salt) • Certain precise details about the margarines: type of oil (IE. of sunflower, colza, corn, mixed, etc.), hard or soft margarine • Certain precise details about the mayonnaises, salad dressings and vinaigrettes: (IE. Ranch, Cesar, Italian, true mayonnaise)
PREPARED MEALS	• Commercial products (IE. frozen or refrigerated, canned pasta, quiches, pizza) - type, product name, weight on packing, and brand name. • Home made meals – recipe, ingredients and measurements. • Restaurant meals – name of restaurant, meal description, water, bread, condiments and others additional flavourings, etc. **N.B.** For pizzas, specify: where it was purchased (IE. frozen commercial, restaurant), the type of crust (IE. Thin, thick or regular, whole wheat or stuffed crust), the type of dressings (tomato sauce, type of meat, cheese, types of vegetables, with extras) the size (small, medium, large, extra-large (or the diameter in inches), for both frozen or restaurant products.

Appendix 4. Published Protocol for Manuscript 2

Open access Protocol

BMJ Open

Diet quality during preconception or pregnancy and gestational weight gain: protocol for a systematic review and meta-analysis

Yamei Yu ,[1] Isabelle Hardy ,[2] Wenguang Sun,[3] Dean A Fergusson,[1,4] William Fraser,[2,5] Lise Dubois[1]

To cite: Yu Y, Hardy I, Sun W, *et al*. Diet quality during preconception or pregnancy and gestational weight gain: protocol for a systematic review and meta-analysis. *BMJ Open* 2020;**10**:e033130. doi:10.1136/bmjopen-2019-033130

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2019-033130).

Received 23 July 2019
Revised 11 January 2020
Accepted 16 January 2020

For numbered affiliations see end of article.

Correspondence to
Dr Lise Dubois;
ldubois@uottawa.ca

ABSTRACT

Introduction Inappropriate gestational weight gain (GWG), including inadequate and excessive GWG, has become pandemic across nations and continents. This review aims to synthesise the evidence on the correlation between diet quality and GWG. If this association is confirmed, improving diet quality could become an intervention target in the efforts to reduce inappropriate GWG.

Methods and analysis We will conduct a systematic review of all prospective cohort studies on diet quality in preconception or pregnancy and GWG. Our secondary outcomes include gestational diabetes, pre-eclampsia and birth weight. A comprehensive search of all published articles in MEDLINE ALL (Ovid), Embase (Ovid), Food Science and Technology Abstracts (Ovid) and CINAHL (EBSCOHost), from database creation to 20 April 2019, will be conducted. Studies will be screened for eligibility by title, abstract and full text in duplicate by two independent reviewers. Study quality and risk of bias will be assessed using the adapted Newcastle–Ottawa Scale. Results will be reported following the meta-analysis of observational studies in epidemiology guidelines. If sufficient data are available, a meta-analysis will be conducted to synthesise the effect size reported as OR with 95% CI using both fixed-effect and random-effect models. I^2 statistics and visual inspection of the forest plots will be used to assess heterogeneity and identify the potential sources of heterogeneity. Publication bias will be assessed by visual inspections of funnel plots and Egger's test.

Ethics and dissemination Formal ethical approval is not required as no primary data will be collected. We aim to publish the results of this study in a peer-reviewed journal and present them at conferences and scientific meetings to promote knowledge transfer.

PROSPERO registration number CRD42019128732

Strengths and limitations of this study

- Compared with diet quantity, or single nutrients/food groups, the importance of overall diet quality has not been evaluated in correlation with gestational weight gain and subsequent maternal and childhood outcomes. This study is the first to synthesise the evidence regarding the association between diet quality and gestational weight gain.
- We will only include prospective cohort studies to avoid recall bias in dietary assessment and reverse causation in case–control and cross-sectional studies.
- The main methodological limitations of this systematic review are the exclusion of abstracts and foreign-language publications.
- Another potential limitation we anticipate is that we might encounter different definitions of diet quality and the secondary outcomes, which will limit our ability to pool the results in meta-analysis.

INTRODUCTION

Defining diet quality

Diet quality is a relatively new concept measured by scoring diet in terms of '*a priori*' defined adherence to dietary guidelines or a specific pattern. Compared with single nutrient or single food group measures, diet quality enables research on overall diet using broader components of food groups, based on the best available knowledge concerning associations between diet and health. Diet quality indices also differentiate from a data-driven dietary pattern analysis which is studied '*a posteriori*' using factor or cluster analysis.[1] Some diet quality indices are based on national dietary guidelines, such as the Healthy Eating Index (HEI)[2 5] in USA, which was developed in 2008 to assess the alignment of diet to Dietary Guidelines for Americans. Newer versions (HEI-2010[4] and HEI-2015[5]) correspond to evolving versions of the dietary guidelines. Other diet quality indices evaluate adherence to certain healthy dietary patterns such as Mediterranean-style patterns[6] or dietary approaches to stop hypertension-style patterns.[7] Systematic reviews have identified a list of diet quality indices including Diet Quality Index, Dietary Guideline Index, Dietary Diversity Score, Recommended Food Score and so on.[8 9]

Defining gestational weight gain (GWG) and its importance

Appropriate weight gain during pregnancy is important for maternal and infant health. In 2009,[10] the Institute of Medicine (IOM; now known as the National Academy of Medicine) updated the GWG guidelines[11] to provide specific recommendations regarding the ideal GWG. The new guideline incorporated WHO categories of maternal body mass index (BMI) and recommended less GWG for overweight and obese women. Briefly, the IOM recommended 12.5–18 kg of total GWG for singleton pregnancies with a prepregnancy BMI categorised as underweight (BMI<18.5), 11.5–16 kg for normal weight (BMI 18.5–24.9), 7–11.5 kg for overweight (BMI 25–29.9) and 5–9 kg for obese (BMI≥30). Total GWG within the IOM recommendations will be considered as appropriate GWG, above the recommendations will be considered as excessive GWG and below the recommendations will be considered as inadequate GWG.

Inappropriate GWG has a significant effect on perinatal outcomes, independent of maternal BMI. A systematic review and meta-analysis[12] found that excessive GWG is associated with an increased risk of large for gestational age (OR 1.85, 95% CI 1.76 to 1.95), macrosomia (1.95, 1.79 to 2.11) and caesarean delivery (1.30, 1.25 to 1.35). Low GWG is related to increased risk of small for gestational age (1.53, 1.44 to 1.64) and preterm birth (1.70, 1.32 to 2.20). Higher maternal GWG is also associated with higher risks of gestational hypertensive disorders, pre-eclampsia, preterm birth and gestational diabetes.[13] Although overweight and obese women present high rates of both excessive GWG, and gestational diabetes and pre-eclampsia, GWG has not been consistently found to mediate these complications.[12 14]

Inappropriate GWG also has long-term effects on maternal and offspring health. In a meta-analysis,[15] women with a GWG above recommended levels retained, on average, an additional 3.06 kg (95% CI 1.50 to 4.63) after 3 years, and 4.72 kg (2.94 to 6.50) after ≥15 years post partum, compared with women with GWG within the recommendations. In non-overweight women, excessive GWG has been found to triple the risk of becoming overweight after pregnancy (3.19, 1.87 to 5.44).[16] In the offspring, excessive maternal GWG has been associated with increased adiposity[17] and an increased risk of overweight/obesity[18] during childhood.

Considering the global epidemic of inappropriate GWG, with prevalence of excessive and inadequate GWG, respectively, reaching 50% and 20% across continents and ethnicities,[19] it is urgent that effective interventions be put in place.

Association between diet quality and GWG

Pregnancy is a critical period when energy and nutrient intake must support growth of maternal and fetal tissues. Low diet quality characterised by high saturated fat, refined grains, free sugars, low fibre intake may contribute to excessive energy intake which may be a risk factor for excessive GWG and inadequate vital nutrient intake. Thus, adjusting diet quality could be a target for nutritional intervention to reduce excessive weight gain.

Although dietary patterns are difficult to change, pregnancy appears as a window of opportunity where women are willing to adopt healthier dietary habits.[20] Thus, pregnancy is a critical intervention period to implement dietary interventions targeting both women and their families. Considering that the offspring share similar dietary patterns with the parents, a good diet pattern can be transmitted to the next generation with potential long-lasting effects on health.

Why is it important to do this review?

With the recent development of prospective birth cohorts, evidence of an association between diet quality and GWG is accumulating. However, no systematic review has evaluated this association. One systematic review evaluated the relationship between macronutrients intake and GWG,[21] but none has reviewed the evidence on the relationship between global diet quality and GWG. Consequently, diet quality has been neglected as a risk factor and potential intervention target for inappropriate GWG. We would like to fill this knowledge gap by providing a robust evidence synthesis on the subject. This work will guide effective interventions and policy making to prevent inappropriate GWG, and its short-term and long-term consequences.

Research objectives

The objective of our study is to systematically review prospective cohort studies that explore the association between diet quality and GWG. Our secondary aim will be to explore whether this association is mediated by energy intake, and whether diet quality has further impact on clinical outcomes including gestational diabetes, pre-eclampsia and birth weight. If significant heterogeneity is identified, we will conduct subgroup analyses to explore potential factors that modify the association between diet quality and GWG. Potential effect modifying factors include the origin of the study population (developed/developing countries, urban/rural areas), the characteristics of the population (overweight or obese/general pregnant women) and the timing of dietary evaluation (preconception/trimester of pregnancy).

METHODS AND ANALYSIS

Patient and public involvement

Patients and the public were not involved in the design and conception of this study.

Eligibility criteria

Studies will be screened and selected according to the criteria specified below.

Study designs

Only prospective cohort studies of human subjects will be included in this systematic review. Case–control studies will be excluded because they are retrospective and may lead to recall bias in dietary assessment.[22] Secondary

analysis of the control arm of randomised control trials will be included, since this design mimics a prospective cohort and excludes the effect of the intervention. In order to avoid recall bias in dietary assessment and avoid reverse causation, we will only include studies where dietary assessment is completed before the outcome measurement. We will exclude other study types such as narrative and systematic reviews, experimental or quasi-experimental trials, case–control studies, cross-sectional studies, case series and case reports.

Publication type

Only full-text articles published in scholarly peer-reviewed journals in English will be included. Only articles published in English will be included. We will exclude abstracts, unpublished grey literature, commentaries, letters, reviews and editorials, meeting proceedings, theses and dissertations, books, treatment guidelines or manuals.[23]

Participants

We are interested in studies of women from the general population in the preconception period or pregnancy. Studies including only women with a specific disease, such as heart disease, diabetes, hypertension or gestational diabetes, will be excluded because these populations may already adhere to specifically prescribed dietary patterns, which might lead to reverse causation in the association between diet and the outcomes. Studies of diet quality in the general population including some women with a specific disease will be included. Studies of women with overweight or obesity will also be included. Most included women are expected to be 18–45 years at the time of study participation, but general population studies including some minor or older participants will be included. We will exclude studies focusing only on participants <18 years old such as studies of teenagers.

Exposure

We are interested in the difference in the outcomes of women exposed to high diet quality, compared with women exposed to low diet quality in the same population. Diet quality will be assessed systematically using prespecified scoring scales and validated dietary assessment methods including food diaries, food recalls or food frequency questionnaires. Diet quality analysed as both categorical and continuous variables will be included. Studies with exposures defined as a single or few nutrients or food groups will be excluded.

Outcomes

Our primary outcome is GWG according to the IOM recommendations, and our secondary outcomes include gestational diabetes, pre-eclampsia, preterm delivery, delivery by caesarean section and birth weight for gestational age. We will not exclude studies based on the definition of the outcomes because we anticipate that there will be discrepancies in the definition of outcomes in the target studies. We will extract outcomes in all data forms (eg, dichotomous, continuous) as reported in the included studies. The definition of the outcomes in each study will be recorded.

Information sources

Four databases will be searched: MEDLINE ALL (Ovid), Embase (Ovid), Food Science and Technology Abstracts (Ovid) and CINAHL (EBSCOHost). All databases will be searched from the date of database creation to the cut-off date of 20 April 2019. In order to further ensure a comprehensive literature search, reference lists of included studies and relevant review articles identified through the search will be checked for additional references. Authors of relevant published abstracts will be contacted to verify if full-text manuscripts have been published. Finally, we will circulate a bibliography of the included articles to the systematic review team for feedback.

Search strategy

Both medical subject headings and text keywords were used to develop the search strategies. Two groups of keywords were used: 'preconception or pregnancy', and diet quality. The Medline search strategy was developed with inputs from the whole research team and the health science librarian (LS) with expertise in systematic review research strategies. After the Medline search strategy was finalised, it was adapted to the syntax of other databases. The search terms were then peer reviewed by a second health science librarian not otherwise associated with the project.[24] The detailed search terms used in OVID Medline are shown in online supplementary file 1.

Study selection

The publications identified with the search process will be uploaded to the Covidence software, which is an online service working in partnership with Cochrane to improve the production and use of systematic reviews for health and well-being. Two review authors (YY and IH) will independently screen the titles and abstracts of the search results to exclude articles that do not meet the eligibility criteria. All articles that seem to meet the inclusion criteria in the title and abstract screening or those with uncertainties will be assessed with full text. Reasons for exclusion in the full-text screening will be recorded. Any disagreement arising during the selection process will be resolved by discussion with a third reviewer. The process of study selection will be reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.[25]

Data collection process

YY and IH will independently extract all information related to the research question from the included studies for both narrative synthesis and potential meta-analysis. A predefined extraction sheet will be used. We will also contact the authors if related data are ambiguous or not included in the publications. Any disagreement arising during the extraction process will be resolved by discussion with a third reviewer LD.

The following data will be extracted from all studies meeting the inclusion criteria:

1. Study authors.
2. Year of study.
3. Country/countries where study was conducted.
4. Population characteristics (including their ethnicity, age, parity and so on) with inclusion/exclusion criteria.
5. Study design and characteristics.
6. Number of participants.
7. Exposure information on diet quality, including diet assessment method, definition of diet quality, calculation, time of measurement (preconception or gestational age).
8. Outcomes: definition and time of measurement.
9. Conflicts of interest and funding.
10. Statistical analysis.
11. Confounders adjusted for in the statistical analysis.
12. Selected main findings.

Risk of bias in individual studies

YY and IH will independently assess the quality and risk of bias of the included studies in duplicates. Discrepancies between the two reviewers will be resolved by discussion. If necessary, a third author of the team will be consulted to achieve consensus. The quality of the studies will be assessed with the Newcastle–Ottawa Scale.[20] In this scale, a maximum of 9 points can be awarded to each cohort study: 4 for selection, which evaluates selection bias ascertainment of exposure; 2 for comparability, which requires control of appropriate confounders and 3 for the outcome, which requires a high quality measurement of the outcomes and follow-up. The sum of points for all subscale items will be used to categorise overall study quality as either high (>7), moderate (5–7) or low (<5) to decide on the likelihood of reliability of the outcome reports. Justification from the study report will be supplied to support the judgement as appropriate.

Data synthesis

Risk ratios with 95% CI will be used to summarise the association between diet quality (the highest vs lowest levels of diet quality scores) and GWG (excessive or insufficient GWG compared with appropriate GWG category according to IOM guideline) and the association between diet quality and other categorical outcomes. Weighted mean differences with 95% CI will be used for continuous outcomes. We are anticipating different scales of reporting diet quality across studies, including 1 absolute unit increase, 1 SD increase, tertiles, quartiles, quintiles. The different scales will be transformed to calculate the effect size in the top tertile of diet quality scores compared with the bottom tertile using the method reported in previous studies.[27–29] The homogeneity of the study results will be assessed using I^2 statistic and by visual inspection of the forest plots. The rough guide for interpretation of I^2 are as follows: 0%–40% may present low heterogeneity, 30%–60% may present moderate heterogeneity, 50%–90% may represent substantial heterogeneity and 75%–100% is considerable heterogeneity.[30] If there is a substantial amount of heterogeneity (≥75%), the sources of heterogeneity will be examined through subgroup analyses examining factors including origin of the study population (developed/developing countries, urban/rural areas), the characteristics of the population (overweight or obese/general pregnant women) and the timing of dietary evaluation (preconception/trimesters of pregnancy). Considering the possibility of different covariates used in each study, we are planning to do subgroup analysis separating studies including or not including the important covariates including prepregnancy BMI, socioeconomic background, parity and so on, if a sufficient number of studies are available. If appropriate, we will also make exclusions based on the sensitivity analysis excluding studies with high risk of bias to improve the homogeneity of the results. A quantitative analysis (meta-analysis) will be done using Review Manager (RevMan) V.5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Populational characteristics and exposure/outcome definitions may vary between the target observational studies, so pooling data using a random-effect model may seem more reasonable. But presenting results from both models in a sensitivity analysis may be informative.[31] In this study, both fixed-effect model and random-effect model will be used to estimate the summary statistics and 95% CIs. If there is a sufficient number of studies on the mediation effect of total energy on the association between diet quality and GWG, we will use correlation-based or parameter-based approaches, as appropriate, to conduct a meta-analytic structural equation modelling as reviewed by Cheung and Cheung.[32] If the included studies are not sufficiently homogenous to conduct a meta-analysis or if three or fewer studies use similar measuring methods, a narrative synthesis will be provided to report relevant findings from the included studies.

Publication bias and small study effects

Publication bias will be assessed in all analyses synthesising 10 or more studies to ensure adequate power in the analysis.[30] For investigation of the effect of small studies and publication bias, data from included studies will be entered into a funnel plot asymmetry test if we have at least 10 studies in the meta-analysis. Egger's statistical test will be implemented using STATA/SE V.13 (Stata Corp).

Confidence in cumulative evidence

The quality of supporting evidence will be assessed by the Grades of Recommendation, Assessment, Development and Evaluation.[35]

Amendments

This is an original research protocol, as opposed to an amendment of a previously completed protocol. If the protocol requires major amendments, the changes will be documented and updated via PROSPERO and stated in the final review manuscript.

Author affiliations
[1]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

[2]Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec, Canada
[3]The International Peace Maternity and Child Health Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China
[4]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada
[5]Centre de Recherche du Centre hospitalier Universitaire de Sherbrooke (CRCHUS), Sherbrooke, Ottawa, Canada

Acknowledgements The authors would like to thank Lindsey Sikora (librarian) for counselling in developing the searching strategies. We also thank Dr Jean-Patrice Baillargeon for critical reviews and suggestions in formulating the systematic review protocol.

Collaborators Lindsey Sikora; Jean-Patrice Baillargeon.

Contributions YY is the guarantor of the review. YY, WS, WF and LD contributed to the conception of the research question. YY, IH, WS and DAF contributed to the development of search strategies, eligibility criteria and methodology for data synthesis. YY, IH, WS, LD, WF and DAF contributed to drafting of the protocol and provided approval for the version submitted for publishing. YY and IH will work in duplicate to screen the titles and abstracts of all the materials obtained using the search strategy to exclude the articles that do not meet the eligibility criteria. YY and IH will evaluate the potentially eligible studies with the full text and further exclude studies with documentation of the reason for exclusion. All authors will contribute to the bias assessment strategy and data extraction criteria. YY and IH will independently extract data from the included studies using a predefined extraction sheet. YY and IH will analyse the data and draft the results. All authors will read, provide feedback and approve the final manuscript.

Funding This research project is sponsored jointly by the Canadian Institutes of Health Research (CIHR) (Grant HLT 151517) and the National Natural Sciences Foundation of China (NSFC) (Grant No. 81661128010).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Formal ethical approval is not required as no primary data will be collected. We aim to publish the results of this study in a peer-reviewed journal and present them at conferences and scientific meetings to promote knowledge transfer.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Yamei Yu http://orcid.org/0000-0002-5151-3397
Isabelle Hardy http://orcid.org/0000-0001-9996-2995

REFERENCES

1 Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* 2002;13:3–9.
2 Guenther PM, Reedy J, Krebs-Smith SM. Development of the healthy eating Index-2005. *J Am Diet Assoc* 2008;108:1896–901.
3 Guenther PM, Reedy J, Krebs-Smith SM, *et al*. Evaluation of the healthy eating Index-2005. *J Am Diet Assoc* 2008;108:1854–64.
4 Guenther PM, Casavale KO, Reedy J, *et al*. Update of the healthy eating Index: HEI-2010. *J Acad Nutr Diet* 2013;113:569–80.
5 Krebs-Smith SM, Pannucci TE, Subar AF, *et al*. Update of the healthy eating Index: HEI-2015. *J Acad Nutr Diet* 2018;118:1591–602.
6 Trichopoulou A, Costacou T, Bamia C, *et al*. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* 2003;348:2599–608.
7 Fung TT, Chiuve SE, McCullough ML, *et al*. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. *Arch Intern Med* 2008;168:713–20.
8 Asghari G, Mirmiran P, Yuzbashian E, *et al*. A systematic review of diet quality indices in relation to obesity. *Br J Nutr* 2017;117:1055–65.
9 Wirt A, Collins CE. Diet quality--what is it and does it matter? *Public Health Nutr* 2009;12:2473–92.
10 Rasmussen KM, Yaktine AL, eds. *Weight gain during pregnancy: reexamining the guidelines*. Washington, DC: National Academies Press, 2009.
11 Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation. *Nutrition during pregnancy: Part I weight gain: Part II nutrient supplements*. Washington, DC: National Academies Press (US), 1990.
12 Goldstein RF, Abell SK, Ranasinha S, *et al*. Association of gestational weight gain with maternal and infant outcomes: a systematic review and meta-analysis. *JAMA* 2017;317:2207–25.
13 Santos S, Voerman E, Amiano P, *et al*. Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. *BJOG* 2019;126:984–95.
14 Nohr EA, Vaeth M, Baker JL, *et al*. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. *Am J Clin Nutr* 2008;87:1750–9.
15 Nehring I, Schmoll S, Beyerlein A, *et al*. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. *Am J Clin Nutr* 2011;94:1225–31.
16 Gunderson EP, Abrams B, Selvin S. The relative importance of gestational gain and maternal characteristics associated with the risk of becoming overweight after pregnancy. *Int J Obes Relat Metab Disord* 2000;24:1660–8.
17 Hochner H, Friedlander Y, Calderon-Margalit R, *et al*. Associations of maternal prepregnancy body mass index and gestational weight gain with adult offspring cardiometabolic risk factors: the Jerusalem perinatal family follow-up study. *Circulation* 2012;125:1381–9.
18 Voerman E, Santos S, Patro Golab B, *et al*. Maternal body mass index, gestational weight gain, and the risk of overweight and obesity across childhood: an individual participant data meta-analysis. *PLoS Med* 2019;16:e1002744.
19 Goldstein RF, Abell SK, Ranasinha S, *et al*. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women. *BMC Med* 2018;16:153.
20 Vanstone M, Kandasamy S, Giacomini M, *et al*. Pregnant women's perceptions of gestational weight gain: a systematic review and meta-synthesis of qualitative research. *Matern Child Nutr* 2017;13.
21 Tielemans MJ, Garcia AH, Peralta Santos A, *et al*. Macronutrient composition and gestational weight gain: a systematic review. *Am J Clin Nutr* 2016;103:83–99.
22 Song JW, Chung KC. Observational studies: cohort and case-control studies. *Plast Reconstr Surg* 2010;126:2234–42.
23 Fergusson D, Laupacis A, Salmi LR, *et al*. What should be included in meta-analyses? an exploration of methodological issues using the ISPOT meta-analyses. *Int J Technol Assess Health Care* 2000;16:1109–19.
24 McGowan J, Sampson M, Salzwedel DM, *et al*. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol* 2016;75:40–6.
25 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009;339:b2535.
26 Wells GA, Shea B, O'Connell D, *et al*. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, 2011. Available: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
27 Danesh J, Collins R, Appleby P, *et al*. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. *JAMA* 1998;279:1477–82.
28 Araujo AB, Dixon JM, Suarez EA, *et al*. Clinical review: endogenous testosterone and mortality in men: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2011;96:3007–19.
29 Chia A-R, Chen L-W, Lai JS, *et al*. Maternal dietary patterns and birth outcomes: a systematic review and meta-analysis. *Adv Nutr* 2019;10:685–95.
30 Higgins J, Green S, eds. *Cochrane handbook for systematic reviews of interventions version 5.1.0*. The Cochrane collaboration, 2011.
31 Dekkers OM, Vandenbroucke JP, Cevallos M, *et al*. COSMOS-E: guidance on conducting systematic reviews and meta-analyses of observational studies of etiology. *PLoS Med* 2019;16:e1002742.
32 Cheung MW-L, Cheung SF. Random-effects models for meta-analytic structural equation modeling: review, issues, and illustrations. *Res Synth Methods* 2016;7:140–55.
33 Guyatt GH, Oxman AD, Vist GE, *et al*. Grade: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.

Appendix 5. Proof of Submission for Manuscript 2

De: PLOS ONE <em@editorialmanager.com>
Date: 28 juin 2022 à 17:08:41 HAE
À: Lise Dubois <ldubois@uottawa.ca>
Objet: Submission Confirmation for PONE-D-22-18391 - [EMID:7a02bc067527a120]
Répondre à: PLOS ONE <plosone@plos.org>

Attention : courriel externe | external email

PONE-D-22-18391
Association Between Diet Quality During Preconception or Pregnancy and Perinatal Outcomes: a Systematic Review and Meta-Analysis
PLOS ONE

Dear Dr. Dubois,

Thank you for submitting your manuscript entitled 'Association Between Diet Quality During Preconception or Pregnancy and Perinatal Outcomes: a Systematic Review and Meta-Analysis' to PLOS ONE. Your assigned manuscript number is PONE-D-22-18391.

We will now begin processing your manuscript and may contact you if we require any further information. You will receive an update once your manuscript passes our in-house technical check; you can also check the status of your manuscript by logging into your account at https://www.editorialmanager.com/pone/.

If during submission you selected the option for your manuscript to be posted on the bioRxiv preprint server (http://biorxiv.org), we will be assessing the manuscript for suitability shortly. If suitable, your preprint will be made publicly available on bioRxiv and you will receive an email confirmation from them when it has posted. Please check your response to this question and email us as soon as possible at plosone@plos.org if it has been answered incorrectly. Further information about our partnership with bioRxiv to facilitate the rapid availability of life sciences research is available at http://journals.plos.org/plosone/s/preprints.

If you have any inquiries or other comments regarding this manuscript please contact plosone@plos.org.

Thank you for your support of PLOS ONE.

Kind regards,
PLOS ONE

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/pone/login.asp?a=r). Please contact the publication office if you have any questions.

Appendix 6. Results from the 3D Cohort Study - Association between Diet Quality during Pregnancy and Perinatal Outcomes.

	results from 3D study				pooled results from meta-analysis	
	n	unadjusted OR or beta (95% CI)	n	adjusted* OR or beta (95% CI)	number of studies	OR or beta (95% CI)
excessive gestational weight gain	1451	0.86(0.65,1.15)	1393	1.14(0.83,1.56)	6	0.91(0.76, 1.10)
inadequate gestational weight gain	1451	1.16(0.79,1.69)	1393	1.17(0.78,1.76)	6	0.9(0.70, 1.17)
HDP	1468	0.59(0.35,0.99)	1402	0.52(0.3,0.92)	5	0.87(0.83, 0.92)
preterm birth	1526	0.85(0.62,1.17)	1391	0.89(0.63,1.25)	8	0.77(0.66, 0.89)
SGA	1453	0.92(0.71,1.19)	1387	0.83(0.63,1.1)	6	0.88(0.79, 0.99)
LBW	1459	0.74(0.5,1.09)	1393	0.7(0.46,1.05)	5	0.6(0.37, 0.99)
LGA	1453	0.92(0.69,1.22)	1387	1.02(0.75,1.39)	6	0.9(0.71, 1.15)
Macrosomia	1459	0.91(0.71,1.18)	1393	0.9(0.68,1.19)	3	1.12(0.69, 1.81)
Birth Weight as a Continuous Variable	1528	-13.29(-77.07,50.5)	1396	-9.37(35.59,0)	9	-7.8(-56.0, 40.5)
Birth Weight for Gestational Age Z-score as a continuous variable	1385	-0.1(-0.23,0.02)	1275	-0.08(0.07,0)	3	0(-0.1, 0.2)

Effect estimates for for pregnant women in the top tertile of diet quality scores compared to those in the bottom tertile.
*Adjusted for maternal age, education, household income, marital status, prepregnancy BMI, parity, born in Canada, ethnicity, smoking status, calorie intake. Additionally adjusted for sex of the baby for birth weight related outcomes.

Appendix 7. STROBE-nut Reporting Checklist for Manuscript 3

Adapted from Lachat C et al. (2016) STrengthening the Reporting of OBservational studies in Epidemiology – Nutritional Epidemiology (STROBE-nut): an extension of the STROBE statement. Plos Medicine 13(6) http://dx.doi.org/10.1371/journal.pmed.1002036 pdf or online version.

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.	**nut-1** State the dietary/nutritional assessment method(s) used in the title, abstract, or keywords.	Abstract – Methods p.4
Introduction				
Background rationale	2	Explain the scientific background and rationale for the investigation being reported.		Background p.6-7
Objectives	3	State specific objectives, including any pre-specified hypotheses.		Background p.7
Methods				
Study design	4	Present key elements of study design early in the paper.		Methods (Design, Setting, and Participants) p.7

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
Settings	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.	**nut-5** Describe any characteristics of the study settings that might affect the dietary intake or nutritional status of the participants, if applicable.	Methods (Design, Setting, and Participants) p.7
Participants	6	a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants. (b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed. Case-control study—For matched studies, give matching criteria and the number of controls per case.	**nut-6** Report particular dietary, physiological or nutritional characteristics that were considered when selecting the target population.	Methods (Design, Setting, and Participants) p.7

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	**nut-7.1** Clearly define foods, food groups, nutrients, or other food components. **nut-7.2** When using dietary patterns or indices, describe the methods to obtain them and their nutritional properties.	Methods (Exposures and Measurements, Outcomes and Measurements) p.7-9
Data sources - measurements	8	For each variable of interest, give sources of data and details of methods of assessment (measurement).Describe comparability of assessment methods if there is more than one group.	**nut-8.1** Describe the dietary assessment method(s), e.g., portion size estimation, number of days and items recorded, how it was developed and administered, and how quality was assured. Report if and how supplement intake was assessed. **nut-8.2** Describe and justify food composition data used. Explain the procedure to match food composition with consumption data. Describe the use of conversion factors, if applicable. **nut-8.3** Describe the nutrient requirements, recommendations, or dietary guidelines and the	Methods (Exposures and Measurements) p.7-8

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
			evaluation approach used to compare intake with the dietary reference values, if applicable. **nut-8.4** When using nutritional biomarkers, additionally use the STROBE Extension for Molecular Epidemiology (STROBE-ME). Report the type of biomarkers used and their usefulness as dietary exposure markers. **nut-8.5** Describe the assessment of nondietary data (e.g., nutritional status and influencing factors) and timing of the assessment of these variables in relation to dietary assessment. **nut-8.6** Report on the validity of the dietary or nutritional assessment methods and any internal or external validation used in the study, if applicable.	
Bias	9	Describe any efforts to address potential sources of bias.	**nut-9** Report how bias in dietary or nutritional assessment was addressed, e.g., misreporting,	Methods (Statistical Analyses) p.9 Discussion (Strength) p.22

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
			changes in habits as a result of being measured, or data imputation from other sources	
Study Size	10	Explain how the study size was arrived at.		Methods (Design, Setting, and Participants) p.7 Results p.12-13
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.	**nut-11** Explain categorization of dietary/nutritional data (e.g., use of N-tiles and handling of nonconsumers) and the choice of reference category, if applicable.	Methods (Exposures and Measurements) p. 7-8
Statistical Methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) Cohort study—If applicable, explain how loss to follow-up was addressed.	**nut-12.1** Describe any statistical method used to combine dietary or nutritional data, if applicable. **nut-12.2** Describe and justify the method for energy adjustments, intake modeling, and use of weighting factors, if applicable. **nut-12.3** Report any adjustments for measurement error, i.e,. from a validity or calibration study.	Methods (Statistical Analyses) p. 9

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
		Case-control study—If applicable, explain how matching of cases and controls was addressed. Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy. (e) Describe any sensitivity analyses.		
Results				
Participants	13	(a) Report the numbers of individuals at each stage of the study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed. (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram.	**nut-13** Report the number of individuals excluded based on missing, incomplete or implausible dietary/nutritional data.	Results p. 12-13 Figure 1
Descriptive data	14	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	**nut-14** Give the distribution of participant characteristics across the exposure variables if applicable. Specify if food consumption of total	Results (Table 1 p. 11-12, Figure 1)

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
		(b) Indicate the number of participants with missing data for each variable of interest (c) Cohort study—Summarize follow-up time (e.g., average and total amount)	population or consumers only were used to obtain results.	
Outcome data	15	Cohort study—Report numbers of outcome events or summary measures over time. Case-control study—Report numbers in each exposure category, or summary measures of exposure. Cross-sectional study—Report numbers of outcome events or summary measures.		Results p. 13
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included.	**nut-16** Specify if nutrient intakes are reported with or without inclusion of dietary supplement intake, if applicable.	Methods (statistical analyses) p. 9; Results (Table 2 p.15-16, Table 3 p.18-19)

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
		(b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions and sensitivity analyses.	**nut-17** Report any sensitivity analysis (e.g., exclusion of misreporters or outliers) and data imputation, if applicable.	Results p. 20
Discussion				
Key results	18	Summarize key results with reference to study objectives.		Discussion p.20
Limitation	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	**nut-19** Describe the main limitations of the data sources and assessment methods used and implications for the interpretation of the findings.	Discussion p.22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	**nut-20** Report the nutritional relevance of the findings, given the complexity of diet or nutrition as an exposure.	Discussion p.21

Item	Item nr	STROBE recommendations	Extension for Nutritional Epidemiology studies (STROBE-nut)	Reported on page #
Generalizability	21	Discuss the generalizability (external validity) of the study results.		Discussion p.22-23
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.		Financial Support p.3
Ethics			**nut-22.1** Describe the procedure for consent and study approval from ethics committee(s).	Methods p.7
Supplementary material			**nut-22.2** Provide data collection tools and data as online material or explain how they can be accessed.	Data Sharing p.23

Appendix 8. Proof of Submission for Manuscript 3

Submission Confirmation for Maternal Diet Quality and Multivitamin Intake During Pregnancy Interact in the Association with Offspring Neurodevelopment at 2 Years of Age

T em.ajcn.0.7d714e.1dd99d58@editorialmanager.com on behalf of The American Journal c

To: Yamei Yu Fri 8/19/2022 10:17 AM

Attention : courriel externe | external email

Maternal Diet Quality and Multivitamin Intake During Pregnancy Interact in the Association with Offspring Neurodevelopment at 2 Years of Age

Dear Dr Yu,

Your submission entitled "Maternal Diet Quality and Multivitamin Intake During Pregnancy Interact in the Association with Offspring Neurodevelopment at 2 Years of Age" with manuscript ID (AJCN-D-22-01092) has been received by journal The American Journal of Clinical Nutrition.

You will be able to check on the progress of your paper by logging on to Editorial Manager as an author. The URL is https://www.editorialmanager.com/ajcn/.

Your manuscript will be given a reference number once an Editor has been assigned.

Thank you for submitting your work to this journal.

Kind regards,

The American Journal of Clinical Nutrition

CHAPTER 10. REFERENCES

Following the guidelines from the department for developing the paper-based thesis, a complete reference list is listed here. It includes references cited in all chapters except the article chapters and the appendices chapter. For article chapters and the appendices chapter, references are listed at the end of each individual chapter.

1. Wu Y, Marc I, Bouchard L, et al. Study protocol for the Sino-Canadian Healthy Life Trajectories Initiative (SCHeLTI): a multicentre, cluster-randomised, parallel-group, superiority trial of a multifaceted community-family-mother-child intervention to prevent childhood overweight and obesity. *BMJ Open* 2021; **11**(4): e045192.

2. Last J. A Dictionary of Epidemiology: Oxford University Press, USA; 2000.

3. Schwarzenberg SJ, Georgieff MK, Committee On Nutrition. Advocacy for Improving Nutrition in the First 1000 Days to Support Childhood Development and Adult Health. *Pediatrics* 2018; **141**(2).

4. Koletzko B, Brands B, Grote V, et al. Long-Term Health Impact of Early Nutrition: The Power of Programming. *Ann Nutr Metab* 2017; **70**(3): 161-9.

5. Hanson MA, Bardsley A, De-Regil LM, et al. The International Federation of Gynecology and Obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First". *Int J Gynaecol Obstet* 2015; **131 Suppl 4**: S213-53.

6. Lim SS, Vos T, Flaxman AD. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic

analysis for the Global Burden of Disease Study 2010 (vol 380, pg 2224, 2012). *Lancet* 2013; **381**(9874): 1276-.

7. Lancet T. A future direction for tackling malnutrition. *Lancet* 2020; **395**(10217): 2.

8. Victora CG, Adair L, Fall C, et al. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* 2008; **371**(9609): 340-57.

9. Hawkes C, Ruel MT, Salm L, Sinclair B, Branca F. Double-duty actions: seizing programme and policy opportunities to address malnutrition in all its forms. *Lancet* 2020; **395**(10218): 142-55.

10. Wells JC, Sawaya AL, Wibaek R, et al. The double burden of malnutrition: aetiological pathways and consequences for health. *Lancet* 2020; **395**(10217): 75-88.

11. Sayre RK, Devercelli AE, Neuman MJ, Wodon Q. Investing in Early Childhood Development : Review of the World Bank's Recent Experience, 2015.

12. Krebs-Smith SM, Pannucci TE, Subar AF, et al. Update of the Healthy Eating Index: HEI-2015. *J Acad Nutr Diet* 2018; **118**(9): 1591-602.

13. Health Canada. Prenatal Nutrition Guidelines for Health Professionals. 2019-09-05 2010. https://www.canada.ca/en/health-canada/services/canada-food-guide/resources/prenatal-nutrition/eating-well-being-active-towards-healthy-weight-gain-pregnancy-2010.html.

14. Healthy eating and pregnancy. 2019. https://www.canada.ca/en/public-health/services/pregnancy/healthy-eating-pregnancy.html.

15. Eating Well with Canada's Food Guide 2007. 2007. https://www.canada.ca/en/health-canada/services/canada-food-guide/about/history-food-guide/eating-well-with-canada-food-guide-2007.html.

16. Prenatal Nutrition Guidelines for Health Professionals - Background on Canada's Food Guide. 2009. https://www.canada.ca/en/health-canada/services/publications/food-nutrition/prenatal-nutrition-guidelines-health-professionals-background-canada-food-guide-2009.html.

17. Canada's Food Guide. 2019. https://food-guide.canada.ca/en/.

18. Fowler JK, Evers SE, Campbell MK. Inadequate dietary intakes among pregnant women. *Can J Diet Pract Res* 2012; **73**(2): 72-7.

19. Pick ME, Edwards M, Moreau D, Ryan EA. Assessment of diet quality in pregnant women using the Healthy Eating Index. *J Am Diet Assoc* 2005; **105**(2): 240-6.

20. Crozier SR, Robinson SM, Borland SE, et al. Do women change their health behaviours in pregnancy? Findings from the Southampton Women's Survey. *Paediatr Perinat Epidemiol* 2009; **23**(5): 446-53.

21. Morton SM, Grant CC, Wall CR, et al. Adherence to nutritional guidelines in pregnancy: evidence from the Growing Up in New Zealand birth cohort study. *Public Health Nutr* 2014; **17**(9): 1919-29.

22. Malek L, Umberger W, Makrides M, Zhou SJ. Adherence to the Australian dietary guidelines during pregnancy: evidence from a national study. *Public Health Nutr* 2016; **19**(7): 1155-63.

23. Bodnar LM, Siega-Riz AM. A Diet Quality Index for Pregnancy detects variation in diet and differences by sociodemographic factors. *Public Health Nutr* 2002; **5**(6): 801-9.

24. Morisset AS, Dubois L, Colapinto CK, Luo ZC, Fraser WD. Prepregnancy Body Mass Index as a Significant Predictor of Total Gestational Weight Gain and Birth Weight. *Can J Diet Pract Res* 2017; **78**(2): 66-73.

25. Prentice AM. Overeating: the health risks. *Obes Res* 2001; **9 Suppl 4**: 234S-8S.

26. Diet and Health: Implications for Reducing Chronic Disease Risk. Washington (DC); 1989.

27. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med* 2011; **364**(25): 2392-404.

28. Huang T, Tobias DK, Hruby A, Rifai N, Tworoger SS, Hu FB. An Increase in Dietary Quality Is Associated with Favorable Plasma Biomarkers of the Brain-Adipose Axis in Apparently Healthy US Women. *J Nutr* 2016; **146**(5): 1101-8.

29. Wirt A, Collins CE. Diet quality--what is it and does it matter? *Public Health Nutr* 2009; **12**(12): 2473-92.

30. Guenther PM, Reedy J, Krebs-Smith SM. Development of the Healthy Eating Index-2005. *J Am Diet Assoc* 2008; **108**(11): 1896-901.

31. Guenther PM, Reedy J, Krebs-Smith SM, Reeve BB. Evaluation of the Healthy Eating Index-2005. *J Am Diet Assoc* 2008; **108**(11): 1854-64.

32. Guenther PM, Casavale KO, Reedy J, et al. Update of the Healthy Eating Index: HEI-2010. *J Acad Nutr Diet* 2013; **113**(4): 569-80.

33. Garriguet D. Diet quality in Canada. *Health Rep* 2009; **20**(3): 41-52.

34. Jessri M, Ng AP, L'Abbe MR. Adapting the Healthy Eating Index 2010 for the Canadian Population: Evidence from the Canadian National Nutrition Survey. *Nutrients* 2017; **9**(8).

35. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* 2003; **348**(26): 2599-608.

36. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. *Arch Intern Med* 2008; **168**(7): 713-20.

37. Asghari G, Mirmiran P, Yuzbashian E, Azizi F. A systematic review of diet quality indices in relation to obesity. *Br J Nutr* 2017; **117**(8): 1055-65.

38. Kennedy RAK, Turner MJ. Development of a novel Periconceptual Nutrition Score (PENS) to examine the relationship between maternal dietary quality and fetal growth. *Early Hum Dev* 2019; **132**: 6-12.

39. Katamay SW, Esslinger KA, Vigneault M, et al. Eating well with Canada's Food Guide (2007): development of the food intake pattern. *Nutr Rev* 2007; **65**(4): 155-66.

40. Tsigga M, Filis V, Hatzopoulou K, Kotzamanidis C, Grammatikopoulou MG. Healthy Eating Index during pregnancy according to pre-gravid and gravid weight status. *Public Health Nutr* 2011; **14**(2): 290-6.

41. Shin D, Lee KW, Song WO. Pre-Pregnancy Weight Status Is Associated with Diet Quality and Nutritional Biomarkers during Pregnancy. *Nutrients* 2016; **8**(3): 162.

42. Parker HW, Tovar A, McCurdy K, Vadiveloo M. Associations between pre-pregnancy BMI, gestational weight gain, and prenatal diet quality in a national sample. *PLoS One* 2019; **14**(10): e0224034.

43. Imamura F, Micha R, Khatibzadeh S, et al. Dietary quality among men and women in 187 countries in 1990 and 2010: a systematic assessment. *Lancet Glob Health* 2015; **3**(3): E132-E42.

44. Mozaffarian D, Angell SY, Lang T, Rivera JA. Role of government policy in nutrition-barriers to and opportunities for healthier eating. *BMJ* 2018; **361**: k2426.

45. Vanstone M, Kandasamy S, Giacomini M, DeJean D, McDonald SD. Pregnant women's perceptions of gestational weight gain: A systematic review and meta-synthesis of qualitative research. *Matern Child Nutr* 2017; **13**(4).

46. Gardner B, Croker H, Barr S, et al. Psychological predictors of dietary intentions in pregnancy. *J Hum Nutr Diet* 2012; **25**(4): 345-53.

47. Savard C, Plante AS, Carbonneau E, et al. Do pregnant women eat healthier than non-pregnant women of childbearing age? *Int J Food Sci Nutr* 2020: 1-12.

48. Crozier SR, Robinson SM, Godfrey KM, Cooper C, Inskip HM. Women's dietary patterns change little from before to during pregnancy. *J Nutr* 2009; **139**(10): 1956-63.

49. Savard C, Lemieux S, Carbonneau E, et al. Trimester-Specific Assessment of Diet Quality in a Sample of Canadian Pregnant Women. *Int J Environ Res Public Health* 2019; **16**(3).

50. Lebrun A, Plante AS, Savard C, et al. Tracking of Dietary Intake and Diet Quality from Late Pregnancy to the Postpartum Period. *Nutrients* 2019; **11**(9).

51. Bjerregaard AA, Halldorsson TI, Tetens I, Olsen SF. Mother's dietary quality during pregnancy and offspring's dietary quality in adolescence: Follow-up from a national birth cohort study of 19,582 mother-offspring pairs. *PLoS Med* 2019; **16**(9): e1002911.

52. JM L. A Dictionary of Epidemiology, 2nd ed: New York: Oxford University Press; 1988.

53. Sugiyama T, Shapiro MF. The growing socioeconomic disparity in dietary quality: mind the gap. *JAMA Intern Med* 2014; **174**(10): 1595-6.

54. Doyle IM, Borrmann B, Grosser A, Razum O, Spallek J. Determinants of dietary patterns and diet quality during pregnancy: a systematic review with narrative synthesis. *Public Health Nutr* 2017; **20**(6): 1009-28.

55. Ivers LC, Cullen KA. Food insecurity: special considerations for women. *Am J Clin Nutr* 2011; **94**(6): 1740S-4S.

56. Blumenshine P, Egerter S, Barclay CJ, Cubbin C, Braveman PA. Socioeconomic disparities in adverse birth outcomes: a systematic review. *Am J Prev Med* 2010; **39**(3): 263-72.

57. Kramer MS, Morin I, Yang H, et al. Why are babies getting bigger? Temporal trends in fetal growth and its determinants. *J Pediatr* 2002; **141**(4): 538-42.

58. Dubois L, Girard M. Social position and nutrition: a gradient relationship in Canada and the USA. *Eur J Clin Nutr* 2001; **55**(5): 366-73.

59. Raine KD. Determinants of healthy eating in Canada: an overview and synthesis. *Can J Public Health* 2005; **96 Suppl 3**: S8-14, S8-5.

60. Tarasuk V, Fitzpatrick S, Ward H. Nutrition inequities in Canada. *Appl Physiol Nutr Metab* 2010; **35**(2): 172-9.

61. AprOn, Teams ES. Adherence to Canada's Food Guide Recommendations during Pregnancy: Nutritional Epidemiology and Public Health. *Curr Dev Nutr* 2017; **1**(7): e000356.

62. Jahns L, Davis-Shaw W, Lichtenstein AH, Murphy SP, Conrad Z, Nielsen F. The History and Future of Dietary Guidance in America. *Adv Nutr* 2018; **9**(2): 136-47.

63. Lawlor DA, Andersen AM, Batty GD. Birth cohort studies: past, present and future. *Int J Epidemiol* 2009; **38**(4): 897-902.

64. De-Regil LM, Harding KB, Roche ML. Preconceptional Nutrition Interventions for Adolescent Girls and Adult Women: Global Guidelines and Gaps in Evidence and Policy with Emphasis on Micronutrients. *J Nutr* 2016; **146**(7): 1461S-70S.

65. Larque E, Labayen I, Flodmark CE, et al. From conception to infancy - early risk factors for childhood obesity. *Nat Rev Endocrinol* 2019; **15**(8): 456-78.

66. Patro Golab B, Santos S, Voerman E, et al. Influence of maternal obesity on the association between common pregnancy complications and risk of childhood obesity: an individual participant data meta-analysis. *Lancet Child Adolesc Health* 2018; **2**(11): 812-21.

67. Voerman E, Santos S, Patro Golab B, et al. Maternal body mass index, gestational weight gain, and the risk of overweight and obesity across childhood: An individual participant data meta-analysis. *PLoS Med* 2019; **16**(2): e1002744.

68. Hu Z, Tylavsky FA, Han JC, et al. Maternal metabolic factors during pregnancy predict early childhood growth trajectories and obesity risk: the CANDLE Study. *Int J Obes (Lond)* 2019; **43**(10): 1914-22.

69. Liao XP, Yu Y, Marc I, et al. Prenatal determinants of childhood obesity: a review of risk factors (1). *Can J Physiol Pharmacol* 2019; **97**(3): 147-54.

70. Woo Baidal JA, Locks LM, Cheng ER, Blake-Lamb TL, Perkins ME, Taveras EM. Risk Factors for Childhood Obesity in the First 1,000 Days: A Systematic Review. *Am J Prev Med* 2016; **50**(6): 761-79.

71. Raghavan R, Dreibelbis C, Kingshipp BL, et al. Dietary patterns before and during pregnancy and birth outcomes: a systematic review. *Am J Clin Nutr* 2019; **109**(Suppl_7): 729S-56S.

72. Raghavan R, Dreibelbis C, Kingshipp BL, et al. Dietary patterns before and during pregnancy and maternal outcomes: a systematic review. *Am J Clin Nutr* 2019; **109**(Suppl_7): 705S-28S.

73. Sanchez-Villegas A, Brito N, Doreste-Alonso J, et al. Methodological aspects of the study of dietary patterns during pregnancy and maternal and infant health outcomes. A systematic review. *Matern Child Nutr* 2010; **6 Suppl 2**: 100-11.

74. Chia AR, Chen LW, Lai JS, et al. Maternal Dietary Patterns and Birth Outcomes: A Systematic Review and Meta-Analysis. *Adv Nutr* 2019; **10**(4): 685-95.

75. Kibret KT, Chojenta C, Gresham E, Tegegne TK, Loxton D. Maternal dietary patterns and risk of adverse pregnancy (hypertensive disorders of pregnancy and gestational diabetes mellitus) and birth (preterm birth and low birth weight) outcomes: a systematic review and meta-analysis. *Public Health Nutr* 2018: 1-15.

76. Kirkham JJ, Altman DG, Williamson PR. Bias due to changes in specified outcomes during the systematic review process. *PLoS One* 2010; **5**(3): e9810.

77. In: Rasmussen KM, Yaktine AL, eds. Weight Gain During Pregnancy: Reexamining the Guidelines: Washington, DC: National Academies Press; 2009.

78. Nutrition During Pregnancy: Part I Weight Gain: Part II Nutrient Supplements. Washington (DC); 1990.

79. Goldstein RF, Abell SK, Ranasinha S, et al. Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysis. *JAMA* 2017; **317**(21): 2207-25.

80. Santos S, Voerman E, Amiano P, et al. Impact of maternal body mass index and gestational weight gain on pregnancy complications: an individual participant data meta-analysis of European, North American and Australian cohorts. *BJOG* 2019; **126**(8): 984-95.

81. Goldstein RF, Abell SK, Ranasinha S, et al. Gestational weight gain across continents and ethnicity: systematic review and meta-analysis of maternal and infant outcomes in more than one million women. *BMC Med* 2018; **16**(1): 153.

82. Begum F, Colman I, McCargar LJ, Bell RC. Gestational weight gain and early postpartum weight retention in a prospective cohort of Alberta women. *J Obstet Gynaecol Can* 2012; **34**(7): 637-47.

83. Hillesund ER, Bere E, Haugen M, Averby NC. Development of a New Nordic Diet score and its association with gestational weight gain and fetal growth - a study performed in the Norwegian Mother and Child Cohort Study (MoBa). *Public Health Nutrition* 2014; **17**(9): 1909-18.

84. Fernandez-Barres S, Vrijheid M, Manzano-Salgado CB, et al. The Association of Mediterranean Diet during Pregnancy with Longitudinal Body Mass Index Trajectories and Cardiometabolic Risk in Early Childhood. *J Pediatr* 2019; **206**: 119-27 e6.

85. Fulay AP, Rifas-Shiman SL, Oken E, Perng W. Associations of the dietary approaches to stop hypertension (DASH) diet with pregnancy complications in Project Viva. *European Journal of Clinical Nutrition* 2018; **72**(10): 1385-95.

86. Tielemans MJ, Erler NS, Leermakers ETM, et al. A Priori and a Posteriori Dietary Patterns during Pregnancy and Gestational Weight Gain: The Generation R Study. *Nutrients* 2015; **7**(11): 9383-99.

87. Emond JA, Karagas MR, Baker ER, Gilbert-Diamond D. Better diet quality during pregnancy is associated with a reduced likelihood of an infant born small for gestational age: An analysis of the prospective New Hampshire birth cohort study. *Journal of Nutrition* 2018; **148**(1): 22-30.

88. Ai-Ru C, Mya-Thway T, Chad Yixian H, et al. Adherence to a healthy eating index for pregnant women is associated with lower neonatal adiposity in a multiethnic Asian cohort: the Growing Up in Singapore Towards healthy Outcomes (GUSTO) study. *American Journal of Clinical Nutrition* 2018; **107**(1): 71-9.

89. American Diabetes A. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. *Diabetes Care* 2021; **44**(Suppl 1): S15-S33.

90. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. *Lancet* 2006; **367**(9516): 1066-74.

91. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. *Obstet Gynecol* 2020; **135**(6): e237-e60.

92. Roberts JM, Balk JL, Bodnar LM, Belizan JM, Bergel E, Martinez A. Nutrient involvement in preeclampsia. *J Nutr* 2003; **133**(5 Suppl 2): 1684S-92S.

93. Fulay AP, Rifas-Shiman SL, Oken E, Wei P. Associations of the dietary approaches to stop hypertension (DASH) diet with pregnancy complications in Project Viva. *European Journal of Clinical Nutrition* 2018; **72**(10): 1385-95.

94. Hillesund ER, Overby NC, Engel SM, et al. Associations of adherence to the New Nordic Diet with risk of preeclampsia and preterm delivery in the Norwegian Mother and Child Cohort Study (MoBa). *Eur J Epidemiol* 2014; **29**(10): 753-65.

95. Gicevic S, Gaskins AJ, Fung TT, et al. Evaluating pre-pregnancy dietary diversity vs. dietary quality scores as predictors of gestational diabetes and hypertensive disorders of pregnancy. *PLoS ONE* 2018; **13**(4): e0195103.

96. Arvizu M, Bjerregaard AA, Madsen MTB, et al. Sodium Intake during Pregnancy, but Not Other Diet Recommendations Aimed at Preventing Cardiovascular Disease, Is Positively Related to Risk of Hypertensive Disorders of Pregnancy. *Journal of Nutrition* 2020; **150**(1): 159-66.

97. Wollmann HA. Intrauterine growth restriction: definition and etiology. *Horm Res* 1998; **49 Suppl 2**: 1-6.

98. Macrosomia: ACOG Practice Bulletin Summary, Number 216. *Obstet Gynecol* 2020; **135**(1): 246-8.

99. Hendrix N, Berghella V. Non-placental causes of intrauterine growth restriction. *Semin Perinatol* 2008; **32**(3): 161-5.

100. Ludvigsson JF, Lu D, Hammarstrom L, Cnattingius S, Fang F. Small for gestational age and risk of childhood mortality: A Swedish population study. *PLoS Med* 2018; **15**(12): e1002717.

101. Vinturache AE, Chaput KH, Tough SC. Pre-pregnancy body mass index (BMI) and macrosomia in a Canadian birth cohort. *J Matern Fetal Neonatal Med* 2017; **30**(1): 109-16.

102. Health Status of Canadians 2016: Report of the Chief Public Health Officer - How healthy are we? - Low birth weight. 2016. https://www.canada.ca/en/public-

health/corporate/publications/chief-public-health-officer-reports-state-public-health-canada/2016-health-status-canadians/page-5-how-healthy-are-we-low-birth-weight.html.

103. Birth-related indicators (low and high birth weight, small and large for gestational age, pre-term births), by sex, five-year period, Canada and Inuit regions. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310006401.

104. Public Health Agency of Canada. Perinatal Health Indicators Data Tool, 2020 Edition: Public Health Infobase. Ottawa (ON); 2020.

105. Olsen A, Dennis EL, Evensen KAI, et al. Preterm birth leads to hyper-reactive cognitive control processing and poor white matter organization in adulthood. *NeuroImage* 2018; **167**: 419-28.

106. Mathewson KJ, Chow CH, Dobson KG, Pope EI, Schmidt LA, Van Lieshout RJ. Mental health of extremely low birth weight survivors: A systematic review and meta-analysis. *Psychological bulletin* 2017; **143**(4): 347-83.

107. Mericq V, Martinez-Aguayo A, Uauy R, Iniguez G, Van der Steen M, Hokken-Koelega A. Long-term metabolic risk among children born premature or small for gestational age. *Nature reviews Endocrinology* 2017; **13**(1): 50-62.

108. Wang J, Shen S, Price MJ, et al. Glucose, Insulin, and Lipids in Cord Blood of Neonates and Their Association with Birthweight: Differential Metabolic Risk of Large for Gestational Age and Small for Gestational Age Babies. *J Pediatr* 2020.

109. Smith CA. The effect of wartime starvation in Holland upon pregnancy and its product. *Am J Obstet Gynecol* 1947; **53**(4): 599-608.

110. Kind KL, Moore VM, Davies MJ. Diet around conception and during pregnancy--effects on fetal and neonatal outcomes. *Reprod Biomed Online* 2006; **12**(5): 532-41.

111. The Blackwell Handbook of Early Childhood Development.; 2006.

112. Pomeroy SL, Ullrich NJ. Development of the Nervous System. Fetal and Neonatal Physiology (Third Edition); 2004: 1675-98.

113. Georgieff MK, Ramel SE, Cusick SE. Nutritional influences on brain development. *Acta Paediatr* 2018; **107**(8): 1310-21.

114. Georgieff MK. Nutrition and the developing brain: nutrient priorities and measurement. *Am J Clin Nutr* 2007; **85**(2): 614S-20S.

115. Kretchmer N, Beard JL, Carlson S. The role of nutrition in the development of normal cognition. *Am J Clin Nutr* 1996; **63**(6): 997S-1001S.

116. de Rooij SR, Caan MW, Swaab DF, et al. Prenatal famine exposure has sex-specific effects on brain size. *Brain* 2016; **139**(Pt 8): 2136-42.

117. de Rooij SR, Mutsaerts H, Petr J, et al. Late-life brain perfusion after prenatal famine exposure. *Neurobiol Aging* 2019; **82**: 1-9.

118. Prado EL, Dewey KG. Nutrition and brain development in early life. *Nutr Rev* 2014; **72**(4): 267-84.

119. Borge TC, Aase H, Brantsaeter AL, Biele G. The importance of maternal diet quality during pregnancy on cognitive and behavioural outcomes in children: a systematic review and meta-analysis. *BMJ Open* 2017; **7**(9): e016777.

120. Taylor RM, Fealy SM, Bisquera A, et al. Effects of Nutritional Interventions during Pregnancy on Infant and Child Cognitive Outcomes: A Systematic Review and Meta-Analysis. *Nutrients* 2017; **9**(11).

121. Mahmassani HA, Switkowski KM, Scott TM, et al. Maternal diet quality during pregnancy and child cognition and behavior in a US cohort. *Am J Clin Nutr* 2022; **115**(1): 128-41.

122. USDA. Food Patterns Equivalents Database. https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/docs/fped-overview/.

123. Brisbois TD, Marsden SL, Anderson GH, Sievenpiper JL. Estimated intakes and sources of total and added sugars in the Canadian diet. *Nutrients* 2014; **6**(5): 1899-912.

124. Elvidge Munene LA, Dumais L, Esslinger K, et al. A surveillance tool to assess diets according to Eating Well with Canada's Food Guide. *Health Rep* 2015; **26**(11): 12-20.

125. Guenther PM, Kirkpatrick SI, Reedy J, et al. The Healthy Eating Index-2010 is a valid and reliable measure of diet quality according to the 2010 Dietary Guidelines for Americans. *J Nutr* 2014; **144**(3): 399-407.

126. Yu Y, Feng C, Bedard B, Fraser W, Dubois L. Diet quality during pregnancy and its association with social factors: 3D Cohort Study (Design, Develop, Discover). *Matern Child Nutr* 2022: e13403.

127. Fraser WD, Shapiro GD, Audibert F, et al. 3D Cohort Study: The Integrated Research Network in Perinatology of Quebec and Eastern Ontario. *Paediatr Perinat Epidemiol* 2016; **30**(6): 623-32.

128. Nohr EA, Liew Z. How to investigate and adjust for selection bias in cohort studies. *Acta Obstet Gynecol Scand* 2018; **97**(4): 407-16.

129. LaMorte WW. 2016. https://sphweb.bumc.bu.edu/otlt/mph-modules/bs/bs704-ep713_confounding-em/BS704-EP713_Confounding-EM4.html#:~:text=Residual%20confounding%20is%20the%20distortion,or%20analysis%20of%20a%20study.

130. Bosco JL, Silliman RA, Thwin SS, et al. A most stubborn bias: no adjustment method fully resolves confounding by indication in observational studies. *J Clin Epidemiol* 2010; **63**(1): 64-74.

131. Grech A, Hasick M, Gemming L, Rangan A. Energy misreporting is more prevalent for those of lower socio-economic status and is associated with lower reported intake of discretionary foods. *Br J Nutr* 2021; **125**(11): 1291-8.

132. Yland JJ, Wesselink AK, Lash TL, Fox MP. Misconceptions About the Direction of Bias From Nondifferential Misclassification. *Am J Epidemiol* 2022; **191**(8): 1485-95.

133. Hofler M. The effect of misclassification on the estimation of association: a review. *Int J Methods Psychiatr Res* 2005; **14**(2): 92-101.

134. Crawford PB, Obarzanek E, Morrison J, Sabry ZI. Comparative advantage of 3-day food records over 24-hour recall and 5-day food frequency validated by observation of 9- and 10-year-old girls. *J Am Diet Assoc* 1994; **94**(6): 626-30.

135. Kolar AS, Patterson RE, White E, et al. A practical method for collecting 3-day food records in a large cohort. *Epidemiology* 2005; **16**(4): 579-83.

136. Bingham SA, Cassidy A, Cole TJ, et al. Validation of weighed records and other methods of dietary assessment using the 24 h urine nitrogen technique and other biological markers. *Br J Nutr* 1995; **73**(4): 531-50.

137. Fitzgerald E, Hor K, Drake AJ. Maternal influences on fetal brain development: The role of nutrition, infection and stress, and the potential for intergenerational consequences. *Early Hum Dev* 2020; **150**: 105190.

138. Gernand AD, Schulze KJ, Stewart CP, West KP, Jr., Christian P. Micronutrient deficiencies in pregnancy worldwide: health effects and prevention. *Nat Rev Endocrinol* 2016; **12**(5): 274-89.