ASSOCIATIONS OF DIET AND EXERCISE IN PREGNANCY WITH INFANT GROWTH

EXPLORING ASSOCIATIONS BETWEEN A MATERNAL NUTRITION+EXERCISE INTERVENTION IN PREGNANCY AND INFANT GROWTH AND BODY COMPOSITION

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LAY ABSTRACT

Excessive weight gain in pregnancy can impact fetal and child growth and health. Diet and exercise modifications during pregnancy may improve weight gain but influence on infant outcomes is unknown. It is important to determine if women actually follow such guidance. Our study showed that infants of women randomized to a diet and exercise program compared to usual prenatal care had similar body size and body composition at birth (except length) and age six months. Women in both treatment groups had similar healthy dietary practices in early pregnancy, but with dietary counselling intervention women improved their diet. However, a unique scoring system developed to measure adherence to diet and exercise revealed that it was difficult for women to follow the guidance provided. Our study provides insights into the association of diet in pregnancy and infant growth in a Canadian population, and a novel approach to measuring ability to follow guidance.

ABSTRACT

Background: Pregnancy lifestyle interventions may effectively mediate gestational weight gain and adverse pregnancy outcomes. Whether maternal diet and exercise in pregnancy also benefits offspring body size and composition in infancy is not widely investigated. Further, adherence to interventions in longitudinal studies is often overlooked.

Objectives: 1) Determine the effects of a nutrition+exercise intervention compared with standard prenatal care throughout pregnancy on infant anthropometry and body composition 2) Compare the dietary practices between intervention and control groups 3) Create an algorithm to assess intervention adherence

Study Design: Maternal diet and physical activity were collected from a subset of women at 12-17, 26-28, 36-38 weeks gestation while enrolled in the Be Healthy in Pregnancy randomized controlled trial. Infant birth size was obtained from hospital records, and anthropometry and body composition outcomes were measured at six months postpartum. Percentile values for anthropometric measures were obtained using population reference growth standards. Diet quality was assessed through food frequency questionnaire, and a novel adherence algorithm was created using step counts from an accelerometer and three-day diet record.

Results: For 183 participants of mean age 31 ± 4 years and BMI 25.3 ± 4.7 kg/m$_2$, infant anthropometry and body composition at birth and six months were similar between intervention and control groups with the exception that intervention infants

had significantly higher birth length and a higher proportion categorized above the 97th percentile for reference length measures. In the analysis of healthy dietary practices (N=111) intervention and control participants had similar scores at baseline but only intervention participants improved and maintained their dietary practice scores in mid and late pregnancy. Application of the adherence score incorporating diet and step counts demonstrated increased adherence to the intervention in mid-pregnancy in intervention participants, but this level of adherence was not maintained through the end of pregnancy.

Conclusion: In a healthy pregnant cohort, a lifestyle intervention did not significantly impact infant anthropometry or body composition and most measures were within appropriate reference ranges for age and sex. The novel algorithm to measure intervention adherence demonstrated inconsistent compliance across pregnancy in intervention participants, potentially contributing to null findings.

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LIST OF ABBREVIATIONS

3DDR – 3 Day Diet Record

AGA – Appropriate for gestational age

AMDR – Acceptable Macronutrient Distribution Range

BHIP – Be Healthy in Pregnancy

BMI – Body mass index

CCHS – Canadian Community Health Survey

CHMS – Canadian Health Measures Survey

CPSS – Canadian Perinatal Surveillance System

DASH – Dietary Approaches to Stop Hypertension

DRI – Dietary reference intakes

DXA – Dual-energy x-ray absorptiometry

EAR – Estimated average requirement

EE – Energy expenditure

EER – Estimated energy requirements

FFQ – Food frequency questionnaire

GDM – Gestational diabetes mellitus

GEE – Generalized estimating equations

GWG – Gestational weight gain

HCP – Healthcare provider

IGF-1 – Insulin-like growth factor 1

IOM – Institute of Medicine

LGA – Large for gestational age

PARmed-X – Physical Activity Readiness Medical Examination

pBMI – Pre-pregnancy body mass index

PEAPOD – Air displacement plethysmography

QMR – Quantitative magnetic resonance

RCT – Randomized controlled trial

REDCap – Research Electronic Data Capture

SFT – Skinfold thickness

SGA – Small for gestational age

SOGC/CSEP – Society of Obstetricians and Gynecologists of Canada/Canadian Society for Exercise Physiology

SOP – Standardized operating procedure

WHO – World Health Organization

CHAPTER 1

INTRODUCTION

CHAPTER 1 - INTRODUCTION

1.1 Rationale

Prenatal environmental exposures have been linked to a wide variety of offspring health outcomes, from early infancy and across the life span, which are well documented in epidemiological studies. (1–4) Of particular interest is how maternal lifestyle behaviours across pregnancy impact on fetal and offspring development. Notably, high (or excessive) maternal gestational weight gain (GWG) has been associated with adverse offspring outcomes, including being born large or small for gestational age, macrosomia, and higher incidence of birth trauma, as well as future health implications including metabolic disorders and obesity. (5–10) Such information forms the foundation for clinical concerns since an estimated 50-65% of Canadian women exceed the most recent guidelines for GWG. (11,12)

In an attempt to increase the proportion of pregnant women whose weight gain in pregnancy is within recommendations, reported studies have explored whether alterations in dietary and/or physical activity practices positively impact GWG and maternal health outcomes. (13,14) This approach is suggested to reduce the burden of costs for treatment of adverse health outcomes. (15)

Currently, there is a paucity of research that explores the direct associations between maternal prenatal diet, particularly dietary changes, and infant growth and body composition. (16) Available research completed in randomized controlled trials (RCT) has often presented conflicting results, and often excludes measures in infants

beyond birth. Further, treatment adherence is rarely measured in intervention studies in pregnancy, potentially confounding the reported results.

1.2 Diet and physical activity in pregnancy

1.2.1 Current recommendations

Health Canada has adapted guidelines from the Institute of Medicine surrounding gestational weight gain. (11) making them available in the Gestational Weight Gain section of Health Canada's Prenatal Nutrition Guidelines for Health Professionals. This section provides insight into tracking weight gain in pregnancy, and the importance of diet and exercise in achieving optimal weight gain. (17) Healthy Living with Canada's Food Guide is the primary source of dietary information for Canadians, including pregnant women. The pregnancy guidelines included in the 2007 version of Canada's Food Guide highlight the importance of folic acid supplementation, fish consumption, and intake of 2-3 additional Food Guide servings daily. (17,18,19) Canada's Food Guide was updated in 2020, with pregnant women advised to consume only one, not three, extra daily meals or snacks, in addition to daily supplementation with a multivitamin and folic acid, drinking water, and iron. (20)

Recommendations for physical activity type and duration throughout pregnancy are provided in Canada by the Society of Obstetricians and Gynecologists of Canada and Canadian Society for Exercise Physiology (SOGC/CSEP) (21) and were recently updated. (22) The SOGC/CSEP emphasize the importance of both aerobic and strength-training exercises on a regular basis (Table 1).

Table 1: SOGC/CSEP recommendations for physical activity in pregnancy, 2003 versus 2019

Agency	Type	Duration/Frequency
SOGC/CSEP 2003 (21)	Aerobic and strength-conditioning exercises	Begin with 15 minutes of continuous exercise 3x/week Increase to 30 minute sessions 4x/week
SOGC/CSEP 2019 (22)	Aerobic and resistance training activities Pelvic muscle training	Minimum of 150 minutes moderate-intense weekly physical activity, accumulated over at least 3 days

Physical activity guidelines have emphasized the importance of aerobic exercise during pregnancy. (17,21,23) Walking has been noted as a feasible and accessible exercise option for women to practice throughout the duration of pregnancy, overcoming barriers that might prevent women from exercise (e.g. cost, equipment), and it can be safely practiced in later stages of pregnancy, and is feasible for individuals who are otherwise sedentary. (24,25)

1.2.2 Evidence to support lifestyle interventions in pregnancy

Some systematic reviews of existing observational studies and randomized controlled trials have demonstrated a positive association between lifestyle interventions in pregnancy on mediating GWG. (26,27) Regarding the impact of pregnancy lifestyle interventions on reducing adverse maternal and neonatal outcomes either such outcomes were not included, or results were inconsistent. For example, one systematic review and meta-analysis of 19 randomized and non-randomized clinical trials determined the efficacy of diet, exercise, behavior and/or other lifestyle interventions in pregnancy on maternal outcomes in overweight and obese women. (28)

While overall the interventions reduced GWG, no intervention effect on infant birth weight was observed. (28) Similar results were observed in a systematic review and meta-analysis of 13 RCTs in which no significant effects of dietary interventions on birth weight or preterm birth were determined. (29) An updated Cochrane review explored 65 RCTs employing diet and exercise lifestyle interventions in pregnancy on preventing excessive GWG, in addition to other pregnancy-related outcomes. (30) Overall, interventions using diet, exercise or both reduced the relative risk of excessive GWG by 20% compared to chosen standard prenatal care. (30) In this review 27 studies also included results on incidence of infant macrosomia but found no clear difference between infants born to control or intervention mothers. (30) The largest effect size for infant macrosomia was in a subset of seven exercise-only interventions, which demonstrated a 7% reduction in infant macrosomia. (30)

A particular interest of the Be Healthy in Pregnancy (BHIP) study was in dietary composition and specifically on dietary protein as described in a previous research design paper. (31) Healthy adults are advised to source a minimum of 10% of their energy from protein sources, as per the Acceptable Macronutrient Distribution Range (AMDR) of the Canadian Dietary Reference Intake (DRI) tables; pregnant women are specifically recommended to consume 0.8g of protein per 1 kg of body weight, or roughly 71g of daily protein. (32) A Cochrane Review examined 17 intervention trials employing dietary interventions centered on energy and protein intake in pregnancy. (33) Diet interventions with balanced energy and protein supplementation (N = 12), compared to standard prenatal care with no specified diet, were associated with reduced risk of small for gestational age infants, higher mean

infant birth weight, and significantly lower weekly GWG. (33) In, a prospective cohort study in pregnant women in Portugal (n = 98) a higher dairy intake in early and mid-pregnancy was negatively associated with weight gain in pregnancy (β = -0.007, P = 0.02). (34) Additionally, maternal dairy intake in pregnancy has been found to mitigate some adverse infant outcomes such as low birth weight and being born small for gestational age (SGA), both of which are risks for growth stunting. (35–37) Taken together, these studies suggest that higher dietary protein, and particularly dairy protein, in pregnancy may yield benefits to outcomes for mother and child.

Physical activities during pregnancy such as aerobic exercises, including walking, swimming, dancing, and biking, have been associated with positive outcomes such as improved cardiovascular fitness, reduced risk of excess GWG, and lowered postpartum weight retention. (38,39) A systematic review and meta-analysis of 135 observational studies and intervention trials found that exercise-only RCTs showed a 39% reduction in the likelihood of newborn macrosomia if mothers exercised in pregnancy. (40) Additionally, a Canadian birth cohort (N = 1913) found that higher maternal energy expenditure was associated in reductions in infant birth weight, without increasing the likelihood of infants being born small for gestational age. (41)

A major concern in pregnancy is adherence to the physical activity guidelines. The reasons pregnant women may not adhere to prescribed exercise include the prevailing misconception that exercise can cause undue harm to the fetus, including fetal growth restriction and preterm delivery. (42,43) Other women fail to engage in

physical activity in pregnancy due to time and resource management, including a lack of facilities for exercise. (44,45) As a result, pregnant women from around the world fail to meet physical activity recommendations set by health agencies. (42,46,47)

Lack of adherence to dietary recommendations during pregnancy has also been highlighted as a concern primarily from observational research. An Australian prospective cohort study assessed compliance with dietary recommendations in the Australian Guide to Healthy Eating (AGHE) in pregnancy and post-partum using a food frequency questionnaire. (48) Ultimately, no women met all AGHE food group recommendations. (48) Similarly, a birth cohort in New Zealand found that pregnant women were unsuccessful in meeting national dietary guidelines, with 25% of women failing to meet any recommendations for any food group. (49) A Canadian prospective cohort study found that approximately half of pregnant women classified as normal weight or underweight met Canada's Food Guide recommendations (54% and 50%), but fewer overweight or obese women met the recommendations (47% and 41%). (50) The recommendation to choose reduced-fat milk was achieved by 56% of women, while <1% of women consumed the recommended extra 2-3 servings daily from any food group. (50)

1.3 Physical measures of infant growth

1.3.1 Anthropometric measures

Maternal health status and body composition in pregnancy, including GWG, BMI, and fat mass can have a profound impact on offspring size, fat mass and later life health outcomes. An ongoing surveillance project of the Centre for Disease

Control and Prevention known as the Pregnancy Risk Assessment Monitoring System (PRAMS) utilized questionnaires completed by mothers across the United States to collect data on infant outcomes and maternal characteristics. (9) In examining infant size at birth in a sub-study of PRAMS in relation to maternal pBMI combined with GWG, excessive GWG was a strong indicator of large for gestational age (LGA; defined as birth weight above the 90th percentile for a given gestational age) infants regardless of maternal pBMI ($p < 0.0001$). (9) Similarly, in a retrospective analysis of healthcare records for mother-child dyads ($n = 16,218$) in China, GWG combined with maternal pBMI categorization of overweight or obese significantly increased the likelihood of an infant being born LGA (OR 3.0, $P < 0.001$ for obese pBMI; OR 1.7, $P = 0.001$ for overweight pBMI). (51) Also, inadequate GWG in early pregnancy increased the likelihood of infants being born small for gestational age (SGA) by 40% ($p < 0.001$). (51) For mothers with excessive GWG across pregnancy and across all pBMI categories, infants had a significantly higher increased risk of being born LGA (OR 2.4, $P = 0.001$). (51)

The impact of excess maternal GWG as defined by the IOM GWG recommendations may extend well beyond early infancy. In a systematic review and meta-analysis of 15 observational studies, excess maternal GWG was found to contribute to an increased relative risk (RR) of obesity in children aged 0-5 years (RR=1.91, p=0.04) and 5-18 years (RR=1.32, p<0.001). (8) Similarly, associations between excess GWG and later child obesity were observed in a prospective cohort study in China in children at 3-6 years of age with the highest risk if mothers were overweight or obese prior to pregnancy and gained excessive weight during

pregnancy. (52) Such an association between, maternal obesity and excess GWG and offspring overweight/obese was observed in adolescence and adulthood in an American longitudinal cohort study. (7)

1.3.2 Body composition

Maternal factors such as GWG, presence of diabetes, and overweight/obesity are also thought to be predictors of offspring body composition namely lean and fat mass. Observational studies exploring potential associations between maternal outcomes and infant body composition are summarized in Table 2. Overall, these studies demonstrate that incidence of adverse maternal outcomes, such as gestational diabetes, excessive GWG, and higher pBMI, are related to an increased likelihood of infants having higher fat mass and percent body fat at birth. In addition, observational studies have demonstrated potential associations between increased neonatal body fat and later adverse health outcomes, including childhood obesity and higher abdominal fat accumulation in childhood. (53,54) However, these observational studies have often failed to include mothers of all pBMI and GWG categories and were limited to infant measures at birth and not beyond. Additionally, the individual responsible for providing measurements throughout a study is often inconsistent, and can include self-reporting, physician/delivery room staff measurements without standardized equipment, and measures from one or more research personnel using validated equipment. (55)

Table 2: Association of infant body composition outcomes with maternal gestational weight gain (GWG) or diabetes

Study	Maternal Factor	Impact on Infant
Logan et al., 2017 (56) *Systematic review & meta-analysis (N = 35 observational studies)*	Maternal diabetes status (type 1, type 2, or gestational)	Infants born to mothers with any form of diabetes mellitus in pregnancy had higher overall fat mass at birth than infants born to mothers without diabetes (mean difference 83g, p<0.00001) % body fat was 2.2% higher in infants born to mothers with diabetes, than without (p<0.0001)
Hull et al., 2011 (57) *Observational analysis (N = 306)*	Maternal GWG and pBMI	With appropriate GWG, infants born to obese mothers had greater % body fat (14.6%) at birth than those born to overweight (9.2%, p<0.002) or normal weight (11.2%, p=0.014) mothers Infants born to mothers with excessive GWG had higher fat mass (484.4g) than those with appropriate GWG (303.6g; p = 0.001)
Starling et al., 2015 (58) *Birth cohort (N = 826)*	Maternal GWG and pBMI	1 kg/m2 increase in maternal BMI associated with increases at birth in neonatal fat mass (5.2g; 95% CI 3.5, 6.9g), fat-free mass (7.7g; 4.5, 10.9g), and % body fat (0.12%; 0.08%, 0.16%) 0.1 kg/week increase in GWG associated with higher infant fat mass (24.0g; 95% CI 17.4, 30.5g), fat-free mass (34.0g; 21.4, 46.6g), and % body fat (0.55%; 0.37%, 0.72%) at birth

1.3.3 Interventions in pregnancy & infant outcomes

Previous research demonstrated that diet and exercise lifestyle interventions can successfully reduce not only the risk of excess GWG but also other adverse maternal measurements in pregnancy. (30,59) Less is known about the direct impact of maternal lifestyle interventions on infant outcomes; and those that exist report contradictory results. In a systematic review and meta-analysis of randomized control trials, dietary interventions of a) dietary and nutrition counselling; b) a particular food

or fortified food item; or c) a combination of counselling and promotion of a certain food item were assessed for impact on infant outcomes. (16) All dietary interventions, including those focused on macronutrient intake and/or fortified food products resulted in significantly higher birth weight ($p<0.01$) and lower frequencies of low birth weights ($p<0.01$) compared to control groups. But for size-at-birth indices of macrosomia, LGA and SGA, no differences existed between control and intervention groups in the included studies. (16) In a recent prospective meta-analysis of seven RCTs of lifestyle interventions in pregnancy (60), neither infant birth weight nor the incidence of LGA infants and macrosomia were different between intervention and control groups. A limitation of the latter study is that the seven clinical trials included in this meta-analysis had vastly different interventions, resulting in heterogeneity of responses. Further, reporting on adherence measures to the interventions within the trials was not included.

From the perspective of infant body composition, variable effects were observed between groups with overweight or obese American mothers (N=210) in a racially diverse population who were randomized to a diet and exercise intervention or standard prenatal care. (61) Infants born to intervention compared to control group had greater fat-free mass as measured by air displacement plethysmography (PEAPOD) and quantitative magnetic resonance (QMR). (61) However, no significant differences were found between infant groups in skinfold thickness measurements, gestational age, birth length, birth weight, or occurrence of LGA/SGA infants. (61) While this study did consider intervention adherence as it pertained to attending counselling sessions, there was no noted consideration of complying to the intervention by

pursuing a healthier diet or increased exercise; further, it was noted that attendance to provided exercise classes was poor, calling into question how the impact of physical activity could be legitimately assessed. (61)

The Lifestyle in Pregnancy and Offspring (LiPO) randomized controlled trial in Denmark explored dietary coaching and exercise in obese pregnant women (N=301) designed to lower GWG, and its impact on infant anthropometrics and body composition measured by DXA. (62) Intervention participants received diet coaching on energy intake four times throughout pregnancy, were encouraged to engage in 30-60 minutes of daily exercise, and received a free fitness center membership for 6 months; control participants continued to seek their chosen prenatal care. (62) In infants measured between 2.5 and 3 years of age no differences in BMI z-score, body composition measures by DXA, or other anthropometrics were found between intervention and control groups. (62) The intervention in the LiPO study consisted of dietary counselling, however no measures were put into place to assess the actual dietary behaviours displayed by participants. Additionally, adherence to exercise recommendations was not recorded, despite having the means to (i.e. measuring attendance to offered exercise classes or gym attendance). Moreover, this study only included participants with pBMI categorization of obese, such that any results are not generalizable to broader populations.

1.4 Intervention adherence

As highlighted in the sections above, the influence of prenatal lifestyle interventions on infant immediate and long-term outcomes have null or conflicting

results. As alluded to, a measure of adherence to the intervention(s) is often missing. For example, in a Dutch study that promoted attendance at biweekly exercise classes alongside self-directed physical activity in overweight pregnant women, no effect of the intervention was observed on maternal fasting blood glucose, insulin sensitivity, or infant birth weight. (63) The authors reported low attendance to provided exercise classes but no quantitative measure of physical activity such as step counts or energy expenditure was reported. (63) Overall, few intervention studies employ tools to assess intervention adherence; further, those which consider intervention adherence often rely on a single measure like study attendance, which does not encompass the quantitative measures of the active components of an intervention. (64,65) Assessing intervention adherence allows researchers to better interpret intervention results and success, making adherence measuring tools a valuable resource. (64–66)

Approaches to measurement of adherence to diet or physical activity vary widely thus no validated standardized approach exists. Some countries assessed adherence to national nutrition guidelines using dietary indices or scores; a sample of some national dietary indices are presented in Table 3.

Table 3: Summary of national dietary indices employed in observational research to measure dietary compliance

Tool/Guidelines	Reference	Score allocation
Healthy Eating Index (HEI-2005) Dietary Guidelines for Americans	Guenther et al., 2008 (67)	9 adequacy components with maximum score allocations of 5 or 10 1 moderation components with maximum score allocations of 10 or 20. Max score: 100
Dutch Healthy Diet Index (DHD-Index) Dutch Guidelines for a Healthy Diet	Van Lee et al., 2012 (68)	10 dietary components, each with a maximum score allocation of 10 Max score: 100
Norwegian Food Guide Healthy Eating Index (HEI-NFG) Norwegian Food Guide	Von Ruesten et al., 2014 (69)	3 adequacy components with maximum score allocation of 10 2 range components with maximum score allocation of 5 2 moderation components with maximum allocation score of 10 Max score: 70
Nordic Nutrition Recommendations Healthy Eating Index (HEI-NNR) Nordic Nutrition Recommendations	Von Ruesten et al., 2014 (69)	1 adequacy component with maximum score allocation of 10 4 range components with maximum score allocations of 5 or 10 2 moderation components with maximum score allocation of 5 or 10 Max score: 50
Canadian Healthy Eating Index (HEI-C 2010) Canada's Food Guide (2007)	Jessri et al., 2017 (70)	8 adequacy components with maximum score allocation of 5 or 10 3 moderation components with maximum score allocation of 10 or 20 Max score: 100

While national dietary indices are valuable tools, many intervention studies are not strictly designed around national guidelines. Pharmacotherapeutic intervention adherence has been widely explored in current research, with an 80% medication intake benchmark widely accepted as a compliant population. (71–74) However, measuring or expressing adherence to diet and exercise interventions is often more complex, which has resulted in intervention studies failing to include or report intervention compliance amongst participants.

While not yet widely employed, intervention trials in adults (but not specifically pregnant women) are beginning to utilize scoring systems to quantify and report adherence. Adherence to the Mediterranean diet in interventions can be expressed using the MedDietScore scoring system. (75) The MedDietScore consists of nine dietary components corresponding to the Mediterranean diet recommendations (consumption of fish., olive oil, fruits and vegetables, etc.), and two dietary components not in line with the Mediterranean diet. (75) Participants can receive 0-5 points; the higher the score is, the more adherent a participant was. (75) The Dixon-DASH dietary index is a tool for quantifying adherence to the Dietary Approaches to Stop Hypertension (DASH) diet in intervention studies. The Dixon-DASH index consists of a nine point score, based on recommendations of the DASH Eating Plan included in the 2005 Dietary Guidelines for Americans, and is based on responses to a 137 question FFQ. (76,77) The score comprises eight food group components and one nutrient components; adherence to each component is worth one point, for a maximum possible score of nine. (77,78)

Given the paucity of pregnancy intervention studies that measured adherence to the intervention, it was challenging to find a validated tool by which to measure adherence to the diet and exercise components of the BHIP study. Two studies, including one in a Canadian population, which successfully implemented adherence measures are summarized here. The Fit for Delivery (FFD) study, a randomized controlled intervention trial aimed at preventing excessive GWG through dietary counselling, constructed a unique intervention adherence score. (79) Dietary adherence was assessed using a 43-question FFQ developed for the FFD study. (79) The corresponding adherence score for the FFD study consisted of ten subscales corresponding to intervention dietary recommendations, with a maximum score of 10, and minimum of 0; higher scores represent greater adherence (Appendix 1). (79) Participant scores for the FFD study have since been categorized into tertiles representing low, medium and high adherence, with plans to explore other outcomes of interest using these scores. (79) The Nutrition and Exercise Lifestyle Intervention Program (NELIP) study, a lifestyle intervention in pregnant Canadian women designed to lower the incidence of excess GWG, employed a scored adherence system. (80) This study included both objective (i.e. attendance to study visits) and subjective (i.e. diet records) measures of the employed lifestyle intervention. (80) The score generated consisted of 3 dietary components and 3 exercise components, resulting in a score out of 6. (80) Ultimately, the NELIP study found that participants who gained appropriate amounts of gestational weight had significantly higher intervention adherence scores across all pBMI categories (Appendix 1). (80) Using these two studies as prototypes, I created a novel adherence score, unique to the Be Healthy in Pregnancy (BHIP) study as part of my thesis research.

1.5 Knowledge gaps, objectives, and hypotheses

Current diet and exercise recommendations for pregnant populations lack specific and achievable guidance (81), posing the need for intervention trials to explore potential solutions to better guide pregnancy recommendations, including those surrounding appropriate GWG. Additionally, limited insight exists in current research into the impacts of interventions designed to increase levels of optimal GWG on offspring outcomes at birth and in early infancy. Further, tools to measure adherence to interventions are not widely implemented, potentially overshadowing the validity of intervention results; in pregnant populations, maternal intervention adherence has not been explored in relation to infant anthropometry and body composition.

For this thesis project, I explored the impact of standard care versus a diet+exercise intervention in pregnancy on multiple measures of infant anthropometry and body composition. This was assessed not only at birth, but also in early infancy until six months of age. Additionally, the BHIP study included pregnant women from all pBMI categories, compared to available literature which often focuses solely on overweight and obese populations. Additionally, detailed dietary assessment of diet and physical activity provided insights into lifestyle practices in both the intervention and control group participants. Further, I created an adherence scoring algorithm unique to this intervention, utilizing both self-reported and objectively measured data, to quantify and express maternal intervention adherence. This score was then used to describe adherence in the intervention group across pregnancy.

The aim of this project was to determine the impact of a diet and exercise intervention throughout pregnancy on infant outcomes at birth and in early infancy. The specific objectives of this project are:

1) To determine the effects of a structured maternal nutrition+exercise intervention compared with standard prenatal care throughout pregnancy on:
    i. Infant weight and length at birth; and weight, length, skinfold thickness measures and body fat at six months
    ii. Infant anthropometric outcomes within reference ranges (expressed as percentiles) for appropriate age as defined by the World Health Organization's Child Growth Standards

2) To compare the dietary practices between the intervention and control groups using PrimeScreen diet scores as an indicator of healthy dietary practices.

3) To create an algorithm to describe adherence in the intervention group across pregnancy, and to determine if adherence is maintained across pregnancy

We hypothesized that:

1. Infants born to participants in the nutrition+exercise intervention compared to the control group would have lower weight at birth, and lower weight and body fat at six months. Further, a higher proportion of intervention infants would have anthropometric measures within the normal range of the WHO Child Growth Standards.

2. Intervention compared to control participants would have higher PrimeScreen healthy diet scores maintained across pregnancy.

3. Intervention participants will maintain their adherence to the prescribed intervention from early to late pregnancy, as captured by the adherence algorithm created.

CHAPTER 2

STUDY DESIGN AND METHODS

CHAPTER 2 – STUDY DESIGN AND METHODS

Section A: Study design and methods

A.2.1. Study design

The primary objective of the CIHR-funded Be Healthy in Pregnancy (BHIP) randomized control trial (RCT) (NCT01693510) is to reduce the proportion of women with excess GWG according to Institute of Medicine guidelines. (31) Participants were randomized via the 24-hr centralized online randomization service managed by the Biostatistics Unit at St. Joseph's Healthcare – Hamilton. Ethics approval for the BHIP RCT was acquired from the Research Ethics Board of Hamilton Health Sciences in Hamilton, ON, Joseph Brant Hospital in Burlington, ON, and the University of Western Ontario in London, ON.

Healthy, pregnant women were recruited within the communities of Hamilton, Burlington, and London through primary care, midwifery and obstetrical practitioners offices, with additional recruitment facilitated through advertisements online through Facebook and Kijiji, and in community sites such as libraries, coffee shops, and the YMCA. Once women were informed of the BHIP RCT, they were provided with a consent to contact form, which was forwarded to the BHIP study staff along with their personal contact information. Recruitment was also completed via poster advertisements in community and hospital locations, providing interested individuals with both phone and email contact information. Potential participants participated in a scripted screening call with BHIP study staff to assess eligibility following study inclusion and exclusion criteria (Table 4).

Table 4: Inclusion and exclusion criteria for the BHIP study.

Inclusion Criteria	Exclusion Criteria
✓ Healthy pregnant females > 18 years of age with singleton pregnancies (either nulliparous of multiparous)	✗ Unable to understand some English
✓ Less than 17 weeks gestation	✗ Type I or II diabetes
✓ Pre-pregnant BMI <40 kg/m2	✗ Known contraindications to exercise as recommended by Canadian clinical practice guidelines for pregnancy
✓ Plans to deliver at a Hamilton or London regional hospital or by homebirth	✗ Severe chronic gastrointestinal diseases or conditions
✓ Able to tolerate dairy foods	✗ Refusal to consume dairy foods due to intolerance or dislike
✓ Approval of primary care provider	✗ Any significant heart, kidney, liver or pancreatic diseases
✓ Able to provide signed informed consent	✗ Currently smoking
	✗ A depression score above 12 on the validated Edinburgh depression questionnaire

Eligible participants were scheduled to attend the first study visit for between 12-17 weeks gestation, designated as the 'baseline' time point; during this study visit, written informed consent was obtained. At the second study visit, participants who had completed all of the baseline measurements were randomized to either the intervention or control group and re-consented to the specific treatment group. Randomization was stratified by pBMI and study site. Data was entered into an online Research Electronic Data Capture (REDCap) service hosted at McMaster University in a two-step procedure (entry and verification). (31) REDCap is a secure website for the purpose of data collection for research studies, providing automated data export procedures for use in statistical programming. (31)

A.2.2. Methods

A.2.2.1 Intervention treatments

All participants, regardless of intervention status, were expected to continue to receive standard prenatal care from their chosen healthcare practitioner for the duration of their pregnancy as per National Health Canada Recommendations. (31) Additionally, all participants received counseling from the study nutritionist about Health Canada's nutrition recommendations for pregnancy, and were provided both Canada's Food Guide, and the Pregnancy Weight Gain Calculator. Further, the healthcare providers of all participants were made aware of involvement in the study, and provided with the same resources as participants, namely Health Canada's Prenatal Nutrition Guidelines for Health Professionals: Gestational Weight Gain (11,17) and Canada's Food Guide. The BHIP study methodology has been previously described elsewhere. (31)

Intervention: Participants randomized to the intervention group were counselled in an individualized diet with an emphasis on consumption of high protein, low-fat dairy foods. Participants were encouraged to meet their calculated individualized Estimated Energy Requirements (EER) based on their size, age, and physical activity levels, with additional energy goals added as pregnancy progressed. (17,32) Further, participants were instructed with examples to source at least 25% of their energy from protein sources, an increase from the acceptable macronutrient distribution range (AMDR) of a minimum of 10% of energy from protein sources. (32) Consumption of low-fat dairy foods was an important feature of the BHIP intervention; participants needed to source at least 50% of their protein intake from dairy foods, and aimed to consume 4-6

servings of low-fat dairy, such as milk, cottage cheese and yogurt, daily. To achieve these dietary behaviours, participants in the intervention group participated in biweekly in-person visits with the study nutritionist. The study nutritionist counselled the participants on their individual dietary requirements, providing recipes and diet plans suited to meet energy requirements.

In addition to the dietary component of the BHIP intervention, participants were also counselled in a controlled walking-based exercise program. (31) All participants completed a validated activity questionnaire which was reviewed by a certified exercise physiologist to assess participants' activity levels at baseline. Participants were encouraged to follow guidelines from the PARmed-X for Pregnancy, walking 3-4 times each week for 25 minutes a session, increasing their walking time by 2 minutes a week until they reached 40 minutes. (21) Intervention participants were to aim to walk 10,000 steps daily; any daily forms of physical activity could count towards the step count, including walking sessions at study visits accompanied by research staff and daily habitual activities, and were measured through use of a pedometer. (31)

Control: In addition to receiving standard prenatal care alongside counselling in Canada-specific pregnancy guidelines, control participants had the option to be a part of a nested qualitative study focusing on general well-being during pregnancy, in part to encourage participant retention. (31) This included the option to participate in a focus group and information session in late pregnancy led by a midwife. Discussion focused on topics including breastfeeding practices and pain relief in labor. (31)

As of February 2019, all participants enrolled in the BHIP study completed all study visits up to 6 months postpartum.

Section B: Assessment of maternal treatment on infant anthropometry and body composition

This thesis includes data sourced at baseline, prior to randomization, in addition to post-randomization data to be analyzed by treatment group. The study population for this analysis is a subset of the BHIP study population for whom complete data sets for maternal dietary and physical activity, infant anthropometric and infant body composition measures were available as detailed below. Participants in both treatment groups completed relevant dietary questionnaires and provided physical activity data through the use of an accelerometer. All demographic information for study participants was sourced via questionnaire during the baseline study visit prior to randomization.

B.2.1 Maternal treatment assessment

Diet: Participants in the intervention and control groups completed the PrimeScreen Food Frequency Questionnaire, and were assigned a corresponding PrimeScreen diet score to provide insight into their healthy dietary practices. (82) PrimeScreen scores used in this analysis were generated at three time points throughout pregnancy: 12-17 week gestation (baseline); 26-28 weeks gestation (mid-pregnancy); and 36-38 weeks gestation (late pregnancy).

The adherence score for the dietary components of the maternal intervention, was derived based on data sourced from completed 3-day diet records (3DDR),

completed over the same three-day period during which participants wore accelerometers. Over this three-day period (two weekdays, and one weekend day), participants recorded all food and beverages they consumed. This included information pertaining to the amount of food, the method of preparation, and the brand of food, if applicable. Following the completion of the 3DDR, dietary analysis of the macronutrient and micronutrient profiles were completed using NutritonistPro™ Diet Analysis Software (version 5.2.0; Axxya Systems, Woodinville WA). The completion of 3DDR and the corresponding nutritional analysis via NutritionistPro™ Diet Analysis Software was conducted at three time points during the BHIP study: at 12-17 weeks (baseline), 26-28 weeks (mid-pregnancy), and 36-38 weeks gestation (late pregnancy).

Physical activity: Physical activity in the BHIP study was measured by having participants wear the SenseWear® armband tri-axis accelerometer (Model MF-SW; BodyMedia® Inc., Pittsburgh PA). Participants in the intervention and control groups were asked to wear the accelerometers around their upper left tricep for three consecutive days (one weekend day, two weekdays), only removing the device when entering water (i.e., showering, swimming, bathing, etc). The SenseWear® accelerometer features multiple sensors which measure heat flux, galvanic skin response, skin temperature, and body movement. (83) Using these physiological measures, the accelerometer armband is able to utilize advanced algorithms to provide estimates of energy expenditure (EE; kcal/day), posture, sleep data, time spent at various activity levels, and daily step counts. (83) The accelerometer armband is worn at three time points during the BHIP study, corresponding with the completion of

3DDR: 12-17 weeks (baseline), 26-28 weeks (mid-pregnancy), and 36-38 weeks gestation (late pregnancy).

B.2.2 Infant anthropometry and body composition assessment

Anthropometry: A comparison of infant health outcomes between intervention and control groups was assessed at birth and six months of age. Outcome measures at birth were obtained from hospital/birth records. Primary outcomes obtained at birth were birth weight for gestational age and birth length percentile categorization. Additionally, absolute birth weight and birth length were considered. Infants with birth weights below the 10th percentile for gestational age were considered to be small for gestational age (SGA); those with birth weights above the 90th percentile for gestational age are considered to be large for gestational age (LGA). Infants with birth weights between the 10th and 90th percentile for gestational age are considered to be appropriate for gestational age (AGA). Birth weight for gestational age categorization comes from the Canadian Perinatal Surveillance System (CPSS), and is gender-specific. (84) Birth length is considered to represent abnormal growth if it falls outside the World Health Organization's recommended cut-off values of ±2SD, corresponding to the 3rd and 97th percentiles. (85,86) Appendix 3 provides weight for gestational age percentiles from CPSS used to categorize infant weight at birth, and WHO reference percentiles to categorize infant birth length.

At six months postpartum, participants and their infant returned for an in-person study visit during which infant anthropometric and body composition measures were taken. Infant weight (g) was measured on an electric scale (Medela Inc.,

McHenry, IL), and infant supine length (cm) was measured on a pediatric length board (O'Leary LengthBoard, Ellard Instrumentation Inc., Monroe, WA). Skinfold thickness (SFT) measures of the biceps, triceps and subscapularis were taken using infant calipers (Lange calipers, Beta Technology Inc., Cambridge, MD). Reference ranges for infant weight, length, and skinfold thickness measures for triceps and subscapularis were compared against the World Health Organization's Child Growth Standards for analysis, with measurements outside the 3rd and 97th percentiles considered abnormal (Appendix 3). (85,86) Reference standards for bicep SFT measurements are unavailable. Anthropometric measures expressed as percentiles by sex category from the six-month visit were scaled for infant birth date. Appendix 3 provides the growth charts from the WHO used to categorize infant outcomes at six months of age.

Body composition: At the six-month visit, infant body composition was also assessed via dual-energy X-ray absorptiometry (DXA) scans. DXA scans were completed using the QDR®4500 series Hologic Inc. Discovery™ DXA machine (Waltham, MA; Infant whole body software). Only infants scanned at the McMaster University site were included in this analysis. To be scanned, infants were dressed only in a clean diaper, and swaddled with blankets to prevent limb movement. A standardized operation procedure (SOP) (Appendix 3) to analyze infant scans was created based upon a previous DXA SOP for maternal scans. (87) Infant DXA measures included in this analysis are fat mass (g), lean mass (g), total body mass (g) and percent body fat; results from infant DXA scans are expressed as whole body minus the head for

consistency. [88] Currently, no reference standards exist for infant body composition measures completed via DXA.

B.2.3 Statistical analysis

All data analysis was completed using IBM SPSS Statistics for Mac, Version 26.0 (IBM Corp., Armonk, NY). Descriptive statistics presented as mean (SD), median (Q1, Q3) and/or count (%) presented relevant characteristics of the study participants. Prior to performance of analysis, all continuous data was checked for normality using the Shapiro-Wilks test, Normal P-P plots, and Normal Q-Q plots where applicable; non-normal continuous data was transformed accordingly (Table 5).

Table 5: List of variables included in statistical analysis - variable type and relevant data transformations for non-normalized data.

Variable	Type	Transformation
Maternal age	Continuous	None
Ethnicity	Categorical	None
Parity	Categorical	None
Maternal pBMI	Continuous	None
Education	Categorical	None
Total annual household income	Categorical	None
Marital status	Categorical	None
Method of delivery	Categorical	None
Gestational age	Continuous	None
Birth weight	Continuous/Categorical	None
Birth length	Continuous/Categorical	None
6 month weight	Continuous/Categorical	None
6 month length	Continuous/Categorical	None
6 month subscapular SFT	Continuous/Categorical	None
6 month tricep SFT	Continuous/Categorical	None
6 month bicep SFT	Continuous	None
6 month % body fat (DXA)	Continuous	None
6 month fat mass (DXA)	Continuous	None
6 month lean mass (DXA)	Continuous	None
6 month total mass (DXA)	Continuous	None

Linear regression analysis was performed to determine if differences existed between maternal intervention vs. control groups on the measured anthropometric values of infant birth weight, birth length, six month weight, six month length, six month tricep SFT, six month subscapularis SFT, and six month bicep SFT, controlling for maternal pBMI and study site. The means are presented with standard deviations (SD). Results were determined to be statistically significant if presenting a two-sided p-value of <0.05. The beta coefficient (β) is presented alongside p-values for linear regression analysis.

Binomial logistic regression analyses were performed to explore whether maternal treatment group was associated with the likelihood of infant measures being outside the appropriate reference ranges, denoted as the 10-90th for weight for gestational age, or 3rd-97th percentile for all other anthropometry at birth and six months. This analysis was adjusted for maternal pBMI and study site. The infant outcomes explored were birth weight for gestational age, birth length, six-month weight, six-month length, six-month tricep SFT, and six month subscapularis SFT, all presented as dichotomous outcomes. Results were considered statistically significant if the two-sided p-value was <0.05. Odds ratio (OR) and 95% confidence intervals (CI) are presented alongside p-value for binomial logistic regression results.

Associations between maternal intervention status and infant body composition outcomes measured by DXA at six months (lean mass, fat mass, total mass and % body fat) were explored by performing linear regression. Analysis was adjusted for maternal pBMI; adjustments were not made for study site as only DXA

scans from McMaster were included in this analysis. The beta coefficient (β) and p-value were calculated and statistical significance was defined as $p < 0.05$.

Section C: Method development for maternal intervention adherence score

C.2.1 Analysis of intervention effects using measures of dietary practices and adherence

All participants were assigned a PrimeScreen score derived from the completion of the PrimeScreen FFQ (Appendix 2) that was adapted for the BHIP study from a validated tool that was used to assess dietary quality in non-pregnant groups. (82) The PrimeScreen FFQ is designed to capture the average frequency of consumption of various food items and groups, through 25 questions, from which scores are assigned to one of three diet quality ranges. The PrimeScreen score provides insight into the dietary practices/behaviours of participants and allows the identification of any potential differences between the general dietary practices of the control and intervention participants. This sets the groundwork for assessing the control and intervention participants dietary and physical activity behaviours in relation to the requirements of the BHIP Intervention.

All data analysis was completed using IBM SPSS Statistics for Mac, Version 26.0 (IBM Corp., Armonk, NY). Descriptive statistics presented as mean (SD), median (Q1, Q3) and/or count (%) presented relevant characteristics of the study participants. Prior to performance of analysis, all continuous data was checked for normality using the Shapiro-Wilks test; non-normal continuous data was analyzed using non-parametric tests where necessary.

Descriptive statistics were used to describe and compare the dietary practices between the intervention and control groups using PrimeScreen diet scores as an indicator of healthy dietary practices, obtained from an FFQ.

Generalized estimating equations (GEE) were performed to determine the change in adherence scores across pregnancy (12-17, 26-28, and 36-38 weeks gestation) in intervention group participants. Analysis was controlled for maternal pBMI and study site (McMaster vs Western). An AR(1) repeated measures working correlation matrix was applied. A normal model with identify link function was used.

C.2.2: Measures of intervention adherence

Currently, no gold standard to assess diet and exercise intervention compliance in pregnancy exists. Two studies in Canada and Norway successfully created unique scores to assess adherence to their respective interventions in pregnant women; and these existing approaches guided the creation of a novel adherence score for this project. The adherence score developed for this project was based on four main criteria that comprise the BHIP intervention; three criteria based on dietary practices, and one based on physical activity practices. The data for the dietary criteria was sourced from the maternal 3DDR, providing information on energy intake, protein intake, and intake of protein from dairy food sources. Participant responses to the 3DDR were analyzed for energy and macronutrient breakdown using NutritionistPro™ software. The data for the physical activity criteria was sourced from the average daily step counts obtained from an accelerometer worn over the same three-day period that the 3DDRs were completed.

CHAPTER 3

RESULTS

CHAPTER 3 – RESULTS

Section 3.A: Infant anthropometry and body composition

A.3.1 Maternal characteristics

Of the 274 participants enrolled in the BHIP study at baseline, 241 were randomized, 189 completed the study to 6 months postpartum, and 183 were included in this per protocol analysis based on having measured infant outcomes available at birth and 6 months. The majority of participants included in this analysis were Caucasian, married, had post-secondary education, and an annual household income of > $75,000 (Table 6). Nearly half of the participants were nulliparous and were categorized as overweight or obese by pBMI.

Table 6: Baseline (12-17 weeks gestation) demographic characteristics of study participants (N = 183) included in analysis.

Characteristic	**Descriptive Statistics**	
	Intervention (N = 92)	**Control (N = 91)**
Age (years) at enrolment*	31.2 (3.9)	31.5 (4.2)
Pre-pregnancy BMI (kg/m2)		
Underweight (< 18.5)	2 (2.2)	1 (1.1)
Normal Weight (18.5 - 24.9)	51 (55.4)	49 (53.8)
Overweight (25.0 - 29.9)	26 (28.3)	22 (24.2)
Obese (> 30.0)	13 (14.1)	19 (20.9)
Education Level		
Secondary school	1 (1.1)	4 (4.4)
Post-secondary school or greater	91 (98.9)	87 (95.6)
Total annual household income		
< $30,000	4 (4.3)	8 (8.8)
$30,000-$75,000	27 (29.4)	27 (29.7)
> $75,000	59 (64.1)	51 (56.0)
Marital Status		
Married/living with partner	91 (98.9)	86 (94.5)
Ethnicity		
Caucasian	84 (91.3)	82 (90.1)
Other	8 (8.7)	9 (9.9)
Parity		
Nulliparous	48 (52.2)	42 (46.2)
Primi/Multiparous	44 (47.8)	49 (53.8)

*mean (SD) continuous
All other values are Count (%) categorical

A.3.2 Infant birth outcomes

The infants born to the 183 BHIP participants had a mean gestational age of 39.4±1.2 weeks, with an approximately even split between male and female infants (Table 7).

Table 7: Pre-specified infant birth outcomes by treatment group (N = 183).

Characteristic	**Descriptive Statistics**	
	Intervention (N = 92)	**Control (N = 91)**
Gestational Age (weeks)*	39.5 (1.2)	39.4 (1.3)
Sex		
Male	46 (50.0)	45 (49.5)
Female	46 (50.0)	46 (50.5)
APGAR scores*		
1 minute	8.2 (1.5)	8.5 (1.2)
5 minute	9.0 (0.4)	8.9 (0.4)

*mean (SD) continuous
Count (%) categorical

Recorded birth weight (g) was similar between infants born to control and intervention groups (Table 8). Recorded length at birth (cm) was significantly higher in infants born to intervention compared to the control group, adjusted for study site and maternal pBMI (Table 8). The majority of infants had birth weights categorized as appropriate for gestational age (AGA) in both the Intervention (82.6%) and Control groups (87.9%). Infant birth length was categorized by percentiles defined by the World Health Organization, with values outside the 3rd-97th percentile range considered abnormal. In the intervention group, 65.8% of infants had a birth length

between the 3rd-97th percentile, and 34.2% of infants had a birth length above the 97th percentile; in the control group, 85.5% of infants had birth lengths between the 3rd-97th percentile, with 13.2% of infants having birth lengths above the 97th percentile. Intervention status, pBMI (kg/m2), and study site were not significantly associated with higher odds of infants being born AGA (Table 9). Infants born to control group mothers had 3.07 higher odds of birth length (cm) being between the 3rd-97th percentile, compared to intervention group infants (Tables 10); pBMI and study site were not found to impact this association.

Table 8: Effect of treatment on infant anthropometric measures at birth (N = 183)

Variable	**Intervention**	**Control**	**β**	**P-value**
Weight (g)	3604±492 (N = 92)	3485±439 (N = 91)	0.13	0.09
Length (cm)*	52.1±2.7 (N=73)	51.1±2.1 (N=76)	0.20	0.02

Group differences analyzed by linear regression adjusted for maternal pBMI and study site was performed
*Birth length measures were not recorded on medical charts for some infants

Table 9: Association of infant weight (g) at birth being AGA as defined by CPSS with maternal intervention status, study site, and pBMI.

Maternal Characteristic	**OR**	**95% CI**	**p**
Intervention status	0.58	0.25, 1.33	0.20
pBMI	1.02	0.93, 1.12	0.66
Study site	2.05	0.90, 4.69	0.09

Binomial logistic regression was performed using the following categories: AGA (n =155) vs SGA/LGA(n = 28)
OR = Odds ratio

Table 10: Association of infant length (cm) at birth being within 3rd-97th percentile as defined by WHO Child Growth Standards with maternal intervention status, study site, and pBMI.

Maternal Characteristic	**OR**	**95% CI**	**p**
Intervention status	3.08	1.38, 6.85	0.006
pBMI	1.02	0.94, 1.11	0.60
Study site	1.02	0.56, 2.75	0.60

Binomial logistic regression was performed using the following categories: within preferred recommendations (n = 113) vs outside preferred recommendations (n = 36)
OR = Odds ratio

A.3.3. Six month outcomes

Anthropometric measures of weight, length, tricep SFT, subscapular SFT, and bicep SFT at 6 month of age were similar in infants born to mothers in the intervention group versus control group (Table 11). Infant DXA measures were not included in this analysis if significant limb movement, missing limbs or foreign artifacts in the field of view could not be mediated using limb surrogate analysis, as per an SOP (Appendix 4). Further, scans from the Western University site were not included due to discrepancies in technology. Measures of fat mass, lean mass, total body mass, and % body fat (all reported without head values) by DXA were similar in infants born to mothers in the intervention and control groups (Table 12)

Table 11: Effect of treatment on infant anthropometric measures at six months of age (N = 183)

Variable	Intervention (N = 92)	Control (N = 91)	β	P-value
Weight (g)	7849±989	7744±942	0.05	0.49
Length (cm)	67.9±3.1	67.7±2.9	0.03	0.74
Tricep SFT (mm)	13.9±3.4	13.1±3.4	0.12	0.09
Subscapular SFT (mm)	8.6±1.9	8.1±2.3	0.14	0.06
Bicep SFT (mm)	9.6±3.7	8.9±2.9	0.10	0.20

Group differences were analyzed by linear regression adjusted for maternal pBMI and study site
Values are mean±SD

Table 12: Effect of treatment on infant body composition measures by DXA scanning at six months of age (N = 56)

Variable	Intervention Group (N = 32)	Control Group (N = 24)	β	P-value
Fat mass (g)	2340±654	2188±571	0.21	0.13
Lean mass (g)	4232±640	4211±538	0.006	0.97
Total mass (g)	6661±1054	6489±810	0.20	0.15
% Fat mass	34.8±6.2	33.4±6.4	0.14	0.32

Group differences were analyzed by linear regression adjusted for maternal pBMI .
Values are mean±SD; all values reported exclude head measures

Percentile-based reference standards for infant growth measures at 6 months of age were available from the World Health Organization for weight, length, tricep SFT, and subscapular SFT at 6 months of age, wherein measures outside the 3rd-97th percentiles are considered abnormal. The majority of infants had measured weights between the 3rd-97th percentiles (95.7% in the intervention group, 96.7% in the control

group); similarly, the majority of infants measured lengths between the 3rd-97th percentiles (81.5% in the intervention group, 86.8% in the control group). Infant subscapular SFT measurements were between the 3rd-97th percentiles in 79.3% of intervention group infants, and 81.3% of control group infants. Infant tricep SFT measurements were above the 97th percentile in 54.3% of intervention group infants, and 46.2% of control group infants.

The results from the binomial logistic regression analyses for infant anthropometric measures at 6 months are shown in Tables 13-16. The likelihood of infant weight (g), infant length (cm) or subscapular SFT (mm) being between the 3rd-97th percentile was not significantly associated with maternal intervention status, pBMI, or study site. The likelihood of infant tricep SFT being within the 3rd-97th range was not associated with maternal intervention status, or pBMI. However, regarding study site, infant tricep SFT (mm) was two and a half times more likely to be within the 3rd-97th percentile in infants at the McMaster study site, compared to the Western study site.

Table 13: Association of infant weight (g) at six months being within 3rd-97th percentile as defined by WHO Child Growth Standards with maternal intervention status, study site, and pBMI.

Maternal Characteristic	**OR**	**95% CI**	**p**
Intervention status	0.76	0.16, 3.50	0.72
pBMI	0.95	0.82, 1.11	0.52
Study site	0.77	0.14, 4.16	0.77

Binomial logistic regression was performed using the following categories: within recommendations (n = 176) vs outside recommendations (n = 7)
OR = Odds ratio

Table 14: Association of infant length (cm) at six months being within 3rd-97th percentile as defined by WHO Child Growth Standards with maternal intervention status, study site, and pBMI.

Maternal Characteristic	OR	95% CI	p
Intervention status	0.58	0.25, 1.34	0.20
pBMI	0.94	0.87, 1.02	0.15
Study site	1.35	0.58, 3.13	0.49

Binomial logistic regression was performed using the following categories: within recommendations (n = 155) vs outside recommendations (n = 28)
OR = Odds ratio

Table 15: Association of infant tricep SFT (mm) at six months being within 3rd-97th percentile as defined by WHO Child Growth Standards with maternal intervention status, study site, and pBMI.

Maternal Characteristic	OR	95% CI	p
Intervention status	0.64	0.35, 1.17	0.15
pBMI	1.06	1.00, 1.14	0.07
Study site	2.50	1.30, 4.81	0.006

Binomial logistic regression was performed using the following categories: within recommendations (n = 90) vs outside recommendations (n = 93)
OR = Odds ratio

Table 16: Association of infant subscapular SFT (mm) at six months being within 3rd-97th percentile as defined by WHO Child Growth Standards with maternal intervention status, study site, and pBMI.

Maternal Characteristic	OR	95% CI	p
Intervention status	0.88	0.42, 1.83	0.73
pBMI	0.95	0.88, 1.02	0.18
Study site	0.96	0.44, 2.10	0.92

Binomial logistic regression was performed using the following categories: within recommendations (n = 147) vs outside recommendations (n = 36)
OR = Odds ratio

Section 3.B: Development and application of scores for healthy dietary practices and treatment adherence

B.3.1 Maternal characteristics

Of the 183 women analyzed for the clinical outcomes in Section A, 111 (55 intervention participants, 56 control participants) with completed PrimeScreen FFQ, 3DDR, and accelerometer data across pregnancy (12-17 weeks, 26-28 weeks, and 36-38 weeks gestation) were included in the dietary practices and treatment adherence analysis. This sub-group of 111 had very similar demographic characteristics to the 187 participants in the clinical outcomes analysis (data not shown).

B.3.2 Healthy dietary practices between treatment groups by PrimeScreen diet score

PrimeScreen diet scores were comparable between intervention and control participants at baseline (12-17 weeks gestation) (Figure 1). However, scores rose significantly in intervention participants at 26-28 weeks gestation, and were maintained at 36-38 weeks gestation, while in the control group participants' scores remained constant across pregnancy (Figure 1). PrimeScreen diet scores are measured on a continuous score, with higher scores indicating increasingly healthy general dietary practices.

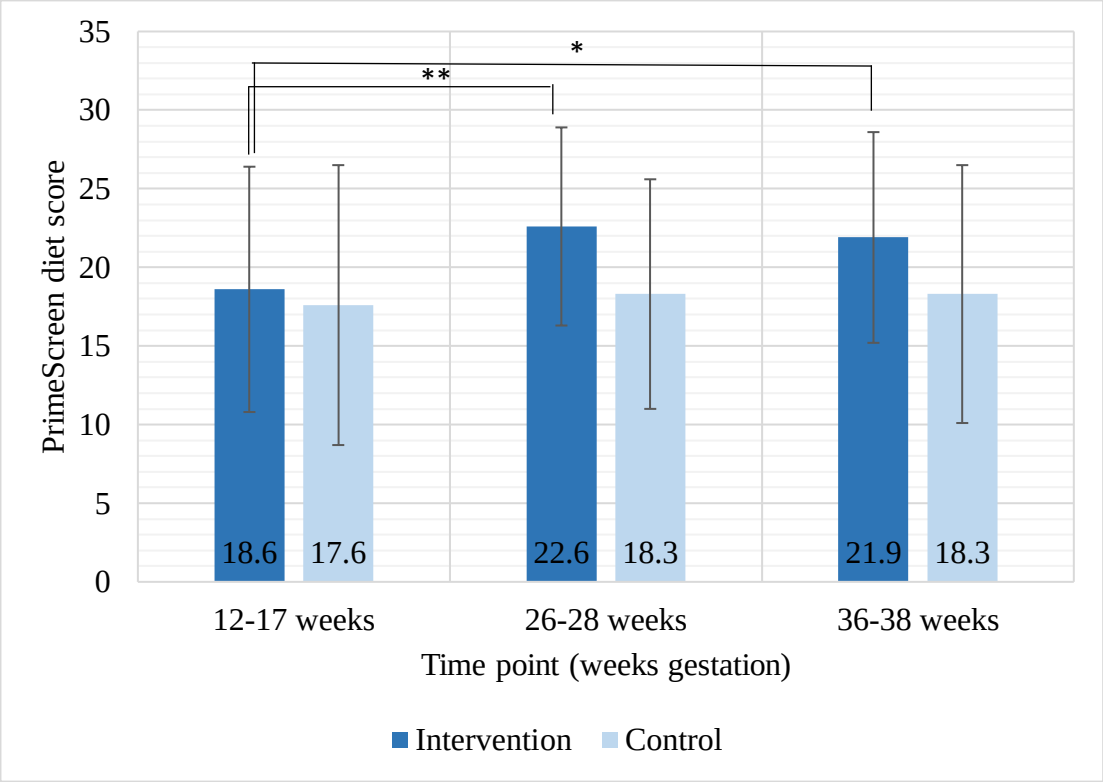

Figure 1: Participant PrimeScreen scores in Intervention (N= 55) and Control groups (N = 56). Bars and whiskers represent mean±SD. Values within bars are means. * $p < 0.008$; ** $p < 0.001$.

B.3.3 Development of adherence score for diet and exercise intervention

A detailed summary of this scoring system can be found in Table 17, and an example of its application can be found in the Appendix 5. Scores awarded to individual participants ranged from 0 to 4, with a higher score corresponding to greater adherence to the BHIP intervention. This adherence score was employed across pregnancy, corresponding with the 3 study visits that all participants completed: 12-17, 26-28, and 36-38 weeks gestation. This provided a sense of how behaviours changed from before the intervention (12-17 weeks gestation) to after the implementation of the intervention (26-28 and 36-38 weeks gestation).

Table 17: Summary of adherence score criteria for BHIP intervention

Criteria	Category	Assessment/Score Attribution	Possible Score Ranges
Are participants meeting their individualized estimated energy requirements (EER)?	Binary	Score 1: If a participant's energy intake (EI) is within 1 population-derived SD of their individualized EER, they are adherent. Score 0: If their energy intake is not within 1 population-derived SD of their EER, they are not adherent.	0 (non-adherent) or 1 (adherent)
Are participants consuming a high protein (25% of kcal sourced from protein) daily diet?	Binary	Score 1: If a participant's protein intake is within 1 population-derived SD of 25% of their energy intake, they are adherent. Score 0: If their energy intake is not within 1 population-derived SD of 25% of their energy intake, they are not adherent.	0 (non-adherent) or 1 (adherent)
Are participants sourcing 50% of their protein from dairy sources?	Binary	Score 1: If a participant's protein intake is within 1 population-derived SD of being 50% sourced from dairy foods, they are adherent. Score 0: If a participant's protein intake is not within 1 population-derived SD of being 50% sourced from dairy foods, they are not adherent.	0 (non-adherent) or 1 (adherent)
Are participants walking 10,000 daily steps?	Continuous	Each participant's daily step count is divided by 10,000 steps, and the fraction value is the point awarded. This is partial adherence. Participants who walk ≥ 10,000 steps will be considered fully adherent.	Score can range anywhere between 0 (no steps, fully non-adherent), to 1 (≥ 10,000 steps, fully adherent). Scores in between account for partial adherence.

B.3.4 Application of adherence scores within the intervention group

The adherence scoring algorithm was comprised of four dietary and physical activity criteria. Fewer participants met estimated energy intake requirements as pregnancy progressed. Higher intakes of protein and dairy protein from baseline were achieved after implementation of the intervention and were maintained to 36-38 week. Figure 2 demonstrates the proportion of participants who were adherent to the dietary components of the intervention, namely energy, protein and dairy protein intake.

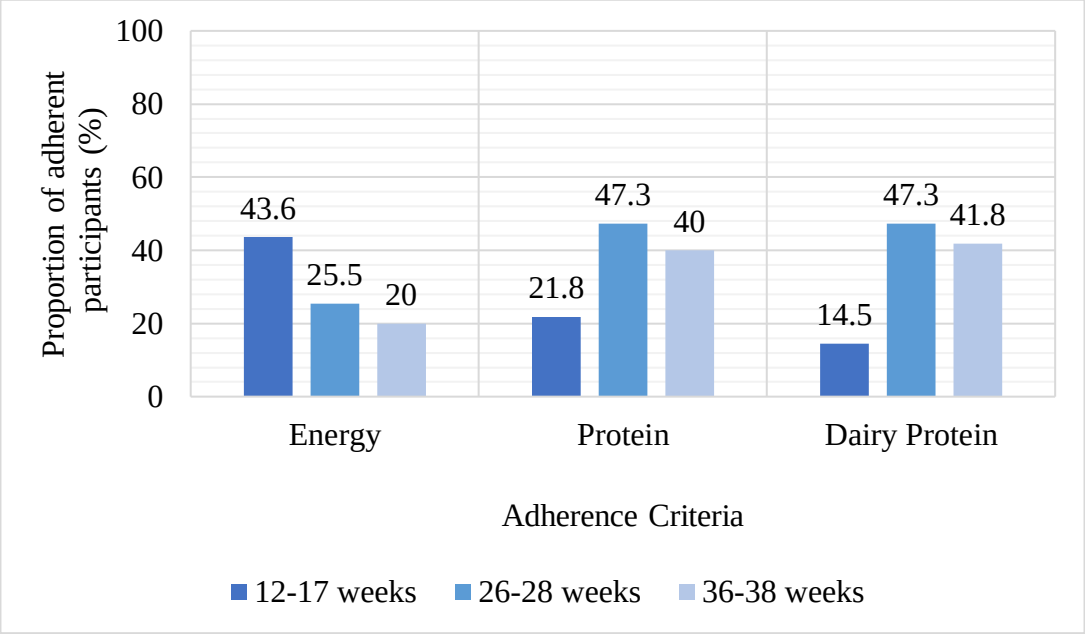

Figure 2: Proportion of intervention participants (N = 55) considered adherent to thedietary components of the BHIP intervention before (12-17 weeks) and after (26-28 and 36-38 weeks) implementation of intervention, as defined by the adherence algorithm. Values displayed are percentages.

Figure 3 demonstrates the mean±SD daily step counts for intervention participants before and after randomization to the intervention. Average daily step counts continued to decline through the end of pregnancy. While 14.5% of intervention participants achieved 10000 average daily steps at 12-17 weeks gestation, this

proportion decreased to 9.1% and 5.5% at 26-28 and 36-38 weeks gestation, respectively.

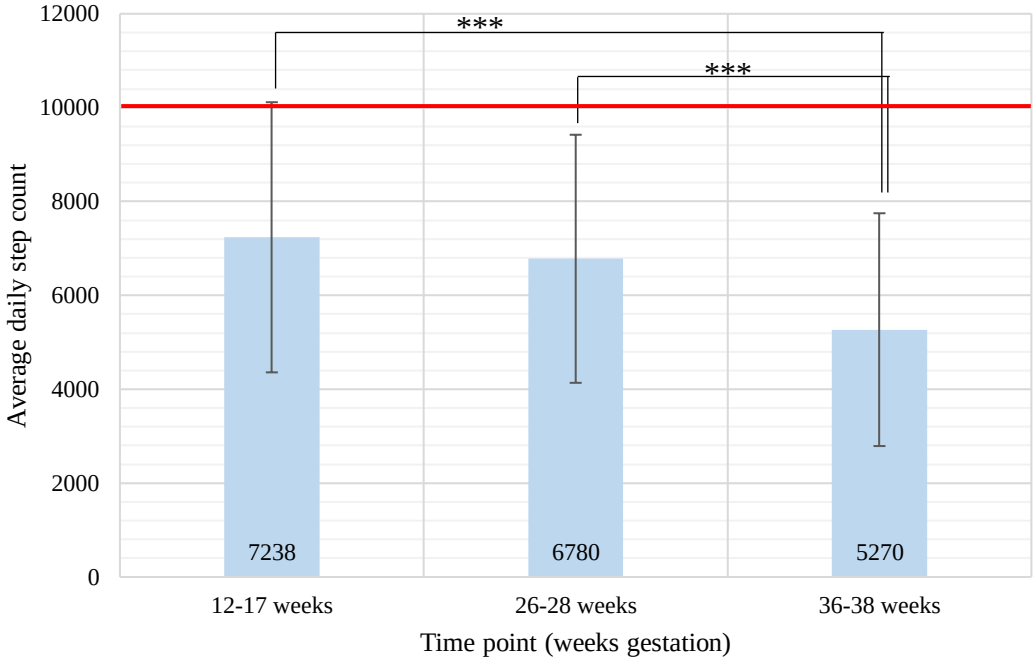

Figure 3: Mean daily step count for intervention participants (N = 55) before (12-17 weeks) and after (26-28 and 36-38 weeks) implementation of intervention. Error bars are standard deviation; line at 10000 steps represents intended daily step count. *** $p < 0.0005$

Figure 4 highlights the range of individual adherence scores within the intervention group. Table 18 demonstrates mean±SD adherence scores through to the end of pregnancy. Adherence scores increased significantly ($p = 0.011$) from baseline to 26-28 weeks gestation indicating that the prescribed intervention was being implemented (Table 19). However, adherence scores declined significantly ($p < 0.0005$) from 26-28 to 36-38 weeks gestation, indicating that the adherence to the prescribed intervention was not being maintained (Table 19). Study site and maternal pBMI were not found to impact adherence scores across pregnancy. In light of the

adherence pattern for dietary components noted in Figure 2 and step count responses noted in Figure 3, the decline in overall adherence scores toward the end of pregnancy appears to be primarily attributed to the decrease in average daily step count and failure to achieve energy intake requirements for a large proportion of participants through to the end of pregnancy.

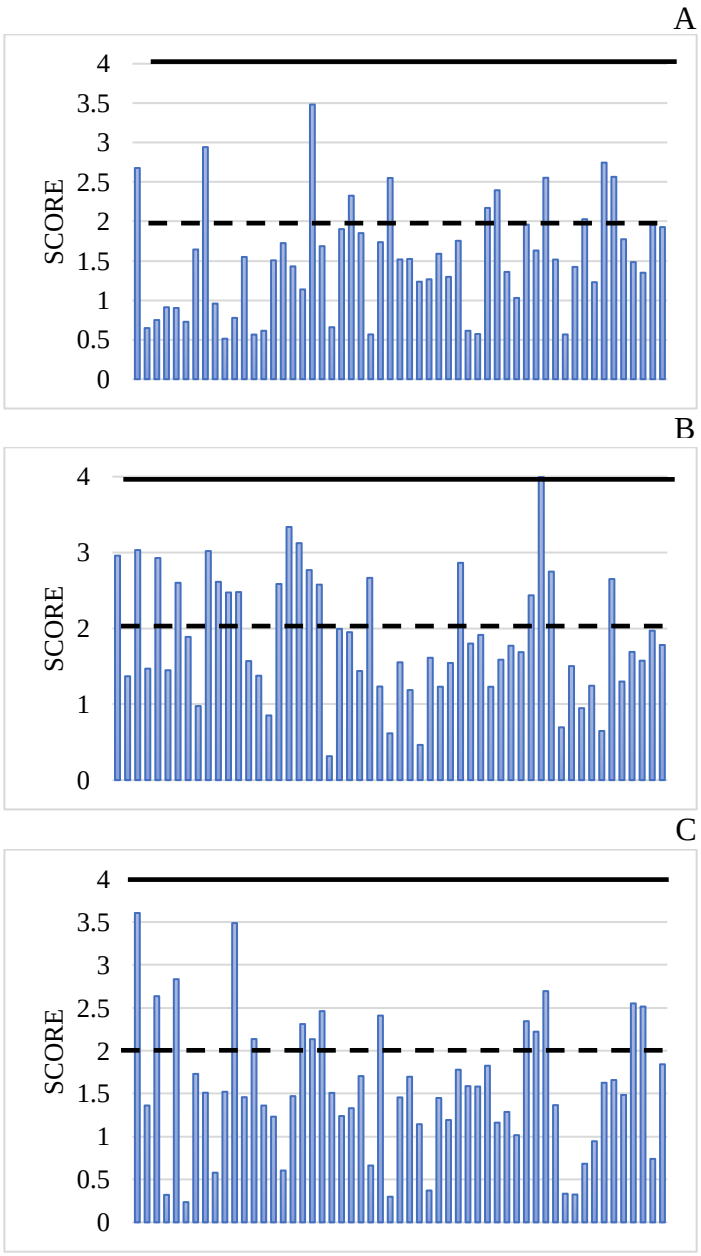

Figure 4: Individual participant adherence scores. A - before intervention implementation at 12-17 weeks gestation; B - after intervention implementation at 26-28 weeks gestational; C - after intervention at 36-38 weeks gestation. Each bar represents a single participant's score. Dashed line indicates 50% adherence; solid line indicates 100% adherence.

Table 18: Adherence scores throughout pregnancy in intervention participants. Continuous variables are mean±SD.

Timepoint	Adherence Score	% Adherence
12-17 weeks gestation*	1.52±0.70	38.0%
26-28 weeks gestation	1.89±0.82	47.3%
36-38 weeks gestation	1.55±0.78	38.8%

*Measures taken before intervention started

Table 19: Change in adherence scores in the intervention group across pregnancy (N = 55)

Parameter	B	95% CI	p-value
Adherence score: 12-17 weeks vs 26-28 weeks	0.35	0.08, 0.63	0.01
Adherence score: 12-17 weeks vs 36-38 weeks	0.02	-0.23, 0.27	0.87
Adherence score: 26-28 weeks vs 36-38 weeks	10.33	-0.51, -0.16	< 0.0005
pBMI	0.009	-0.03, 0.05	0.68
Study site	0.02	-0.45, 0.50	0.93

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CHAPTER 4

DISCUSSION AND CONCLUSION

CHAPTER 4 – DISCUSSION AND CONCLUSION

4.1: Key findings of intervention effects on infant outcomes

In this cohort of relatively healthy, predominantly white, well-educated women, no significant treatment effect of the maternal diet and exercise intervention was demonstrated for most offspring anthropometric and body composition measures at birth and six months of age, namely birth weight, weight and length at six months, and SFT measures of the bicep, subscapular, and tricep. Further, measures of fat mass, lean mass, total mass and percent body fat by DXA were similar in the control and intervention group infants at six months. The lack of an intervention effect in infant body size and composition might be attributed to a number of factors. First, our measure of adherence to the intervention suggested that both the prescribed dietary and exercise components were not completely followed despite counselling and reinforcement by the study team every two weeks. Additionally, while intervention participants increased their healthy dietary practices compared to control participants as measured by the PrimeScreen score, both groups demonstrated relatively similar levels of healthy dietary practices. Secondly, the demographics of the participants demonstrated that the vast majority were Caucasian, well-educated with high income, lived with their partner and were generally healthy; such factors are often characteristic of lower risk of adverse birth and infant outcomes. (89–91) Thirdly, this study was not powered for the secondary outcomes of infant size and body composition. However, the data collected could be used to calculate the sample size required to see an intervention effect.

Interestingly, birth length was significantly higher in intervention compared to the control group infants. The prescribed higher maternal protein intake in the intervention group may provide a possible explanation for this finding. Protein intake in infancy is known to stimulate insulin-like growth factor (IGF-1) synthesis (92–94); thus it is plausible that maternal protein intake in pregnancy may also act as a modulator of IGF-1 in relation to infant growth. (95,96) Another consideration is that birth length was not measured by members of our study team and was instead obtained from birth charts. Infant measures obtained in delivery rooms are often subject to inconsistencies. Notably, any differences in birth length diminished by six months of age as properly measured infant length was similar between the intervention and control groups.

Our observations of a lack of effect of the maternal nutrition+exercise intervention on infant anthropometry and body composition align with a previous systematic review and a few recent studies, although in the latter the type of interventions and specific pregnancy group varied from our study. A meta-analysis of 13 exercise interventions in overweight and obese pregnant women (N = 1439) found no significant differences in reported infant outcomes, including birthweight, macrosomia, and incidence of SGA and LGA infants. (97) Similarly, a Cochrane review of diet and/or exercise pregnancy interventions (N = 65) which included 27 studies reporting on infant macrosomia found no significant differences in incidence of macrosomia in intervention or control born infants; a subset of seven exercise-only interventions demonstrated the largest effect size, reporting a 7% reduction in macrosomia in intervention group infants. (30) Within the BHIP study, 12% of

intervention and 7% of control infants were considered LGA, and 5.5% of intervention and control infants were considered SGA. Interestingly, 22.8% of intervention infants were considered macrosomic at birth compared to 7.7% of control infants. In a single RCT in Brazil (N = 639) employing an exercise intervention for pregnant women of all BMI categories, an intervention effect was not observed for infant birth outcomes of weight, length or head circumference. (98) This trial did include reports of intervention adherence, defined as attendance to exercise sessions offered by the study group. (98) Similarly, a dietary intervention in New Zealand in obese pregnant women (N = 230) designed to decrease the proportion of women with excessive GWG through education sessions with a community health worker found no impact of the intervention (compared to standard care) on birthweight, which was a primary outcome of the study, nor secondary infant outcomes including rate of LGA, SGA and body composition measures. (99) Similarly, our study did not find an intervention effect on body composition measures, nor incidence of SGA or LGA. Adherence to the intervention was not reported despite indications that FFQs were completed by participants. (99) Finally, a diet+exercise behavioural intervention compared to standard prenatal care for obese pregnant women in the United Kingdom (N = 1555) did not yield differences in incidence of LGA and SGA or crown-heel length between the intervention and control group infants. (100) Collectively, the cited studies above infrequently reported measures of adherence, and those which included a measure of adherence reported low levels of compliance. This leads one to speculate that compliance with the intervention may be an important variable mitigating the lack of outcome differences observed between intervention and control group infants.

4.1.1: Infant growth in relation to normative standards from WHO

Most infants included in this analysis had measures of anthropometric growth within acceptable ranges (3rd- 97th percentile) of reference standards at birth and six months of age from WHO (86,101) suggesting adequate nutrition in-utero and in early infancy. Not surprisingly, because of higher absolute length at birth, a higher percentage (34.2%) of infants in the intervention group had birth lengths above the 97th percentile, compared to 13.2% of infants in the control group but this was not sustained as at six months, similar proportions of infants in the intervention and control groups had lengths measures that fell within the 3rd-97th percentile.

The WHO Child Growth Standards have been implemented over regional reference standards in 125 countries, including Canada. (85) The current WHO Child Growth Standards were designed to be globally representative charts, reflecting the growth of children whose circumstances did not impose restrictions on growth and who are receiving sufficient nutrition. (102) These charts are appropriate for use in the BHIP study as they are international standards deemed appropriate for Caucasian populations.

4.2 Assessment of diet quality and adherence to the intervention

4.2.1 Diet quality and physical activity

Diet quality and adherence are not often measured or reported in pregnancy intervention studies. However, both might be a factor explaining the lack of an intervention effect in pregnancy trials, particularly on measures of infant growth. As such, findings of diet quality in both treatment groups, and adherence in the

intervention group were reported. In our study, we found that after about 10 weeks following implementation of the intervention, participants had a higher diet quality PrimeScreen score compared to their habitual self-selected diet at entrance to the study. Intervention participants were able to maintain this higher diet quality through to the end of their pregnancies. In contrast, diet quality scores remained similar in control participants throughout pregnancy. This suggests that the structured and individualized dietary advice with biweekly counseling from the study nutritionist was effective in improving general dietary practices in the intervention group. The PrimeScreen diet score is a continuous score, wherein higher scores reflect a healthier diet. While the control group having lower scores does not necessarily mean they had unhealthy dietary practices, it does indicate that the intervention group's dietary practices were healthier. While more women in pregnancy report the desire to modify their diets compared to non-pregnant populations for the benefit their offspring, many women lack the necessary skills, knowledge or support to adequately make such changes. (103–106) The frequency of knowledge sharing and guided support from the study nutritionist, in addition to the provision of low-fat dairy foods, may have been extra motivating factors for women enrolled in the intervention group to improve their dietary practices.

Application of the adherence score was important to determine compliance with the specific components of the diet and exercise intervention for future reference and clinical application. The overall adherence score indicated that intervention participants were able to change their behaviours to be in line with the intervention; however, they did not maintain this change throughout as noted at the end of

pregnancy. Intervention adherence was ultimately low in the intervention group, with the average intervention participant achieving less than 50% adherence (adherence score < 2 out of a possible 4). However, there was notable individual variability in the overall adherence scores at each time point in pregnancy, demonstrated in Figure 4 in section B.3.4. The adherence scoring algorithm highlights specific components of the intervention that women were less adherent to across pregnancy. While there was a relatively consistent proportion of participants who maintained their protein (47.3% at 26-28 weeks gestation, 40% at 36-38 weeks gestation) and dairy protein intake (47.3% at 26-28 weeks gestation, 41.8% at 36-38 weeks gestation) through to the end of pregnancy, fewer participants were adherent to the individualized requirement for energy intake and the daily step count portion of the intervention. While 43.6% of intervention participants were already meeting their individualized energy intake goals at baseline, this dropped to only 20% by the end of pregnancy.

The goal of 10,000 steps was only achieved by 9.1% of intervention participants at 26-28 weeks gestation, and 5.5% of participants at 36-38 weeks gestation. Disappointingly, average daily step counts continued to drop throughout pregnancy despite continued encouragement and walking sessions accompanied by research staff at the bi-weekly visits. The mean±SD step counts dropped from 7238±2878 at baseline to 5270±2480 by 36-38 weeks gestation. By comparison, the control group achieved step counts of 6571±2629 and 5491±2300 at the same pregnancy time points. Current Canadian pregnancy exercise guidelines recommended accumulating at least 150 minutes of moderate-intensity exercise a week, accumulated over a minimum of three days (22), and do not specify a daily step count. A

longitudinal exercise study in pregnant women GDM (N = 24) in Japan found that daily step counts of at least 6000 was sufficient to significantly reduce blood glucose levels. (107) It is possible that the step counts achieved by our study population may have been sufficient to achieve the recommended 150 weekly minutes pf physical activity. Maintaining 10000 daily steps may not be a reasonable goal, particularly in pregnancy, as it has been questioned for use even in non-pregnant population. (108)

A nested qualitative study within the BHIP study with control participants found that maintaining healthy practices in pregnancy was easier if they had established such behaviours prior to pregnancy (109); this suggests that changes in health behaviours may have felt like an extreme shift for some participants if they were not already making such efforts, making it difficult to maintain these changes until the end of pregnancy. Additionally, a common sentiment echoed by pregnant women attempting to adapt their health behaviours is that despite initial motivation or desire, other commitments such as childcare work responsibilities make it more difficult. (109,110) Approximately half of the participants in our study had at least one other child, which may have presented barriers to modifying dietary and physical activity behaviours. Finally, pregnancy-specific complications, including sore joints and nausea might prevent women from safely engaging in exercise, or opting to follow specific dietary patterns. (109,111–113) Many women also do not engage in exercise during pregnancy due to the misconception that exercise will cause harm to their offspring, despite research suggesting otherwise. (42,43) Particularly given the steady decline in daily step count for the intervention participants, it is plausible that such reasons may have prevented them from continuing to exercise throughout the

intervention. These reasons may have ultimately contributed to the declining adherence seen in intervention participants through the end of pregnancy.

4.2.2 Adherence scores for diet and exercise intervention

Unlike other intervention trials, our study involved the creation and application of a novel scoring system to measure intervention adherence. This score could be applied at multiple timepoints to assess whether intervention compliance changed across pregnancy. This score has the potential to be used in future analyses within the BHIP study to allow for greater interpretation of intervention success in modifying intended outcome measures.

Reporting measures of intervention adherence is important to transparency in research, and to understand the effectiveness of a trial. (114) Our study demonstrated that creating a quantifiable measure of intervention adherence is entirely plausible and can likely be achieved within other interventions. However, there are some important considerations to make when measuring adherence. It is key to define the specific elements of the intervention prior to describing adherence; this may be achieved by considering an intervention as a series of specified steps that must be completed. (115,116) In our study, we considered the main behaviours we asked of our participants to define the intervention, and thus developed four specific criteria. Next, one must ensure the proper measurements or tools are available to measure what was delivered and received, as opposed to the intended intervention effect. (116) For example, to measure adherence in our study we had to determine average daily protein intake. We were actually able to report on this measure, as we had collected data from on daily

food intake through 3DDR and had access to NutritionistPro™ software to complete nutritional analysis, including macronutrient intake. Without these tools, reporting on protein adherence may not have been possible. Taken together, the foregoing considerations allow reporting intervention adherence to be more achievable.

Objective measures of dietary and exercise practices can be difficult to incorporate in assessments of intervention adherence. In our study, we were able to use accelerometer data as an objective measure of daily step count. For dietary adherence our measures were more subjective, although we did employ high quality measurement tools, including 3DDR analyzed by NutritionistPro™ software and PrimeScreen FFQ. In pharmaceutical trials, it is becoming more commonplace to find ways to measure target biomarkers as a more objective understanding of adherence. (117) Successful biomarker measurement methods for dietary components such as offered by metabolomics (118,119) would be a valuable contribution to future adherence measuring practices, particularly to validate potential adherence measures.

4.3 Contributions to clinical practices

Participants in the intervention group increased their daily protein intake, without increased risk of adverse anthropometry and body composition in their offspring. While birth length and incidence of abnormal birth length above the 97th percentile was seen more prominently in the intervention group, there was concern for reporting bias as birth length data were abstracted from medical charts and proper length board measures are not always used in delivery rooms. Further, the difference in length between treatment groups no longer existed at six months of age. This

suggests that protein intake above current recommendations in pregnancy is safe. In fact, recent research has explored the impact of protein intake greater than current recommendations, both in non-pregnant and pregnant populations, on a variety of health outcomes. It has been suggested that the protein requirements for pregnant populations should change, as current recommendations are based on data from non-pregnant populations. (32) A Canadian clinical trial (N = 29) determined adequate protein requirements in pregnant women through measuring the oxidation rate of L-phenylalanine to CO_2 after receiving different protein intake ranges in early and late pregnancy. (120) The results of this study suggest that the EAR for daily protein intake should be 1.22 g/kg body weight and 1.52 g/kg body weight in early and late gestation, respectively, which are above current Canadian EAR of 0.88 g/kg body weight. (120)

The BHIP study contributes self-selected dietary intake data on Canadian pregnant women, which is not currently available in the Canadian Community Health Survey (CCHS) as this national survey does not specifically sample pregnant women. Neither the CCHS nor the Canadian Health Measures Survey (CHMS) collect data on infant growth under one year of age. Thus, our study also contributes data on infant anthropometry and body composition at birth and six months of age that appear to represent a healthy population based on analysis with current WHO reference growth standards.

Our study successfully employed a tool to assess diet quality and created an adherence algorithm which accounted for both dietary and physical activity

components of the intervention, utilizing subjective and objective measurement tools. This has been done in very few interventions, particularly in pregnant populations. These results are now available to guide further research in how to better assess intervention adherence for the purpose of interpretation of results.

4.4 Strengths and limitations

This study had many strengths. First, it was an RCT with longitudinal follow-up of mothers and infants, while significant currently available longitudinal data comes from observational studies. Our study benefited by taking measurements at multiple time points in pregnancy, as opposed to only once. This captured a broad picture of dietary and physical activity behaviours of pregnant women in Southern Ontario, and particularly how such behaviours corresponded with the prescribed intervention. Additionally, many diet and exercise interventions in pregnancy include only participants categorized as overweight and/or obese by pBMI; our study included participants from all pBMI categories, making results more generalizable to the broader population. Our study did adjust all analyses for pBMI, and did not find any significant effects.

For the measures in infants, most intervention studies have only included infant data at birth, with observational/epidemiological studies providing the majority of early infancy and childhood data. The value of the BHIP study is the inclusion of several measures of infant anthropometry at two time points and complete body composition measures at six months of age. Our study used DXA to measure infant body composition, widely considered a gold standard technique. Further, our study

included both absolute infant anthropometry measures and percentile categorizations that were compared to universal reference standards for child growth.

Most studies of dietary interventions in pregnancy have failed to report measures of diet quality or adherence or adjusted for this in their results. We provided two measures – one of general diet quality using the PrimeScreen diet scores and the other an intervention adherence score specifically developed for the BHIP study. The creation and use of a unique adherence score has rarely been achieved in other RCTs, especially those in pregnant populations. This allowed for us to better understand the specific dietary and physical activity behaviour changes participants made throughout the intervention. Our novel adherence score incorporated both subjective and objective measures, allowing for a more comprehensive understanding of intervention compliance. The accelerometer used to capture step count is widely considered to be the gold standard technique, as it captures the most activity; this includes household and caregiving activities which are reported to make up 50-65% of energy expenditure in pregnancy. (121) Further, utilization of 3DDR to capture dietary intake lowered the risk of recall bias from participants; nutrition analysis with NutritionistPro™ Diet Analysis Software captured in depth dietary information, including energy intake and macronutrient distribution.

This study is not without some limitations. First, this study was not powered for measuring infant outcomes; thus, results presented are exploratory.

The relatively homogeneous demographics of the study sample may limit the generalizability of our findings to the general pregnant population in Canada. Most participants in both the intervention and control group were Caucasian, had a secondary education, and a high annual household income (> $75000). Thus, the results of this study might not be replicated in pregnant populations with different sociodemographic characteristics. A systematic review of 106 observational studies reported consistent associations between socioeconomic disadvantages such as low income, lack of post-secondary education, and unemployment, and increased risk of adverse birth outcomes including low birth weight, preterm birth, and incidence of SGA. (122)

The participants in our study were predominantly recruited from midwifery clinics; access to midwifery clinics in Canada is relatively low, with an estimated 6.1% of the Canadian population using midwifery services in pregnancy. (123) Comparatively, midwives attended 16% of births in Ontario in 2017. (124) Despite this, a recent qualitative descriptive study in Ontario found that access to midwifery care was reduced in populations of low-socioeconomic status, potentially contributing to disparities in prenatal care. (125) This may contribute to our results not being generalizable to the broader Ontarian and Canadian pregnant population.

Finally, few cases for measured infant outcomes compared against the WHO Child Growth Standard percentiles were outside the 3rd-97th percentile and thus deemed abnormal. Small sample sizes increase the likelihood of Type II errors in

analysis, leading to the non-rejection of the null hypothesis. A larger sample size may have increased statistical power, benefitting our analysis.

4.5 Future directions

While the novel adherence score cannot definitively demonstrate whether adherence levels directly impacted the reported outcomes, it may provide transparency into the behaviours of the BHIP study population to support interpretation of future results. Further, metabolomics research will be undertaken to identify potential biomarkers indicative of protein and dairy protein intake, to better understand dietary behaviours in line with the proposed intervention.

Beyond the BHIP study, future research should aim to explore the impact of intervention trials on maternal and neonatal outcomes beginning in the preconception period; preconception health is continually identified as an important indicator of offspring health, with some suggesting that waiting to start interventions in pregnancy is too late. (126,127) Future pregnancy interventions should also aim to follow offspring beyond infancy, to view potential long-term effects of such interventions. Such studies should incorporate infant outcomes as primary outcomes of interest, to adequately power studies. Additionally, potential barriers to or misconceptions around healthy dietary and physical activity practices should be evaluated. Such findings should drive the information shared with pregnant women, or those planning to conceive, by their respective HCPs. A thorough understanding of the nutrition and exercise resources shared by HCPs in pregnancy is needed, alongside a determination of what is unclear or missing from the patients' perspectives. Inclusion of ethnically and

socioeconomically diverse study populations in pregnancy interventions should be prioritized, such that results can be generalized to broader populations.

CHAPTER 5

APPENDICES

CHAPTER 5 - APPENDICES

5.1 Appendix 1 – Examples of adherence scores in available literature

Two examples of scores created to reflect intervention adherence in pregnant populations are currently available in the literature. The first, the Fit for Delivery (FFD) study was an RCT aimed at preventing excessive GWG through dietary counseling. (79) A breakdown of the FFD diet score is presented below.

Dietary recommendations	Related FFQ question(s)	Response alternatives and coding	Calculations	Possible range of each subscale	Median = cut-off	Dietary behaviour associated with scoring
1. Eat regular meals	How often do you eat – breakfast – lunch – dinner – evening meal/supper	Never = 0 Less than once a week = 0.5 Once a week = 1 Twice a week = 2 Three times a week = 3 Four times a week = 4 Five times a week = 5 Six times a week = 6 Every day = 7	Sum of answers to the four questions	0–28 meals a week	Test: 26 Retest: 25	Test: ≤25 meals week^{-1} = 0 ≥26 meals week^{-1} = 1 Retest: ≤24 meals week^{-1} = 0 ≥25 meals week^{-1} = 1
2. Drink water when thirsty	How often do you drink – tap water – bottled water – carbonised water – whole-fat milk – low-fat milk – skimmed milk – juice – fruit drinks or nectar – sugar-containing beverages – artificially sweetened beverages – alcohol-containing beverages	Never = 0 Less than once a week = 0.5 Once a week = 1 Twice a week = 2 Three a week = 3 Four times a week = 4 Five times a week = 5 Six times a week = 6 Every day = 7 Several times a day = 10	Sum of water intake events (frequency) divided by sum of all other drink intake events (frequency) multiplied by 100	0–100%	Test: 40% Retest: 38%	Test: <40% of drinking events is water = 0 ≥40% of drinking events is water = 1 Retest: <38% of drinking events is water = 0 ≥38% of drinking events is water = 1
3. Eat vegetables with dinner every day	How often do you eat vegetables with dinner?	Never to daily (0–7)	No calculation	0–7	Test: 5 Retest: 4	Test: <5 times week^{-1} = 0 ≥5 times week^{-1} = 1 Retest: <4 times week^{-1} = 0 ≥4 times week^{-1} = 1
4. In between meals – choose fruits or vegetables	How often do you eat fruits or vegetables as an in-between meal? How often do you eat in-between meals?	Never to several times a day (0–10)	Frequency of eating fruits or vegetables in between meals divided by frequency of having in-between meals multiplied by 100	0–100%	Test: 80% Retest: 86%	Test: Fruits/vegetables <80% of in-between meals = 0 Fruits/vegetables ≥80% of in-between meals = 1 Retest: Fruits/vegetables <86% of in-between meals Fruits/vegetables ≥86% of in-between meals
5. Eat sweets and snacks only when you really appreciate it	How often do you eat sweets or unhealthy foods without really appreciating it?	Never to several times a day (0–10)	No calculation	0–10	Test: 0.5 Retest: 0.5	Test and retest: Never eating sweets without appreciation = 1 Sometimes eating sweets without appreciation = 0
6. Buy small portion sizes of unhealthy foods	Which size of the following three items do you usually buy? – crisps – chocolate – soda	Small = 0 Big = 1	Sum of three answers	0–3	Test: 3 Retest: 3	Test and retest: Buying small portion size of at least one of the three items = 1 Buying big size of all three items = 0
7. Limit your intake of added sugar	How often do you have – sugar-sweetened fruit drinks – soda – cookies/crackers – sweet breads – cake/muffins – sugar-containing cereals – sugar-containing fruit yoghurt – chocolate/sweets How often do you add sugar to your food?	Never to several times a day (0–10)	Sum of answers to the nine questions	0–90	Test: 10 Retest: 10	Test and retest: <10 (approximately equivalent to eating food with added sugar once a day or less) = 1 ≥10 (approximately equivalent to eating food with added sugar more than once a day) = 0
8. Limit your intake of salt	How often do you eat – salted crackers – noodles – crisps or other salted snacks – hot dogs from kiosk/gas station – fried potato chips from fast-food restaurants – canned or freeze-dried food How often do you add salt to your food?	Never to several times a day (0–10)	Sum of answers to the seven questions	0–70	Test: 7.5 Retest: 7.5	Test and retest: <7.5 (fast-foods, snacks or salting of food no more than once a day) = 1 ≥7.5 (fat-foods, snacks or salting of foods more than once a day = 0
9. Do not eat beyond satiety	How often do you eat beyond satiety?	Never to several times a day (0–10)	No calculation	0–10	Test: 1 Retest: 1	Test and retest: Less than once a week = 1 Once a week or more = 0
10. Read nutrition labels on foods before buying		Never = 1 Sometimes = 2 Usually = 3 Always = 4	No calculation	1–4	Test: 2 Retest: 2	Test and retest: Never reading labels = 0 sometimes or often reading labels = 1
Total FFD score			Sum of the 10 dichotomised subscales	0–10	Test: 5 Retest: 5	Adherence test and retest: ≤3.5 = low 4–5.5 = medium ≥6 = high

FFD, fit for delivery; FFQ, food frequency questionnaire.

The Nutrition and Exercise Lifestyle Intervention Program (NELIP) study, based in Canada, created a unique score to measure adherence to a lifestyle intervention designed to prevent excessive GWG in pregnant women. (80) The calculation of the NELIP adherence score is listed below.

Goals of the program	Description of calculation	Points allocated
Nutrition goal: total average daily energy intake	Average daily intake throughout the program of: 2000 kcal day^{-1} ± 10%, (1800–2200 kcal day^{-1})	/1
Nutrition goal: total average daily carbohydrate intake	Average daily intake throughout the program of: 200–250 g	/1
Nutrition goal: submission of food intake records (FIR)	Total number of FIRs submitted ÷ total number of expected FIRs (based on number of weeks on the program; 1 submission per week)	/1
Total nutrition score		/3
Exercise goal: face-to-face lab visit for one walking session	Attending one walking session in the lab per week	/1
Exercise goal: walking one time on their own	Walking one time on their own for a total of 2 walking sessions per week	/1
Exercise goal: walking a second time on their own	Walking two times on their own for a total of 3 walking sessions per week	/1
Total exercise score	An average of how many times they walked per week was calculated for a total score out of 3 for exercise. If participants walked on average more than 3 times per week, they were still assigned a score of 3 for meeting all exercise goals.	/3
Total adherence score	Total nutrition + total exercise score	/6

5.2 Appendix 2 – PrimeScreen Food Frequency Questionnaire

Higher positive values indicate healthier dietary behaviours, while negative values indicate less healthy dietary behaviours. Values are summed to generate the PrimeScreen diet score.

1. Dark green leafy vegetables (spinach, romaine lettuce, mesclun mix, kale, turnip greens, bok choy, swiss chard):
   - Less than once per week …… 0
   - Once per week …….. 1
   - 2-4 times per week…… 2
   - Nearly daily or daily ……. 3
   - Twice or more per day…… 4

2. Broccoli, broccoli rabe, cauliflower, cabbage, brussel sprouts:
   - Less than once per week…….. 0
   - Once per week …… 1
   - 2-4 times per week …….. 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

3. Carrots:
   - Less than once per week…….. 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…….. 4

4. Other vegetables (e.g. peas, corn, green beans, tomatoes, squash):
   - Less than once per week…….. 0
   - Once per week …….. 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

5. Citrus fruits (e.g. oranges, grapefruits):
   - Less than once per week…….. 0
   - Once per week …… 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3
   - Twice or more per day…… 4

6. Other fruits (e.g. fresh apples or pears, bananas, berries, grapes, melons):
   - Less than once per week…….. 0
   - Once per week …….. 1
   - 2-4 times per week …… 2
   - Nearly daily or daily…… 3

Twice or more per day……. 4

7. Whole milk dairy foods (whole milk, hard cheese, butter, ice cream):

Less than once per week…… 0
Once per week ……. -1
2-4 times per week …… -2
Nearly daily or daily…… -3
2 – 3 times per day…… -4
4 - 6 times per day…… -5

8. Low-fat milk (e.g., skim, 1%, 2%):

Less than once per week…… 0
Once per week ……. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
2 – 3 times per day…… 4
4 - 6 times per day…… 5

9. Low-fat Greek yogurt (0%, 2%):

Less than once per week…… 0
Once per week ……. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
2 – 3 times per day…… 4
4 - 6 times per day…… 5

10. Low-fat regular yogurt:

Less than once per week…… 0
Once per week ……. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
2 – 3 times per day…… 4
4 - 6 times per day…… 5

11. Cottage cheese:

Less than once per week…… 0
Once per week ……. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
2 – 3 times per day…… 4
4 - 6 times per day…… 5

12. Fortified milk alternatives (e.g. soy, almond, rice milk):

Less than once per week…… 0
Once per week ……. 1

2-4 times per week ……. 2
Nearly daily or daily…… 3
2 – 3 times per day…… 4
4 - 6 times per day…… 5

13. Whole eggs:
Less than once per week…… 0
Once per week …….. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
Twice or more per day…… -1

14. Dried beans, split peas or lentils:
Less than once per week…… 0
Once per week …….. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
Twice or more per day…… 4

15. Nuts and/or nut butter (e.g. peanut, almond, soy butters):
Less than once per week…… 0
Once per week …….. 1
2-4 times per week …… 2
Nearly daily or daily…… 3
Twice or more per day…… 4

16. Beef, pork or lamb:
Less than once per week…… 0
Once per week …….. -1
2-4 times per week …… -2
Nearly daily or daily…… -3
Twice or more per day…… -4

17. Processed meats (sausages, salami, bologna, hot dogs, bacon):
Less than once per week…… 0
Once per week …… -1
2-4 times per week ……. -2
Nearly daily or daily…… -3
Twice or more per day…… -4

18. Turkey or chicken:
Less than once per week…… 0
Once per week …… 1
2-4 times per week ……. 2
Nearly daily or daily…… 3
Twice or more per day…… 4

19. Fish/Seafood (not fried, but broiled, baked, poached or canned):

Less than once per month……..	0
Once per month ……..	1
2-3 times per month ……	2
Weekly……..	3
Twice or more per week…….	4

20. Refined grains (e.g. white bread, white rice):

Less than once per week……..	0
Once per week ……	-1
2-4 times per week ……	-2
Nearly daily or daily……	-3
Twice or more per day……	-4

21. Whole grain breads and cereals (whole wheat, oatmeal, brown rice, barley):

Less than once per week…….	0
Once per week ……	1
2-4 times per week …….	2
Nearly daily or daily……	3
Twice or more per day……	4

22. Baked products (muffins, doughnuts, cookies, cake, pastries):

Less than once per week……..	0
Once per week ……	-1
2-4 times per week …….	-2
Nearly daily or daily……	-3
Twice or more per day……	-4

23. Sugar-sweetened beverages (e.g. Regular soda, fruit drinks, Nestea, Gatorade):

Less than once per week……..	0
Once per week ……	-1
2-4 times per week …….	-2
Nearly daily or daily……	-3
Twice or more per day……	-4

24. Deep fried foods:

Less than once per week……..	0
Once per week ……	-1
2-4 times per week …….	-2
Nearly daily or daily……	-3
Twice or more per day……	-4

25. How often do you add salt to food at the table?

Less than once per week……..	0
Once per week ……	-1
2-4 times per week …….	-2

Nearly daily or daily…… -3
Twice or more per day…… -4

Total: _____

RATING SCALE: Continuous variable – higher score = healthier diet

Adapted from the PrimeScreen Questionnaire, President and Fellows of Harvard College, Harvard School of Public Health,

Copyright 1999

Source: Rifas-Shiman, SL, Willett, WC et a.l PrimeScreen, a brief dietary screening tool reproducibility and comparability with both a longer food frequency questionnaire and biomarkers. *PubHealNut.*1999:4 (2), 249-254

5.3 Appendix 3 – Reference standards for infant anthropometry

Reference standards from the Canadian Perinatal Surveillance System, used to categorization birth weight for gestation age, are listed in tables below.

Birth Weight (in g) for GA in Completed Weeks Canadian Male Singletons

GA	3%ile	5%ile	10%ile	50%ile	90%ile	95%ile	97%ile	Mean	SD
22	338	368	401	490	587	627	659	501	111
23	406	434	475	589	714	762	797	598	114
24	468	498	547	690	844	902	940	697	125
25	521	557	617	795	981	1,048	1,092	800	147
26	571	614	686	908	1,125	1,200	1,251	909	178
27	627	677	763	1,033	1,278	1,358	1,416	1,026	209
28	694	752	853	1,173	1,445	1,532	1,598	1,159	241
29	780	845	964	1,332	1,629	1,729	1,809	1,312	273
30	885	959	1,099	1,507	1,837	1,955	2,053	1,487	306
31	1,012	1,098	1,259	1,698	2,069	2,209	2,327	1,682	339
32	1,164	1,266	1,444	1,906	2,319	2,478	2,614	1,896	369
33	1,344	1,460	1,648	2,127	2,580	2,750	2,897	2,123	391
34	1,552	1,677	1,866	2,360	2,851	3,029	3,184	2,361	410
35	1,783	1,907	2,091	2,600	3,132	3,318	3,475	2,607	428
36	2,024	2,144	2,321	2,845	3,411	3,604	3,759	2,855	443
37	2,270	2,384	2,552	3,080	3,665	3,857	4,003	3,091	449
38	2,498	2,605	2,766	3,290	3,877	4,065	4,202	3,306	448
39	2,684	2,786	2,942	3,465	4,049	4,232	4,361	3,489	445
40	2,829	2,927	3,079	3,613	4,200	4,382	4,501	3,638	447
41	2,926	3,025	3,179	3,733	4,328	4,512	4,631	3,745	459
42	2,960	3,070	3,233	3,815	4,433	4,631	4,773	3,800	485
43	2,954	3,081	3,249	3,864	4,528	4,747	4,941	3,793	527

Birth Weight (in g) for GA in Completed Weeks
Canadian Female Singletons

GA	3%ile	5%ile	10%ile	50%ile	90%ile	95%ile	97%ile	Mean	SD
22	332	347	385	466	552	576	576	472	72
23	379	403	450	557	669	706	726	564	95
24	424	456	513	651	790	839	887	656	121
25	469	508	578	751	918	982	1,060	754	152
26	516	562	645	858	1,060	1,139	1,247	860	186
27	569	624	717	976	1,218	1,313	1,446	976	222
28	634	697	802	1,109	1,390	1,499	1,657	1,107	254
29	716	787	903	1,259	1,578	1,701	1,885	1,256	286
30	814	894	1,022	1,427	1,783	1,918	2,121	1,422	319
31	938	1,026	1,168	1,613	2,004	2,150	2,347	1,604	345
32	1,089	1,184	1,346	1,817	2,242	2,399	2,578	1,808	368
33	1,264	1,369	1,548	2,035	2,494	2,664	2,825	2,029	389
34	1,467	1,581	1,768	2,266	2,761	2,948	3,097	2,266	409
35	1,695	1,813	1,998	2,506	3,037	3,242	3,384	2,512	426
36	1,935	2,052	2,227	2,744	3,307	3,523	3,660	2,754	439
37	2,177	2,286	2,452	2,968	3,543	3,752	3,886	2,981	443
38	2,406	2,502	2,658	3,169	3,738	3,931	4,061	3,181	439
39	2,589	2,680	2,825	3,334	3,895	4,076	4,202	3,350	434
40	2,722	2,814	2,955	3,470	4,034	4,212	4,331	3,486	434
41	2,809	2,906	3,051	3,576	4,154	4,330	4,444	3,588	439
42	2,849	2,954	3,114	3,655	4,251	4,423	4,554	3,656	448
43	2,862	2,975	3,159	3,717	4,333	4,495	4,685	3,693	459

Infant birth length, in addition to weight, length, subscapular SFT and triceps SFT at six months were compared against the WHO Child Growth Standards. These reference standards are listed below.

Weight-for-age BOYS
Birth to 5 years
(percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 0	0	2.5	2.9	3.3	3.9	4.3
0: 1	1	3.4	3.9	4.5	5.1	5.7
0: 2	2	4.4	4.9	5.6	6.3	7.0
0: 3	3	5.1	5.6	6.4	7.2	7.9
0: 4	4	5.6	6.2	7.0	7.9	8.6
0: 5	5	6.1	6.7	7.5	8.4	9.2
0: 6	6	6.4	7.1	7.9	8.9	9.7

Weight-for-age GIRLS
Birth to 5 years
(percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 0	0	2.4	2.8	3.2	3.7	4.2
0: 1	1	3.2	3.6	4.2	4.8	5.4
0: 2	2	4.0	4.5	5.1	5.9	6.5
0: 3	3	4.6	5.1	5.8	6.7	7.4
0: 4	4	5.1	5.6	6.4	7.3	8.1
0: 5	5	5.5	6.1	6.9	7.8	8.7
0: 6	6	5.8	6.4	7.3	8.3	9.2

Length-for-age BOYS
Birth to 2 years
(percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 0	0	46.3	47.9	49.9	51.8	53.4
0: 1	1	51.1	52.7	54.7	56.7	58.4
0: 2	2	54.7	56.4	58.4	60.5	62.2
0: 3	3	57.6	59.3	61.4	63.5	65.3
0: 4	4	60.0	61.7	63.9	66.0	67.8
0: 5	5	61.9	63.7	65.9	68.1	69.9
0: 6	6	63.6	65.4	67.6	69.8	71.6

Length-for-age GIRLS
Birth to 2 years
(percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 0	0	45.6	47.2	49.1	51.1	52.7
0: 1	1	50.0	51.7	53.7	55.7	57.4
0: 2	2	53.2	55.0	57.1	59.2	60.9
0: 3	3	55.8	57.6	59.8	62.0	63.8
0: 4	4	58.0	59.8	62.1	64.3	66.2
0: 5	5	59.9	61.7	64.0	66.3	68.2
0: 6	6	61.5	63.4	65.7	68.1	70.0

Subscapular skinfold-for-age BOYS
3 months to 5 years (percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 3	3	5.7	6.5	7.7	9.2	10.8
0: 4	4	5.5	6.3	7.5	9.0	10.5
0: 5	5	5.4	6.2	7.3	8.8	10.3
0: 6	6	5.3	6.0	7.2	8.6	10.1

Subscapular skinfold-for-age GIRLS
3 months to 5 years (percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 3	3	5.6	6.5	7.8	9.5	11.2
0: 4	4	5.4	6.3	7.5	9.2	10.8
0: 5	5	5.3	6.1	7.3	8.9	10.6
0: 6	6	5.2	6.0	7.2	8.7	10.4

Triceps skinfold-for-age BOYS
3 months to 5 years (percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 3	3	7.1	8.2	9.8	11.6	13.3
0: 4	4	6.9	8.0	9.6	11.5	13.3
0: 5	5	6.7	7.8	9.4	11.3	13.2
0: 6	6	6.5	7.6	9.2	11.1	13.0

Triceps skinfold-for-age GIRLS
3 months to 5 years (percentiles)

World Health Organization

Year: Month	Months	3rd	15th	Median	85th	97th
0: 3	3	6.9	8.1	9.8	11.7	13.4
0: 4	4	6.7	7.9	9.6	11.6	13.4
0: 5	5	6.5	7.7	9.4	11.4	13.3
0: 6	6	6.3	7.4	9.1	11.2	13.1

5.4 Appendix 4 – Standard operating procedure for analyzing infant DXA scans

Likert scale classifying the analysis procedure for infant DXA scans.

Code	Issue	Procedure
0	**N/A**	• No issues with scan or less than a whole finger (with no arm). In this case, no action required. • If a small object is in the frame, a region of interest will be performed to see if the amount of "unusable data can be removed or replaced with an ROI of the corresponding/opposite limb
1	**Limb missing/movement**	• If one limb is out of frame or has a movement artifact, but the other limb is fully intact (could be classified as a "0"), a limb surrogate will be performed – further steps described below.
2	**Significant movement in extremity**	• If large amounts of movement in limb, one can attempt to perform a limb surrogate • One will have to exclude the scan if: 1. Large amounts of movement (movement artifacts) are found throughout the body or 2. If large regions of interest are present, blocking the scan *Note these scans will be excluded from full body but may be useable in other analysis
3	**Movement in more than one appendage/body part**	• If multiple limbs (i.e. one arm and one leg) have a movement artifact, attempt a surrogate • If movement in multiple appendages occur on the same side of the body (i.e. movement in left arm and leg), a lateral half body measure may be feasible • If neither surrogate or lateral half body scan would be successful, note scan for exclusion
4	**Large amounts of movement/large amounts of body not in scan field**	• If possible, attempt to perform a lateral half body measure • If poor quality of scan in abdominal area, use for bone only • Otherwise, note scan for exclusion

5.5 Appendix 5 – Sample application of adherence scoring system

The following is an example of the application of the adherence scoring algorithm.

Requirement	Criteria to be considered adherent	Actual Value	Point awarded
Energy	2243 kcal/daily Population SD: 196 kcal	2450 kcal	0; not adherent
Protein	153 g/daily Population SD: 43	121 g	1; adherent
Dairy Protein	60.5 g/daily Population SD: 16	53 g	1; adherent
Step count	10,000 steps daily	8647	0.8647; partially adherent
		Total Score:	2.8647

5.6 Appendix 6 – Participant protein intake

Completion of 3DDR completed by intervention and control participants provides information in protein intake by participants throughout pregnancy. Mean protein intake in early pregnancy was 83.6+24.8g in intervention participants and 88.7+24.7g in control participants. In the intervention group, protein intake was 105.2+27.8g and 104.1+27.7g in mid and late pregnancy, respectively. In the control group, participant protein intake remained constant through the end of pregnancy, measuring 85.5+20.8g and 87.9+24.0g in mid and late pregnancy.

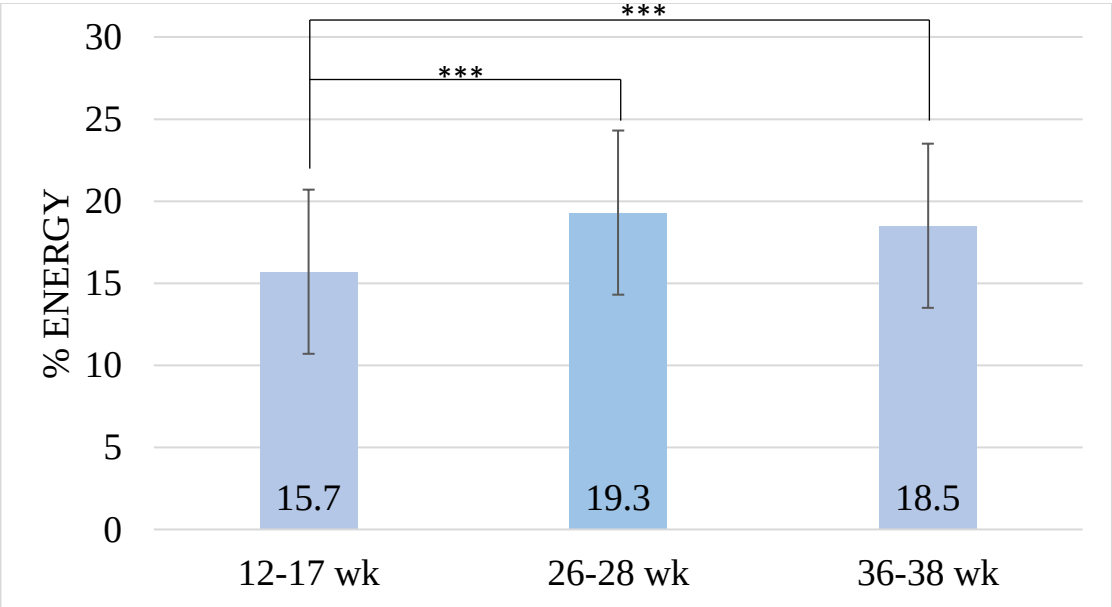

Table 1: Proportion of energy intake sourced from protein sources by intervention participants (N = 55); *** = P < 0.0001

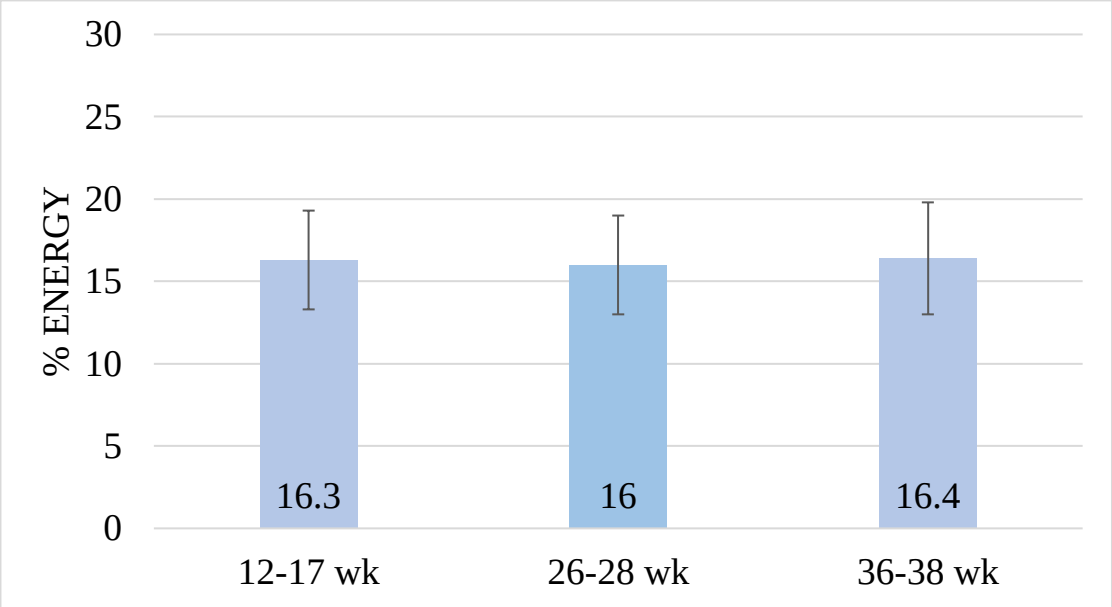

Table 2: Proportion of energy intake sourced from protein sourced by control participants (N = 56)

REFERENCES

REFERENCES

1. Barker DJP, Eriksson JG, Forsén T, Osmond C. Fetal origins of adult disease: Strength of effects and biological basis. *Int J Epidemiol*. 2002;31(6):1235-1239. doi:10.1093/ije/31.6.1235
2. Carolan-Olah M, Duarte-Gardea M, Lechuga J. A critical review: early life nutrition and prenatal programming for adult disease. *J Clin Nurs*. 2015;24(23-24):3716-3729. doi:10.1111/jocn.12951
3. Cohen JM, Beddaoui M, Kramer MS, Platt RW, Basso O, Kahn SR. Maternal antioxidant levels in pregnancy and risk of preeclampsia and small for gestational age birth: A systematic review and meta-analysis. *PLoS One*. 2015;10(8). doi:10.1371/journal.pone.0135192
4. Borge TC, Aase H, Brantsæter 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):1-14. doi:10.1136/bmjopen-2017-016777
5. Mcgiveron A, Foster S, Pearce J, Taylor MA, Mcmullen S, Langley-Evans SC. Limiting antenatal weight gain improves maternal health outcomes in severely obese pregnant women: Findings of a pragmatic evaluation of a midwife-led intervention. *J Hum Nutr Diet*. 2015;28(s1):29-37. doi:10.1111/jhn.12240
6. Santos Ferreira DL, Williams DM, Kangas AJ, et al. Association of pre-pregnancy body mass index with offspring metabolic profile: Analyses of 3 European prospective birth cohorts. *PLoS Med*. 2017;14(8):1-19. doi:10.1371/journal.pmed.1002376
7. Rooney BL, Mathiason MA, Schauberger CW. Predictors of obesity in

childhood, adolescence, and adulthood in a birth cohort. *Matern Child Health J*. 2011;15(8):1166-1175. doi:10.1007/s10995-010-0689-1

8. Mamun AA, Mannan M, Doi SAR. Gestational weight gain in relation to offspring obesity over the life course: A systematic review and bias-adjusted meta-analysis. *Obes Rev*. 2014;15(4):338-347. doi:10.1111/obr.12132
9. Shin D, Song WO. Prepregnancy body mass index is an independent risk factor for gestational hypertension, gestational diabetes, preterm labor, and small- and large-for-gestational-age infants. *J Matern Neonatal Med*. 2015;28(14):1679-1686. doi:10.3109/14767058.2014.964675
10. Zhang X, Decker A, Platt RW, Kramer MS. How big is too big? The perinatal consequences of fetal macrosomia. *Am J Obstet Gynecol*. 2008;198(5):517.e1-517.e6. doi:10.1016/j.ajog.2007.12.005
11. Medicine I of, Council NR. *Weight Gain During Pregnancy: Reexamining the Guidelines*. (Rasmussen KM, Yaktine AL, eds.). The National Academies Press; 2009. doi:10.17226/12584
12. McDonald SD, Woolcott C, Chapinal N, Guo Y, Murphy P, Dzakpasu S. Interprovincial variation in pre-pregnancy body mass index and gestational weight gain and their impact on neonatal birth weight with respect to small and large for gestational age. *Can J Public Heal*. 2018;109(4):527-538. doi:10.17269/s41997-018-0086-x
13. Gardner B, Wardle J, Poston L, Croker H. Changing diet and physical activity to reduce gestational weight gain: A meta-analysis. *Obes Rev*. 2011;12(7):12-14. doi:10.1111/j.1467-789X.2011.00884.x
14. Barger MK. Maternal nutrition and perinatal outcomes. *J Midwifery Women's*

Heal. 2010;55(6):502-511. doi:10.1016/j.jmwh.2010.02.017

15. Quinlivan JA, Lam LT, Fisher J. A randomised trial of a four-step multidisciplinary approach to the antenatal care of obese pregnant women. *Aust New Zeal J Obstet Gynaecol*. 2011;51(2):141-146. doi:10.1111/j.1479-828X.2010.01268.x
16. Gresham E, Byles JE, Bisquera A, Hure AJ. Effects of dietary interventions on neonatal and infant outcomes : 2014;(2). doi:10.3945/ajcn.113.080655.Nutrition
17. Canada H. Prenatal Nutrition Guidelines for Health Professions. Published online 2010. http://www.hc-sc.gc.ca/fn-an/alt_formats/pdf/nutrition/prenatal/ewba-mbsa-eng.pdf)
18. Canada H. Food Guide Servings. Published online 2011:2.
19. Expert Advisory Group on National Nutrition Pregnancy Guidelines. Prenatal nutrition guidelines for health professional: iron. *Heal Canada*. 2015;1. doi:10.1017/CBO9781107415324.004
20. Health Canada. *Canada's Dietary Guidelines for Health Professionals and Policy Makers*.; 2019. https://food-guide.canada.ca/static/assets/pdf/CDG-EN-2018.pdf
21. Davies GAL, Wolfe LA, Mottola MF, MacKinnon C. Joint SOGC/CSEP clinical practice guideline: Exercise in pregnancy and the postpartum period. *Can J Appl Physiol*. 2003;28(3):330-341. doi:10.1139/h03-024
22. Mottola MF, Davenport MH, Ruchat SM, et al. No. 367-2019 Canadian Guideline for Physical Activity throughout Pregnancy. *J Obstet Gynaecol Canada*. 2018;40(11):1528-1537. doi:10.1016/j.jogc.2018.07.001

23. Davies GAL, Maxwell C, McLeod L, et al. Obesity in pregnancy: No. 239, february 2010. *Int J Gynecol Obstet*. 2010;110(2):167-173. doi:10.1016/j.ijgo.2010.03.008

24. Connolly CP, Conger SA, Montoye AHK, et al. Walking for health during pregnancy: A literature review and considerations for future research. *J Sport Heal Sci*. 2019;8(5):401-411. doi:10.1016/j.jshs.2018.11.004

25. Lee IM, Buchner DM. The importance of walking to public health. *Med Sci Sports Exerc*. 2008;40(7 SUPPL.1):512-518. doi:10.1249/MSS.0b013e31817c65d0

26. Lamminpää R, Vehviläinen-Julkunen K, Schwab U. A systematic review of dietary interventions for gestational weight gain and gestational diabetes in overweight and obese pregnant women. *Eur J Nutr*. 2018;57(5):1721-1736. doi:10.1007/s00394-017-1567-z

27. Shieh C, Cullen DL, Pike C, Pressler SJ. Intervention strategies for preventing excessive gestational weight gain: systematic review and meta-analysis. *Obes Rev*. 2018;19(8):1093-1109. doi:10.1111/obr.12691

28. Oteng-Ntim E, Varma R, Croker H, Poston L, Doyle P. Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: Systematic review and meta-analysis. *BMC Med*. 2012;10:10-12. doi:10.1186/1741-7015-10-47

29. Tanentsapf I, Heitmann BL, Adegboye ARA. Systematic review of clinical trials on dietary interventions to prevent excessive weight gain during pregnancy among normal weight, overweight and obese women. *BMC Pregnancy Childbirth*. 2011;11(82).

30. Muktabhant B, Theresa L, Pisake L, Malinee L. : Diet or exercise, or both, for preventing excessive weight gain in pregnancy SO-: Cochrane Database of Systematic Reviews YR-: 2015 NO-: 6. *Cochrane Database Syst Rev*. 2015;(6). doi:10.1002/14651858.CD007145.pub3.www.cochranelibrary.com

31. Perreault M, Atkinson SA, Mottola MF, et al. Structured diet and exercise guidance in pregnancy to improve health in women and their offspring: Study protocol for the Be Healthy in Pregnancy (BHIP) randomized controlled trial. *Trials*. 2018;19(1):1-15. doi:10.1186/s13063-018-3065-x

32. Manore MM, Meacham SL. *New Dietary Reference Intakes Set for Energy, Carbohydrates, Fiber, Fat, Fatty Adds, Cholesterol, Proteins, and Amino Acids*. Vol 7.; 2003.

33. Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. *Cochrane Database Syst Rev*. 2015;2015(6). doi:10.1002/14651858.CD000032.pub3

34. Abreu S, Santos PC, Montenegro N, Mota J. Relationship between dairy product intake during pregnancy and neonatal and maternal outcomes among Portuguese women. *Obes Res Clin Pract*. 2017;11(3):276-286. doi:10.1016/j.orcp.2016.07.001

35. Clark DC. Association of Dairy Protein Intake During Pregnancy with Birth Weight. *Food Nutr Bull*. 2018;39(2_suppl):S54-S59. doi:10.1177/0379572118775824

36. Lise Brantsæter A, Olafsdottir A, Forsum E, Olsen S, Thorsdottir I. Does milk and dairy consumption during pregnancy influence fetal growth and infant birthweight? A systematic literature review. *Food Nutr Res*. 2012;56(1):20050.

doi:10.3402/fnr.v56i0.20050

37. Olmedo-Requena R, Amezcua-Prieto C, Luna-Del-Castillo J de D, et al. Association Between Low Dairy Intake During Pregnancy and Risk of Small-for-Gestational-Age Infants. *Matern Child Health J*. 2016;20(6):1296-1304. doi:10.1007/s10995-016-1931-2

38. Nascimento SL, Surita FG, Cecatti JG. Physical exercise during pregnancy: A systematic review. *Curr Opin Obstet Gynecol*. 2012;24(6):387-394. doi:10.1097/GCO.0b013e328359f131

39. Perales M, Santos-Lozano A, Ruiz JR, Lucia A, Barakat R. Benefits of aerobic or resistance training during pregnancy on maternal health and perinatal outcomes: A systematic review. *Early Hum Dev*. 2016;94:43-48. doi:10.1016/j.earlhumdev.2016.01.004

40. Davenport MH, Meah VL, Ruchat SM, et al. Impact of prenatal exercise on neonatal and childhood outcomes: A systematic review and meta-analysis. *Br J Sports Med*. 2018;52(21):1386-1396. doi:10.1136/bjsports-2018-099836

41. Bisson M, Croteau J, Guinhouya BC, et al. Physical activity during pregnancy and infant's birth weight: Results from the 3D Birth Cohort. *BMJ Open Sport Exerc Med*. 2017;3(1):1-9. doi:10.1136/bmjsem-2017-000242

42. Gjestland K, Bø K, Owe KM, Eberhard-Gran M. Do pregnant women follow exercise guidelines? Prevalence data among 3482 women, and prediction of low-back pain, pelvic girdle pain and depression. *Br J Sports Med*. 2013;47(8):515-520. doi:10.1136/bjsports-2012-091344

43. Barakat R, Perales M, Bacchi M, Coteron J, Refoyo I. A program of exercise throughout pregnancy. is it safe to mother and newborn? *Am J Heal Promot*.

2014;29(1):2-8. doi:10.4278/ajhp.130131-QUAN-56

44. Evenson KR, Moos MK, Carrier K, Siega-Riz AM. Perceived barriers to physical activity among pregnant women. *Matern Child Health J*. 2009;13(3):364-375. doi:10.1007/s10995-008-0359-8

45. Santos PC, Abreu S, Moreira C, et al. Impact of compliance with different guidelines on physical activity during pregnancy and perceived barriers to leisure physical activity. *J Sports Sci*. 2014;32(14):1398-1408. doi:10.1080/02640414.2014.893369

46. Walsh JM, McGowan C, Byrne J, McAuliffe FM. Prevalence of physical activity among healthy pregnant women in Ireland. *Int J Gynecol Obstet*. 2011;114(2):154-155. doi:10.1016/j.ijgo.2011.02.016

47. Mudd LM, Evenson KR. Review of impacts of physical activity on maternal metabolic health during pregnancy. *Curr Diab Rep*. 2015;15(2). doi:10.1007/s11892-014-0572-3

48. Blumfield ML, Hure AJ, MacDonald-Wicks LK, Patterson AJ, Smith R, Collins CE. Disparities exist between National food group recommendations and the dietary intakes of women. *BMC Womens Health*. 2011;11. doi:10.1186/1472-6874-11-37

49. Morton SMB, 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):1919-1929. doi:10.1017/S1368980014000482

50. Jarman M, Bell RC, Nerenberg K, Robson PJ. Adherence to Canada's Food Guide Recommendations during Pregnancy. *Curr Dev Nutr*. 2017;1(7):e000356. doi:10.3945/cdn.116.000356

51. Broskey NT, Wang P, Li N, et al. Early Pregnancy Weight Gain Exerts the Strongest Effect on Birth Weight, Posing a Critical Time to Prevent Childhood Obesity. *Obesity*. 2017;25(9):1569-1576. doi:10.1002/oby.21878

52. Guo L, Liu J, Ye R, Liu J, Zhuang Z, Ren A. Gestational weight gain and overweight in children aged 3-6 years. *J Epidemiol*. 2015;25(8):536-543. doi:10.2188/jea.JE20140149

53. Crozier SR, Inskip HM, Godfrey KM, et al. Weight gain in pregnancy and childhood body composition: Findings from the Southampton Women's Survey. *Am J Clin Nutr*. 2010;91(6):1745-1751. doi:10.3945/ajcn.2009.29128

54. Gishti O, Gaillard R, Manniesing R, et al. Fetal and infant growth patterns associated with total and abdominal fat distribution in school-age children. *J Clin Endocrinol Metab*. 2014;99(7):2557-2566. doi:10.1210/jc.2013-4345

55. West J, Manchester B, Wright J, Lawlor DA, Waiblinger D. Reliability of routine clinical measurements of neonatal circumferences and research measurements of neonatal skinfold thicknesses: Findings from the Born in Bradford study. *Paediatr Perinat Epidemiol*. 2011;25(2):164-171. doi:10.1111/j.1365-3016.2010.01181.x

56. Logan KM, Gale C, Hyde MJ, Santhakumaran S, Modi N. Diabetes in pregnancy and infant adiposity: Systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed*. 2017;102(1):F65-F72. doi:10.1136/archdischild-2015-309750

57. Hull HR, Thornton JC, Ji Y, et al. Higher infant body fat with excessive gestational weight gain in overweight women. *Am J Obstet Gynecol*. 2011;205(3):211.e1-211.e7. doi:10.1016/j.ajog.2011.04.004

58. Starling AP, Brinton JT, Glueck DH, et al. Associations of maternal BMI and gestational weight gain with neonatal adiposity in the Healthy Start study. *Am J Clin Nutr*. 2015;101(2):302-309. doi:10.3945/ajcn.114.094946

59. International T, Management W, Group C. Effect of diet and physical activity based interventions in pregnancy on gestational weight gain and pregnancy outcomes: meta-analysis of individual participant data from randomised trials. *BMJ*. 2017;358:j3119. doi:10.1136/bmj.j3119

60. Peaceman AM, Clifton RG, Phelan S, et al. Lifestyle Interventions Limit Gestational Weight Gain in Women with Overweight or Obesity: LIFE-Moms Prospective Meta-Analysis. *Obesity*. 2018;26(9):1396-1404. doi:10.1002/oby.22250

61. Gallagher D, Rosenn B, Toro-Ramos T, et al. Greater Neonatal Fat-Free Mass and Similar Fat Mass Following a Randomized Trial to Control Excess Gestational Weight Gain. *Obesity*. 2018;26(3):578-587. doi:10.1002/oby.22079

62. Tanvig M, Vinter CA, Jørgensen JS, et al. Anthropometrics and body composition by dual energy x-ray in children of obese women: A follow-up of a randomized controlled trial (the Lifestyle in Pregnancy and Offspring [LiPO] study). *PLoS One*. 2014;9(2):1-8. doi:10.1371/journal.pone.0089590

63. Oostdam N, Van Poppel MNM, Wouters MGAJ, et al. No effect of the FitFor2 exercise programme on blood glucose, insulin sensitivity, and birthweight in pregnant women who were overweight and at risk for gestational diabetes: Results of a randomised controlled trial. *BJOG An Int J Obstet Gynaecol*. 2012;119(9):1098-1107. doi:10.1111/j.1471-0528.2012.03366.x

64. Vitolins MZ, Rand CS, Rapp SR, Ribisl PM, Sevick MA. Measuring adherence

to behavioral and medical interventions. *Control Clin Trials*. 2000;21(5 SUPPL. 1):S188-S194. doi:10.1016/S0197-2456(00)00077-5

65. Colditz GA, Taylor PR. Prevention Trials: Their Place in How We Understand the Value of Prevention Strategies. *Annu Rev Public Health*. 2010;31(1):105-120. doi:10.1146/annurev.publhealth.121208.131051

66. Martin KA, Bowen DJ, Dunbar-Jacob J, Perri MG. Who will adhere? Key issues in the study and prediction of adherence in randomized controlled trials. *Control Clin Trials*. 2000;21(5 SUPPL. 1):S195-S199. doi:10.1016/S0197-2456(00)00078-7

67. Guenther PM, Reedy J, Krebs-Smith SM. Development of the Healthy Eating Index-2005. *J Am Diet Assoc*. 2008;108(11):1896-1901. doi:10.1016/j.jada.2008.08.016

68. Van Lee L, Geelen A, Hooft van Huysduynen EJC, de Vries JHM, van't Veer P, Feskens EJM. The Dutch Healthy Diet index (DHD-index): an instrument to measure adherence to the Dutch Guidelines for a Healthy Diet. *Nutr J*. 2012;11(49).

69. Von Ruesten A, Brantsæter AL, Haugen M, et al. Adherence of pregnant women to Nordic dietary guidelines in relation to postpartum weight retention: Results from the Norwegian Mother and Child Cohort Study. *BMC Public Health*. 2014;14(1). doi:10.1186/1471-2458-14-75

70. Jessri M, Ng AP, L'Abbé MR. Adapting the healthy eating Index 2010 for the canadian population: Evidence from the Canadian national nutrition survey. *Nutrients*. 2017;9(8). doi:10.3390/nu9080910

71. DiMatteo MR. Variations in patients' adherence to medical recommendations:

A quantitative review of 50 years of research. *Med Care*. 2004;42(3):200-209. doi:10.1097/01.mlr.0000114908.90348.f9

72. Fischer MA, Stedman MR, Lii J, et al. Primary medication non-adherence: Analysis of 195,930 electronic prescriptions. *J Gen Intern Med*. 2010;25(4):284-290. doi:10.1007/s11606-010-1253-9

73. Huurne KK Ter, Movig K, Van Der Valk P, Van Der Palen J, Brusse-Keizer M. Differences in adherence to common inhaled medications in COPD. *COPD J Chronic Obstr Pulm Dis*. 2015;12(6):643-648. doi:10.3109/15412555.2014.995292

74. Hansen RA, Farley JF, Droege M, Maciejewski ML. A retrospective cohort study of economic outcomes and adherence to monotherapy with metformin, pioglitazone, or a sulfonylurea among patients with type 2 diabetes mellitus in the united states from 2003 to 2005. *Clin Ther*. 2010;32(7):1308-1319. doi:10.1016/j.clinthera.2010.07.011

75. Panagiotakos DB, Pitsavos C, Arvaniti F, Stefanadis C. Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore. *Prev Med (Baltim)*. 2007;44(4):335-340. doi:10.1016/j.ypmed.2006.12.009

76. USDA/DHHS. Dietary Guidelines for Americans by U.S.Department of Health and Human Services and U.S.Department of Agriculture_ _. *[Monograph on the Internet]*. 2005;6th Editio(Available at: http://www.health.gov/dietaryguidelines/dga2005/document/):Accessed June 7, 2007.

77. Dixon LB, Subar AF, Peters U, et al. Adherence to the USDA Food Guide, DASH Eating Plan, and Mediterranean Dietary Pattern Reduces Risk of Colorectal Adenoma. *J Nutr*. 2007;137(11):2443-2450. doi:10.1093/jn/137.11.2443

78. Miller PE, Cross AJ, Subar AF, et al. Comparison of 4 established DASH diet indexes: Examining associations of index scores and colorectal cancer. *Am J Clin Nutr*. 2013;98(3):794-803. doi:10.3945/ajcn.113.063602

79. Øverby NC, Hillesund ER, Sagedal LR, Vistad I, Bere E. The Fit for Delivery study: Rationale for the recommendations and test-retest reliability of a dietary score measuring adherence to 10 specific recommendations for prevention of excessive weight gain during pregnancy. *Matern Child Nutr*. 2015;11(1):20-32. doi:10.1111/mcn.12026

80. Nagpal TS, Prapavessis H, Campbell C, Mottola MF. Measuring Adherence to a Nutrition and Exercise Lifestyle Intervention: Is Program Adherence Related to Excessive Gestational Weight Gain? *Behav Anal Pract*. 2017;10(4):347-354. doi:10.1007/s40617-017-0189-5

81. Poston L, Harthoorn LF, Van Der Beek EM. Obesity in pregnancy: Implications for the mother and lifelong health of the child. A consensus statement. *Pediatr Res*. 2011;69(2):175-180. doi:10.1203/PDR.0b013e3182055ede

82. Rifas-Shiman SL, Willett WC, Lobb R, Kotch J, Dart C, Gillman MW. PrimeScreen, a brief dietary screening tool: reproducibility and comparability with both a longer food frequency questionnaire and biomarkers. *Public Health Nutr*. 2001;4(2):249-254. doi:10.1079/phn200061

83. Manns PJ, Haennel RG. SenseWear armband and stroke: Validity of energy expenditure and step count measurement during walking. *Stroke Res Treat*. 2012;2012. doi:10.1155/2012/247165

84. Joseph KS, Kramer MS, Allen AC, Mery LS, Platt RW, Wen SW. Implausible birth weight for gestational age. *Am J Epidemiol*. 2001;153(2):110-113. doi:10.1093/aje/153.2.110

85. de Onis M, Onyango A, Borghi E, et al. Worldwide implementation of the WHO Child Growth Standards. *Public Health Nutr*. 2012;15(9):1603-1610. doi:10.1017/S136898001200105X

86. World Health Organization. WHO Child Growth Standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. *Dev Med Child Neurol*. 2009;51(12):1002-1002. doi:10.1111/j.1469-8749.2009.03503.x

87. Rodrigopulle DJ, Atkinson SA. Validation of surrogate limb analysis for body composition in children by dual energy X-ray absorptiometry (DXA). *Eur J Clin Nutr*. 2014;68(6):653-657. doi:10.1038/ejcn.2014.44

88. Gordon CM, Bachrach LK, Carpenter TO, et al. Dual Energy X-ray Absorptiometry Interpretation and Reporting in Children and Adolescents: The 2007 ISCD Pediatric Official Positions. *J Clin Densitom*. 2008;11(1):43-58. doi:10.1016/j.jocd.2007.12.005

89. Campbell EE, Seabrook JA. The Influence of Socio- economic Status on Adverse Birth Outcomes Influence du statut socio- économique sur les issues de naissance indésirables. *Can J Midwifery Pract Res J Midwifery Pract Res*. 2016;15(2):10-20.

90. Cheng ER, Rifas-Shiman SL, Perkins ME, et al. The influence of antenatal partner support on pregnancy outcomes. *J Women's Heal*. 2016;25(7):672-679. doi:10.1089/jwh.2015.5462

91. Cohen K, Capponi S, Nyamukapa M, Baxter J, Crawford A, Worly B. Partner Involvement During Pregnancy and Maternal Health Behaviors. *Matern Child Health J*. 2016;20(11):2291-2298. doi:10.1007/s10995-016-2048-3

92. Ong KK, Langkamp M, Ranke MB, et al. Insulin-like growth factor I concentrations in infancy predict differential gains in body length and adiposity: The Cambridge Baby Growth Study. *Am J Clin Nutr*. 2009;90(1):156-161. doi:10.3945/ajcn.2008.27408

93. Larnkjaer A, Ingstrup HK, Schack-Nielsen L, et al. Early programming of the IGF-I axis: Negative association between IGF-I in infancy and late adolescence in a 17-year longitudinal follow-up study of healthy subjects. *Growth Horm IGF Res*. 2009;19(1):82-86. doi:10.1016/j.ghir.2008.06.003

94. Madsen AL, Larnkjær A, Mølgaard C, Michaelsen KF. IGF-I and IGFBP-3 in healthy 9month old infants from the SKOT cohort: Breastfeeding, diet, and later obesity. *Growth Horm IGF Res*. 2011;21(4):199-204. doi:10.1016/j.ghir.2011.05.003

95. Switkowski KM, Jacques PF, Must A, Kleinman KP, Gillman MW, Oken E. Maternal protein intake during pregnancy and linear growth in the offspring. *Am J Clin Nutr*. 2016;104(4):1128-1136. doi:10.3945/ajcn.115.128421

96. Geraghty AA, O'Brien EC, Alberdi G, et al. Maternal protein intake during pregnancy is associated with child growth up to 5 years of age, but not through insulin-like growth factor-1: Findings from the ROLO study. *Br J Nutr*.

2018;120(11):1252-1261. doi:10.1017/S0007114518002611

97. Du MC, Ouyang YQ, Nie XF, Huang Y, Redding SR. Effects of physical exercise during pregnancy on maternal and infant outcomes in overweight and obese pregnant women: A meta-analysis. *Birth*. 2019;46(2):211-221. doi:10.1111/birt.12396

98. da Silva SG, Hallal PC, Domingues MR, et al. A randomized controlled trial of exercise during pregnancy on maternal and neonatal outcomes: Results from the PAMELA study. *Int J Behav Nutr Phys Act*. 2017;14(1):1-11. doi:10.1186/s12966-017-0632-6

99. Okesene-Gafa KAM, Li M, McKinlay CJD, et al. Effect of antenatal dietary interventions in maternal obesity on pregnancy weight-gain and birthweight: Healthy Mums and Babies (HUMBA) randomized trial. *Am J Obstet Gynecol*. 2019;221(2):152.e1-152.e13. doi:10.1016/j.ajog.2019.03.003

100. Poston L, Bell R, Croker H, et al. Effect of a behavioural intervention in obese pregnant women (the UPBEAT study): A multicentre, randomised controlled trial. *Lancet Diabetes Endocrinol*. 2015;3(10):767-777. doi:10.1016/S2213-8587(15)00227-2

101. De Onis M. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatr Int J Paediatr*. 2006;95(SUPPL. 450):76-85. doi:10.1080/08035320500495548

102. de Onis M, Garza C, Victora CG, Onyango AW, Frongillo EA, Martines J. The WHO Multicentre Growth Reference Study: Planning, study design, and methodology. *Food Nutr Bull*. 2004;25(1 SUPPL. 1):15-26. doi:10.1177/15648265040251s104

103. Szwajcer EM, Hiddink GJ, Koelen MA, van Woerkum CMJ. Nutrition awareness and pregnancy: Implications for the life course perspective. *Eur J Obstet Gynecol Reprod Biol*. 2007;135(1):58-64. doi:10.1016/j.ejogrb.2006.11.012

104. Fowles ER, Fowles SL. Healthy eating during pregnancy: Determinants and supportive strategies. *J Community Health Nurs*. 2008;25(3):138-152. doi:10.1080/07370010802221727

105. Phelan S. Pregnancy: a "teachable moment" for weight control and obesity prevention. *Am J Obstet Gynecol*. 2010;202(2):135.e1-135.e8. doi:10.1016/j.ajog.2009.06.008

106. Forbes LE, Graham JE, Berglund C, Bell RC. Dietary change during pregnancy and women's reasons for change. *Nutrients*. 2018;10(8):1-10. doi:10.3390/nu10081032

107. Hayashi A, Oguchi H, Kozawa Y, Ban Y, Shinoda J, Suganuma N. Daily walking is effective for the management of pregnant women with gestational diabetes mellitus. *J Obstet Gynaecol Res*. 2018;44(9):1731-1738. doi:10.1111/jog.13698

108. Lee IM, Shiroma EJ, Kamada M, Bassett DR, Matthews CE, Buring JE. Association of Step Volume and Intensity with All-Cause Mortality in Older Women. *JAMA Intern Med*. 2019;179(8):1105-1112. doi:10.1001/jamainternmed.2019.0899

109. Murray-Davis B, Grenier L, Atkinson SA, et al. Experiences regarding nutrition and exercise among women during early postpartum: A qualitative grounded theory study. *BMC Pregnancy Childbirth*. 2019;19(1):1-11.

doi:10.1186/s12884-019-2508-z

110. McKinley MC, Allen-Walker V, McGirr C, Rooney C, Woodside J V. Weight loss after pregnancy: Challenges and opportunities. *Nutr Res Rev*. 2018;31(2):225-238. doi:10.1017/S0954422418000070

111. Connelly M, Brown H, van der Pligt P, Teychenne M. Modifiable barriers to leisure-time physical activity during pregnancy: A qualitative study investigating first time mother's views and experiences. *BMC Pregnancy Childbirth*. 2015;15(1):1-7. doi:10.1186/s12884-015-0529-9

112. Coll CVN, Domingues MR, Gonçalves H, Bertoldi AD. Perceived barriers to leisure-time physical activity during pregnancy: A literature review of quantitative and qualitative evidence. *J Sci Med Sport*. 2017;20(1):17-25. doi:10.1016/j.jsams.2016.06.007

113. Sytsma TT, Zimmerman KP, Manning JB, et al. Perceived Barriers to Exercise in the First Trimester of Pregnancy. *J Perinat Educ*. 2018;27(4):198-206. doi:10.1891/1058-1243.27.4.198

114. Craig P, Dieppe P, Macintyre S, Mitchie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: The new Medical Research Council guidance. *Bmj*. 2008;337(7676):979-983. doi:10.1136/bmj.a1655

115. Hawe P, Shiell A, Riley T. Complex interventions: How "out of control" can a randomised controlled trial be? *Bmj*. 2004;328(7455):1561. doi:10.1136/bmj.328.7455.1561

116. Graham L, Wright J, Walwyn R, et al. Measurement of adherence in a randomised controlled trial of a complex intervention: supported self-management for adults with learning disability and type 2 diabetes. *BMC Med*

Res Methodol. 2016;16(1):1-11. doi:10.1186/s12874-016-0236-x

117. Baumgartner PC, Haynes RB, Hersberger KE, Arnet I. A systematic review of medication adherence thresholds dependent of clinical outcomes. *Front Pharmacol*. 2018;9(NOV). doi:10.3389/fphar.2018.01290

118. Wellington N, Shanmuganathan M, Souza RJ De, Desai D, Anand SS, Britz-mckibbin P. and Western Diets from Food Provisions : Identifying Robust Biomarkers of Short-Term Changes in.

119. Wild J, Shanmuganathan M, Hayashi M, Potter M, Britz-Mckibbin P. Metabolomics for improved treatment monitoring of phenylketonuria: Urinary biomarkers for non-invasive assessment of dietary adherence and nutritional deficiencies. *Analyst*. 2019;144(22):6595-6608. doi:10.1039/c9an01642b

120. Stephens T V, Payne M, Ball RO, Pencharz PB, Elango R. Protein Requirements of Healthy Pregnant Women during Early and Late Gestation Are Higher than Current Recommendations. *J Nutr*. 2015;145(1):73-78. doi:10.3945/jn.114.198622

121. Dodd JM, Cramp C, Sui Z, et al. The effects of antenatal dietary and lifestyle advice for women who are overweight or obese on maternal diet and physical activity: The LIMIT randomised trial. *BMC Med*. 2014;12(1):1-19. doi:10.1186/s12916-014-0161-y

122. 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):263-272. doi:10.1016/j.amepre.2010.05.012

123. Abdullah P, Gallant S, Saghi N, Macpherson A, Tamim H. Characteristics of patients receiving midwife-led prenatal care in Canada: Results from the

Maternity Experiences Survey (MES). *BMC Pregnancy Childbirth*. 2017;17(1):1-7. doi:10.1186/s12884-017-1350-4

124. Canadian Association of Midwives (CAM). No Title. Midwifery across Canada.

125. Darling EK, Grenier L, Nussey L, Murray-Davis B, Hutton EK, Vanstone M. Access to midwifery care for people of low socio-economic status: a qualitative descriptive study. *BMC Pregnancy Childbirth*. 2019;19(1):416. doi:10.1186/s12884-019-2577-z

126. Barker M, Dombrowski SU, Colbourn T, et al. Intervention strategies to improve nutrition and health behaviours before conception. *Lancet*. 2018;391(10132):1853-1864. doi:10.1016/S0140-6736(18)30313-1

127. 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. doi:10.1016/S0140-6736(18)30311-8