Dietary patterns in pregnancy and offspring growth outcomes: a multi-country analysis of birth cohorts

Camilla Nykjær

Submitted in accordance with the requirements for the degree of
Doctor of Philosophy

The University of Leeds
School of Food Science and Nutrition

October, 2016

Declaration

The candidate confirms that the work submitted is his/her own, except where work which has formed part of jointly-authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

This thesis features secondary analyses of established data sets. The candidate is extremely grateful to all the individuals/families who took part in these studies, the healthcare professionals for their help in recruiting them, and the whole study teams, which include interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, midwives and nurses. The candidate was not involved in design, data collection or primary data processing of these studies (the Avon Longitudinal Study of Parents and Children (ALSPAC), the Danish National Birth cohort (DNBC) and the Caffeine and Reproductive Health study (CARE)). Credit for these data is detailed in the Acknowledgements. The candidate's contributions included data cleaning, data manipulation, analysis and interpretation.

Chapter 4 of this thesis will include work which has been published in jointly authored publications.

Publication details:

Camilla Nykjaer, Nisreen A Alwan, Darren C Greenwood, Nigel A B Simpson, Alastair W M Hay, Kay L M White, Janet E Cade (2014) **Maternal alcohol intake prior to and during pregnancy and risk of adverse birth outcomes: evidence from a British cohort.** Journal of Epidemiology & Community Health; 68: 542-549 doi:10.1136/jech-2013-202934

Author contributions: The CARE study was designed by and carried out under the leadership of JEC and NABS. CN conducted the statistical analysis with assistance from DCG and NAA and led the drafting of the manuscript. AH and KW did the laboratory investigations. All authors contributed to subsequent drafts of the manuscript and have read and approved the final manuscript.

Chapter 5 of this thesis will include work which has been submitted to a journal for publication and is currently under editorial assessment.

Publication details:

Camilla Nykjaer, Charlotte Higgs, Janet E Cade, Darren C Greenwood, Nigel AB Simpson, Nisreen A Alwan. **Maternal fatty fish intake prior to and during pregnancy and risk of adverse birth outcomes: findings from a British birth cohort.** Submitted to BMC Pregnancy & childbirth. Status: Editorial assessment.

Author contributions: The CARE study was designed by and carried out under the leadership of JEC and NABS. CN & CH conducted the statistical analysis with assistance from DCG and NAA and led the drafting of the manuscript. All authors contributed to subsequent drafts of the manuscript and have read and approved the final manuscript.

Acknowledgements

First and foremost thank you to my supervisors Nisreen Alwan, Janet Cade and Darren Greenwood who have been very supportive throughout these past years. Thank you for your helpful comments, your patience, shared wisdom and encouragement throughout.

This research made extensive use of data from three large prospective cohort studies, the Avon Longitudinal Study of Parents and Children (ALSPAC), the Danish National Birth cohort (DNBC) and the Caffeine and Reproductive Health study (CARE). I would like to acknowledge the DNBC creators and funders including the March of Dimes Birth Defects Foundation, the Danish Heart Association, the Danish Medical Research Council, the Sygekassernes Helsefond, Danish National Research Foundation, Danish Pharmaceutical Association, Ministry of Health, National Board of Health and Statens Serum Institut. Similarly I would like to acknowledge the core support providers for the ALSPAC study; the UK MRC, the Wellcome Trust and the University of Bristol. And finally acknowledgement goes to the funding body of the CARE study which was supported by a grant from the Food Standard Agency, UK (T01033).

I must also thank the Rank Prize Foundation and the Medical Research Council (MRC) for funding this joint studentship.

Furthermore, thank you to the fetal programming group at Statens Serum Institute (Denmark), in particular Sjurdur Frodi Olsen, for having me stay with them on a prolonged research visit and guiding me through the sometimes overwhelming quantities of DNBC data.

Thank you to my colleagues in the Nutritional Epidemiology Group, in particular the CARE database manager Neil Hancock for his patience with my never ending queries about food groups and 24 hour recall data! I am also grateful for the advice of my Assessors Drs Nigel Simpson and Victoria Burley.

Never-ending thanks are owed to my parents, for always believing I could achieve anything; and for providing a home for me this summer where I could write up in peace.

Finally a massive thank you to my friends, the “guys”, who are like sisters to me and have been so supportive throughout this whole process. There are too many wonderful people to name but a special thank you to Dan and Cat for letting me stay at their home these final weeks of write up.

Abstract

Fetal life and early childhood are periods of rapid growth and development and both serve as important indicators of health in later life. Maternal diet during pregnancy has been recognised as one of the major lifestyle factors influencing both fetal growth and long term health. The link between maternal dietary patterns and fetal growth has been examined to some extent, little however is known on the potential long term effects on child growth. Using data from three large international cohort studies, this thesis aimed to assess the effect of maternal dietary components and patterns during pregnancy on offspring growth.

The literature review revealed a heterogeneous body of studies that was generally supportive of a positive association between a health conscious maternal dietary pattern during pregnancy characterised by high intakes of fruit, vegetables, water and wholegrains and offspring size at birth. The evidence relating later child growth to maternal diet in pregnancy was inconclusive mainly due to a lack of research as well as heterogeneity amongst studies.

Analyses of the association between maternal alcohol intake and fatty fish consumption prior to and during pregnancy and offspring size at birth was explored; providing further support on the evidence of alcohol as a teratogen, even in low amounts in the first trimester of pregnancy. The evidence for fatty fish intake however was inconclusive.

In order to facilitate between study comparisons, a common food grouping system was applied to dietary data from the three cohorts and principal component analysis was performed on energy adjusted dietary data.

Two, four and seven components were derived from each cohort. However, the dietary patterns identified from the different cohorts did share some commonalities. In particular, a dietary pattern characterised by high positive correlations with fruit, water and unrefined grains and negative correlations with refined grains and chips, seemed to be present in all three datasets. These were also the components that showed the most convincing associations with offspring growth outcomes at birth and around 7 years of age, even after taking into account known confounders and assessing possible mediation by birth weight and gestational weight gain as well as effect modification by breastfeeding and maternal pre-pregnancy BMI status.

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Abbreviations

AA	Arachidonic acid
AGA	Appropriate for gestational age
AHEI	Alternative Healthy Eating Index
AHEI-P	Alternative Healthy Eating Index for Pregnancy
ALSPAC	Avon Longitudinal Study of Parents and Children
ANOVA	Analysis of Variance
ASA24	Automated Self-Administered 24hr Dietary Assessment
BP	Blood pressure
BMI	Body mass index
CARE	Caffeine and Reproductive Health study
CDSR	Cochrane Database of Systematic Reviews
CI	Confidence interval
CRD	Centre for Reviews and Disseminations
CVD	Cardiovascular decease
DH	Department of Health
DHA	Docosahexaenoic acid
DK	Denmark
DM	Diabetes Mellitus
DNBC	Danish National Birth Cohort
EFA	Essential Fatty Acids
ELISA	Enzyme- Linked Immunosorbent Assay
FBDG	Food based dietary guidelines
FFQ	Food Frequency Questionnaire
FGR	Fetal growth restriction
FSA	Food Standards Agency
GDM	Gestational diabetes mellitus
GWG	Gestational Weight Gain
HEI	Healthy Eating Index
HHANES	Hispanic Health and Nutrition Examination Survey
HIV	Human Immunodeficiency Virus
HNFI	Healthy Nordic Food Index
HT	Hypertension
IFS	Infant Feeding Survey
IMD	Index of Multiple Deprivation
INMA	Infancia y Medio Ambiente Project
IQR	Interquartile range
IUGR	Intra-uterine growth restriction
IVF	In vitro fertilization
KCAL	Kilocalorie
KG	Kilograms
LA	Linoleic Acid
LBW	Low Birth Weight
LCPUFA	Long Chain Polyunsaturated Fatty Acids
LGA	Large for gestational age
LBW	Low birth weight
LNA	Linolenic Acid
LRNI	Lower Reference Nutrient Intake
MD	Mediterranean Diet
MeSH	Medical Subject Headings
MUFA	Monounsaturated Fatty Acids
NCD	Non-Communicable Disease
NICE	National Institute for Health and Care Excellence

NDNS	National Diet and Nutrition Survey
NND	New Nordic Diet
OR	Odds ratio
PCA	Principle component analysis
POP	Persistent organic pollutants
RCGOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised controlled trial
RNI	Reference Nutrient Intake
SACN	Scientific Advisory Committee on Nutrition
SD	Standard Deviation
SFA	Saturated Fatty Acid
SGA	Small for gestational age
UK	United Kingdom
UKWCS	UK Women's Cohort Study
US	United States
WHO	World Health Organization

1 Introduction

1.1 Chapter overview

This chapter provides some general background to the relevance of my research and places the research in context. The aims and objectives are described and related to the relevant sections of the thesis. The overall flow of the thesis is also presented.

1.2 Offspring growth and health

Fetal life and early childhood are periods of rapid growth and development and both serve as important indicators of health in later life. Poor growth in utero has been linked to increased risk of developing chronic diseases such as cardiovascular diseases (CVDs) and diabetes II in adult life (Barker, 1997) (WHO, 2002); on the other end of the spectrum, high birthweight has been linked to increased risk of certain cancers (Silva Idos et al., 2008; Signorello and Trichopoulos, 1998) as well as childhood obesity (Ong et al, 2000). Child overweight and obesity often track into adult life (Singh et al., 2008), where it becomes associated with an increased risk of mortality from non-communicable diseases (NCDs) (Reilly and Kelly, 2011; Global BMI Mortality Collaboration, 2016). Child height has been found to serve as an indicator of child health (de Onis, 2013; Silventoinen, 2003) as well as a predictor of adult height (Power et al., 1997; Kramer et al., 2000), which in turn has been found to be inversely associated with certain CVDs and cancers (Batty et al., 2009). In the UK, around 7 million people live with CVD and it causes over one quarter of all deaths in the UK with a huge burden to the wider economy of over £15 billion. The prevalence of obesity (defined as a BMI above or equal to 30 kg/m^2) is even greater with around 25% of the adult population (16+ years) being obese, a number that has more than doubled in the last twenty five years and has an even greater economic cost (HSE, 2015).

Early prediction of possible markers of these diseases is therefore important and of potential clinical interest should preventive measures or intervention strategies become available that could help reduce future morbidity and mortality.

1.3 Offspring growth and development

The Scientific Advisory Committee on Nutrition (SACN, 2011) has defined normal growth and development in fetal life and early childhood as a process “*characterised by a regulated increase in the size, mass and complexity of function of tissues and* *organs.*”(SACN, 2011)(p.28). The measurement of growth is therefore an important tool for assessing fetal, infant and child health (SACN, 2011).

1.3.1 Fetal growth

Prenatal development and growth can be divided into an embryonic period and a fetal period. The embryonic period is confided to the first trimester and begins with fertilization of the ovum (SACN, 2011). The placenta starts forming around week 2 of gestation and is usually established by week 4 where organogenesis begins. The placenta has a role both in terms of maternal nutrition but also as a conduct of nutrients from the mother to the fetus, of which glucose forms the primary source of energy. Fetal growth and development therefore is dependent upon a well-functioning maternal-placental unit (British Nutrition Foundation, 2013). The first three months of a pregnancy is a period of rapid growth where the embryo is transformed into a fetus and is one of the reasons why the 1st trimester is considered to be the most vulnerable period to external factors. During the fetal period, the major organs are fully formed and the nervous and immune systems developed. In the second trimester, the fetus starts laying down fat and it is critical that sources of the PUFAs n-3 and n-6 are available as these are needed for development of the brain and retina (British Nutrition Foundation, 2013). The fetus is entirely dependent upon the mother for its nutritional requirements and successful transfer of nutrients is constrained by factors other than her immediate dietary intake or overall nutritional status (British Nutrition Foundation, 2013).

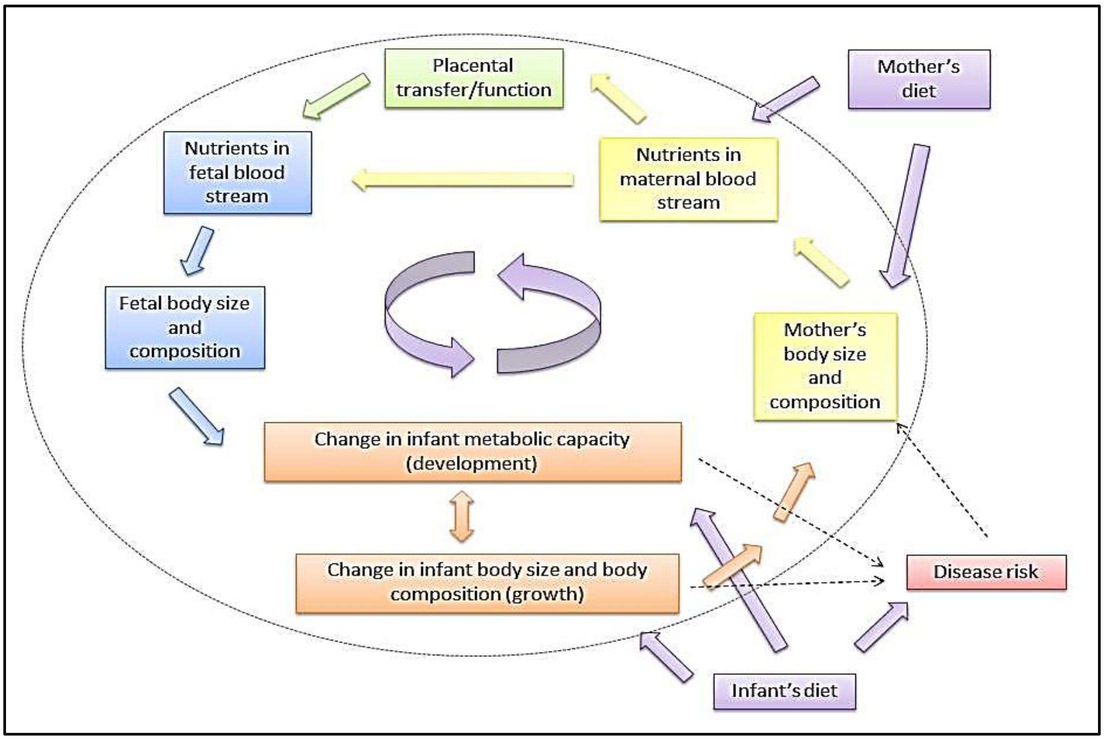
1.3.2 Determinants of growth

There are a multitude of factors which affect fetal (and post-natal) growth and development, including genetic, epigenetic and environmental factors. Maternal smoking as well as alcohol abuse in pregnancy are perhaps the most well-known environmental factors to negatively influence fetal growth, and recent evidence has suggested an independent link between the former and offspring risk of excess weight in children up to 10 years of age (Gravel et al., 2011). Population level factors such as poverty as well as maternal education have also been linked to adverse offspring growth as has pathological conditions such as gestational diabetes and preeclampsia which both influence fetal nutrient supply. The size of the mother can also affect growth with smaller mothers giving birth to lower birth weight babies due to the smaller size of the uterus (BNF, 2013). Maternal BMI as well as gestational weight gain similarly act as determinants of size at birth (WHO, 2002). Other non-modifiable factors liable to affect growth include maternal ethnicity and age. The primary driver of growth however is thought to be nutritional.

1.3.3 Nutritional programming: the effect of nutrition on growth and development

As stated earlier, nutrition appears to be the main driver of growth. Fetal undernutrition can occur because of an inadequate maternal diet, an inability of the mother to mobilize and transport sufficient nutrients, or an impaired vascular and placental supply line to the fetus. It can also occur if there is high fetal demand, for example because of faster growth (Nestlé Nutrition Institute, 2012). This will then cause adaptations to reduce nutrient demand, by slowing fetal growth or prioritizing essential organs which may in turn change fetal metabolism, and consequently alter growth or body composition unfavourably later in life (BNF, 2013).

Figure 1 below adapted from the SACN (2011) report 'The influence of maternal, fetal and child nutrition on the development of chronic disease in later life', illustrates how diet (in purple) modify nutritional status throughout the reproductive cycle. Maternal considerations such as nutrients in the blood stream, body size and composition are shown in yellow; placental considerations in green; fetal in blue and offspring in orange.

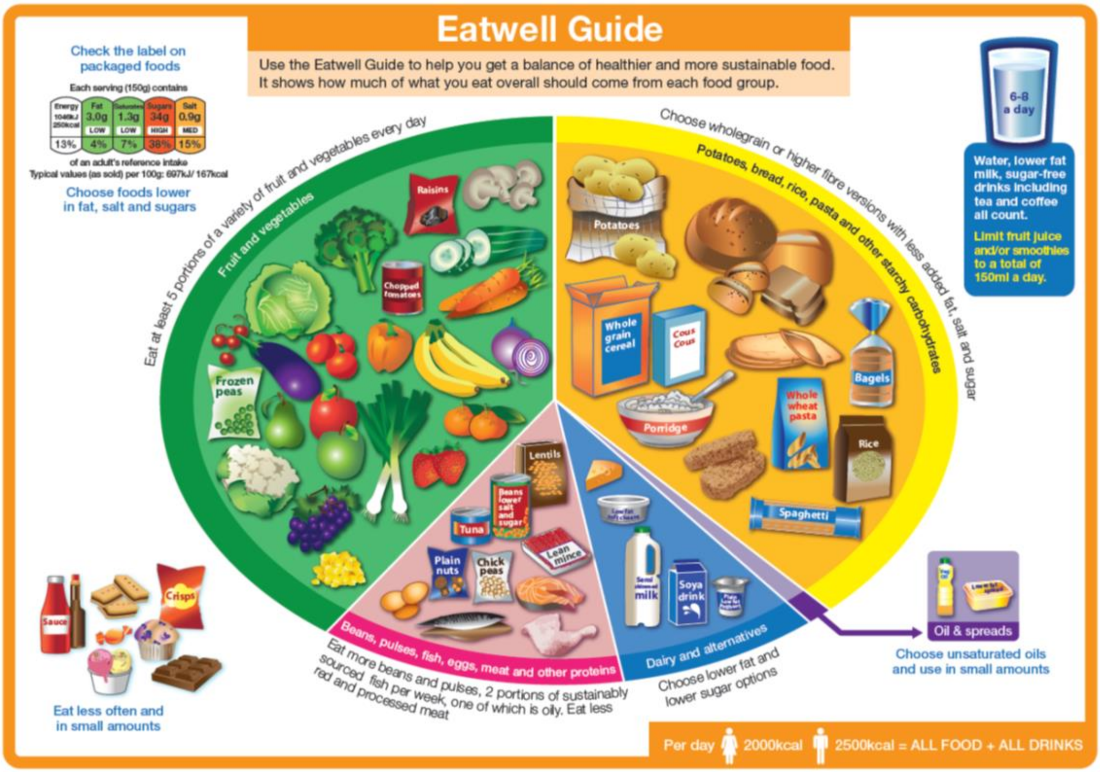


Adapted from: Early life nutrition (SACN, 2011)

Figure 1 Intergenerational aspects of maternal, fetal and infant nutrition on development and predisposition to disease risk

1.3.4 Current pregnancy dietary guidelines in the UK

The current advice for pregnant women in the UK is to follow the official dietary guidelines for healthy eating for the general population which are promoted using a pictorial illustration; the ‘Eatwell Guide’ (Figure 2).



Source: Public Health England in association with the Welsh Government, Food Standards Scotland and the Food Standards Agency in Northern Ireland (Public Health England, 2016)

Figure 2. The UK food based dietary guidelines: The Eatwell Guide

In addition to these, advice has been put in place regarding consumption of certain food groups during pregnancy (NHS, 2017) which can be found in Table 1 below.

Table 1. Food based dietary guidelines in the UK: additional recommendations for pregnant women

Foods	Recommendation for general population	Additional recommendations for pregnant women
Fruit and vegetables	5 portions of a variety per day (1 portion= 80 g)	Same
Fish	2 portions per week, one of which should be fatty (~140 g each)	Maximum of 2 portions of oily fish per week (~140 g per portion) Limit intake of predatory fish (max 100 g; most common include tuna and swordfish) 4 cans of tuna per week (140 g per can , drained)- if this is one of the portions of fish per week then avoid fresh tuna as oily fish Avoid cod liver oil (contains large quantities of Vitamin A)
Starchy foods	Should constitute 1/3 of daily food intake - roughly 2 portions at each meal. Choose wholemeal or wholegrain.	Same

Meat and Protein	Cut down to 70 g of red meat (beef, lamb and pork) or processed meat per day (=490 g per week). Choose eggs and pulses (including beans, nuts and seeds) as alternative sources of protein. Choose lean meat.	Same as for the general population but: - Avoid cold cured meats (pre-packed meats, e.g. ham, are fine) - Avoid all pates and liver + liver products
Dairy and alternatives	2-3 portions per day (1 portion= 1/3 ltr) Choose low fat options.	Same as for the general population but: - Avoid mould-ripened soft cheese and soft blue-veined cheeses - Choose pasteurised products
Fats	Cut down on fat and choose foods that contain unsaturated fat	Same
Salt	Eat food with less salt	Same
Foods high in sugar	Only have as a treat	Same
Drinks	Drink 6-8 cups/glasses of fluid a day. Water, lower fat milk and sugar-free drinks including tea and coffee all count. Alcohol should be limited to no more than 14 units per week.	Same as for the general population but: - No more than 200 mg caffeine per day - equates to about 2 mugs of instant coffee or 3 mugs of tea - Avoid alcohol

1.4 Maternal dietary patterns versus single foods/nutrients

Because nutrients are not consumed in isolation, and intakes will often be highly correlated, it is difficult to identify a true association between nutrients and offspring growth. This may be resolved by the use of dietary patterns that encompass multiple dietary components (Hu, 2002). The SACN Subgroup on Maternal and Child Nutrition (SMCN) (2011) has recommended future research in this area, particularly emphasising the need for data which better characterise dietary patterns and patterns of pre and postnatal growth. In a public health context, identifying patterns in dietary intake that are beneficial to fetal and child growth as well as maternal health will also be of great advantage when implementing dietary recommendations as these appear to be more intuitive than the single food or nutrient approach.

1.5 Thesis aim & objectives

The primary aim of this thesis is to assess the effect of maternal dietary patterns during pregnancy on size at birth and child growth outcomes (height and weight) in three large prospective birth cohorts: the Danish National Birth Cohort (DNBC), the Caffeine & Reproductive Health study (CARE), and the Avon Longitudinal Study of Parents and Children (ALSPAC). It will however also consider maternal alcohol consumption during pregnancy as well as fatty fish consumption in relation to size at birth within the CARE study where associations with these components are as of yet unexplored. Both alcohol and fatty fish intake during pregnancy have received particular attention in the literature and evidence surrounding these remains somewhat contradictive. To address the overarching aim of this research a set of objectives are listed below.

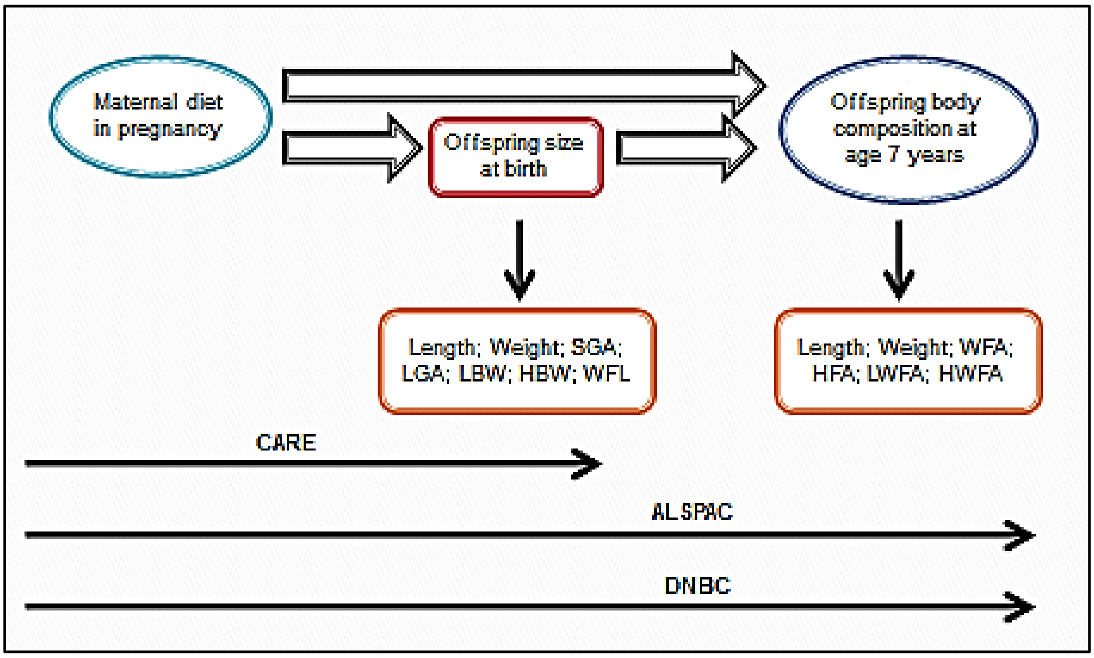
Hypothesis: optimal perinatal nutrition, gained from a healthy maternal dietary pattern, leads to favourable pregnancy outcomes in terms of offspring growth

1.5.1 Objectives

1. Review the evidence linking dietary patterns to offspring growth outcomes (Chapter 2)
2. Characterise dietary patterns in pregnancy using data from English and Danish birth cohorts (Chapters 6,7 & 8)
3. Examine the relationship of maternal alcohol consumption in pregnancy with offspring size at birth in the CARE study (Chapter 4)
4. Examine the relationship of maternal fatty fish intake in pregnancy with offspring size at birth in the CARE study (Chapter 5)
5. Examine the relationship between maternal dietary patterns in pregnancy and offspring size at birth (Chapters 6,7 & 8)
6. Examine the relationship between maternal dietary patterns in pregnancy and offspring growth outcomes at age 7 years (Chapters 7 & 8)
7. Compare and contrast dietary patterns of pregnant women living in England and Denmark (Chapters 8 & 9)
8. Discuss how evidence from this research fits in with the fetal programming hypothesis (Chapter 9)

1.6 Thesis overview

As stated above, this thesis uses data from three sources. An outline of how these studies fit together to address the hypothesis under investigation is illustrated in Figure 3.



CARE: Caffeine and Reproductive Health study (Chapters 4, 5 & 6)
ALSPAC: The Avon Longitudinal Study of Parents and Children (Chapter 7)
DNBC: The Danish National Birth Cohort (Chapter 8)

Figure 3. Thesis cohort and chapter overview

The *second chapter* of this thesis is a review of the existing evidence surrounding maternal dietary patterns in pregnancy and offspring growth outcomes, followed by a methods chapter (*Chapter 3*) detailing the data and methods used. *Chapter 4 and 5* are the first analysis chapters and investigate the association between maternal alcohol consumption and fatty fish intake in pregnancy respectively and offspring size at birth using data from the CARE study. This is followed by an analysis within the same cohort of maternal dietary patterns in pregnancy and an assessment of any relation to offspring size at birth (*Chapter 6*). In *Chapter 7* and *Chapter 8*, data from the ALSPAC study and the DNBC respectively are used to analyse dietary patterns in pregnancy and investigate both their relationship with offspring size at birth as well as child growth outcomes at 7.5 years of age. The final chapter of the thesis, *Chapter 9,* provides a synthesis of the findings from the three cohorts, relating them to each other and discussing how they fit in with the fetal programming hypothesis. The implications for public health and policy will be identified and recommendations for future research suggested.

2 Literature review

2.1 Chapter overview

This chapter present the results of a narrative systematic review of the literature investigating maternal dietary patterns during pregnancy in relation to offspring growth outcomes. Literature relating to the analyses in chapter 4 and 5 has been described in those specific chapters.

The literature search was carried out on several databases in two separate phases (2013 and 2016), using a pre-established protocol. Findings were presented separately for size at birth outcomes and offspring growth outcomes in early childhood. A total of 21 articles were identified which fit the inclusion criteria, 18 of these assessed maternal dietary patterns in relation to size at birth and 4 in relation to later offspring growth outcomes. In addition to this, one literature review was identified in the update search which assessed the evidence base relating maternal dietary patterns in pregnancy to infant size at birth.

Findings relating to infant size at birth were largely in keeping with the hypothesis that optimal perinatal nutrition, gained from a healthy maternal dietary pattern, leads to favourable pregnancy outcomes in terms of size at birth. The review however identified several methodological issues which limit the confidence in these results. The evidence was not clear for child growth outcomes, partly due to heterogeneity and lack of studies.

The increasing interest in this area of research, as evidenced by the recentness of the publications, suggests that this is a worthwhile area of further investigation, however findings are somewhat mixed and it is clear that a uniform approach to dietary pattern analysis is needed in order to facilitate in between study comparisons. This synthesis of the evidence helps to identify the methodological challenges researchers in this area of nutritional epidemiology are faced with and helps set the context for the analyses in later chapters.

2.2 Introduction

The overall aim of this thesis is to determine the extent to which maternal dietary patterns during pregnancy influences offspring size at birth as well as later child growth outcomes. Before investigating this however, it is necessary to consider the existing evidence base, both to assess whether there are grounds for further research, but also to help make informed decisions in regards to future analyses. As highlighted in Chapter 1, the use of dietary patterns is a relatively new phenomenon in nutritional epidemiological research and has only recently been explored in relation to maternal and child health outcomes.

This chapter presents the results of a systematic search of the literature with a narrative synthesis of findings relevant to the research objectives outlined in Chapter 1. The objectives of this review chapter are to examine and synthesise any published evidence on associations between the following:

- Maternal dietary pattern during pregnancy and size at birth;
- Maternal dietary patterns during pregnancy and offspring infant/child growth outcomes.

2.3 Methods

2.3.1 Literature searches

The work for this literature review was conducted in two phases: the initial search conducted in July 2013 and a second phase in July 2016, in which the initial search was updated. The searching of literature was done following a pre-established protocol in accordance with the recommendations made by the Centre for Reviews and Disseminations (CRD) (CRD, 2009) which detailed the search strategy, criteria, and methods for data extraction and synthesis. The searching involved firstly identifying any existing reviews, secondly, searching selected databases; and thirdly, citation searching.

The literature search was carried out using the following databases: the Cochrane Database of Systematic Reviews (CDSR) (in the initial search only), MEDLINE, EMBASE and Maternity and Infant Care. These databases were thought suitable, as they cover many aspects of nutrition and health.

The search strategy was developed for the Ovid databases, and adapted to suit the CDSR. The search terms for each component are listed in Table 2 below and were combined using the Boolean operator ‘AND’. Where possible the search terms were mapped to subject headings in order to cover a full range of terms using the advanced search function in the Ovid database and MeSH headings for CDSR. The search was not limited by date or country of origin. However, due to the resources available, only English language articles were included. For the same reason, the decision was taken to also exclude grey literature (unpublished articles, theses and dissertations and non-peer reviewed articles), and include only those papers that reported findings from original research in humans.

Table 2. Literature review search terms

Search component	Search terms
Dietary pattern	diet* quality' or vegan or 'seventh day Adventist' or 'healthy eating index' or 'diet* score' or 'food intake' or nutrition or eating or 'dietary intake' or diet* or vegetarian or macrobiotic or Mediterranean or 'dietary pattern' or 'principal component analysis' or 'cluster analysis
Pregnancy	pregnan* or gestation*
Growth	height or 'body mass' or 'body size' or weight or height or hip or waist or 'body composition' or grow* or BMI or birthweight
Offspring	child* or infan* or offspring or foetal or fetal

2.3.2 Screening of articles and criteria for inclusion

Search results from each database were imported into an EndNote X6 library for de-duplication across the databases. Titles of articles were then screened and excluded if they seemed highly irrelevant. Abstracts were assessed against the pre-defined inclusion criteria presented in Figure 4 below and given exclusion codes according to the stage of exclusion. That way it was easy to identify studies which could prove informative, such as those investigating single foods in relation to offspring growth outcomes (exclusion code 5). Where decisions could not be made based on the abstract, the full article was retrieved and examined against the inclusion criteria.

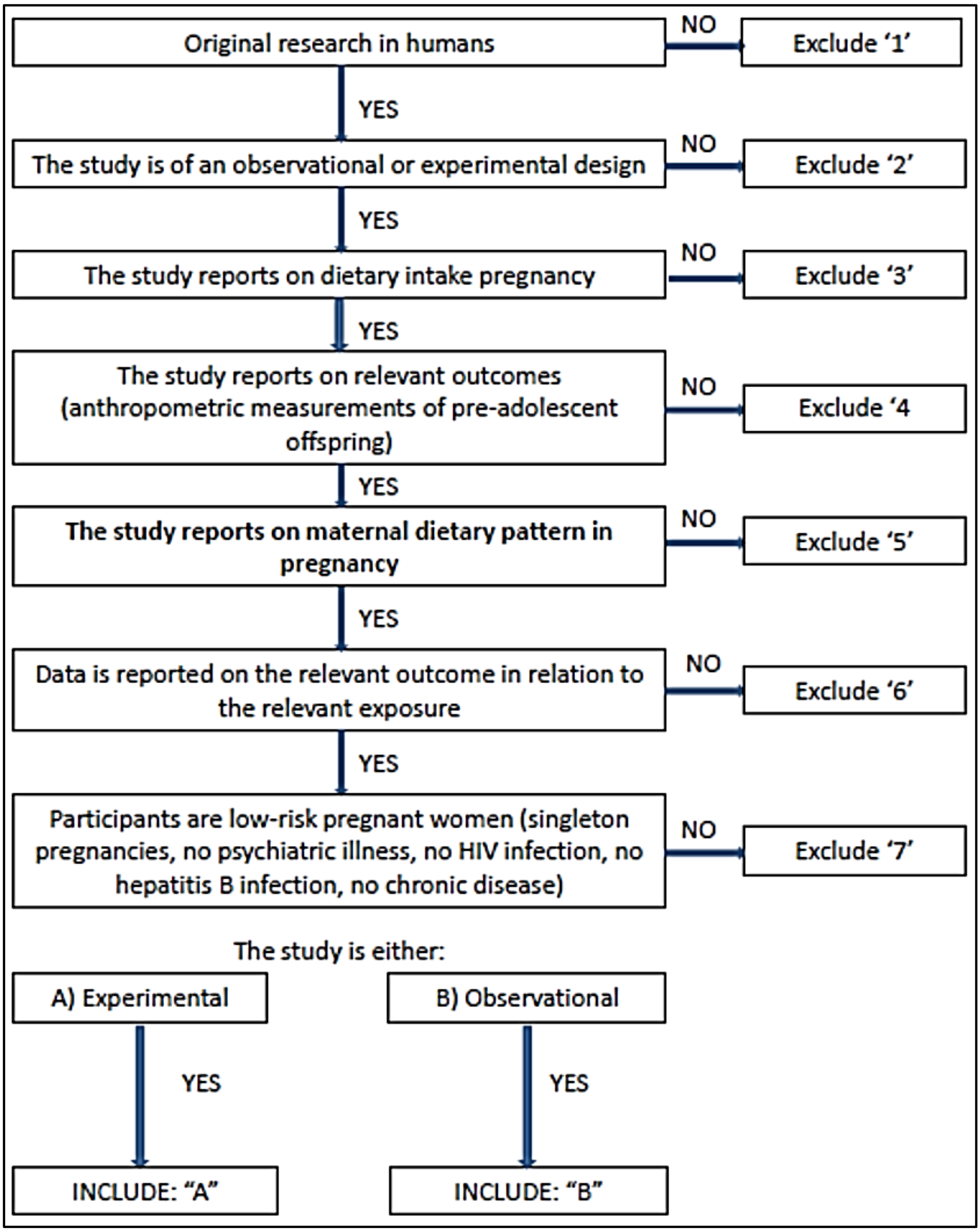


Figure 4. Study inclusion criteria

2.3.3 Data extraction

Extraction of data from literature is a process which can be prone to human error as subjective decisions are often required. Therefore, for consistency, a data extraction form was developed which was deemed relevant to the area of study (see Appendix A: Literature review data extraction form). Extracted data were organised into tables in Excel, and are presented alongside a narrative synthesis of the findings.

2.3.4 Data analysis/synthesis

Due to heterogeneity of study designs it was decided a meta-analysis of study results would not be undertaken. A narrative synthesis of the evidence instead seeks to organise the literature in a logical manner.

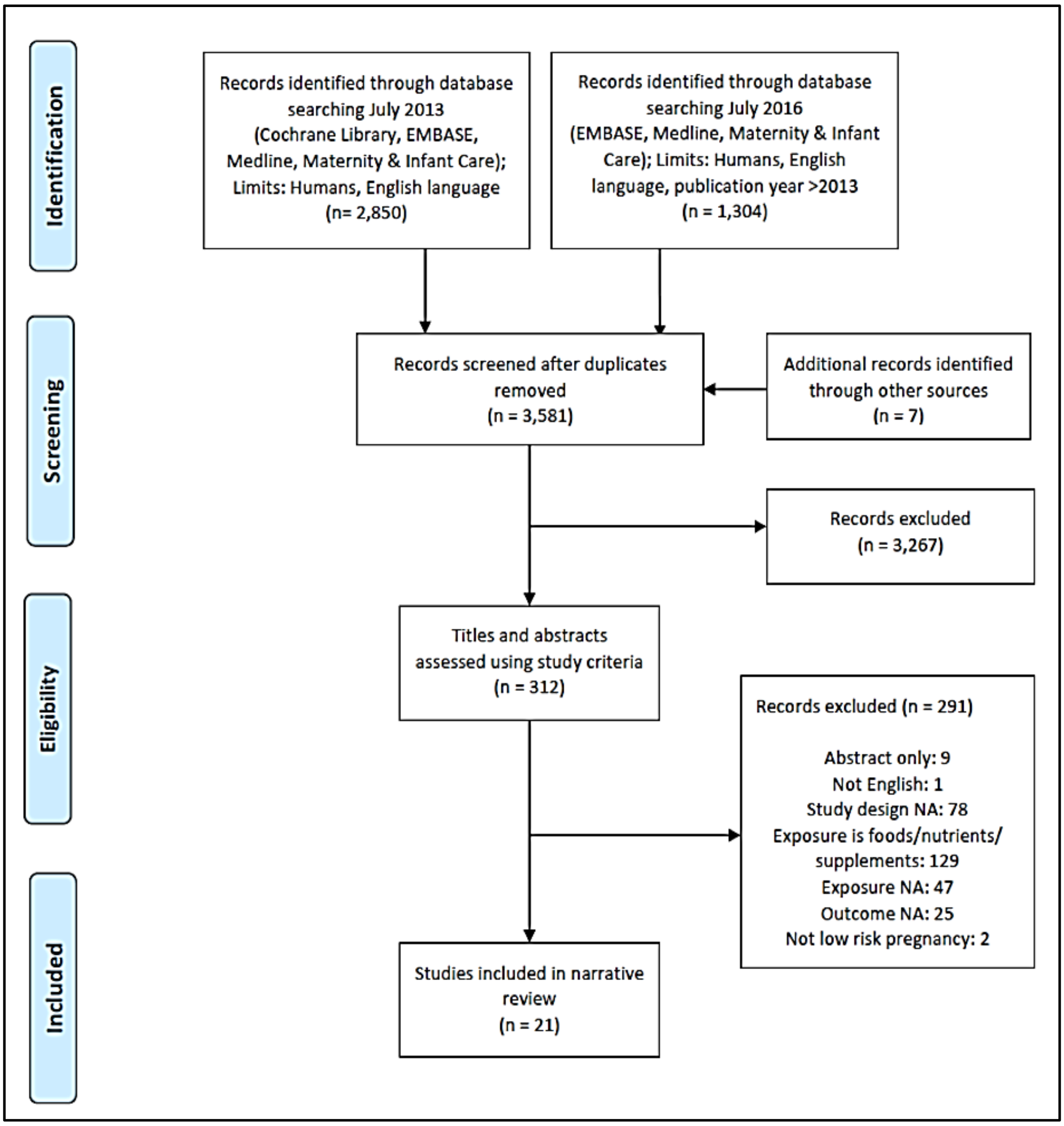
2.3.5 Quality appraisal

Methodological quality of studies was not evaluated using a formal scoring approach but aspects of study quality, such as appropriateness of study design, risk of bias brought about through sampling, method of dietary assessment, dietary data analysis, outcome measures, statistical techniques used and the quality of reporting and generalisability were assessed.

2.4 Results

The search strategy was systematically followed. After removing duplicates in EndNote, titles and abstract were screened for eligibility against the inclusion/exclusion criteria. Out of 3,581 references from the combined searches, 312 articles were retrieved for further evaluation of which 21 met the inclusion criteria, all of which investigated maternal dietary patterns in pregnancy in relation to offspring growth outcomes. Adapted from *The PRISMA Group, (Moher et al., 2009))*

Figure 5 below shows a flow chart of the study selection process. Results have been presented according to offspring growth outcomes at birth and in infancy/childhood respectively.



Adapted from The PRISMA Group, (Moher et al., 2009))

Figure 5. Study selection process

2.4.1 Existing reviews

In addition to the 21 articles identified through the literature searches, one literature review was identified in the July 2016 update search. The review was published in June 2016 and assessed the evidence concerning the relationship between maternal dietary patterns and pregnancy outcomes (Chen et al., 2016). The authors reviewed evidence published up to November 2015 and from a search in PubMed they included 54 articles out of a total of 2,972 potentially relevant. Of these, 11 articles assessed growth outcomes in relation to maternal dietary patterns. In their review, Chen et al. (2016) state that only articles relating diet during pregnancy with health outcomes in the mother and infant were included. Despite this, two of the studies assessed child growth expressed as bone size and bone mineral density as well as forearm fractures at 9 years and 16 years respectively and were included in their description of evidence related to fetal growth. Of the 4 studies assessing SGA, Chen et al. (2016) highlighted significantly protective effects of a maternal 'traditional' dietary pattern as well as a higher adherence to a Mediterranean diet against having a SGA infant, whereas a maternal ‘Western’ dietary pattern and a ‘Wheat products’ dietary pattern appeared to significantly increase the risk of having a SGA infant. Evidence relating to fetal growth expressed as birth weight and first trimester crown-rump length from 3 studies appeared to be contradictive with a ‘health conscious’ dietary pattern, but also a ‘snack’ and ‘energy-rich’ dietary pattern showing positive associations. The review identified some important limitations in the evidence assessed, including comments on: misclassification & recall bias from dietary assessment, the subjective nature of naming dietary patterns derived from *a posteriori* techniques as well as inconsistencies in the names used for *a priori* diet scores with very similar contents. The authors highlighted the need for a formal development of taxonomy and classification to enable better comparison between studies, but ultimately concluded that diets with higher intakes of fruits, vegetables, legumes and fish have positive pregnancy outcomes in general and that this evidence should be communicated to women (Chen et al., 2016).

2.4.2 Maternal dietary patterns and offspring size at birth

2.4.2.1 Study design & setting

Eighteen studies were identified which investigated the association between maternal dietary patterns in pregnancy and size at birth. Characteristics of these studies are presented in Table 3 below. All but two studies were of a prospective cohort design, whereas the remaining two were of a case-control (Thompson et al., 2010) and cross-sectional survey design (Wolff and Wolff, 1995). Studies were based in a variety of countries, two used data from a large Dutch birth cohort study; Generation R (Bouwland-Both et al., 2013, Timmermans et al., 2012), two used data from the Spanish INfancia y Medico Ambiente Project (INMA) (Chatzi et al., 2012, Rodriguez-Bernal et al., 2010), one from Crete (Chatzi et al., 2012), five from the US (Colon-Ramos et al., 2015, Poon et al., 2013, Rifas-Shiman et al., 2009, Shapiro et al., 2016, Wolff and Wolff, 1995), one from Brazil (Coelho Nde et al., 2015), one from Norway (Hillesund et al., 2014), one from Denmark (Knudsen et al., 2008), one from China (Lu et al., 2016), one from the UK (Northstone et al., 2008), one from Japan (Okubo et al., 2012), one from the French West Indies (Saunders et al., 2014), one from New

Zealand (Thompson et al., 2010) and one from Australia (Wen et al., 2013). In terms of inclusion criteria all but two studies restricted their analyses to singleton births and of these 7 were restricted according to gestational age (ranging from >32 weeks to >37 weeks gestation). Several studies applied further exclusion criteria by excluding mothers who had diabetes mellitus (DM) or hypertension (HT) leading up to pregnancy or who developed gestational diabetes mellitus (GDM). The ages of the pregnant women were fairly similar ranging from 24 years in the US Hispanic Health and Nutrition Examination Survey (HHANES) (Wolff and Wolff, 1995) to 32 years in the US Project Viva cohort study (Rifas-Shiman et al., 2009). Sample sizes were generally large ranging from 368 to 66,597 participants with a mean of 7,842.

2.4.2.2 Dietary assessment

The majority of studies assessed diet using a food frequency questionnaire (FFQ), which varied somewhat in design and application. The number of food items included ranged from 29 to 360 items and reference periods ranged from 1 week to the whole of pregnancy. Some were interviewer-administered whereas others were self-reported. Two studies used other methods of dietary assessment, namely automated self-reported 24 hour dietary recalls (ASA24) (Shapiro et al., 2016) and face-to-face interviews (Wen et al., 2013). The timing of assessment varied, with two assessing diet in the first trimester (Chatzi et al., 2012; Rodriguez-Bernal et al., 2010), six in the second (Chatzi et al., 2012; Colon-Ramos et al., 2015; Hillesund et al., 2014; Knudsen et al., 2008; Lu et al., 2016; Timmermans et al., 2012), two in the third (Northstone et al., 2008; Poon et al., 2013), two at several time points throughout pregnancy (Rifas-Shiman et al., 2009; Shapiro et al., 2016) and three post-partum assessing intakes throughout pregnancy (Saunders et al., 2014), in the first and third trimester (Thompson et al., 2010) and current diet 5 years post-partum (Wolff and Wolff, 1995). For three studies, maternal diet was assessed at varying time points depending upon the gestational age at the mother’s enrolment (Bouwland-Both et al., 2013; Okubo et al., 2012; Wen et al., 2013) and one study had no details on the timing of dietary assessment (Coelho Nde et al., 2015). Prior to analyses of dietary data the majority of studies excluded mothers with incomplete FFQs or, where nutrient intake was estimated, implausible values for total energy intake with varying criteria (e.g. >5000 kcal/day or <1000 kcal/day).

2.4.2.3 Dietary pattern analysis

Of the 18 studies, 10 used *a posteriori* techniques to derive dietary patterns and eight evaluated dietary patterns using *a priori* techniques.

2.4.2.3.1 A posteriori analyses

For the studies using *a posteriori* methods, seven used PCA to derive dietary patterns (Bouwland-Both et al., 2013; Colon-Ramos et al., 2015; Coelho Nde et al., 2015; Knudsen et al., 2008; Northstone et al., 2008; Thompson et al., 2010; Wolff and Wolff, 1995), two used cluster analysis (Lu et al., 2016; Okubo et al., 2012) and one study used logistic regression analysis to predict the occurrence of IUGR as a function of 21 food groups (Timmermans et al., 2012). All but three of the 10 studies (Colon-Ramos et al., 2015; Northstone et al., 2008; Thompson et al., 2010) aggregated the dietary data collected from FFQs into main food groups based on nutritional profiles and culinary usage before applying statistical techniques. The types and number of food groups varied from study to study depending to some degree upon the setting, but tended to include fruit, vegetables, potatoes, snacks, cakes or sweets, cereal products, meat, fish, eggs, dairy, fats, sauces & condiments and soft drinks. Some studies included a food group for meat substitutes (Thompson et al., 2010; Colon-Ramos et al., 2015; Northstone et al., 2008), alcoholic beverages (Timmermans et al., 2012; Okubo et al., 2012; Knudsen et al., 2008; Bouwland-Both et al., 2013; Thompson et al., 2010) and tea and coffee (Knudsen et al., 2008; Northstone et al., 2008; Okubo et al., 2012; Thompson et al., 2010). Others differentiated between high-fat and low-fat dairy products (Knudsen et al., 2008; Wolff and Wolff, 1995), types of meat (Bouwland-Both et al., 2013; Knudsen et al., 2008; Lu et al., 2016; Northstone et al., 2008; Okubo et al., 2012; Wolff and Wolff, 1995; Colon-Ramos et al., 2015; Thompson et al., 2010), types of fish (Knudsen et al., 2008; Lu et al., 2016; Okubo et al., 2012), types of soft drinks (SSB vs. non-SSB) (Bouwland-Both et al., 2013; Knudsen et al., 2008) and refined vs. unrefined breads (Knudsen et al., 2008; Northstone et al., 2008). Whereas for some studies food items with dissimilar nutritional profiles and/or culinary usage had been grouped together, e.g. Coelho Nde et al. (2015) grouped eggs together with pork and sausages and Timmermans et al. (2012) had a food group covering soya and diet products (with no clarification of what constituted a diet product). One study standardised the dietary data before (Knudsen et al., 2008) and one standardised dietary scores after analysis (Thompson et al., 2010), one energy adjusted the data (Timmermans et al., 2012), and two studies both standardised and energy adjusted dietary data before analysis (Northstone et al., 2008; Okubo et al., 2012). For the studies using PCA, only one reported on whether it was based on the correlation or covariance matrix (Coelho Nde et al., 2015). The choice of components to retain tended to depend on the percentage variance explained, the scree plot and/or general interpretability. Details of the dietary patterns derived from *a posteriori* analyses can be found in Table 3 below. Briefly the number of components or cluster solutions from studies ranged from 3 to 7 and explained between 14% (Thompson et al., 2010) and 59% (Wolff and Wolff, 1995) of the variance in the dietary data. The majority of studies derived a component high in processed and red meats, animal fat and high-fat processed foods such as pizza and pastries and labelled it either ‘Western’ (Bouwland-Both et al., 2013; Coelho Nde et al., 2015; Knudsen et al., 2008), ‘Processed’ (Colon-Ramos et al., 2015) or ’Meat’ (Lu et al., 2016; Okubo et al., 2012). A dietary pattern which was consistent with general dietary guidelines for healthy eating was also prevalent amongst studies and labelled as either ‘Health conscious’(Knudsen et al., 2008; Northstone et al., 2008), ‘Healthy’(Colon-Ramos et al., 2015), ‘Prudent’(Coelho Nde et al., 2015), ‘Mediterranean’(Bouwland-Both et al., 2013) or ‘Nutrient dense’(Wolff and Wolff, 1995) and was characterised by high intakes of fruit, vegetables, white meat (chicken or fish) and for some studies breakfast cereals and non-white bread. Several studies also derived a somewhat healthy dietary pattern considered traditional to the setting, e.g. Northstone et al. (2008) derived a component with high intakes of green vegetables and root vegetables, potatoes, peas and to some extent red meat and poultry and labelled it ‘traditional’, based on the familiar British ‘Meat and two veg’ diet. Similarly, Thompson et al. (2010) derived a component considered traditional to a New Zealand diet which included apples/pears, citrus fruit, kiwifruit/feijoas, bananas, green vegetables, root vegetables, peas/maize, dairy food/yogurt and water.

2.4.2.3.2 A priori analyses

Of the eight studies using *a priori* methods, three studies assessed adherence to a Mediterranean diet using slightly different versions of the Mediterranean diet (MD) score (Chatzi et al., 2012; Poon et al., 2013; Saunders et al., 2014), four studies assessed diet quality using alternate versions of the Healthy Eating Index (HEI) (Rifas-Shiman et al., 2009; Rodriguez-Bernal et al., 2010; Poon et al., 2013; Shapiro et al., 2016), one study assessed adherence to a New Nordic Diet (NND) score (Hillesund et al., 2014) and one study categorised mothers into ‘Junk food’ or ‘No junk food’ based on answers to a range of dietary behaviour questions (Wen et al., 2013) (see Table 3 below for further details). Four studies energy adjusted dietary data before analysis

(Chatzi et al., 2012; Rifas-Shiman et al., 2009; Rodriguez-Bernal et al., 2010; Shapiro et al., 2016).

2.4.2.4 Assessment of offspring anthropometry at birth

Data on offspring anthropometry at birth was extracted from hospital records for all but three studies. Okubo et al. (2012) used self- reported data collected 2-9 months post-partum, Wen et al. (2013) collected information on birth weight via telephone interviews six months post-partum and Wolff & Wolff (1995) used self-reported birth weight 5 years post-partum. Gestational age and sex adjusted SD scores or Z-scores were used in several studies and constructed using either country specific standards (Bouwland-Both et al., 2013; Lu et al., 2016; Okubo et al., 2012; Knudsen et al., 2008; Poon et al., 2013; Rifas-Shiman et al., 2009; Thompson et al., 2010) or the 2006 child growth standards created by the World Health Organization (WHO) (Colon-Ramos et al., 2015). Definitions of FGR varied from study to study in terms of the choice of parental characteristics they took into account in their predictions, all but one study however defined FGR as <10th infant sex-and-age specific birth weight centile. Rodriguez-Bernal et al. (2010) took into account parental as well as infant characteristics (sex and age) in their predictions and defined FGR as birth weight less than the lower limit of the 80% confidence intervals for predictions (Rodriguez-Bernal et al., 2010). In terms of SGA, it was defined as <10th birth weight centile (or birth length & head circumference centile) and was either infant sex specific (Hillesund et al., 2014), infant sex-and-age specific (Lu et al., 2016; Okubo et al., 2012; Poon et al., 2013; Rifas-Shiman et al., 2009) or neither (Thompson et al., 2010). Knudsen et al. (2008) defined SGA as <2.5th infant sex specific birth weight Z-scores. LGA was defined as >90th birth weight and was similarly either infant sex specific or both age-and-infant sex specific.

2.4.2.5 Statistical analyses

Of the 18 studies, 17 used multivariable regression techniques to assess the association between dietary patterns and offspring size at birth, whereas one study used univariable regression (Northstone et al., 2008). The regression techniques used included linear, logistic, multinomial or poisson regression. Stepwise multiple linear and logistic regression were used in six studies and consequently the selection of confounders varied greatly between studies (see Table 3 below). Of the 17 studies using multivariable regression, all but two (Coelho Nde et al., 2015; Wen et al., 2013) adjusted for both infant's sex and gestational age either in the regression models or in the outcome definition (e.g. sex-and-age adjusted birth weight Z-scores). The majority of studies adjusted for established confounders such as maternal age, smoking status, ethnicity, educational status, pre-pregnancy BMI or height and weight separately either in the regression models or in the definition of outcomes, and those which did not tended to use stepwise regression. Wen et al. (2013) used stepwise regression and had the least adjusted model with only maternal weight and gestational age as significant confounders at a 5% accepted significance level. Gestational weight gain (GWG) was included as a confounder by Okubo et al. (2012), Rodriguez-Bernal et al. (2010) and Saunders et al. (2014), and GDM was adjusted for by Hillesund et al. (2014) and Lu et al. (2016) respectively. Of the 11 studies which did not energy adjust the dietary data before the dietary pattern analysis, three adjusted for energy intake in the regression models (Hillesund et al., 2014; Poon et al., 2013; Saunders et al., 2014), whereas Chatzi et al. (2012) appeared to have adjusted for energy intake both in their assessment of Mediterranean diet adherence and later on in their regression models, resulting in a total of 11 studies which adjusted for energy intake either before or after the dietary pattern analysis. Consideration was given to possible effect modification by maternal age, BMI, infant’s sex, educational status and smoking status in some studies and two studies assessed dietary patterns derived at different time points during pregnancy in relation to size at birth (Rifas-Shiman et al., 2009; Thompson et al., 2010). Of the six studies which categorised their exposure into tertiles, quartiles or quintiles, only one study assessed for linearity across categories (Rodriguez-Bernal et al., 2010) and one adjusted for multiple testing (Okubo et al., 2012).

Table 3. Study characteristics: studies investigating maternal dietary patterns and offspring birth size

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure
Bouwland-Both et al. (2013)	Generation R Study (Netherlands)	Prospective cohort 2002–2006	847	Dutch women; singleton birth	Self-administered 293 item FFQ (<24 wks; past 3 m)	A posteriori PCA on 20 food groups. Number of components based on % variance	Mediterranean; Energy rich; Western % variance: 29.8
Chatzi et al. (2012)	INfancia y Medio Ambiente Project (INMA) (Spain)	Prospective cohort 2004-2008	2,461	>16 yrs, singleton birth; no ART, residents of study area	Interviewer administered 100 item FFQ (T1; since LMP)	A priori 8 item score: veg, legumes, fruits & nuts, cereals, fish & seafood, dairy products, meat, fat (ratio of MUFA: SFA). Data residually energy-adjusted. '0' assigned for intakes < median and '1' for intakes > median for beneficial items & vice versa for detrimental items	Mediterranean diet score (0 (low) to 8 (high))
	Rhea (Crete)	Prospective cohort 2007-2008	889	Singleton birth, residents of study area	250 item FFQ (T2; since LMP)	As above	As above
Coelho Nde et al. (2015)	Social Capital & Psychosocial Factors associated with Prematurity & Low Birth Weight (Brazil)	Prospective cohort 2007 – 2008	1,298	Singleton term birth	29 item FFQ (not stated; T3)	A posteriori: PCA on 20 food groups. Number of components based on scree plot, % variance & interpretability.	Prudent; Traditional; Western; Snack % variance: 36.4
Colon-Ramos et al. (2015)	The Conditions Affecting Neurocognitive Development & Learning in Early Childhood (US)	Prospective cohort 2006 -2011	1,151	16-40 yrs; 16-28 wks gestation; low risk singleton pregnancy; English literate, residents of study area	Interviewer administered 111 item FFQ (T2; past 3 m)	A posteriori PCA on all FFQ items. Number of components based on scree plot, % variance & interpretability. Combined dietary patterns created based on participants' rank order in the Healthy, Processed & Southern components.	Healthy; Processed; Southern; Healthy-processed; Healthy-Southern; Southern-processed; Mixed % variance: 15.4
Hillesund et al. (2014)	The Norwegian Mother and Child Cohort Study (Norway)	Prospective cohort 1999 - 2008	66,597	Singleton term birth; no DM before pregnancy	Self-administered 255 item FFQ (T2; first 4 m of pregnancy)	A priori 10 item score: (1) meal pattern; (2) Nordic fruits; (3) root veg; (4) cabbages; (5) potatoes relative to rice & pasta; (6) whole grain breads relative to refined	New Nordic Diet score (0 (low) to 10 (high))

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure
						breads; (7) oatmeal porridge consumption (8) game, fish, seafood and native berries consumption; (9) unsweetened milk relative to fruit juice (10) water relative to SSB. Same scoring as Chatzi et al. (2012).	
Knudsen et al. (2008)	Danish National Birth Cohort (Denmark)	Prospective cohort 1997-2002	44,612	Singleton term birth	Self-administered 360 item FFQ (T2; past 1 m)	A posteriori PCA on 36 food groups. Dietary data standardised. Number of components based on scree plot, % variance & interpretability. Combined dietary patterns created based on participants' rank order in the Western & Health Conscious component.	Western; Health Conscious; Intermediate % variance: NR
Lu et al. (2016)	Born in Guangzhou Cohort Study (China)	Prospective cohort 2012-2015	6,954	Singleton term birth; no hypertension or DM before pregnancy	Self-administered 64 item FFQ (T2; past wk)	A posteriori Cluster analysis on 30 food groups. Cluster solution selected by comparing the ratio of between-cluster variance to within-cluster variance divided by the number of clusters & on the nutritional meaningfulness of clusters.	Cereals, eggs & Cantonese soups; Dairy; Fruits, nuts & Cantonese desserts; Meats; Vegetables; Varied
Northstone et al. (2008)	The Avon Longitudinal Study of Parents and Children (UK)	Prospective cohort 1990-1992	12,053	Pregnant residents in study area	Self-administered 44 item FFQ (T3; past 2 wks)	A posteriori PCA on 44 food groups. Dietary data standardised & energy adjusted using the residual method. Number of components based on scree plot & interpretability.	Health conscious; Traditional; Confectionary; Vegetarian % variance: 32.4
Okubo et al. (2012)	Prospective cohort study- Osaka Maternal and Child Health Study (Japan)	Prospective cohort 2001 - 2003	803	Singleton term birth (37-41 wks)	Self-administered 150 item FFQ (5–39 wks; past month)	A posteriori Cluster analysis on 33 food groups. Dietary data standardised & energy adjusted using the energy-density method	Meat & eggs; Wheat products; Rice, fish & vegetables (RFV)
Poon et al. (2013)	The Infant Feeding Practices Study II (IFPSII)(US)	Prospective cohort 2005	893	Healthy singleton; >35 wks gestation; ≥5 pounds; no intensive care unit for >3 days	Self-administered FFQ (T3; past 1 m) modified version of the Diet History questionnaire (DHQ)	A priori AHEI-P: 13 items based on modified version of US 2010 dietary guidelines for healthy eating: veg (≥5 servings/d), whole fruit (≥4 servings/d), whole grains (75 g/d), nuts & legumes (≥1 serving/d), long-	Alternate Healthy Eating Index for Pregnancy (AHEI-P) (0 (low) to 130 (high))

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure
						chain (n-3) fats (250 mg/d), PUFA %Energy (≥10), folate (≥600 µg/d), calcium (≥1200 mg/d) & iron (≥27 mg/d) from foods, SSB (0 servings/d), red & processed meat (0 servings/d), trans fat % of Energy (≤0.5), sodium (mg/d, lowest decile). Max score of 10 for each component. Intakes scored proportionally. aMED: 8 items: Same as Chatzi et al. (2012) but with the removal of dairy and separate groups for fruit & nuts.	The alternate Mediterranean diet (aMED) (0 (low) to 8 (high))
Rifas-Shiman et al. (2009)	Project Viva (US)	Prospective cohort 1999 - 2002	1,777 (T1); 1,666 (T2)	Singleton birth, <22 wks gestation at recruitment, English literate	Self-administered 166 item FFQ (T1 & T2; past 3 m)	A priori 9 items score (modified HEI-1995): Unless specified, same intake criteria as Poon et al. (2013): veg, fruit, ratio of white meat (fish and poultry) to red meat (≥4:1), cereal fibre (25 g/d), trans fat, ratio of PUFA to SFA (≥1), folate, calcium & iron. Residually energy-adjusted nutrients.	Alternate Healthy Eating Index for Pregnancy (AHEI-P) (0 (low) to 90 (high))
Rodriguez-Bernal et al. (2010)	INMA (Spain)	Prospective cohort (Valencia area only) 2004 - 2005	787	>16yrs, singleton birth, residing in study area, no chronic HT	Interviewer administered 101 item FFQ (T1; since LMP)	A priori 10 items score (modified HEI-1995): Same items as Rifas-Shiman et al. (2009) with the addition of nuts and soy (≥1 serving/d). Residually energy-adjusted nutrients. Max score of 10 for each component, 1 point subtracted for each 10% decrease in intake	Alternate Healthy Eating Index (AHEI) (0 (low) to 100 (high))
Saunders et al. (2014)	TIMOUN Mother–Child Cohort Study (French West Indies)	Prospective cohort 2004-2007	728	Singleton birth without birth defects	Interviewer administered 217 item FFQ (post-partum; pregnancy)	A priori 9 items score: same as Chatzi et al. (2012) with the inclusion of alcohol	Mediterranean diet score (0 (low) to 9 (high))

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure
Shapiro et al. (2016)	The Healthy Start Study(US)	Prospective cohort 2010-2014	1,079	⩾16 years; GA>32 wks; singleton birth; no GDM	Automated Self-Administered 24-h Dietary Recall (ASA24); multiple recalls throughout pregnancy (mean:2, range: 1-8)	A priori 12 items score based on US 2010 guidelines for healthy eating: total fruit, whole fruit, total veg, greens and beans, whole grains, dairy, total protein foods, seafood & plant proteins, ratio of PUFA/ MUFA:SFA, refined grains, sodium, empty calories. Based on energy densities (amount per 1000 kcal). Max score of 10 for whole grains, dairy, fatty acids, refined grains, sodium; max score of 20 for empty calories; max score of 5 for remaining items.	Healthy Eating Index-2010 (HEI-2010) (0 (low) to 100 (high))
Thompson et al. (2010)	The Auckland Birthweight Collaborative Study (New Zealand)	Case-control study 1995-1997	1,714	Singleton birth; no birth defects; live in study area	Self-administered 71 item FFQ (two post-partum;T1 & T3)	A posteriori PCA on 71 food groups. Number of components based on scree plot & % variance explained. Standardised scores.	Fusion; Junk; Traditional % variance: 13.84
Timmermans et al. (2012)	Generation R study (Netherlands)	Prospective cohort 2001-2006	3,207	Singleton birth; no fertility treatment or drug abuse	Self-administered 293 item FFQ (T2: past 3 m)	A posteriori Logistic regression analysis used to predict the occurrence of IUGR as a function of 21 food groups. Dietary data residually energy adjusted	Mediterranean diet adherence
Wen et al. (2013)	The Healthy Beginnings RCT (Australia)	Longitudinal study sample from RCT 2008	368	>16 yrs; 1st pregnancy; 24-34 wks gestation, English literate; live in study area	Face-to-face interview during T2-T3	A priori Women categorised into 'Junk food ' or 'No junk food' if they consumed: ≥ 2 cups of soft drinks/d, ≥ 2 fast food meals/wk, ≥ 2 times processed meat/wk, or ≥ 2 times chips/wk	Junk food diet
Wolff & Wolff (1995)	Hispanic Health and Nutrition Examination Survey (HHANES) (US)	Cross-sectional survey 1982-1984	549 mothers; 778 infants	Women whose children were included in HHANES; singleton birth; no DM; US birth	57 item FFQ (5 yrs post-partum; current diet)	A posteriori PCA on 18 food groups (47 of the 57 foods were included in the analysis and condensed into 18 food groups). Number of components based on eigenvalues >1	Nutrient dense; Traditional; Transitional; Nutrient dilute; Protein rich; HF dairy; Mixed dishes % variance: 59

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure

ART, assisted reproduction; d, day; FFQ, food frequency questionnaire; LMP, last menstrual period; m, month; MUFA, monounsaturated fatty acids; n, number; NR, not reported; PUFA, polyunsaturated fatty acids; RCT, randomized controlled trial; SD, standard deviation; SFA, saturated fatty acids; SSB, sugar-sweetened beverages; T, trimester; yrs, years; wks, weeks

2.4.2.6 Quality of studies

All of the studies were observational in design, and are therefore similarly at risk of the bias commonly associated with observational studies. Sixteen were of a prospective cohort design, one was a case-control study and one was cross-sectional in design. The latter two are, according to the CRD's hierarchy of evidence, more susceptible to bias (CRD, 2009). The main differences between these three types of study designs relate to when the exposure and the outcome of interest is measured. For cohort studies the exposure is measured in the present and the outcome is assessed in the future, whereas for case-control studies, the outcome is measured before the exposure and for cross-sectional studies, both the exposure and the outcome is measured at the same time point (Margetts and Nelson, 1997). For the latter this means that temporality becomes impossible to ascertain. For cohort studies this often results in loss to follow-up, however for pregnancy outcome studies with a relatively short follow-up, dropout rates should be minimal. But even for studies of the same design, differences in terms of sampling, methods of data collection and analysis may have introduced bias.

For the majority of studies mothers were recruited by researchers at pre-natal visits in routine care at hospitals or GPs. All participated on a voluntarily basis and no incentives were given. It is therefore likely that the study populations differ from the general population in certain aspects and selection bias may have been introduced. The sample sizes differed greatly between studies with only two using nationally representative samples (Hillesund et al., 2014; Knudsen et al., 2008). Despite being nationally representative, not all mothers initially recruited had data on dietary exposures and it could be argued that those who did not might differ from the study sample in some way, something which is recognised (but not tested) by both studies mentioned in the above. Many of the studies assessed whether respondents differed from non-respondents in terms of characteristics such as age, smoking, educational status, social class and ethnicity and more often than not respondents tended to be older women with a higher educational and social class status and less likely to smoke. This implies that the samples were unrepresentative of the sampling frame and the target population and therefore the external validity and generalisability of the findings of the study sample to the general population should be questioned; however, that is not to say that the internal validity of the findings was affected.

Study quality also differed in the validity of data collection methods, in particular dietary assessment. Measuring diet in an accurate way is one of the greatest challenges faced by research in nutritional epidemiology (Willett, 2013; Margetts and Nelson, 1997). As

Margetts & Nelson have highlighted in their book ‘Design Concepts in Nutritional Epidemiology’ (1997) no matter how you measure diet there will always be errors; if you use prospective methods such as food diaries you are likely to actually change the dietary behaviour and if you use retrospective methods such as FFQs or 24 hour recalls you are reliant on memory as well as honesty (Margetts and Nelson, 1997). This holds true even for measures which are interviewer administered. In particular for FFQs, the most commonly used approach in the studies reviewed, assumptions about food portion sizes have been made and not all studies reviewed provided guidance for participants on these. In addition, a FFQ is only as good as its foods listed and may therefore not capture total diet something which is better assessed by 24 hour recalls. Rather, a well-designed FFQ gives a good proxy of habitual intake and is less prone to within-person day to day variation which is something daily consumption methods are more vulnerable to. The FFQs used in the reviewed studies varied greatly in number of items and there is as yet no clear consensus on how many items to include in order to best assess dietary intake. Cade et al. (2004) suggest using a comprehensive food list and using single food items rather than food groups to avoid losing important information (Cade et al., 2004b). It could therefore be argued that those studies which used FFQs limited in number of food items were more prone to error in their assessment of diet.

A poor measure of diet is likely to obscure any exposure-outcome relationship. However, steps have been taken to assess the degree to which the observed intake is likely to differ from the true intake in the form of validation studies, where the dietary measure (the test measure) is compared to another measure, usually a more involved and therefore more accurate method. For a validation study to be useful the test measure and the reference measure should be administered to the same individuals, ideally a sub-group within the study population (if it is a large study population), or at least a comparative population and should be administered at similar time frames. It is common to assess the association between either nutrient intakes or consumption frequencies of food groups from the test and reference measure using a correlation coefficient. It is then assumed that if the correlation coefficient is high (which it would be as, unless using biomarkers, they measure the same thing, namely diet) and statistically significant the test measure is a suitable proxy for the reference measure. However, there may be poor agreement between the measures even though the correlation is high. Approaches to describing the agreement between test and reference measures are available and include Bland-Altman plots of the difference between the reference and test measure plotted against the average of the two measures or the Kappa statistic if the data are categorical (Giavarina, 2015; Altman and Bland, 1983).

Of the 18 studies assessing maternal dietary patterns in relation to size at birth, 16 reported on some measure of validation, using a variety of reference measures such as 24 hour recalls, food diaries, weighed records and biomarkers. For the dietary measure used in the Rhea cohort (which was analysed concurrently with data from INMA), Chatzi et al. (2013) reported no details of validation and neither did Wolff & Wolff (1995) in their analysis of the HHANES data, nor Coelho Nde et al (2015) who used a 29 item FFQ simplified from an 80 item validated FFQ. The majority of studies used correlation as a validation measure of association (Bouwland-Both et al., 2013; Chatzi et al., 2012; Colon-Ramos et al., 2015; Knudsen et al., 2008; Lu et al., 2016; Poon et al., 2013; Rodriguez-Bernal et al., 2010; Timmermans et al., 2012), others reported on correlation as well as comparable classification (Hillesund et al., 2014; Okubo et al., 2012; Saunders et al., 2014) and one study used regression techniques (Rifas-Shiman et al., 2009). Some measures were only validated in relation to certain dietary exposures, e.g. for the ALSPAC study, only maternal fish consumption was assessed against concentrations of n-3 LC-PUFA26 and mercury concentrations in maternal blood (Daniels et al., 2004; Williams et al., 2001). None of the studies assessed agreement between the methods and four studies did not report on the measure of association used in the validation study (Poon et al., 2013; Shapiro et al., 2016; Thompson et al., 2010; Wen et al., 2013). Where validation results were not reported, it is assumed that the validated tools were a close enough proxy of the reference method as none of the studies attempted to make adjustments to any measurement errors.

Only five studies validated the dietary assessment tool in a sub-sample of the original pregnancy cohort (Hillesund et al., 2014; Knudsen et al., 2008; Northstone et al., 2008; Saunders et al., 2014; Lu et al., 2016). Two studies used tools validated in similar pregnant populations (Rifas-Shiman et al., 2009; Timmermans et al., 2012; Bouwland-Both et al., 2013), whereas tools used in other studies were validated in comparable adult populations (Chatzi et al., 2012; Rodriguez-Bernal et al., 2010; Wen et al., 2013). Three studies used tools validated in populations not representative of the study population (e.g. children, elderly or diseased) (Thompson et al., 2010; Colon-Ramos et al., 2015; Okubo et al., 2012) and Poon et al. (2013) used a modified version of the validated Diet History Questionnaire (DHQ), which had not been validated in a pregnant population. Shapiro et al. (2016) did not provide any details on the validation of ASA24, this tool however has been validated in adults and kids, but not in a pregnant population.

In addition to the error arising from a poor measurement of dietary intake researchers are reliant of food composition tables to estimate nutrient intakes, which can be out of date or lacking in certain foods. For example for Saunders et al.'s (2014) French-Caribbean cohort, no Caribbean food tables were available and they therefore had to use a mixture of food composition tables from the US, France and Canada which may not only be missing essential items but might also provide different estimates of nutrient profiles for foods. In addition, in their analysis of data from the Cretan Rhea cohort, Chatzi et al. (2012) used UK food composition tables which are likely to be missing out on several items specific to a Cretan diet.

As has been highlighted in the previous section on dietary pattern analysis (section 2.4.2.3) the decisions concerning data preparation as well as analysis of dietary patterns are subjective in nature which can influence the quality of the studies. In terms of *a posteriori* techniques, PCA as well as cluster analysis are data transformation methods and as such there are no inherent assumptions to be met. Some studies chose to standardise data before analysis in order to remove the extraneous effect of variables with large variances whereas others did not. Some chose to assess relative dietary intake and energy adjusted data prior to PCA whereas others adjusted for energy intake at a later stage or not at all. As highlighted by Walter Willett (2013), the adjustment of energy intake in nutritional epidemiology deserves special consideration as it is important to demonstrate that any association between diet and disease is independent of caloric intake (Willett, 2013). For example when it comes to dietary patterns that represent a diet high in energy dense foods any association observed with offspring growth outcomes may not be a real effect of the foods themselves, rather an association with actual energy intake. It is therefore concerning that several studies failed to adjust for energy intake. Of the studies adjusting for energy intake, some did so prior to and others did so after deriving dietary patterns. Northstone et al. (2008) examined the effect of the timing of energy adjustment on maternal dietary patterns extracted using PCA on data collected via a FFQ and their association with birth weight. As expected, correlations between food items and components were reduced for the energy adjusted dietary data compared to the unadjusted dietary data and one component, the 'processed' component, was lost. Nevertheless, they found no notable difference in the size of the effects of the dietary pattern scores on birth weight, whether energy was adjusted for before entry into the PCA or after (Northstone et al., 2008). Therefore, studies which adjusted for energy intake were considered of similar quality regardless of the timing of adjustment.

The reasoning behind the aggregation of food data into a set number of food groups as well as choice of components to retain from a PCA was sometimes unclear and varied from study to study. Both of which are likely to influence the results of any dietary pattern analysis; as evidenced by Wolff & Wolff (1995) who had the smallest sample size as well as number of food groups entered into a PCA, yet they retained 7 components based on one criterion of observed eigenvalues above 1. They did not assess the general interpretability of the patterns nor the scree plot (Wolff and Wolff, 1995).

As for dietary patterns identified *a priori* there were two approaches used, those based on set cut-off values (e.g. the HEI) and those based on population intake values such as the median (e.g. the MD or the NND score where 0 is assigned to values below the median and 1 to values above). There are pros and cons to both approaches. Set values lend themselves better to between study comparisons; however this comparison is seldom useful (or insightful) when study or country specific portion sizes and food composition tables are used to estimate food and nutrient intakes. Alternatively, the median may not be related to a healthy value, nor will it be the same for different populations. The major advantage of using this approach is the straight forward scoring system resulting in a clear differentiation between subjects (Waijers et al., 2007). As was the case with dietary patterns identified using *a posteriori* techniques, not all studies energy adjusted the dietary data when deriving the index scores or in their regression models thus introducing similar bias to their findings.

In terms of statistical analysis the quality of the studies was found to be predominantly good with the majority of studies using appropriate and well-considered statistical analyses that adjusted for important confounders. Only one study did not assess confounding as this would have influenced the purpose of their analysis (Northstone et al., 2008) and another study only adjusted for maternal weight and gestational age, explained by the use of stepwise regression. Stepwise regression is a data driven approach in its choice of confounders and therefore gives no consideration to the existing evidence on important confounders from the literature and it can lead to an overestimation of parameters, incorrect variance estimates of those parameters resulting in small standards errors and narrow confidence intervals (Harrell, 2001). Despite this it was used in 5 out of the 18 studies. Even with the adjustment for many important factors residual confounding remain an issue in observational studies such as these as it is impossible to fully adjust for confounding.

The studies which used a more exhaustive FFQ, appropriate food composition tables to estimate nutrient intakes which had been validated in terms of a range of nutrients in a comparable population, adjusted for energy intake, based the decision of components to retain from PCA on more than just the amount of variance explained and included important confounders (Chatzi et al., 2012; Hillesund et al., 2014; Rifas-Shiman et al., 2009; Rodriguez-Bernal et al., 2010; Timmermans et al., 2012) were considered of a higher quality than those that used simplified FFQs with no clear evidence of validation or validation in inappropriate populations, neglected to adjust for energy intake and omitted other important confounders.

2.4.2.7 Findings

Findings from studies investigating size at birth in relation to maternal dietary patterns during pregnancy are presented in Table 4 below. All effect estimates presented were extracted from maximally adjusted models.

2.4.2.7.1 Birth weight & weight-for-age

Eleven studies reported results on birth weight expressed in grams or standard deviation scores (or Z-scores) in relation to maternal dietary patterns. Of these, nine found significant associations (P<0.05). Chatzi et al. (2012) found in their analysis of the Mediterranean INMA cohort that mothers with a higher MD adherence had babies weighing nearly 90 g more (SE: 33.4 g, P=0.009) compared to mothers with a low MD adherence. In agreement with this, Timmermans et al. (2012) found that compared to mothers with a high MD adherence, those with a low adherence had babies born with a 72 g lower birth weight and 0.2 lower birth weight SD score (Timmermans et al., 2012). They tested for possible effect modification by maternal educational status as well as smoking during pregnancy by introducing the variables as interaction terms in the models and found that for high educated mothers, compared to those with high MD adherence, those with middle and low adherence had babies born with a 131 g and 160 g lower birth weight respectively. Similarly, compared to non-smoking mothers with a high MD adherence, smoking mothers with a high MD adherence had babies born with a 66 g lower birth weight, whereas smoking mothers with a low MD adherence had babies born with a birth weight over 200 g lower (Timmermans et al., 2012). They also tested for effect modification by parity, BMI and folic acid use, but found no significant interaction (all interaction terms P>0.10). Chatzi et al. (2012) found no significant association with the MD score for the Atlantic INMA cohort or the Rhea cohort (Chatzi et al., 2012) and neither did Poon et al. (2013) in their analysis of data from a US birth cohort.

Coelho Nde et al. (2015) observed positive associations between a ‘Snack’ based dietary pattern and birth weight, which appeared strongest in age stratified analyses where younger mothers (aged 10-19 years) had babies born with an increased birth weight of 57 g (P=0.04) for every 1 unit increase in the Snack dietary pattern score. They did not however assess the interaction between age and the dietary patterns and found no significant association with a Prudent, Traditional or Western dietary pattern. Wen et al. (2013) found that compared to mothers consuming a ‘Junk food diet’ non-consumers had 74% lower odds of having babies born with high birth weight (>4 kg), they however did not test whether this effect was more pronounced in younger mothers nor did they adjust for maternal age. Bouwland-Both et al. (2013) found insignificant positive associations between birth weight SD scores and an ‘Energy-rich’ dietary pattern.

Lu et al. (2016) found that compared to mothers eating a ‘Cereals, eggs & Cantonese soups’ dietary pattern, mothers eating a ‘Fruits, nuts and Cantonese desserts’ dietary pattern and mothers eating a ‘Varied’ dietary pattern had babies born with around 0.05 higher birth weight Z-scores (Lu et al., 2016). Northstone et al. (2008) found in their univariable analysis positive associations with a ‘Health conscious’ dietary pattern (Northstone et al., 2008). Similarly, Wolff & Wolff (1995) observed an increase of 20 g in birth weight for every one unit increase in a ‘Nutrient dense’ dietary pattern score, characterised by high intakes of fruits, vegetables and low fat dairy products. They found higher (36 g increase in birth weight) but less significant effects with a ‘Protein rich’ dietary pattern characterised by high intakes of dairy desserts, low fat meats and processed meats and observed negative association with birth weight for a ‘Nutrient dilute’ dietary pattern characterised by high intakes of salty snacks, non-dairy and sugar (Wolff and Wolff, 1995). Okubo et al. (2012) found that women with a ‘Rice, fish and vegetables’ dietary pattern had babies born with a higher birth weight compared to mothers with a ‘Wheat products’ and a ‘Meat and eggs’ dietary pattern (Okubo et al., 2012).

Poon et al. (2013) and Shapiro et al. (2016) found no significant associations with the AHEI-P and HEI-2010 respectively, whereas Rodriguez-Bernal et al. (2010) showed that compared to women with the lowest AHEI-P scores women with higher scores had babies born with higher birth weight, with the highest effect observed for the 4th quintile (126 g, 95% CI: 39, 214, P_{trend}=0.009).

Colon-Ramos et al. (2015) reported result on WFA Z-scores and found no significant association when comparing mothers following ‘Healthy-processed’, ‘Healthy Southern’, ‘Mixed’, ‘Processed’, ‘Processed-Southern’ or ‘Southern’ dietary patterns to a ‘Healthy’ dietary pattern characterised by high intakes of vegetables, fruits, non-fried fish and chicken, and water (Colon-Ramos et al., 2015).

2.4.2.7.2 Birth length & length-for-age

Two studies reported findings on birth length. Similarly to the results for birth weight, Chatzi et al. (2012) only observed significant positive finding for the Mediterranean INMA cohort, where compared to women with low MD scores, those with high MD adherence had babies born 0.3 cm longer (SE:0.15, P=0.04) (Chatzi et al., 2012). Whereas Okubo et al. (2012) observed no significant differences in birth length between mothers consuming a ‘Rice, fish & vegetable’ dietary pattern, a ‘Wheat products’ dietary pattern and a ‘Meat & eggs’ dietary pattern (Okubo et al., 2012). Similarly, Colon-Ramos et al. (2015) found no significant association with length-for-age Z-scores when comparing mothers following ‘Healthy-processed’, ‘Healthy Southern’, ‘Mixed’, ‘Processed’, ‘Processed-Southern’ or ‘Southern’ dietary patterns to a ‘Healthy’ dietary pattern (Colon-Ramos et al., 2015).

2.4.2.7.3 Head circumference

Four studies reported findings on head circumference. As opposed to the findings reported on birth weight and birth length, Chatzi et al. (2012) only observed a significant association with the MD score in the Rhea cohort and only for mothers with a medium level of adherence where babies were born with a 0.23 cm smaller head circumference compared to babies born of mothers in the lowest adherence level category (P=0.05) (Chatzi et al., 2012). Colon-Ramos et al. (2015) found that compared to mothers consuming a ‘Healthy’ dietary pattern, characterised by high intakes of vegetables, fruits, non-fried fish/chicken and water, mothers consuming a ‘Healthy-processed’ dietary pattern had babies born with 0.36 higher head circumference Z-scores (P<0.05) (Colon-Ramos et al., 2015). Similarly, Okubo et al. (2012) found that mothers with a ‘Rice, fish and vegetable’ dietary pattern, characterised by high intakes of rice, potatoes, nuts, pulses, fruits, green and yellow vegetables, white vegetables, mushrooms, seaweeds, Japanese and Chinese tea, fish, shellfish, sea products, miso soup and salt-containing seasoning, had babies born with a higher head circumference (Okubo et al., 2012). Rodriguez-Bernal et al. (2010) found that mothers in the 2nd and 4th quintile of the AHEI-P had babies born with a significantly higher head circumference (0.30 cm and 0.38 cm respectively) compared to babies born of mothers in the lowest quintile category, the P for trend however was not significant.

2.4.2.7.4 Fat-free mass (FFM), Fat mass (FM)

Only one study reported results on FFM and FM. Shapiro et al. (2016) assessed the HEI-2010 score expressed as a binary variable (≤57 & > 57) in relation to FFM and FM. They observed no significant association with FFM but found that compared to mothers with HEI scores ≤57, mothers with HEI scores >57 had babies born with a higher FM expressed in grams (21 g, 95% CI: 1.49, 40.0, P<0.05) and as a percentage (0.58% 95% CI:0.07, 1.1, P<0.05).

2.4.2.7.5 Fetal growth restriction (FGR)

Three studies reported on FGR for birth weight (Chatzi et al., 2012; Rodriguez-Bernal et al., 2010; Saunders et al., 2014), two on FGR for birth length and two on FGR for head circumference (Chatzi et al., 2012; Rodriguez-Bernal et al., 2010). Of the studies which reported results on FGR for birth weight, Chatzi et al. (2012) found similarly to their results for birth weight only a significant association in the Mediterranean INMA cohort, where mothers with higher MD adherence had 50% lower odds of having a baby born FGR (95% CI: 0.28, 0.90, P=0.02) compared to mothers with a low MD adherence (Chatzi et al., 2012). Saunders et al. (2014) on the other hand found in their cohort of French Caribbean mothers no significant association between FGR for birth weight and the MD score. Stratifying by maternal BMI and infant sex did not alter those results (Saunders et al., 2014). Rodriguez-Bernal et al. (2010) found that women with higher AHEI-P scores were less likely to have babies born FGR. Mothers in the highest quintile category had 76% lower odds (95% CI: 0.10, 0.55, P_{trend}=0.001) of having FGR born babies compared to those in the lowest quintile (Rodriguez-Bernal et al., 2010). There were no significant associations observed with FGR for birth length or FGR for head circumference.

2.4.2.7.6 Weight-for-length (WFL)

Two studies reported on result for WFL and neither found any significant associations with maternal dietary patterns derived from PCA (Colon-Ramos et al., 2015) nor with adherence to the aMED score (Poon et al., 2013).

2.4.2.7.7 Large for gestational age (LGA)

Four studies reported on result for LGA, of which only one observed a significant association. Hillesund et al. (2014) found in their analysis of data from a large Norwegian birth cohort that mothers with high adherence to a NND score (see Table 3 above for a description of the NND score) had 7% higher odds of having babies born LGA compared to mothers in the lowest adherence category (95% CI: 1.00, 1.15) (Hillesund et al., 2014). Poon et al. (2013) found no significant association between LGA and the aMED. And neither Poon et al. (2013) nor Rifas-Shiman et al. (2009) observed any significant associations with the AHEI-P, the latter of which tested for associations with AHEI-P in both the 1st and 2nd trimester separately (Rifas-Shiman et al., 2009).

2.4.2.7.8 Small for gestational age (SGA)

Seven studies reported on findings for SGA for birth weight with one study additionally reporting on SGA for birth length and head circumference (Hillesund et al., 2014; Knudsen et al., 2008; Poon et al., 2013; Rifas-Shiman et al., 2009; Thompson et al., 2010). There were no significant associations observed for SGA for birth length or SGA for head circumference (Okubo et al., 2012). Four studies showed significant associations with SGA for birth weight. Hillesund et al. (2014) found a protective effect of a higher NND score against the odds of having babies born SGA. But as with LGA, the effect size was small with mothers in the highest NND tertile category having 8% lower odds of having babies born SGA (95% CI: 0.86, 0.99, P=0.025) compared to mothers in the lowest tertile category (Hillesund et al., 2014). Similarly, Knudsen et al. (2008) found that mothers with a ‘Health conscious’ dietary pattern characterised by high intakes of fruits, vegetables, fish, poultry, breakfast cereals, vegetable juice and water had lower odds of having babies born SGA (OR: 0.74 95% CI: 0.64, 0.86, P=0.0001) compared to women with a ‘Western dietary pattern’ characterised by high intakes of high-fat dairy, refined grains, processed and red meat, animal fat (butter and lard), potatoes, sweets, beer, coffee and high-energy drinks. Conversely, mothers in the intermediate dietary pattern (with high intakes of low-fat dairy and fruit juice and with consumption of the remaining food groups in between the ‘Western’ and the ‘Health conscious’ dietary patterns) had even lower odds of having babies born SGA; 32% (95% CI: 0.55, 0.84, P=0.0004) vs. 26% in the ‘Health conscious’ dietary pattern (Knudsen et al., 2008). Okubo et al. (2012) found that compared to women in the ‘rice, fish and vegetables’ pattern (a more traditional dietary pattern for a Japanese population), those in the ‘wheat products’ pattern, characterised by high intakes of bread, confectioneries, fruit & vegetable juice and soft drinks, had significantly higher odds of having a baby born SGA (OR: 5.24, 95% CI: 1.13, 24.4). Similarly, Thompson et al. (2010) showed that a dietary pattern considered traditional to their New Zealand case-control study of pregnant women, characterised by high intakes of apples/pears, citrus fruit, kiwifruit/feijoas, bananas, green vegetables, root vegetables, peas/maize, dairy food/yogurt and water, had a protective effect against the odds of having a baby born SGA. For every 1 unit increase in the ‘traditional’ dietary pattern score the mothers had over 20% lower odds of having a baby born SGA (95% CI: 0.66, 0.96). This association was only apparent for dietary patterns in the 1st trimester not the 3rd trimester.

Table 4. Study results: Maternal dietary patterns and offspring birth size

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
Bouwland-Both et al. (2013)	Tertiles (low, med, high); continuous score	BW SD score (sex & GA adjusted) n=847		Stepwise MLR	Height, BMI, education, parity, smoking, DBP, SBP, age, folic acid supplement, duration of LMP, paternal height & BMI, infant's sex	Energy-rich: Low: ref (0) Med: 0.05 (95% CI:-0.013, 0.23) High: 0.15 (95% CI:-0.03, 0.33) Continuous: 0.04 (95% CI:-0.04, 0.11) Mediterranean: NS - estimates NR Western: NS - estimates NR
Chatzi et al. (2012)	Categories of MD score: Low: <3; Med: 4-5; High: 6-8	BW (g)	INMA - Atlantic n=1,074	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, parity, BMI, paternal education, parental social class	Low: ref (0) Med: -26.5 g (SE:26.0, P=0.31) High: -82.9 g (SE:47.7, P=0.08)
		BW (g)	INMA-Mediterranean n=1,387	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, parity, parental BMI, social class	Low: ref (0) Med: 55.2 g (SE:23.5, P=0.019) High: 87.8 g (SE:33.4, P=0.009)
		BW (g)	RHEA n=889	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, BMI, education	Low: ref (0) Med: -33.7 g (SE:31.8, P=0.29) High: -20.4 g (SE:42.3, P=0.63)
		BL (cm)	INMA - Atlantic n=1,074	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, parity, BMI, paternal age, social class	Low: ref (0) Med: -0.16 cm (SE:0.12, P=0.19) High: -0.25 cm (SE:0.22, P=0.245)
		BL (cm)	INMA-Mediterranean n=1,387	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, parity, BMI & social class	Low: ref (0) Med: 0.13 cm (SE: 0.10, P=0.20) High: 0.30 cm (SE: 0.15, P=0.04)
		BL (cm)	RHEA n=889	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, height, education	Low: ref (0) Med: -0.43 cm (SE: 0.18, P=0.08) High: -0.06 cm (SE: 0.24, P=0.79)
		HC (cm)	INMA - Atlantic n=1,074	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, parity, BMI, education	Low: ref (0) Med: 0.03 cm (SE: 0.09, P=0.77) High: -0.06 cm (SE: 0.16, P=0.71)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
		HC (cm)	INMA-Mediterranean n=1,387	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, parity, BMI, education, alcohol intake	Low: ref (0) Med: 0.03 cm (SE: 0.07, P=0.65) High: 0.16 cm (SE: 0.10, P=0.12)
		HC (cm)	RHEA n=889	Stepwise MLR	Infant's sex, GA, smoking status, age, energy intake, BMI, education	Low: ref (0) Med: -0.23 cm (SE: 0.12, P=0.05) High:-0.20 cm (SE: 0.16, P=0.21)
		FGR-BW (<10th centile, adjusted for GA, sex, parental height, weight, parity)	INMA - Atlantic n=96/1,074	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, social class	Low: ref (1) Med:1.24 (95%CI:0.81,1.89,P=0.33) High: 0.97 (95%CI:0.42,02.26, P=0.94)
		FGR-BW (as above)	INMA-Mediterranean n=143/1,387	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, BMI, social class	Low: ref (1) Med: 0.76 (95%CI:0.54,1.06, P=0.11) High: 0.50 (95%CI:0.28,0.90, P=0.02)
		FGR-BW (<10th centile, adjusted for GA, sex, parental height, weight & interaction of GA with weight)	RHEA n=71/889	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, education, paternal age	Low: ref (1) Med: 1.82 (95%CI:0.95, 3.49, P=0.07) High: 1.96 (95%CI:0.90, 4.25, P=0.09)
		FGR-BL (<10th centile, adjusted for GA, sex, parental height, weight, parity)	INMA - Atlantic n=98/1,074	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, education	Low: ref (1) Med: 1.33 (95%CI:0.0.87,2.04, P=0.19) High: 0.63 (95%CI:0.23,1.76, P=0.38)
		FGR-BL (as above)	INMA-Mediterranean n=128/1,387	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, education	Low: ref (1) Med: 1.01 (95%CI:0.70,1.47, P=0.95) High: 0.95 (95%CI:0.55, 1.62, P=0.84)
		FGR-BL (<10th centile, adjusted for GA, sex, parental height, weight & interaction of GA with weight)	RHEA n=60/889	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, paternal education	Low: ref (1) Med: 1.39 (95%CI:0.72, 2.68, P=0.33) High: 0.90 (95%CI:0.35, 2.30, P=0.82)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
		FGR-HC (<10th centile, adjusted for GA, sex, parental height, weight, parity)	INMA - Atlantic n=103/1,074	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, paternal age, BMI, education	Low: ref (1) Med: 0.88 (95%CI:0.57,1.346, P=0.54) High: 1.11 (95%CI:0.53,2.33, P=0.78)
		FGR-HC (as above)	INMA-Mediterranean n=137/1,387	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, BMI, alcohol intake, education, social class.	Low: ref (1) Med: 1.15 (95%CI:0.80,1.62, P=0.46) High: 1.07 (95%CI:0.63,0.83, P=0.80)
		FGR-HC (<10th centile, adjusted for GA, sex, parental height, weight & interaction of GA with weight)	RHEA n=74/889	Stepwise MLoR	Infant's sex, GA, smoking status, age, energy intake, alcohol intake, education.	Low: ref (1) Med: 1.63 (95%CI:0.89, 2.96, P=0.11) High: 1.64 (95%CI:0.76, 3.56, P=0.21)
Coelho Nde et al. (2015)	Continuous scores (per 1 unit increase)	BW (g) n=1,298		MLR	Other dietary patterns, age, education, marital status, social class, parity, pre-pregnancy BMI, prenatal care adequacy, smoking, delivery type, infant's sex	Positive association between Snack pattern and BW (data NR)
		BW (g)	Maternal age: 10-19 yrs n=NR	MLR	Same as for whole sample	Prudent: 55.35 g (P=0.13) Traditional: 11.45 g (P=0.72) Western: 15.88 g (P=0.62) Snack: 56.64 g (P=0.04)
		BW (g)	Maternal age: ≥20 yrs n=NR	MLR	Same as for whole sample	Prudent: 12.57 g (P=0.46) Traditional: 19.90 g (P=0.24) Western: 10.17 g (P=0.55) Snack: 6.57 g (P=0.75)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
Colon-Ramos et al. (2015)	Continuous scores (per 1 unit increase)	WFL Z-score (sex and GA adjusted) n=923		MLR	(if independently & significantly associated with exposure & outcome in bivariate models) Age, ethnicity, pre-pregnancy BMI, education, alcohol, GWG	Healthy: ref (0) Healthy-processed: 0.16 (SE:0.16) Healthy-Southern: 0.17 (SE:0.19) Mixed: 0.15 (SE:0.14) Processed: 0.23 (SE:0.14) Processed-Southern: -0.07 (SE:0.19) Southern: -0.28 (SE:0.19)
		WFA Z-score (sex and GA adjusted) n=1,011		MLR	Same as for WFL	Healthy: ref (0) Healthy-processed: 0.12 (SE:0.11) Healthy-Southern: -0.09 (SE:0.14) Mixed: -0.01 (SE:0.10) Processed: -0.03 (SE:0.14) Processed-Southern: -0.15 (SE:0.14) Southern: -0.07 (SE:0.14)
		LFA Z-score (sex and GA adjusted) n=1,008		MLR	Same as for WFL	Healthy: ref (0) Healthy-processed: 0.07 (SE:0.15) Healthy-Southern: 0.05 (SE:0.18) Mixed: -0.09 (SE:0.14) Processed: -0.17 (SE:0.19) Processed-Southern: -0.12 (SE:0.18) Southern: 0.17 (SE:0.18)
		HC Z-score (sex and GA adjusted) n=999		MLR	Same as for WFL	Healthy: ref (0) Healthy-processed: 0.36 (SE:0.15, P≤0.05) Healthy-Southern: 0.04 (SE:0.18) Mixed: 0.09 (SE:0.14) Processed: -0.18 (SE:0.19) Processed-Southern: -0.06 (SE:0.19) Southern: 0.05 (SE:0.18)
Hillesund et al. (2014)	Categories of NND score: Low: 0–3	LGA (>90th sex-specific BW centile)		Multinomial LoR	Age, parity, pre-pregnancy BMI, height, education, smoking, GDMs, exercise during pregnancy, energy intake	Low: ref (1) Med: 1.04 (95% CI: 0.97, 1.12) High: 1.07 (95% CI: 1.00, 1.15, P=0.048)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
	Medium: 4–5 High: 6–10	n=7,427/66,597				
		SGA (<10th sex-specific BW centile) n=6,959/66,597		Multinomial LoR	Same as for LGA	Low: ref (1) Med: 0.95 (95% CI: 0.89, 1.02) High: 0.92 (95% CI: 0.86, 0.99, P=0.025)
Knudsen et al. (2008)	Continuous scores (per 1 unit increase)	SGA (<2.5th centile of sex & GA specific BW Z-score) n=1,112/44,612		Multinomial LoR	Age, smoking status, parity, height, pre-pregnancy weight, paternal height	Western diet: ref (1) Intermediate: 0.68 (95% CI: 0.55, 0.84, P=0.0004) Health conscious: 0.74 (95% CI: 0.64, 0.86, P=0.0001)
Lu et al. (2016)	Continuous scores (per 1 unit increase)	BW Z-score (sex & GA adjusted) n=6954		MLR	Age, education level, monthly income, parity, passive smoking during pregnancy, alcohol intake, folic acid supplement use, pre-pregnancy BMI, GDM	Cereals, eggs & Cantonese soups: ref (0) Dairy: 0.02 (95% CI:-0.03, 0.13) Fruits, nuts, and Cantonese desserts: 0.05 (95% CI:0.07, 0.24, P<0.05) Meats: -0.01 (95% CI:-0.11, 0.05) Veg: 0.01 (95% CI:-0.04, 0.11) Varied: 0.04 (95% CI:0.01, 0.16, P<0.05)
		LGA (>90th centile of sex & GA specific BW Z-score) n=733/6,954		MLoR	Same as for BW	Cereals, eggs & Cantonese soups: ref (1) Dairy: 1.01 (95% CI:0.75, 1.35) Fruits, nuts, and Cantonese desserts: 1.14 (95% CI:0.84, 1.54) Meats: 0.75 (95% CI:0.56, 1.02) Veg: 1.03 (95% CI:0.79, 1.36) Varied: 1.10 (95% CI:0.85, 1.42)

Reference	**Exposure expression**	**Outcome (s)**	**Comparison/ Subgroup**	**Statistical analysis**	**Adjustments***	**Results**
		SGA (<10^{th} centile of sex & GA specific BW Z-score) n=505/6,954		MLoR	Same as for BW	Cereals, eggs & Cantonese soups: ref (1) Dairy: 0.87 (95% CI:0.63, 1.21) Fruits, nuts, and Cantonese desserts: 0.76 (95% CI:0.53, 1.10) Meats: 0.95 (95% CI:0.69, 1.30) Veg: 0.77 (95% CI:0.56, 1.05) Varied: 0.77 (95% CI:0.57, 1.04)
Northstone et al. (2008)	Continuous scores (per 1 unit increase)	BW (g) n=12,053		LR	(dietary data energy adjusted using the residual method before PCA)	Health conscious: 34.99 g (95% CI: 25.46, 44.52, P<0.05) Traditional: 7.24 g (95% CI:-2.31, 16.8) Confectionary: -1.05 g (95% CI: -10.6, 8.5) Vegetarian: -17.06 g (95% CI: -26.63, -7.48)
Okubo et al. (2012)	Continuous scores (per 1 unit increase)	BW (g) (GA adjusted) n=803		MLR	Age, parity, height, pre-pregnancy BMI, GWG, GA at baseline survey, smoking, change in diet in the previous 1 month, supplement use, PA level, family structure, occupation, family income, education, season of data collection, medical problems in pregnancy, infant's sex	RFV: 3,153 g (95%CI: 3,104, 3,203) Wheat products: 3,073 g (95% CI: 3,036, 3,111) Meat & eggs: 3,105 g (95% CI: 3,069, 3,141) P (adjusted for multiple testing)= 0.045
		BL (cm) (GA adjusted) n=803		MLR	Same as for BW (g)	RFV: 49.2 cm (95%CI: 48.9, 49.4) Wheat products: 48.9 cm (95% CI: 48.7, 49.1) Meat & eggs: 48.9 cm (95% CI: 48.7, 49.1) P (adjusted for multiple testing)=0.177

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
		HC (cm) (GA adjusted) n=803		MLR	Same as for BW (g)	RFV: 33.6 cm (95%CI: 33.3, 33.8) Wheat products: 33.2 cm (95% CI: 33.0, 33.4) Meat & eggs: 33.4 cm (95% CI: 33.2, 33.5) P (adjusted for multiple testing)=0.036
		SGA-BW (<10th sex & GA specific BW centile) n=34/803		MLoR	Same as for BW (g)	RFV: ref (1) Wheat products: 5.24 (95% CI: 1.13, 24.4) Meat & eggs: 4.32 (95% CI: 0.92, 20.3)
		SGA-BL (<10th sex & GA specific BL centile) n=60/803		MLoR	Same as for BW (g)	RFV: ref (1) Wheat products: 0.98 (95% CI: 0.46, 2.09) Meat & eggs: 1.04 (95% CI: 0.50, 2.16)
		SGA-HC (<10th sex & GA specific HC centile) n=70/803		MLoR	Same as for BW (g)	RFV: ref (1) Wheat products: 1.07 (95% CI: 0.53, 2.16) Meat & eggs: 1.12 (95% CI: 0.56, 2.24)
Poon et al. (2013)	Continuous aMED score (per 1 unit increase)	BW Z-scores (sex adjusted) n=815		MLR	Energy intake, age, ethnicity, education, poverty index ratio, pre-pregnancy BMI, smoking, alcohol intake, GA	Per 1 unit increase in aMED score -0.003 (95% CI: -0.036, 0.031)
	Continuous aMED score (per 1 unit increase)	WFL Z-scores (sex adjusted) n=815		MLR	Same as for BW	Per 1 unit increase in aMED score 0.03 (95% CI: -0.03, 0.08)
	aMED score: Low: 0-3; Med:4-5; High: 6-8	LGA (≥90th sex & GA specific BW centile) n=82/775		Poisson regression	Energy intake, age, ethnicity, education, poverty index ratio, pre-pregnancy BMI, smoking, alcohol intake	aMED: Low: ref (1) Med: 0.71 (95% CI: 0.44, 1.14) High: 0.71 (95% CI: 0.37, 1.35)
	aMED score: Low: 0-3; Med:4-5; High: 6-9	SGA (≤10th sex & GA specific BW centile) n=71/755		Poisson regression	Same as for LGA	aMED: Low: ref (1) Med: 0.75 (95% CI: 0.44, 1.29) High: 0.94 (95% CI: 0.48, 1.81)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
	Continuous AHEI-P score (per 1 unit increase)	BW Z-scores (sex adjusted) n=815		MLR	Same as for BW	Per 1 unit increase in AHEI-P score 0.002 (95%CI:-0.003, 0.008)
	Continuous AHEI-P score (per 1 unit increase)	WFL Z-scores (sex adjusted) n=815		MLR	Same as for BW	Per 1 unit increase in AHEI-P score 0.005 (95% CI: -0.004, 0.013)
	AHEI-P: Low: 33-52; Med: 53-62; High: 63-98	LGA (≥90th sex & GA specific BW centile) n=82/775		Poisson regression	Same as for LGA	AHEI-P: Low: ref (1) Med: 0.73 (95% CI: 0.41, 1.31) High: 0.93 (95% CI: 0.49, 1.75)
	AHEI-P: Low: 33-52; Med: 53-62; High: 63-99	SGA (≤10th sex & GA specific BW centile) n=71/755		Poisson regression	Same as for LGA	AHEI-P: Low: ref (1) Med:0.74 (95% CI: 0.43, 1.26) High: 0.92 (95% CI: 0.50, 1.69)
Rifas-Shiman et al. (2009)	Continuous score	LGA (≥90th sex & GA specific BW centile)	T1 AHEI-P score n=243/1,777	Multinomial LoR	Age, BMI, parity, education, ethnicity	Per 5 point increment in AHEI-P score 0.95 (95% CI: 0.89, 1.02)
		SGA (≤10th sex & GA specific BW centile)	T1 AHEI-P score n=98/1,777	Multinomial LoR	Same as for LGA	Per 5 point increment in AHEI-P score 0.92 (95% CI: 0.82, 1.02)
		LGA (≥90th sex & GA specific BW centile)	T2 AHEI-P score n=NR/1,666	Multinomial LoR	Age, BMI, parity, education, ethnicity	Per 5 point increment in AHEI-P score 0.99 (95% CI: 0.92, 1.07)
		SGA (≤10th sex & GA specific BW centile)	T2 AHEI-P score n=NR/1,666	Multinomial LoR	Same as for LGA	Per 5 point increment in AHEI-P score 1.00 (95% CI: 0.90, 1.10)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
Rodriguez-Bernal et al. (2010)	Quintiles (Q) of AHEI-P score: Q1: 35-47 Q2: 48-51 Q3: 52-55 Q4: 56-60 Q5: 61-75	BW (g) (GA adjusted) n=787		Stepwise MLR	Ethnicity, smoking, parity, GWG, infant's sex, log pre-pregnancy BMI, maternal & paternal height	Q1: ref (0) Q2: 92.69 g (95% CI: 3.24, 182.16, P=0.04) Q3: 83.45 g (95% CI: -7.53, 174.43, P=0.07) Q4: 126.25 g (95% CI: 38.53, 213.96, P=0.005) Q5: 114.15 g (95% CI: 27.07, 201.23, P=0.01) P_{trend}= 0.009
		BL (cm) (GA adjusted) n=787		Stepwise MLR	Height, paternal height, log pre-pregnancy BMI, GWG, parity, smoking, T1 caffeine intake, infant's sex	Q1: ref (0) Q2: 0.20 cm (95% CI: -0.20, 0.59, P=0.33) Q3: 0.24 cm (95% CI: -0.17, 0.64, P=0.25) Q4: 0.47 cm (95% CI: 0.08, 0.86, P=0.017) Q5: 0.41 cm (95% CI: 0.03, 0.80, P=0.0036) P_{trend}= 0.013
		HC (cm) (GA adjusted) n=787		Stepwise MLR	Education, smoking, T1 alcohol intake, T1 caffeine intake, parity, GWG, infant's sex, log pre-pregnancy BMI, maternal and paternal height, calcium supplement use, iron supplement use	Q1: ref (0) Q2: 0.30 cm (95% CI: 0.01, 0.59, P=0.039) Q3: 0.23 cm (95% CI: -0.06, 0.52, P=0.13) Q4: 0.38 cm (95% CI: 0.09, 0.66, P=0.008) Q5: 0.25 cm (95% CI: -0.03, 0.53, P=0.08) P_{trend}= 0.078
		FGR-BW (adjusted for weight, parity, parental height, infant sex, GA; defined as BW < lower limit of the 80% CI) n=78/787		Stepwise MLR	Smoking, T1 GWG, folic acid supplement use	Q1: ref (1) Q2: 0.55 (95% CI:0.28, 1.08, P=0.08) Q3: 0.35 (95% CI: 0.16, 0.76, P=0.008) Q4: 0.51 (95% CI: 0.26, 0.99, P=0.048) Q5: 0.24 (95% CI: 0.10, 0.55, P=0.001) P_{trend}= 0.001
		FGR-BL (same adjustments as for FGR-BW; defined as BL < lower limit of the 80% CI) n=69/787		Stepwise MLR	Smoking, T1 GWG, height	Q1: ref (1) Q2: 1.28 (95% CI:0.60, 2.73, P=0.52) Q3: 0.62 (95% CI: 0.25, 1.54, P=0.30) Q4: 1.15 (95% CI: 0.54, 2.46, P=0.72) Q5: 0.78 (95% CI: 0.34, 1.80, P=0.57) P_{trend}= 0.54

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
		FGR- HC (same adjustments as for FGR-BW; defined as BL < lower limit of the 80% CI) n=72/787		Stepwise MLR	Smoking, T1 caffeine intake, parity, height, T1 GWG	Q1: ref (1) Q2: 0.46 (95% CI:0.21, 0.99, P=0.047) Q3: 0.49 (95% CI: 0.22, 1.08, P=0.08) Q4: 0.60 (95% CI: 0.29, 1.23, P=0.17) Q5: 0.40 (95% CI: 0.17, 0.90, P=0.03) P_{trend}= 0.07
Saunders et al. (2014)	Continuous MD score	FGR (<10th BW centile; adjusted for age, weight, height, parity, sex, GA) n=93/728		MLoR	Maternal place of birth, marital status, pre-pregnancy BMI, education, enrolment site, GWG, energy intake, smoking	Per 1 unit increase in MD score 1.0 (95% CI: 0.8, 1.1)
		FGR (as above)	Maternal BMI<25 n=42/429	MLoR	Maternal place of birth, marital status, education, enrolment site, GWG, energy intake, smoking	Per 1 unit increase in MD score 0.8 (95% CI: 0.7, 1.1) Interaction P=0.03
		FGR (as above)	Maternal BMI≥25 n=51/299	MLoR	Maternal place of birth, marital status, education, enrolment site, GWG, energy intake, smoking	Per 1 unit increase in MD score 1.2 (95% CI: 0.9, 1.5)
		FGR (as above)	Infant's sex: male n=39/370	MLoR	Same as for whole sample analysis	Per 1 unit increase in MD score 0.9 (95% CI: 0.7, 1.1) Interaction P=0.69
		FGR (as above)	Infant's sex: female n=54/358	MLoR	Same as for whole sample analysis	Per 1 unit increase in MD score 1.0 (95% CI: 0.8, 1.2)
Shapiro et al. (2016)	HEI-2010 category: ≤57 (n=647) >57 (n=432)	BW (g)		MLR	Age, BMI, ethnicity, infant's sex, GA, household income, energy intake, smoking, PA, chronic HT, gestational HT, preeclampsia	>57: ref (0) ≤57: 27.86 g (95% CI:−21.16, 76.89, P=0.35)
		FFM (g)		MLR	Same as for BW (g)	>57: ref (0) ≤57: 7.30 g (95% CI: −29.71, 44.31, P=0.97)

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
		FM (g)		MLR	Same as for BW (g)	>57: ref (0) ≤57: 20.74 g (95% CI: 1.49, 40.0, P<0.05)
		FM (%)		MLR	Same as for BW (g)	>57: ref (0) ≤57: 0.58% (95% CI:0.07, 1.1, P<0.05)
Thompson et al. (2010)	Continuous scores (per 1 unit increase)	SGA (<10th BW centile)	T1 DPs n=844/1714	Stepwise MLoR	GA, infant's sex, smoking, height, weight, parity, ethnicity, maternal HT, dietary scores in late pregnancy	Fusion: 1.15 (95% CI: 0.91, 1.14) Junk: 0.99 (95% CI: 0.82, 1.18) Traditional: 0.79 (95% CI: 0.66, 0.96)
		SGA (<10th BW centile)	T3 DPs n=844/1714	Stepwise MLoR	GA, infant's sex, smoking, height, weight, parity, ethnicity, maternal HT, dietary scores in early pregnancy	Fusion:0.91 (95% CI: 0.90, 1.18) Junk: 0.99 (95% CI: 0.83, 1.17) Traditional:1.01 (95% CI: 0.84, 1.23)
Timmermans et al. (2012)	Tertiles of MD score: Low, Med, High	BW SD score (GA adjusted) n=3,207		MLR	Age, height, weight, parity, infant's sex, education, smoking, folic acid use	High: ref (0) Med: -0·16 (95% CI -0·24, -0·07) Low: -0.21 (95% CI -0.30, -0.12)
		BW (g) n=3,207		MLR	Same as for BW (SD score)	High: ref (0) Med: -58.0 g (95% CI -95.8, -20.3) Low: -72.0 g (95% CI -110.8, -33.3)
		BW (g)	Low education n=100	MLR	Age, height, weight, parity, infant's sex, folic acid use, smoking	High: NS - estimates NR Med: NS - estimates NR Low: -160 g (-271.4, -50.2) P for interaction <0.10
		BW (g)	Medium education n=1,207	MLR	Age, height, weight, parity, infant's sex, folic acid use, smoking	High: NS - estimates NR Med: NS - estimates NR Low: -131 g (95% CI: -180.9, -81.2)
		BW (g)	High education n=1,900	MLR	Age, height, weight, parity, infant's sex, folic acid use, smoking	High: ref (0) Med: NS - estimates NR Low: NS - estimates NR
		BW (g)	Non-smokers n=2,382	MLR	Age, height, weight, parity, infant's sex, folic acid use, education	High: ref (0) Med: NS - estimates NR Low: NS - estimates NR

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
		BW (g)	Smokers n=825	MLR	Age, height, weight, parity, infant's sex, folic acid use, education	High: -66 g (95% CI: -130.6, -2.5) Med: sig. difference of ca. -70 g (read from figure) Low: -214 g (95% CI:-269.3, -159.6) P for interaction <0.10
Wen et al. (2013)	Junk food diet: Yes n=246 No n=122	High BW (>4kg) n=42/368		Stepwise MLoR	Weight, GA	Yes: ref (1) No: 0.36 (95% CI: 0.14, 0.91, P=0.03)
Wolff & Wolff (1995)	Continuous scores (per 1 unit increase)	BW (g) n=778		Stepwise MLR	Age, BMI, haemoglobin, smoking, number of days the infant was born prior to the expected due date, infant's sex	Nutrient dense: 20.4 g (SE:4.6, P=0.0001) Traditional: NS - estimates NR Transitional: NS - estimates NR Nutrient dilute: -22.2 g (SE:10.0, P=0.05) Protein rich: 36.1 g (SE:14.1, P=0.05) High fat dairy: NS - estimates NR Mixed dishes: NS - estimates NR

*If not otherwise indicated these refer to maternal characteristics. AHEI, Alternate Healthy Eating Index; BL, birth length; BW, birth weight; BMI, body mass index; DBP, diastolic blood pressure; EM, effect modification; FFM, fat free mass; FGR, fetal growth restriction; FM, fat-mass; GA, gestational age; GDM, gestational diabetes; GWG, gestational weight gain; HC, head circumference; HT, hypertension; LF, low fat; LFA, length-for-age; LMP, last menstrual period; LR, linear regression; MD, Mediterranean diet; Med, medium; MLR, multiple linear regression; MLoR, multiple logistic regression; n, number; NND, New Nordic Diet; NR, not reported; NS, non-significant; NSB, non-sweetened beverages; PA, physical activity; RFV, Rice, fish and vegetables; SE, standard error; SBP, systolic blood pressure; veg, vegetables; WFL, weight-for-length; WFA, weight-for-age;

2.4.3 Maternal dietary patterns and offspring infant/child growth outcomes

2.4.3.1 Study design & setting

Four studies were found which assessed offspring infant and/or child growth outcomes in relation to maternal dietary patterns (Cole, Z.A. et al., 2009; Fernandez-Barres et al., 2016; Poon et al., 2013; van den Broek et al., 2015). Characteristics of these studies are presented in Table 5 below. All were of a prospective cohort design. Studies were from a range of developed countries including the UK (Cole, Z.A. et al., 2009), Spain (Fernandez-Barres et al., 2016), the US (Poon et al., 2013) and the Netherlands (van den Broek et al., 2015). All studies limited their analyses to singleton births and one study further restricted analyses to singletons delivered after 35 weeks gestation weighing ≥ 5 pounds (~≥ 2.3 kg) (Poon et al., 2013). Cole et al. (2009) included only mothers without DM or HRT and Poon et al. (2013) recruited only healthy pregnancies. Two studies considered the ethnicity of the samples, with Cole et al. (2009) including only Caucasian mothers in their analysis of UK data and van den Broek et al. (2015) only Dutch mothers in their analysis of data from the Dutch Generation R cohort. The ages of the mothers were fairly similar across studies ranging from 27 to 32 years old. Sample sizes varied and ranged from 198 to 2,689 participants with an average of around 1,400; much smaller than the average of 7,842 participants from the studies reporting on size at birth.

2.4.3.2 Dietary assessment

All studies assessed diet using FFQs. Three of the studies analysed data from birth cohorts previously described in the results section for studies reporting on offspring size at birth and their methods of dietary assessment are not described in detail here (INMA (Fernandez-Barres et al., 2016), Generation R (van den Broek et al., 2015) and IFPSII (Poon et al., 2013) respectively) (see section 2.4.2.2 for details). As opposed to Chatzi et al. (2009) who assessed size at birth in the INMA cohort in relation to dietary data collected in the 1st trimester, Fernandez-Barres et al. (2016) used the average of dietary data collected in the INMA cohort in both the 1st and 3rd trimester from a 101 item FFQs (assessing dietary intake throughout pregnancy) for their dietary patterns analysis. Cole et al. (2009) assessed dietary intake using a 100 item self-administered FFQ administered in both the 2nd and 3rd trimester assessing the previous 3 month's intake. Poon et al. (2013) used a modified version of the Diet History Questionnaire (DHQ) administered in the 3rd trimester assessing the past month's intake, with no details provided on number of food items (Poon et al., 2013). Only Poon et al. (2013) reported excluding mothers with extreme energy intakes (top 2% and bottom 1%).

2.4.3.3 Dietary pattern analysis

Of the four studies, two used *a posteriori* techniques to derive dietary patterns and two evaluated dietary patterns using *a priori* techniques.

2.4.3.3.1 A posteriori dietary pattern analyses

Cole et al. (2009) and van den Broek et al. (2015) both used PCA to generate dietary patterns. Both aggregated dietary data collected from the FFQs into main food groups based on nutritional profiles and culinary usage prior to the PCA. Cole et al. (2009) combined data from a 100 item FFQ into 49 food groups whereas van den Broek et al. (2015) derived 23 food groups from a 293 item FFQ. The food grouping were similar although Cole et al. (2009) with their more exhaustive list differentiated better between certain food groups, e.g. different types of meat, types of vegetables, types of fruit, boiled vs. fried/roast potatoes, types of sweets/desserts, cereal products, i.e. separate food groups for rice, pasta, breakfast cereal, wholemeal bread and white bread, whereas van den Broek et al. (2015) included main food groups for vegetables, fruit, potatoes, sugar/confections and high-fiber and low-fiber cereals. Both shared common food groups such as eggs, fats & oils, spreads and margarine, SSB, non-SSB, soy products (or vegetable dishes), and both included alcohol as well as tea and coffee. Neither differentiated between fish and shellfish and van den Broek et al. (2015) appeared to have included nuts in two food groups, ‘Nuts, seeds and olives’ as well as the ‘Snack’ food group, the latter which included peanuts and beer nuts. Cole et al. (2009) included food groups specific to a UK diet such as Yorkshire puddings and quiche and in addition to having low-fat and high fat milk food groups they also had separate food groups for yoghurt, cheese and cream, whereas van den Broek et al. (2015) included these items in their high-fat and low-fat dairy food groups. As opposed to van den Broek et al. (2015) Cole et al. (2009) had no information on water nor sauces or condiments. Neither study standardised nor energy adjusted dietary data prior to PCA. Only van den Broek et al. (2015) reported on the criteria set for choice of components to retain (the scree plot, the Kaiser criterion and interpretability). The PCA by Cole et al. (2009) resulted in one component labelled ‘prudent’ due to large positive coefficients for fruit and vegetables, wholemeal bread, rice, and pasta, yogurt, cheese, fish, and reduced fat milk, but large negative coefficients for white bread, added sugar, tinned vegetables, full fat milk, and crisps. No information was provided on the amount of variance explained by this component. Van den Broek et al. (2015) derived 3 dietary patterns from their PCA labelled ‘vegetable, fish, and oils’; ‘nuts, soy, and high-fiber cereals’; and ‘margarine, snacks, and sugar’, explaining 26% of the variance in the dietary data.

2.4.3.3.2 A priori dietary pattern analyses

Both Fernandez-Barres et al. (2016) and Poon et al. (2013) evaluated dietary patterns using alternate versions of the MD score (see Table 5 below for details) with Poon et al. (2015) additionally assessing diet quality using the AHEI-P (as reported in the results for birth outcomes, section 2.4.2.3.2). Fernandez-Barres et al. (2016) assessed adherence to the rMED using the average of dietary data collected via FFQs in the 1st and 3rd trimesters of pregnancy. As opposed to the scoring of other diet indices, intakes were expressed as grams per 1000 kcal/day and split into tertiles which were assigned values of 0, 1 and 2, positively scoring higher intakes for beneficial items and vice versa for meat and dairy, resulting in a possible score range of 0-16 (Fernandez-Barres et al., 2016).

2.4.3.4 Offspring anthropometry assessment

Both Cole et al. (2009) and van den Broek et al. (2015) assessed offspring body composition using dual-energy X-ray absorptiometry (DXA). Cole et al. (2009) reported results on offspring fat mas (FM) and lean mass at 9 years, both expressed in grams, whereas van den Broek et al. (2015) evaluated offspring fat free mass (FFM) and FM at 6 years calculated as indexes [lean mass (kg) or fat mass (kg) + bone mass (kg)]/[height^2 (m)] (van den Broek et al., 2015). They additionally assessed BMI (kg/m^2) derived from offspring height and weight measured at the 6 year follow-up. Fernandez-Barres et al. (2016) similarly assessed offspring BMI expressed as age and sex-specific Z-scores at 4 years calculated using the 2007 WHO referent. They also assessed offspring waist circumference at the 4 year follow-up and further categorised offspring as being abdominally obese at 4 years if they had a waist circumference above the 90th sex-specific centile and overweight as having at BMI Z-score at 4 years above the 85th centile (Fernandez-Barres et al., 2016). All anthropometric measurements were carried out by trained staff for the three studies above. Poon et al. (2013) used the Centre for Disease Control and Prevention (CDC) 2000 growth reference charts to derive offspring WFL Z-scores at 4-6 months based on self-reported infant length and weight collected via questionnaires at 5, 7 and 12 months follow-ups (Poon et al., 2013).

2.4.3.5 Statistical analyses

All studies used multivariable regression including linear and logistic techniques. Similar to the studies reporting on size at birth, two of the studies used stepwise regression and as a result thereof the adjustment of confounders varied greatly between studies (see Table 6 below). All four studies adjusted for offspring age and sex, with Fernandez-Barres et al. (2016), Poon et al. (2013) and van den Broek et al. (2015) additionally adjusting for confounders similar to those accounted for in the studies reporting on size at birth (see section 2.4.2.5 for details). Fernandez-Barres et al. (2016) also considered potential mediators such as breastfeeding, GDM, birth weight, rapid growth from birth to 6 months (defined as a Z-score weight gain greater than 0.67 SD) and child diet. They additionally tested for effect modification by pre-pregnancy BMI, smoking status during pregnancy, physical activity status during pregnancy, maternal educational status, child sex and child birth weight category (Fernandez-Barres et al., 2016). Similarly, Poon et al. (2013) adjusted for size at birth in their models but not breastfeeding (Poon et al., 2013). van den Broek et al. (2015) adjusted for breastfeeding but not birth weight and additionally adjusted for offspring TV watching at 2 years as well as sports participation at 6 years of age. They performed sensitivity analyses with and without maternal energy intake and considered effect modification by maternal pre-pregnancy BMI, maternal folic acid use, maternal smoking during pregnancy, vomiting during pregnancy, nausea during pregnancy and maternal energy intake (van den Broek et al., 2015). Both studies which categorised their dietary pattern exposure reported trend tests but did not adjust for multiple testing.

Table 5. Study characteristics: studies investigating maternal dietary patterns and infant/child growth outcomes

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure
Cole et al. (2009)	(UK)	Prospective cohort 1991-1992	198	No DM; no HRT; Caucasian; >16 yrs; singleton births	Interviewer administered 100 item FFQ (T2 & T3; past 3 m)	A posterior PCA on 49 food groups	Prudent % variance: NR
Fernandez-Barres et al. (2016)	INMA (Spain)	Prospective cohort 2003- 2008	1827	>16 yrs, singleton birth; no assisted reproduction; Spanish literate, delivery at ref hospital	Interviewer administered 101 item FFQ (T1 & T3; T1, T2 & T3)	A priori 8 item score: vegetables, fruits & nuts, cereals, legumes, fish, olive oil, total meat and dairy products. Intakes measured as g/1000 kcald-1. Split into tertiles and assigned values of 0, 1 and 2 positively scoring higher intakes for beneficial items and vice versa for meat and dairy.	Relative Mediterranean diet score (rMED) (0 (low) to 16 (high))
Poon et al. (2013)	The Infant Feeding Practices Study II (IFPSII) (US)	Prospective cohort2005	893	Healthy singleton; >35 wks gestation; ≥5 pounds; no intensive care unit for >3 days	Self-administered FFQ (T3; past 1 m) modified version of the Diet History questionnaire (DHQ)	A priori AHEI-P: 13 items based on modified version of US 2010 dietary guidelines for healthy eating: veg (≥5 servings/d), whole fruit (≥4 servings/d), whole grains (75 g/d), nuts & legumes (≥1 serving/d), long-chain (n-3) fats (250 mg/d), PUFA %Energy (≥10), folate (≥600 µg/d), calcium (≥1200 mg/d) & iron (≥27 mg/d) from foods, SSB (0 servings/d), red & processed meat (0 servings/d), trans fat % of Energy (≤0.5), sodium (mg/d, lowest decile). Max score of 10 for each component. Intakes scored proportionally. aMED: 8 items: veg, legumes, fruits, nuts, cereals, fish & seafood, meat, fat (ratio of MUFA: SFA). ‘0’ assigned for intakes < median and ‘1’ for intakes > median for beneficial items & vice versa for detrimental items	Healthy Eating Index for Pregnancy (AHEI-P) (0 (low) to 130 (high)) The alternate Mediterranean diet (aMED) (0 (low) to 8 (high))

Reference	Study name (Country)	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Dietary pattern identification method	Dietary pattern exposure
van den Broek et al. (2015)	Generation R study (Netherlands)	Prospective cohort 2002-2006	2,689	Dutch women; singleton birth	Self-administered 293 item FFQ (<24 wks gestation; past 3 m)	A posterior PCA on 23 food groups. Number of components based on scree plot, the Kaiser criterion & interpretability	Veg, fish & oil; Nuts, soy & high-fibre cereals; Margarine, snacks & sugar % variance: 25.8

ART, assisted reproduction; d, day; FFQ, food frequency questionnaire; LMP, last menstrual period; m, month; MUFA, monounsaturated fatty acids; n, number; NR, not reported; PUFA, polyunsaturated fatty acids; RCT, randomized controlled trial; SD, standard deviation; SFA, saturated fatty acids; SSB, sugar-sweetened beverages; T, trimester; yrs, years; wks, weeks

2.4.3.6 Quality of studies

All of the studies reviewed were of a prospective cohort design with differing lengths of follow-up. Cole et al. (2009) had the longest period of follow-up with their assessment of offspring lean and fat mass at nine years, whereas Poon et al. (2013) had the shortest period of follow-up at 4-6 months. Longitudinal studies such as these are likely to suffer from a loss to follow-up as evidenced by the studies included in this review where two had response rates of <50% (Cole, Z.A. et al., 2009; Poon et al., 2013) and two just over 65% (Fernandez-Barres et al., 2016; van den Broek et al., 2015). The issues related to non-response have been highlighted in the assessment of the quality of studies reporting on size at birth (see section 2.4.2.6). Cole et al. (2009) investigated whether study participants differed from non-respondents and found no notable differences. Poon et al. (2013) who had the lowest response rate despite having the shortest period of follow-up did not report on any steps taken to assess bias introduced by non-response. Both Fernandez-Barres et al. (2016) and van den Broek et al. (2015) used multiple imputation (20 vs. 10 imputed datasets) to replace missing values on covariates in order to prevent bias arising from missing data.

In terms of dietary assessment, all studies used FFQs but the administration, reference period, timing of assessment as well as number of items differed which could have an effect on study quality. Some of the problems inherent to dietary assessments and their validation have been highlighted in the section on assessment of the quality of studies reporting on size at birth (see section 2.4.2.6). As previously stated, Poon et al. (2009) used a modified version of the validated DHQ which had not been validated in a pregnant population and it was therefore unclear how successful this tool was at measuring dietary intake during pregnancy. Both Fernandez-Barres et al. (2016) and van den Broek et al. (2015) used tools that had been validated in similar pregnant populations, whereas Cole et al. (2009) validated their FFQ against prospective 4-day food diaries in a sub-sample of the original cohort. None of the studies measured agreement but rather assessed the association between the test method and the reference methods using correlation, reporting moderate to high coefficients. Three of the four studies used country specific food composition tables to obtain nutrient intakes, whereas Cole et al. (2009) only reported on frequencies of consumption.

Neither of the studies energy adjusted their data prior to analysis, however all but Cole et al. (2009) included energy intake either in their fully adjusted regression models or in sensitivity analyses (van den Broek et al., 2015). The importance of adjusting for energy intake in nutritional epidemiological research has been highlighted in section 2.4.2.6.

In terms of statistical analysis, three of the studies were found to be of similar quality, adjusting for important confounders and considering both mediators and effect modifiers. Cole et al. (2009) however only adjusted for age and child sex and therefore there is potential for residual confounding and their findings should be interpreted with care.

Taking into consideration the above, the studies by Fernandez-Barres et al. (2016) and van den Broek et al. (2015) appeared to be of the highest quality followed by Poon et al. (2013) and then Cole et al. (2009).

2.4.3.7 Findings

Findings from studies investigating offspring infant and child growth outcomes in relation to maternal dietary patterns during pregnancy are presented in Table 6 below. All effect estimates presented were extracted from maximally adjusted models.

2.4.3.7.1 Lean mass, fat mass & fat-free mass

Two studies reported findings on fat mass and fat-free mass (FFM) and one study on lean mass. Cole et al. (2009) assessed offspring lean and fat mass in relation to a maternal prudent dietary pattern in the 2nd and 3rd trimester characterised by high intakes of fruit and vegetables, wholemeal bread, rice, and pasta, yogurt, and breakfast cereals and low intakes of chips and roast potatoes, sugar, white bread, processed meat, crisps, tinned vegetables, and soft drinks. They found that mothers with a higher prudent diet score in the 2nd trimester had offspring with a higher lean mass at 9 years (656.0 g, 95% CI: 304.3, 1007.7) and observed a similar association for the 3rd trimester diet score. Van den Broek et al. (2015) on the other hand found no significant association between a more health conscious dietary pattern in the first half of pregnancy with high intakes of nuts, soy, high-fibre cereals, fruits and fish and offspring FFM at 6 years. Neither study observed any significant associations with fat mass at 9 years or 6 years respectively.

2.4.3.7.2 Body Mass Index

Two studies reported on offspring BMI. van den Broek et al. (2015) assessed offspring BMI at 6 years in relation to maternal dietary patterns in the first half of pregnancy (<24 weeks gestation) and Fernandez-Barres et al. (2016) reported on BMI Z-scores at 4 years in relation to rMED adherence in pregnancy. Neither study found any significant associations. Sub-group analyses by van den Broek et al. (2015) however showed a significant interaction between maternal folic acid supplement use and the nuts, soy, and high-fiber cereals dietary pattern on BMI of the child ($P<0.01$). They did not report any effect estimates hence the direction of the association was unclear (van den Broek et al., 2015). Fernandez-Barres et al. (2016) additionally assessed offspring overweight and abdominal obesity and observed no significant association with maternal rMED adherence in pregnancy. Sub-group analyses by several covariates did not alter findings (Fernandez-Barres et al., 2016).

2.4.3.7.3 Waist circumference

Fernandez-Barres et al. (2016) assessed offspring waist circumference at 4 years in relation to maternal rMED adherence during pregnancy. They found a significant negative association between increasing rMED scores and offspring waist circumference. Similarly, compared to mothers in the lowest tertile category, mothers in the highest rMED tertile category had children with a 0.62 cm lower waist circumference (95% CI: -1.10, -0.14, $P_{trend}=0.009$). No evidence of effect modification was evident in stratified analyses by selected variables (child sex, maternal pre-pregnancy BMI, smoking status, maternal physical activity, social class, educational level and infant birth weight) and the inclusion of child diet measured at 4 years of age did not alter the results (data not shown) (Fernandez-Barres et al., 2016).

2.4.3.7.4 Weight-for-length

Poon et al. (2013) assessed offspring WFL Z-scores at 4-6 months in a sample of 426 children in relation to both maternal MD adherence (aMED) and AHEI-P scores in the final trimester of pregnancy. As was the case with WFL at birth, they observed no significant associations with either diet scores (Poon et al., 2013).

Table 6. Study results: Maternal dietary patterns and offspring infant/child growth outcomes

Reference	Exposure expression	Outcome (s)	Comparison/ Subgroup	Statistical analysis	Adjustments*	Results
Cole et al. (2009)	Continuous SD scores (per 1 unit increase)	Lean mass at 9 yrs (g) n=198	T2 prudent diet score	MLR	Age, sex	Prudent dietary pattern score 656.0 g (95% CI: 304.3, 1007.7)
		Lean mass at 9 yrs (g) n=198	T3 prudent diet score	MLR	Age, sex	Similar to T2 results - estimates NR
		FM at 9 yrs (g) n=198	T2 prudent diet score	MLR	Age, sex	NS - estimates NR
		FM at 9 yrs (g) n=198	T3 prudent diet score	MLR	Age, sex	NS - estimates NR
Fernandez-Barres et al. (2016)	Continuous (per 2 units increase) & tertiles of rMED score: Low: 1-7; Med: 8-9; High: 10-15	BMI Z-scores at 4 yrs (age & sex specific) n=1,827		Stepwise MLR	Child sex & age, region, energy intake, education, smoking, PA, pre-pregnancy BMI, GWG, child BW & rapid growth from birth to 6 m, GDM	Continuous rMED: -0.02 (95% CI: -0.03, 0.01) Low: ref (0) Med: -0.06 (95% CI:-0.20, 0.02) High: -0.09 (95% CI: -0.20, 0.02) P_{trend}=0.113
		WC at 4 yrs (cm) n=1,398		Stepwise MLR	Child sex & age, region, energy intake, education, smoking, PA, pre-pregnancy BMI, GWG, child BW & rapid growth from birth to 6 m, child height, breastfeeding duration	Continuous rMED: -0.18 (95% CI: -0.33, -0.03) Low: ref (0) Med: -0.34 (95% CI: -0.78, 0.11) High: -0.62 (95% CI: -1.10, -0.14) P_{trend}=0.009
		Overweight at 4 yrs (>85th BMI Z-score centile) n=298/1827		Stepwise MLoR	Child sex & age, region, energy intake, education, smoking, PA, pre-pregnancy BMI, GWG, child BW & rapid growth from birth to 6 m, GDM	Continuous rMED: 0.98 (95% CI: 0.89, 1.07) Low: ref (1) Med: 0.88 (95% CI: 0.67, 1.15) High: 0.94 (95% CI: 0.71, 1.24) P_{trend}=0.59

		Abdominal obesity at 4 yrs (WC >90th sex specific centile) n=NR/1398	Stepwise MLoR	Child sex & age, region, energy intake, education, smoking, PA, pre-pregnancy BMI, GWG, child BW & rapid growth from birth to 6 m, breastfeeding duration	Continuous rMED: 0.89 (95% CI: 0.76, 1.05) Low: ref (1) Med: 0.84 (95% CI: 0.53, 1.32) High: 0.62 (95% CI: 0.37, 1.03) P_{trend}=0.064
Poon et al. (2013)	Continuous score (per 1 unit increase)	WFL at 4-6 m (Z-scores) n= 426	MLR	Energy intake, age, race, education, poverty index ratio, pre-pregnancy BMI, smoking, alcohol intake, GA, birth WFL Z-scores	aMED score 0.06 (95% CI: -0.03, 0.14)
	Continuous (per 1 unit increase)	WFL at 4-6 m (Z-scores) n= 426	MLR	Energy intake, age, race, education, poverty index ratio, pre-pregnancy BMI, smoking, alcohol intake, GA, birth WFL Z-scores	AHEI-P score 0.009 (95% CI: -0.004, 0.023)
van den Broek et al. (2015)	Quartiles (Q) of scores Q1 (low) to Q4 (high)	BMI at 6 yrs n=2689	Stepwise MLR	Age, GA at dietary assessment, smoking, folic acid supplement use, alcohol intake, education, family income, parity, pre-pregnancy BMI, stress during pregnancy, child sex, breastfeeding, TV watching at 2 y, participation in sports at 6 y	Veg, fish and oil: Q1: ref (0) Q4: -0.07 (95% CI: -0.16, 0.02), P_{trend}= 0.21 Nuts, soy & high-fibre cereals: Q1: ref (0) Q4: 0.07 (95% CI: -0.02, 0.17, P>0.05) P_{trend}= 0.03 Margarine, snacks and sugar: Q1: ref (0) Q4: -0.02 (95% CI: -0.17, 0.13), P_{trend}= 0.46
		FFM index at 6 yrs n=2520	Stepwise MLR	Same as BMI at 6 yrs	Veg, fish and oil: Q1: ref (0) Q4: 0.00 (95% CI: -0.10, 0.11), P_{trend}= 0.79 Nuts, soy & high-fibre cereals: Q1: ref (0) Q4: 0.12 (95% CI:-0.01, 0.23, P>0.05) P_{trend}= 0.01 Margarine, snacks and sugar:

				Q1: ref (0) Q4: -0.16 (95% CI: -0.33, 0.01, P>0.05) P_{trend}= 0.01
	FM index at 6 yrs n=2520	Stepwise MLR	Same as BMI at 6 yrs	Veg, fish and oil: Q1: ref (0) Q4: -0.09 (95% CI: -0.18, 0.001), P_{trend}=0.30 Nuts, soy & high-fibre cereals: Q1: ref (0) Q4: 0.04 (95% CI:-0.05, 0.13), P_{trend}= 0.25 Margarine, snacks and sugar: Q1: ref (0) Q4: 0.03 (95% CI: -0.11, 0.17), P_{trend}= 0.33

*If not otherwise indicated these refer to maternal characteristics. AHEI-P, Alternate Healthy Eating Index in Pregnancy; BMI, body mass index; FFM, fat free mass; FM, fat-mass; GA, gestational age; GDM, gestational diabetes; GWG, gestational weight gain; m, month; rMED, Relative Mediterranean diet score; Med, medium; MLR, multiple linear regression; MLoR, multiple logistic regression; NR, not reported; NS, non-significant; PA, physical activity; veg, vegetables

2.5 Discussion

This chapter sought to review the literature published to date which has investigated the association between maternal dietary patterns in pregnancy and offspring growth outcomes. The literature was searched in a systematic manner, and data were extracted and organised into two sections according to offspring birth growth outcomes and infant/child growth outcomes.

Despite the increasing research in this area (all but 5 of the included articles were published after 2010), only one review assessing the association between maternal dietary patterns and birth growth outcomes was identified (Chen et al., 2016). The literature searches identified no reviews assessing infant and later childhood growth outcomes. Therefore, this chapter was necessary to comprehensively assess the evidence around maternal dietary patterns in pregnancy and offspring growth outcomes.

2.5.1 Maternal dietary patterns during pregnancy and offspring size at birth

All but one of the 18 studies assessed maternal dietary patterns during pregnancy that somewhat conformed to current guidelines on healthy eating (e.g. Mediterranean diet, NND, HEI, or *a posteriori* derived dietary patterns containing healthy foods, see section 2.4.2.3.1) in relation to size at birth. The most common outcome measure was birth weight either expressed as grams or SD scores, followed by SGA and FGR. Birth weight is used as a measure of both maternal and infant health but is also recognised as a predictor of future adult health, where adults born with lower birth weights are more predisposed to developing certain NCDs (Barker, 1997). Only few studies assessed birth length and never as the sole outcome measure. This may be explained by the fact that less is known about birth length as an independent predictor of adult health, although it has been found to be associated with child and adult height which in turn have been linked to adult health status. Similarly, only four studies included head circumference as one of their outcome measures. It could be argued that abdominal circumference may serve as a better indicator of nutritional status as head circumference is likely to be affected by the fetal ‘brain-sparing effect’ whereby there is a diversion of blood flow to the fetal brain at expense of other bodily functions when the fetus is under conditions of stress (Godfrey and Barker, 2001). Twelve studies found positive significant associations with at least one of their outcome measures (Chatzi et al., 2012; Colon-Ramos et al., 2015; Hillesund et al., 2014; Knudsen et al., 2008; Lu et al., 2016; Northstone et al., 2008; Okubo et al., 2012; Rodriguez-Bernal et al., 2010; Shapiro et al., 2016; Thompson et al., 2010; Timmermans et al., 2012; Wolff and Wolff, 1995) and five observed no association with any measure of size at birth (Bouwland-Both et al., 2013; Coelho Nde et al., 2015; Poon et al., 2013; Rifas-Shiman et al., 2009; Saunders et al., 2014). The evidence appeared to be most convincing for birth weight (expressed in grams as well as FGR and SGA), with the AHEI showing the strongest association, where mothers with a dietary pattern that scored highly on the AHEI had offspring with the biggest increase in birth weight (126 g) and the greatest reduction in risk of FGR for birth weight (76 % reduced odds). No studies found any significant negative associations between a healthy maternal dietary pattern and size at birth.

In terms of more unhealthy dietary patterns the evidence was less uniform. As mentioned earlier, the majority of studies using *a posteriori* techniques derived a dietary pattern high in red meat and processed foods and low in nutrient dense foods (see section 2.4.2.3.1). Of the eight studies, two found significant negative associations with birth weight (Wen et al., 2013; Wolff and Wolff, 1995), five studies showed no associations with infant size at birth (Bouwland-Both et al., 2013; Colon-Ramos et al., 2015; Lu et al., 2016; Northstone et al., 2008; Okubo et al., 2012) and one study observed a significant positive association between a ‘Snack’ dietary pattern and birth weight (Coelho Nde et al., 2015).

In addition to statistical significance it is also important to assess the clinical significance. Large sample sizes are likely to produce significant estimates, but this does not infer that they are clinically important, as evidence by Hillesund et al. (2014) who found in their sample of over 66,000 mother-child pairs an 8% reduction in the odds of having an infant born SGA in mothers with higher NND adherence. Chatzi et al. (2012) found positive significant associations between maternal MD adherence and size at birth in the larger INMA-Mediterranean cohort but not in the smaller Rhea and INMA-Atlantic cohorts. Some significant associations were observed in smaller cohorts (n<1000), e.g. Colon-Ramos et al. (2015) and Rodriguez-Bernal et al. (2010), they could however be caused by type 1 errors as often several group comparisons were made with borderline significance values and huge confidence intervals, and no attempts were made to adjust for multiple testing. In addition, despite efforts made to adjust for important confounders for these associations, residual confounding will always be present in studies of an observational design.

The findings from studies should be considered and interpreted within the context of their quality assessment (see section 2.4.2.6) and some of the methodological considerations have been outlined in section 2.5.3 below.

2.5.2 Maternal dietary patterns during pregnancy and infant/child growth outcomes

Studies focusing on infant and child growth outcomes, which included lean mass, fat mass, BMI, waist circumference and WFL, were too few and too heterogeneous to draw sound conclusions. Of the two studies which used PCA to derive dietary patterns, one found a positive association with child lean mass and a ‘prudent’ dietary pattern (Cole, Z.A. et al., 2009) whereas the other found no association between more health conscious dietary patterns and offspring body composition (van den Broek et al., 2015). Two studies assessed MD adherence and only one observed a positive significant association with offspring waist circumference, but not with child BMI or abdominal obesity (Fernandez-Barres et al., 2016).

As with the studies reporting on size at birth, these findings should be considered and interpreted within the context of their quality assessment (see section 2.4.3.6).

2.5.3 Methodologies

As highlighted in previous sections, the studies included in this review have used a variety of approaches and this heterogeneity itself underlines how difficult it is to investigate dietary patterns and their effects on health outcomes. Despite 19 out of 21 studies being of the same prospective cohort design, they were all different in terms of setting, dietary assessment method, dietary patterns analysis, outcome measures and analytical approaches and it is therefore not surprising that results are inconsistent.

None of the studies were randomized controlled trials (RCTs), which according to the CRD (2009) present the highest form of evidence (CRD, 2009). However, as RCTs are often not feasible or ethical in a pregnant population; in their absence it is necessary to consider other forms of evidence, of which the prospective cohort design is considered to be of highest quality. It is important to note however that because of the absence of trial evidence, causal relationships cannot be established and conclusions drawn from the literature will be limited.

The majority of studies used *a posteriori* techniques to derive dietary patterns, but even within this method discrepancies were present making in between study comparisons problematic. Preparation of dietary data prior to analysis varied from study to study and the number of food groups entered into a PCA ranged from 18 to 111. Even studies which entered similar food groups and applied the same criteria on the choice of components to retain produced different numbers of components. It appeared that those who aggregated the dietary data substantially in relation to the original number of items on the FFQ lost diet variety resulting in a smaller set of components, whereas studies that entered all dietary items or collapsed the number of items by less than half retained a higher number of components, regardless of the size of the study population. However this was not the case for studies with longer follow-up. For example, Cole et al. (2009) entered 49 food groups from a 100 item FFQ into a PCA which only resulted in one ‘prudent’ component. This could be explained by the fact that those participating in follow-up are likely to be more health conscious and might therefore be a more homogenous sample in terms of dietary habit. Similarly, van den Broek et al. (2015) identified 3 maternal dietary patterns in pregnancy at their 6 year follow-up, of which the two had high factor loadings with healthy foods such as fish, vegetable & oil and nuts, soy & fibre respectively. Another problem arising from *a posteriori* techniques stems from the naming of components or clusters, as highlighted by Chen et al. (2016). What is viewed as a Western dietary pattern in the Netherlands is not necessarily the same as what constitutes a Western dietary pattern in Brazil. It is misleading for between study comparisons and at the same time it is also difficult to draw comparisons between studies where dietary patterns are named differently but share commonalities. The naming should be informative and not too generic. It would makes sense to name patterns after the foods with the highest factor loadings, as done by some of the studies included in this review.

Discrepancies were also present for the studies using *a priori* techniques. Studies assessing diet quality used alternate versions of the HEI; one used a HEI based on the 2010 US dietary guidelines for healthy eating (Shapiro et al., 2016), whereas the others used a modified HEI adapted for pregnancy; the AHEI-P (Poon et al., 2013, Rifas-Shiman et al., 2009, Rodriguez-Bernal et al., 2010). The adaptations however were not consistent between studies and were based on different versions of the US dietary guidelines for healthy eating, namely the 1995 and 2010 releases, resulting in a different number of items for each score as well as differing criteria for each item and a different scoring system (although all were scored proportionally to the extent to which the dietary guidelines were met). The issues mentioned above were less prevalent for the studies assessing MD adherence. Saunders et al. (2014) used the 9 item MD score developed by Trichopoulou et al. (2003), whereas Chatzi et al. (2012), Fernandez-Barres et al. (2016) and Poon et al. (2013) chose to remove alcohol with the latter additionally removing dairy and including separate groups for fruit and nuts and Fernandez-Barres et al. (2016) swapping fats with olive oil. These differences complicate between study comparisons.

The timing of dietary assessment also differed greatly between studies as reported in section 2.4.2.2 and 2.4.3.2 on dietary assessment. It has been argued that overall dietary patterns in pregnancy do not change notably from trimester to trimester (Crozier et al., 2009; Rifas-Shiman et al., 2006) and only two studies investigated the importance of timing of exposure (Rifas-Shiman et al., 2009; Thompson et al., 2010), one of which found a positive association between a ‘traditional’ dietary pattern in the first but not the third trimester and SGA. Trajectories of fetal growth and development are set early in pregnancy; results from this review however are inconclusive when it comes to timing of exposure.

Another problem arises from inconsistencies in outcome measures used by studies and in addition to this; some studies used dated growth references in their prediction of FGR (e.g. Bouwland-Both et al. (2013) used growth standards from 1969). Birth weight might not be the best indicator of a healthy pregnancy or indeed the most useful predictor of future health; it is however a valuable measure when it comes to between study comparisons and one that was more commonly used than birth length or head circumference in the studies included in this review.

Finally, the adjustment for confounders varied greatly from study to study and none adjusted for the same factors, further complicating comparisons and preventing definite conclusions to be drawn. In addition, only one study excluded mothers receiving fertility treatment (Timmermans et al., 2012) and the remainder did not assess mode of conception as a possible confounder, despite in vitro fertilised (IVF) babies being known to be slightly smaller than spontaneously conceived babies. Furthermore, it stands to reason that for outcomes such as child growth any relationship will be more difficult to ascertain due to participant selection bias as well as the higher potential for confounding along the causal pathway. Of the four studies which assessed later offspring growth outcomes, three included variables thought to be on the causal pathway such as birthweight, infant growth and breastfeeding. This could potentially obscure any true effect and result in associations biased toward the null as by adjusting for an intermediate variable the total causal effect of dietary patterns on offspring growth cannot be consistently estimated (Schisterman et al., 2009).

2.5.4 Implications

Chapter 1 set out the conceptual framework which motivated this literature review. The hypothesis emphasizes prenatal nutrition as a key determinant for the increased risk of diseases later in life (Barker, 1997) and it was therefore further hypothesised that maternal diet during pregnancy could have a substantial influence on offspring growth. This literature review set out to establish evidence in support of or in opposition to this hypothesis. The synthesis of evidence presented above support to some degree the link between maternal nutrition and size at birth. Mothers who followed a dietary pattern that adhered to dietary guidelines on healthy eating during pregnancy tended to have more positive pregnancy outcomes in terms of infant size at birth. The evidence for longer term offspring child growth outcomes however was inconclusive.

Due to the mixed findings, the key implications from this review relate to future research, rather than implications for policy or interventions. The results indicate a lack of evidence on child growth outcomes despite the inferences of the fetal programming hypothesis linking maternal nutrition to child health outcomes. There were also several issues found with the quality of studies published (see section 2.4.2.6 and 2.4.3.6), in particular in terms of dietary assessment, dietary pattern analysis as well as the sometimes poor and inconsistent consideration of confounders. There is much scope for improvement in future studies of this kind and it is clear that when it comes to *a posteriori* techniques in particular, a more uniform method of dietary patterns analysis is needed.

2.5.5 Strengths and limitations

As opposed to the only other review identified in this area; studies were included from multiple online database searches and covered literature from over two decades (since Wolff & Wolff's study from 1995). There are several limitations to the review by Chen et al. (2016); firstly only one database was searched and the search used only three terms for the dietary pattern exposure, namely 'dietary pattern', 'diet' and 'dietary'. This has likely affected both the quantity and type of evidence assessed and may also help explain why only two studies assessing Mediterranean diet adherence using a diet index score were included and no studies assessing diet quality using Healthy Eating Index (HEI) were reviewed. Secondly, there was no evidence of an assessment of the quality of the individual studies but rather the authors listed the limitations inherent in dietary assessment without considering variations between studies. Thirdly, despite having highlighted the usefulness of statistical approaches such as PCA and cluster analysis in deriving dietary patterns, no consideration was given to the preparation of the dietary data beforehand and how that might influence results from such techniques. Finally, several important methodological study details were absent from tables and text such as study design, sample size and characteristics, recruitment period, timing of dietary assessment (and assessment period) and confounder adjustment.

This is the first work to review the evidence linking maternal dietary patterns during pregnancy to offspring growth outcomes in childhood rather than just size at birth. Despite this novelty, certain practical limitations should be considered. Firstly, the search was restricted to literature published in English in peer-reviewed publications. A second limitation is the problem of publication bias, where positive results or results in support of a certain hypothesis are more likely to be published and non-significant results may be largely unreported, leading to false conclusions resulting from type-I errors (Dickersin, 1990). Thirdly, for practical reasons, only one reviewer was involved in the assessment of the quality of studies and as this was a qualitative rather than a quantitative review this likely has introduced some element of bias. Due to the heterogeneity of studies a meta-analysis was not feasible, however a thorough assessment of study quality for each study reviewed was done; something which has not been done to date. Finally, the review can only be as good as the quality of the studies contributing to it, as all studies were observational in nature there will always be the issue of residual confounding, as well as measurement error associated with not only assessment of diet and their associated dietary patterns but also outcomes and covariates.

2.6 Conclusion

This literature review was necessary to draw together the evidence base relating to the potential impact of maternal dietary patterns during pregnancy on not only size at birth but later child growth outcomes. There were no reviews identified which had comprehensively addressed this. The recentness of most publications indicates that this is an area of increasing attention and a synthesis of studies was warranted. Findings from the existing literature remain largely inconclusive in particular when it comes to offspring growth outcomes in childhood. The following chapters attempt to address some of the discrepancies identified, in particular when it comes to dietary pattern analysis and adjustment of confounders, by applying a uniform method of dietary pattern analysis and statistical modelling to data from three large prospective birth cohorts.

3 Methods

3.1 Chapter overview

Chapter 1 provided an introduction and overview to this thesis together with its aims and objectives. Chapter 2 reviewed existing literature in this area and now Chapter 3 will provide a description of the data and the methods used to produce the results described in chapters 4-8.

This thesis used existing data from large prospective birth cohorts both in the UK and DK which have been set up to examine environmental factors as well as genetic factors and their associations with maternal and offspring health. In the following an overview of the three different cohorts will be given providing details of the study designs and populations, the exposure and outcome measures as well as an overview of the assessment of covariates. This will be followed by an outline of the statistical methods applied in order to meet the thesis objectives outlined in Chapter 1. Methods relevant to specific results chapters will be further expanded upon and put into context in their related chapters.

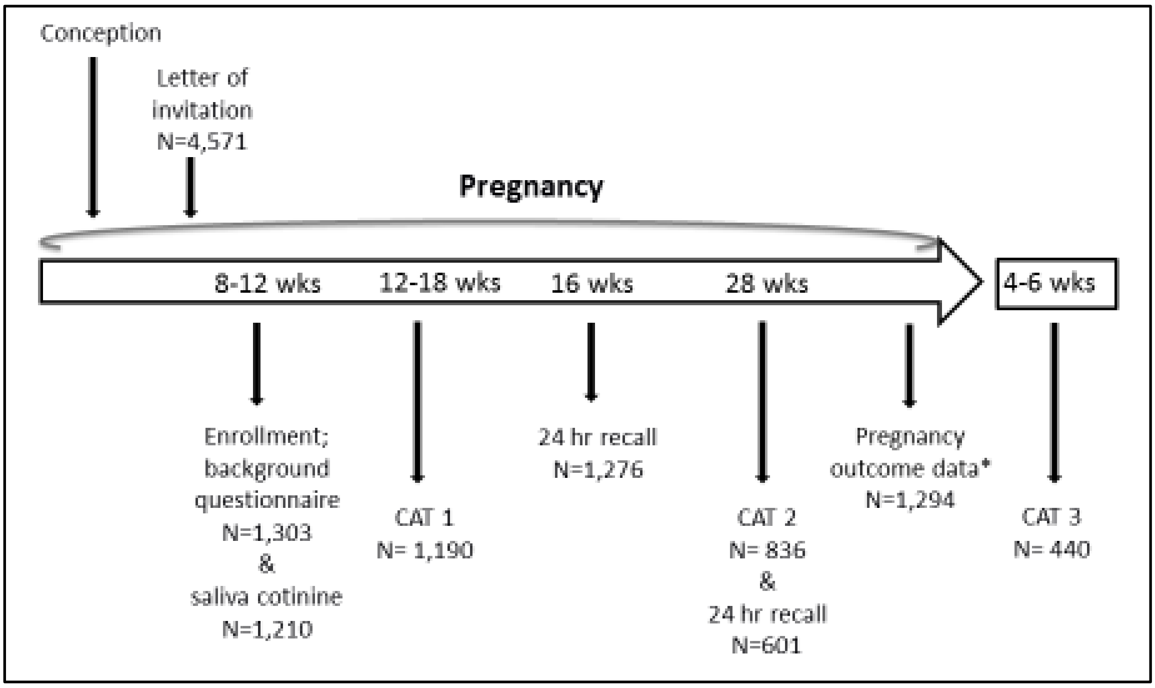
3.2 Study design and study populations

Data were used from three large prospective birth cohorts (see Table 7 for an outline of cohort profiles). A description of the cohorts is presented in the sections below.

3.2.1 CARE

The CARE study is a region(s) based prospective birth cohort. It is a multi-centre study with cohorts in both Leeds & Leicester and it was set up to examine the association between maternal caffeine intake and adverse birth outcomes (CARE, 2008). The Leeds cohort has extensive dietary data collected in the form of 24 hour recalls, unlike the Leicester cohort, and therefore for the purpose of this thesis, only the Leeds data have been used.

Between 2003 and 2006 pregnant women were recruited from the Leeds Teaching Hospitals maternity units. Only mothers aged 18 years and over, with a spontaneous conception, a singleton pregnancy of less than 20 weeks gestation and no previous or current history of medical disorder were considered for inclusion. Women with multiple pregnancy, conception following IVF/ICSI, HIV/Hepatitis B, who used recreational drugs/antidepressants at the time of recruitment, had a current or past history of diabetes outside or whilst pregnant or a current or past history of hypertension or pre-eclampsia were not eligible. Eligible mothers were identified via pre-booking maternity notes and letters of invitation with study information provided to them. Those who agreed to participate either phoned back or were contacted by midwives to arrange an at-home visit. A total of 4,571 mothers were invited to participate of which 1,303 consented and were enrolled into the study (see Figure 6). At enrolment, around 8-12 weeks gestation, mothers were given a self-reported questionnaire collecting data on demographics as well as weight, height and family and medical history. Samples of saliva cotinine levels were also collected as a biomarker of smoking status. The mothers were followed throughout pregnancy to collect data on trimester specific lifestyle behaviours using self-reported questionnaires (caffeine assessment tools (CAT)) with additional follow-up of a sub-sample postpartum (n=440). Of the original 1,303 mothers, 1,294 had data available on pregnancy outcomes and of these 1,270 were live births. The original study protocol was to follow up mothers several weeks after delivery to investigate how their caffeine metabolism had returned to normal. To reduce costs, all cases (SGA or LBW infants; n=191) but only a sample of controls, taken to be the two closest births in time that were not SGA or LBW, were recruited. Data from the third trimester were collected retrospectively on this sub-sample of the cohort. Nearly 80% of the women approached returned data for the 3rd trimester of pregnancy.



*Only singleton pregnancies recruited. CAT, caffeine assessment tool; wks, weeks

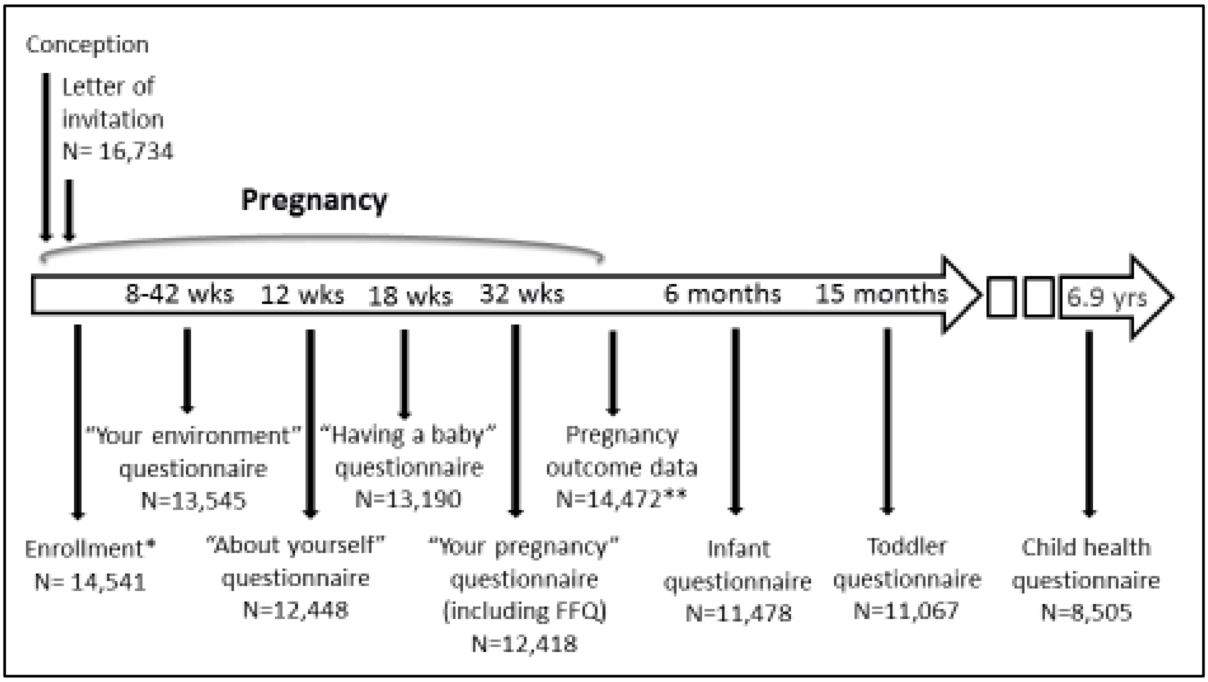
Figure 6. CARE study data collection points

3.2.2 ALSPAC

ALSPAC is a region based prospective birth cohort. It was established to understand how genetic and environmental characteristics influence health and development in parents and children (Fraser et al., 2013). Between 1990 and 1992 all pregnant women residing in the study area of South West of England and with an expected date of delivery between 1st April 1991 and 31st December 1992 were considered for inclusion. Both the media and health services were used to promote the study and distribute “expression of interest” cards.

A total of 16,734 pregnant women were approached and of these 15,717 expressed an interest and were sent study information (Boyd et al., 2013). 14,541 pregnant women were enrolled and information was collected throughout pregnancy at 4 time points using self-reported questionnaires. The timing of the questionnaires depended upon the time of entry into the study as women were allowed to enrol at any time during their pregnancy. In the figure below an overview is given of data collection time points throughout pregnancy for a woman who enrolled in trimester 1.

Of the enrolled mothers, 69 had no data on birth outcomes and 195 were twins, 3 were triplet and 1 was quadruplet resulting in 14,472 pregnancies with known outcomes and 14,676 known foetuses. These pregnancies resulted in 14,062 live births of which 13,988 were alive at 1 year. Follow-up data on both mother and child have been collected at multiple time points via self-reported questionnaires, medical records as well as clinical measures. Only relevant data collection points to the purpose of this thesis are presented in Figure 7 below. More information regarding the cohort's aims, structure, and progress can be found via the study website http://www.bris.ac.uk/alspac/.



*Pregnant women were allowed to enter the study at any time during their pregnancy. Number represents pregnancies enrolled, not fetuses. ** Pregnancies with outcome data (not number of fetuses). Wks, weeks; yrs, years; N, number

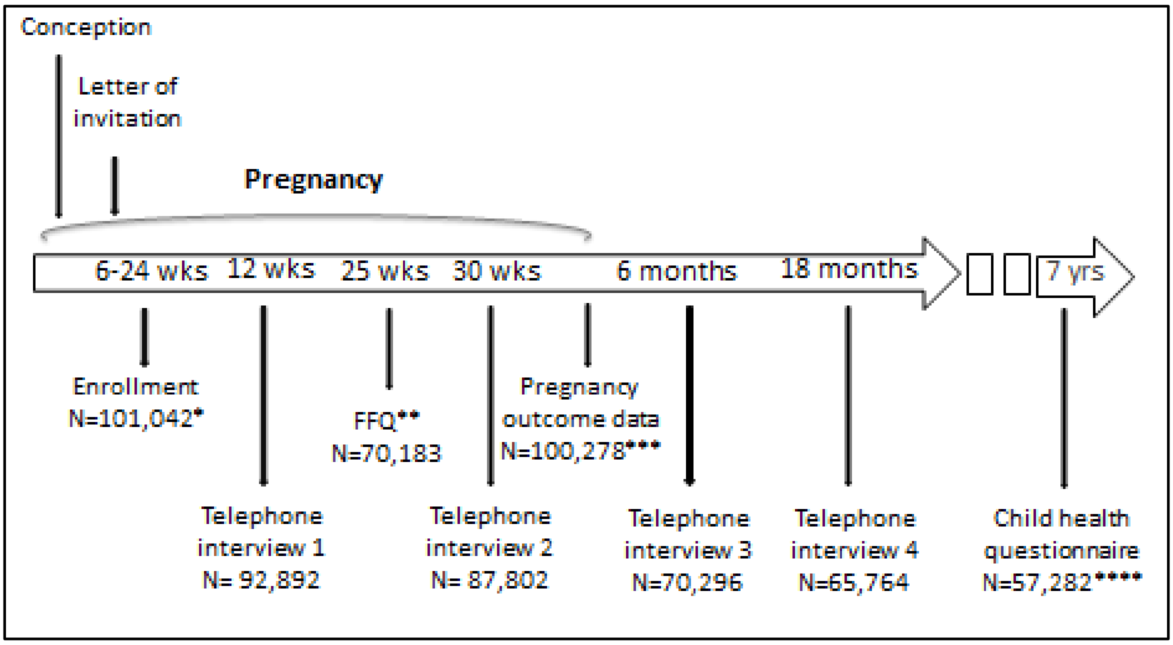
Figure 7. ALSPAC study data collection points

3.2.3 DNBC

The DNBC is a nation based prospective birth cohort set up to study pregnancy complications and diseases in offspring as a function of factors operating in pregnancy/fetal and early life (Olsen, J. et al., 2001). Between 1996 and 2002, over 100,000 pregnant women enrolled into the DNBC. All pregnant women who lived in Denmark and who could speak Danish and planned to carry to term were eligible. No other exclusion criteria were used. Around 60% of women falling pregnant during the study recruitment period received an invitation, 30% did not and 10% failed to meet the inclusion criteria (Olsen, S.F. et al., 2007).

Pregnant women were invited into the study and given oral and printed information at their first pregnancy related general practitioner (GP) visit, usually in weeks 6-12 of pregnancy but later enrolment until week 24 of gestation was allowed. Women who decided to participate returned signed consent forms. Of the women receiving an invitation, approximately 60% consented and were enrolled into the study. The women were followed up throughout pregnancy and after birth and exposure information were collected using computerised telephone interviews as well as self-reported questionnaires. Further data were collected using national registers. In Denmark every citizen has a unique identification number (Central Person Register number) which allows collected data to be linked to data from population based registers on diseases, demography and social conditions (Pedersen, 2011).

A total of 101,042 pregnancies were entered into the study (mothers were allowed to enter multiple pregnancies) and of these, 1 pregnancy outcome was unknown, 47 women emigrated during pregnancy and 3 were deceased leaving 100,278 pregnancies with available outcome data (see Figure 8 below for an overview of the study data collection points). Of these pregnancies 94,809 resulted in live births with 92,668 being live born singletons (Kirkegaard, 2015). More information regarding the cohort's aims, structure, and progress can be found on the study website (http://www.dnbc.dk).



*Mothers were allowed to enter multiple pregnancies. The first pregnancy enrolment consisted of 91,827 women. **Only 94 541 FFQs were sent out. *** Pregnancies with outcome data (not number of fetuses). ****91,256 participants were invited. wks, weeks; yrs, years.

Figure 8. DNBC study data collection points

3.3 Ethical considerations and participant consent

All cohort participants gave written informed consent and all cohorts have had ethical approval which covered the analysis planned for this thesis:

- ALSPAC: Approved by the ALSPAC Ethics & Law Committee (ALEC) and the local research ethics committees, and procedures were in accordance with the Helsinki Declaration of 1975 as revised in 1983.
- CARE study: Approved by the Leeds West Local Research Ethics Committee (reference number 03/054).
- DNBC: Approved by the Danish National committee for Biomedical research Ethics, Copenhagen by protocol nos. KF-01-471 and KF-01-012/97.

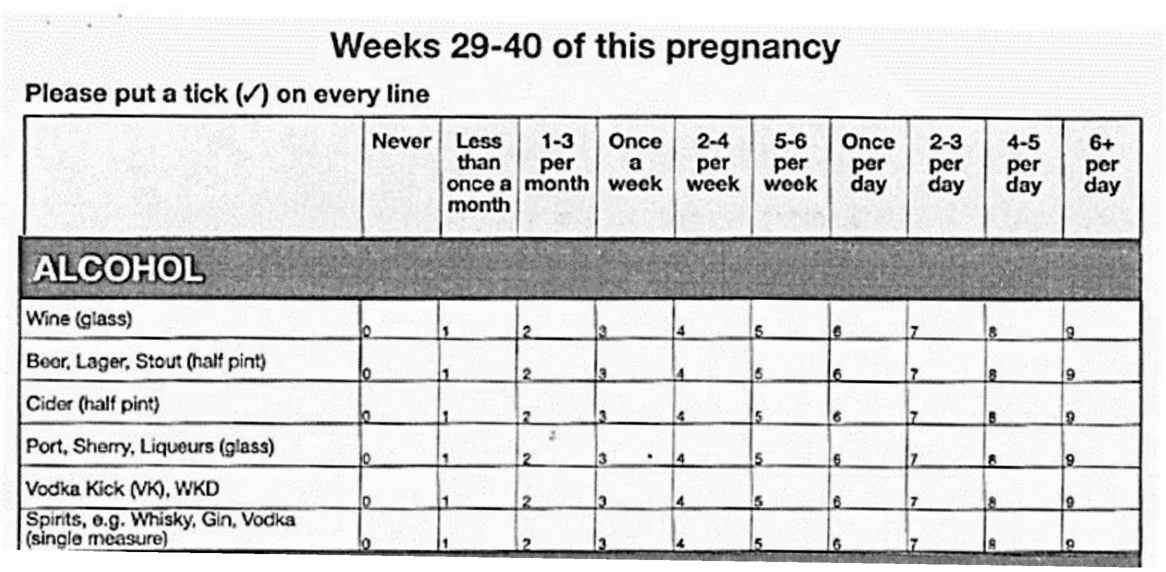
3.4 Measurement of diet

Dietary intake was assessed using different methods and at a different stage in pregnancy for each cohort. The dietary measures used for the three cohorts are outlined below.

3.4.1 CARE

3.4.1.1 Questionnaire based assessment of dietary components

Maternal intakes of specific foods was assessed using a frequency type self-reported questionnaire (CAT) adapted from the UK Women's Cohort Study (Cade et al., 2004a) and administered at 12–18 weeks gestation, week 28 and postpartum (see Figure 6). The questionnaire was developed to ascertain caffeine intake and therefore included a detailed list of caffeine containing foods such as energy drinks, chocolate, tea & coffee (Boylan et al., 2008). In addition to these, participants were asked how often (never; less than once/month; 1–3 times/month; once/week; 2–4 times/week; 5–6 times/week; once/day; 2–3 times/day; 4–5 times/day and >6 times/day) they consumed several food items known to either affect caffeine metabolism or act as a confounder in the association between maternal caffeine intake and birth outcomes (see example given assessing 3rd trimester alcohol intake).



Weeks 29-40 of this pregnancy

Please put a tick (✓) on every line

	Never	Less than once a month	1-3 per month	Once a week	2-4 per week	5-6 per week	Once per day	2-3 per day	4-5 per day	6+ per day
ALCOHOL										
Wine (glass)	0	1	2	3	4	5	6	7	8	9
Beer, Lager, Stout (half pint)	0	1	2	3	4	5	6	7	8	9
Cider (half pint)	0	1	2	3	4	5	6	7	8	9
Port, Sherry, Liqueurs (glass)	0	1	2	3	4	5	6	7	8	9
Vodka Kick (VK), WKD	0	1	2	3	4	5	6	7	8	9
Spirits, e.g. Whisky, Gin, Vodka (single measure)	0	1	2	3	4	5	6	7	8	9

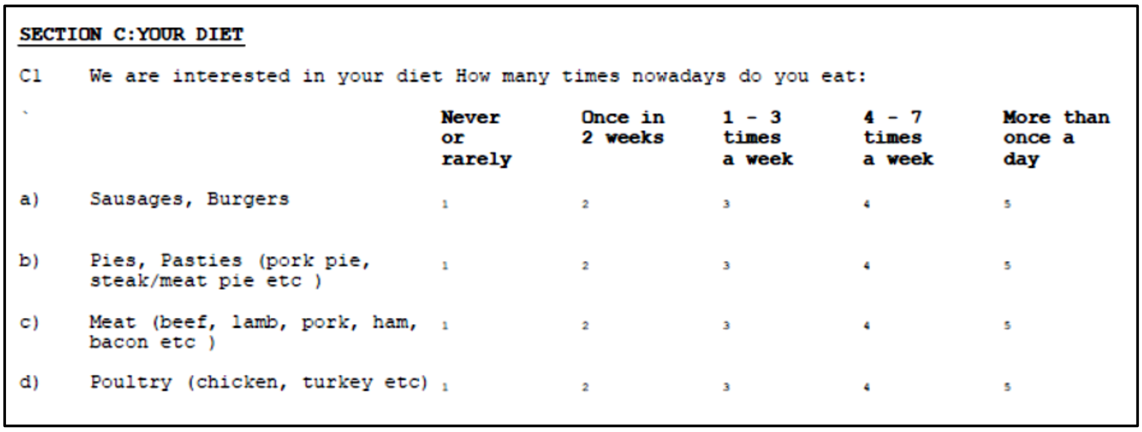
Figure 9. A section from the CARE questionnaire (CAT) relating to intake of alcohol

3.4.1.2 24 hour dietary recall

Dietary intake in pregnancy was assessed using multiple 24 hour dietary recalls administered by a research midwife at 14-18 weeks gestation and 28 weeks gestation (Appendix B: CARE study 24 hour recall form). Participants were asked to report all the food and drink they had consumed in a 24 hour period (12 midnight to 12 midnight) including portion sizes and drink amounts. Total energy intake (kcal/day) and nutrient intakes of foods were estimated by multiplying intakes with the nutrient content of that food using the 5th edition of McCance and Widdowsons `The Composition of Foods' and its supplements (MAFF, 1988; MAFF, 1989; MAFF, 1991a; MAFF, 1991b; MAFF, 1992a; MAFF, 1992b; MAFF, 1993; Ministry of Agriculture, 1993).

3.4.2 ALSPAC

Dietary data were collected using a self-reported dietary questionnaire administered at 32 weeks gestation. The questionnaire was broadly split into two sections of which the first part consisted of a 43 item FFQ where participants were asked how often (never or rarely, once in 2 weeks, 1-3 times/week, 4-7 times/week and >once/day) they consumed a range of foods (see example given in Figure 10 below of consumption categories). Answers were then converted to weekly frequencies by assigning values of 0 to “never”, 0.5 to “once in 2 weeks”, 2 to “1-3 times a week”, 5.5 to “4-7 times a week” and 10 to “more than once a day”. Weekly intakes in grams of each food were calculated by multiplying the frequency of consumption of a food by the standard portion of that food using the Ministry of Agriculture Fisheries and Food guidelines on food portion sizes (Ministry of Agriculture, 1993)[1] .



SECTION C:YOUR DIET

C1 We are interested in your diet How many times nowadays do you eat:

`		**Never or rarely**	**Once in 2 weeks**	**1 - 3 times a week**	**4 - 7 times a week**	**More than once a day**
a)	Sausages, Burgers	1	2	3	4	5
b)	Pies, Pasties (pork pie, steak/meat pie etc)	1	2	3	4	5
c)	Meat (beef, lamb, pork, ham, bacon etc)	1	2	3	4	5
d)	Poultry (chicken, turkey etc)	1	2	3	4	5

Figure 10. A section from the ALSPAC FFQ

The second part of the dietary questionnaire consisted of questions regarding dietary behaviours (e.g. consumption of fat on meat, type of fat used) as well as more in depth questions regarding bread, milk, tea, coffee and cola consumption. Participants were asked how many pieces of bread they consumed in a day (less than 1, 1-2, 3-4 and 5 or more) which was converted into weekly intakes of 0, 10.5, 24.5 and 42 respectively and multiplied with an average portion size of a slice of bread.

---

[1] Some of the FFQ items covered a range of foods, e.g. question on fresh fruit encompassed all fruit with examples of apple, pear, banana, orange and a bunch of grapes given. Due to the differences in portion sizes for each specific food included in some of the FFQ items an average standard portion size was generated by the ALSPAC team for each FFQ item and were used when generating intakes in grams.

They were also asked as to the type of bread (white, brown/granary, wholemeal, chapati/nan) they usually consumed. To allow for differentiation between types of bread consumed, bread preference was combined with weekly intake of bread in grams in order to create two new bread variables, white bread & dark bread (participants who reported consuming chapati/nan only were assigned missing values as this bread category consisted of a mixture of white (nan) and wholemeal (chapati) bread; n=8). Milk consumption was calculated by summing the likely amount of milk drunk in tea and coffee, in breakfast cereal, in puddings and in milky drinks. Participants were asked about daily coffee and tea consumption as well as weekly cola consumption and intakes were estimated by multiplying each item by their respective portion sizes. A new variable for root vegetables was also created by collapsing the two variables expressing carrot and root vegetable (excluding carrots) intake.

Nutrient intakes of foods have been generated by multiplying weekly intakes with the nutrient content of that food using the 5th edition of McCance and Widdowsons `The Composition of Foods' and its supplements (MAFF, 1988; MAFF, 1989; MAFF, 1991a; MAFF, 1991b; MAFF, 1992a; MAFF, 1992b; MAFF, 1993; Ministry of Agriculture, 1993). These were then converted to daily intakes and approximate daily intakes were calculated for energy, protein, total fat, SFA, MUFAs and PUFAs, total sugar, non-milk-extrinsic sugar, dietary fibre (using Southgate analysis), nine vitamins and five minerals[2].

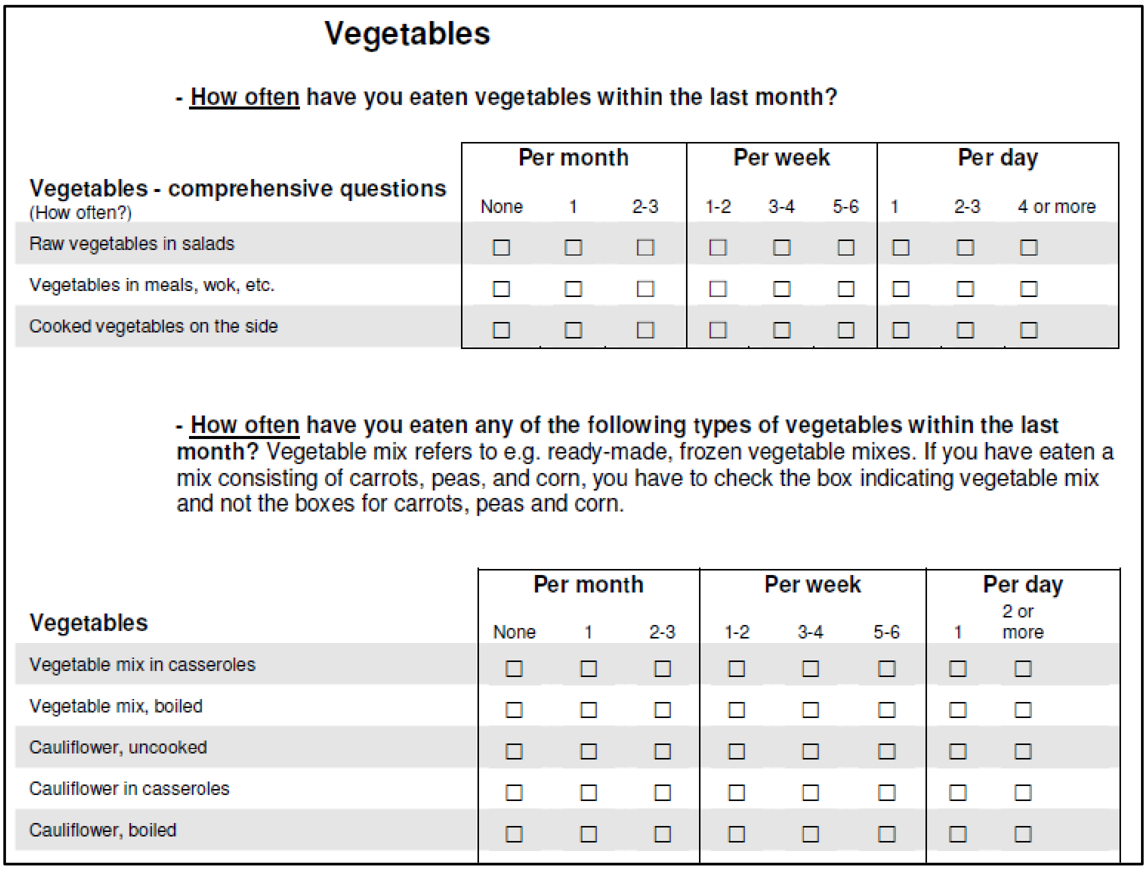
3.4.3 DNBC

Dietary were was obtained using a 360 item self-reported semi-quantitative FFQ around the 25th week of gestation, assessing the previous month’s intake. The FFQ had three main components: food frequency, dietary supplements and other information (Olsen et al., 2007). The questionnaire was developed from one used by the Danish Cancer Registry (Overvad et al., 1991) and has been validated against a 7-day weighed food diary and biomarkers of particular nutrients in a small sub-sample of the cohort (n=88) (Mikkelsen et al., 2006). It was structured in a way so that first women were asked about their meal patterns (e.g. how often they ate breakfast, lunch etc. within the last month) and then it moved onto more specific question in regards to consumption of types of foods such as vegetables, fruits, and beverages.

---

[2] Nutrient data provided by ALSPAC team (not estimated in this analysis)

For most of the food items, women were given 7-11 categories of response options (see example given in Figure 11 below of consumption categories). Nutrient intakes have been calculated by multiplying frequencies with standardized portions and using Danish food composition tables.



Vegetables

- **How often have you eaten vegetables within the last month?**

Vegetables - comprehensive questions (How often?)	Per month None	 1	 2-3	Per week 1-2	 3-4	 5-6	Per day 1	 2-3	 4 or more
Raw vegetables in salads	☐	☐	☐	☐	☐	☐	☐	☐	☐
Vegetables in meals, wok, etc.	☐	☐	☐	☐	☐	☐	☐	☐	☐
Cooked vegetables on the side	☐	☐	☐	☐	☐	☐	☐	☐	☐

- **How often have you eaten any of the following types of vegetables within the last month?** Vegetable mix refers to e.g. ready-made, frozen vegetable mixes. If you have eaten a mix consisting of carrots, peas, and corn, you have to check the box indicating vegetable mix and not the boxes for carrots, peas and corn.

Vegetables	Per month None	 1	 2-3	Per week 1-2	 3-4	 5-6	Per day 1	 2 or more
Vegetable mix in casseroles	☐	☐	☐	☐	☐	☐	☐	☐
Vegetable mix, boiled	☐	☐	☐	☐	☐	☐	☐	☐
Cauliflower, uncooked	☐	☐	☐	☐	☐	☐	☐	☐
Cauliflower in casseroles	☐	☐	☐	☐	☐	☐	☐	☐
Cauliflower, boiled	☐	☐	☐	☐	☐	☐	☐	☐

Figure 11. A section from the DNBC FFQ relating to intake of vegetables

3.5 Measurement of child growth outcomes

There is a range of 13 years between enrolment into the different cohorts and they are therefore at different stages in their follow-up. The CARE study only has birth outcome data. Therefore, maternal diet in CARE has been assessed in relation to size at birth and for ALSPAC & DNBC maternal dietary patterns have been assessed in relation to child height and weight at 7 years as well as size at birth.

3.5.1 CARE

Information regarding birth weight and gestational age was collected from hospital maternity records. Birth weight was recorded in grams and expressed as birth weight centiles which take into account gestational age, maternal height, weight, ethnicity, parity, infant’s sex and birth weight (Gardosi, 2004).

Gestational age was calculated from the date of the last menstrual period, and confirmed by ultrasound scans dating at around 12 and 20 weeks gestation. Babies measuring less than the 10th centile on the customised centile charts were considered small for gestational age (SGA) and those measuring higher than the 90th centile large for gestational age (LGA). Actual birth weight was also analysed as a secondary measure and expressed as a continuous variable in grams.

3.5.2 ALSPAC

Birth weight was collected from hospital records and measurement of birth length was done by trained ALSPAC staff at the maternity hospitals. Low birth weight (LBW) was defined as a birth weight <2,500 g and high birth weight (HBW) as a weight at birth >4,500 g. Children born to the ALSPAC mothers were invited to attend a follow-up examination, which included anthropometric measurements, at about age 7.5 years. Height and weight were measured to the nearest 0.1 cm and 0.1 kg respectively by trained ALSPAC staff.

3.5.3 DNBC

Measurements of birth weight were done by midwives attending child birth according to standard procedures issued by the Danish National Board of Health. As with ALSPAC, no birth centile measure was available. Information on child height and weight was collected via the 7 year follow-up self-reported questionnaire. Mothers were asked to record their child’s most recent GP height & weight measurements together with the date of these.

Measurements were not necessarily done when the child was 7 years old which lead to a range in the children’s age of measurements at the 7 year follow-up. Details of the 7 year follow-up questionnaire can be found on the study website. http://www.ssi.dk/English/RandD/Research%20areas/Epidemiology/DNBC/Questionnaires/7-year%20follow-up.aspx

3.6 Anthropometric indices

Weight or height in itself are not useful indicators of child growth without being related to age and often these two measures are used in combination (e.g. BMI) for the interpretation of anthropometric measurements. In children the three most common anthropometric indices to assess growth status are: weight-for-age (WFA), height-for-age (HFA) and weight-for-height/length (WFH or WFL) (WHO, 1995).

To enable comparisons to be made between cohorts, age specific Z-scores for child height and weight were generated using the World Health Organisation (WHO) growth reference for school aged children. This growth reference was released in 2007 in answer to the then newly released 2006 WHO child growth standards for preschool children and the growing concern that the recommended WHO growth reference for children above 5 years of age (the 1977 National Center for Health Statistics (NCHS)/WHO reference) had become outdated (de Onis et al., 2007). The 1977 growth reference was based on three merged datasets, two of which were from the American Health Examination Survey (HES) Cycle II (6–11 years) and Cycle III (12–17 years), with the third being from the Health and Nutrition Examination Survey (HANES) Cycle I (birth to 74 years), from which only data from the 1 to 24 years age range were used (de Onis et al., 2007). The study authors used this original sample, supplemented with data from the WHO growth standards for preschool children, and applying the same statistical methods they used to generate those, to derive the new 2007 growth reference (de Onis et al., 2007). The charts are based on healthy term born children whose mothers did not smoke before, during, or after pregnancy, and who were fed according to feeding recommendations for breast and complementary feeding (Flegal and Ogden, 2011).

The Z-score system expresses the height and weight as a number of standard deviations (Z-scores) below or above the reference mean or median (WHO, 1995). It is the observed value subtracted by the reference median value and divided by the reference population standard deviation (SD) of that value (see equation below).

$$\boldsymbol{Z - score = \frac{observed\ value - \ median\ reference\ value}{SD\ of\ reference\ population\ value}}$$

There are several advantages to Z-scores, both in terms of usage and interpretation. Firstly, the Z-scores are sex independent thus permitting the evaluation of children's growth status by combining sexes. Secondly, the Z-score scale is linear and therefore a fixed interval of Z-scores results in a fixed difference in for example height for children of the same age. So for a 7 year old girl the difference between a Z-score in height-for-age of -2 to -1 (e.g. 2 cm) is the same as the difference found between a Z-score of 0 to +1. Thirdly, Z-scores usually follow a normal distribution and can be subjected to summary statistics such as the mean and standard deviation (WHO, 1995).

In accordance with the WHO Global Database on Child Growth and Malnutrition, Z-score cut-off points of <-2 SD were also used to classify low weight-for-age (LWFA) and low height-for-age (LHFA) children in ALSPAC and DNBC. Software-macros and documentation of the WHO reference-standards can be downloaded from: http://www.who.int/childgrowth/software/en/

3.7 Measurement of participant characteristics

As with dietary assessment, the measurements of participant characteristics varied between studies and are presented below.

3.7.1 CARE

Maternal characteristics including age, ethnicity (Caucasian vs. Asian, Afro-Caribbean, African or Mixed/Other), pre-pregnancy weight (kg), height (cm), parity (nulli/multiparous), educational level (university degree vs. no degree), maternal intake of dietary supplements (yes/no), vegetarian diet (yes/no) as well as information regarding medical conditions such as GDM and GHT and history of previous miscarriages were self-reported in the enrolment questionnaire. Maternal socio-economic status was evaluated using the Index of Multiple Deprivation (IMD). This index combines multiple indicators chosen to cover a range of economic, social and housing issues into a single deprivation score for each small area in England and ranks areas relative to one another according to their level of deprivation. The IMD is thus an area, and not an individual, deprivation measure.

Caffeine intake (mg/day) and alcohol consumption (units/day) were assessed throughout pregnancy using the CAT (Figure 6). Salivary cotinine levels were measured at enrolment using enzyme- linked immunosorbent assay (ELISA) (Cozart Bioscience, Oxfordshire, UK). Participants were classified on the basis of cotinine concentrations as active smokers (>5 ng/ml), passive smokers (1-5 ng/ml), or non-smokers (<1 ng/ml).

3.7.2 ALSPAC

Parental characteristics were obtained via self-reported questionnaires during pregnancy and at follow-up (see Figure 7) and included information on: maternal age years), maternal pre-pregnancy weight (kg), height (cm), parity (nulli/multiparous), educational level as a marker of socioeconomic status (university degree/ A-level or equivalent), maternal smoking during pregnancy (non-smoker/smoker in both the 1st and 3rd trimester), maternal intake of dietary supplements (yes/no), gestational weight gain (g/week), paternal height (cm) and breastfeeding duration (<=3 months, 4–6 months, and >=7 months) as well as information regarding medical conditions such as GDM and GHT.

3.7.3 DNBC

Information on maternal and paternal characteristics including maternal age (years), maternal pre-pregnancy weight (kg), height (cm), parity (nulli/multiparous), parental SES (high, medium, skilled, student, unskilled, unemployed), maternal smoking during pregnancy (non-smoker, occasional smoker, <15 cigarettes/day, ≥15 cigarettes/day), maternal energy-adjusted alcohol intake (g/day), maternal intake of dietary supplements (yes/no), gestational weight gain (g/week) paternal height (cm) and breastfeeding duration (<=3 months, 4–6 months, and >=7 months) was obtained via telephone interviews (see Figure 8) and national registries.

3.8 Exclusions

For all datasets analyses were limited to live born singleton pregnancies this was done as a lowered birth weight may arise from different causes in singleton and twin births. Where multiple entries of pregnancies were allowed, only the first enrolled pregnancy was used in order to avoid dependencies among correlated measures. Only women with maternal dietary data and child anthropometric data for the DNBC and ALSPAC analyses and birth outcome data for the CARE analysis were included.

Further exclusions were applied to the ALSPAC and DNBC analyses, where mothers whose babies had a gestational age at delivery of <259 days and >294 days, (i.e. three weeks before and two weeks after expected date of delivery) were excluded in order to avoid strata with few observations and to exclude infants with pathologies that may be irrelevant to the purpose of this analysis. This latter exclusion was applied to the CARE dietary pattern analysis (Chapter 6) in order to facilitate between cohort comparisons. For the ALSPAC analysis only, mothers with more than 10 missing FFQ items were excluded and in order to avoid undue influence of extreme values from possible under or over reporting implausible values for energy intake were excluded (see individual analysis chapters for details). The summary table below (Table 7) presents relevant information on the three cohorts. Individual cohort participant flow charts are presented and described in each analysis chapter.

Table 7. Cohort profiles

Study setting	Design & recruitment	Study size	Inclusion criteria	Dietary assessment	Offspring anthropometric measures	Offspring anthropometric assessment
Caffeine And Reproductive Health Study (CARE) Leeds, UK	Prospective cohort 2003-2006	1,303	>18 years; singleton pregnancy <20 wks gestation; no previous or current history of medical disorder; no IVF/ICSI; no recreational drugs	Interviewer administered 24 hr recall (T2 & T3)	BW (g); BW centile (takes into account GA, maternal height, weight, ethnicity, parity, infant's sex & BW)	BW and GA extracted from hospital maternity records
Avon Longitudinal Study of Parents & Children (ALSPAC) Avon, UK	Prospective cohort 1990-992	15,541	All pregnant residents in study area	Self-administered 44 item FFQ (T3; past 2 wks)	BW (g), birth length (cm) Child height (cm) & weight (kg) at 7.5 years	BW & BL: Extracted from hospital records. Child height & weight: measured by trained staff
Danish National Birth Cohort (DNBC) Denmark	Prospective cohort 1997-2002	101,042	All Danish speaking pregnant women in Denmark	Self-administered 360 item FFQ (T2; past 1 m)	BW (g), birth length (cm) Child height (cm) & weight (kg) at 7 years	BW & BL: Extracted from the National Patient Registry of Denmark. Child height & weight: Last GP measurements on self-reported questionnaire

BL, birth length; BW, birth weight; FFQ, food frequency questionnaire; GA, gestational age; hr, hour; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; m, month; T, trimester; wks, weeks

3.9 Data cleaning

All three datasets have been widely used for research and have undergone extensive data cleaning in the past. The DNBC dataset however consisted of some variables (all child and parental anthropometric data) pulled from the original “raw” collected data and were therefore cleaned to ensure the data used for the statistical analyses were appropriate. Variables with extremely large or small values were investigated. These were converted to ‘missing’ where they were deemed as biologically implausible measurements, e.g. 0 g, 1 g and 9999 g for birth weight for term births and 1 cm and 1000 cm for paternal height. This was done as the remaining measurements for that participant may still be valid and would have been lost had the participant been excluded. For the CARE data, where possible any dubious observations were checked with the original records held at the University of Leeds and were only set as missing if there was evidence that the value was incorrect.

3.10 Statistical analysis

This section details the statistical methods used that are common to many of the following chapters containing results; for example the selection of covariates for adjustment, sensitivity analysis and handling large amounts of missing data. Post-hoc sample size calculations will be presented within the methods section for each of the results chapters.

Statistical analyses were performed using the Statistical Analysis System (SAS) version 9.3 for the DNBC dataset and Stata IC & SE version 13 & 14 for the UK datasets. All tests calculated two sided P values and 95% confidence intervals and accepted statistical significance level was 5 % for main analyses; however for stratified analyses, in order to reduce the risk of type I error due to multiple statistical testing, a 1 % statistical significance level was deemed acceptable.

3.10.1 Dietary pattern analysis

3.10.1.1 Harmonisation of dietary data and food groupings across cohorts

As mentioned earlier, dietary data were obtained using different tools in each cohort with different degrees of detail. In order to enable comparison between cohorts and because the number and nature of food data entered into a PCA will influence the resulting patterns, a common food grouping was used. This food grouping consisted of the 65 food groups used to derive the DNBC dietary patterns using PCA (Rasmussen et al., 2014). To facilitate interpretation the 65 food groups have been allocated to 14 main food groups (vegetables, potatoes, nuts, pulses & legumes, fruit & berries, meat, ice cream/sweets/cakes, cereal products, fats, fish, beverages, dairy products, snacks, eggs) as outlined in the table below (Table 8). In addition to the 65 food groups resulting from the Danish dietary data, several food items characteristic of a British population were added. The table below lists the food groups entered into the PCA for each of the cohorts along with their cohort specific descriptions.

For the ALSPAC food data this was relatively straight forward although several food groups were missing as the FFQ was much less comprehensive than that used in the DNBC (43 items vs. 360 items). Where more detailed dietary data on food groups were available, e.g. herbal tea for the tea food group, these data were retained rather than collapsed to prevent loss of possibly relevant details. For both the ALSPAC & CARE data separate groups for breakfast cereal types, which included oat based, wholegrain/bran based and other breakfast cereal were created as well as food groups for baked beans, pastries/savouries, pizza and puddings. This resulted in a total of 44 food groups for the ALSPAC dietary data.

For the CARE food data, 1,770 food items were recorded from the 1st 24 hr recall which were matched to the 65 food groups on the basis of similarity of nutrient composition and comparable usage. There were several composite dishes which could not be assigned to a food group and therefore a new food group for vegetable dishes was created as well as food groups for meat dishes and fish dishes. A food group for soups was also created (see Table 8 below). The addition of these cohort specific foods and those mentioned above resulted in a total of 73 food groups for the CARE dietary data.

Table 8. Food groups and food group descriptions for each cohort

Main food group	Main sub-group description	Sub-group	DNBC food group description (65 items)	CARE food group description (73 items)	ALSPAC food group description[1] (44 items)
Vegetables	Cabbage		Cauliflower, white or red cabbage, sprouts, broccoli, kale	Broccoli, Brussel sprouts, red or white cabbage, savoy cabbage, cauliflower	Cabbage, Brussel sprouts, kale and other green leafy vegetables
	Onions		Spring onions, onion, leeks, garlic, chives	Spring onions, onion, leeks, garlic	
	Mushrooms		Canned & raw	Canned and raw	
	Corn		Frozen, canned & raw corn	Frozen, canned & raw corn	
	Salad		Chinese cabbage (pe-tsai), lettuce, iceberg, radicchio rosso, spinach, romaine lettuce	Cos or Webs lettuce, lettuce, iceberg lettuce, watercress, herb salad, salad leaves, raw spinach	Salad (lettuce, tomato, cucumber etc.)
	Tomatoes		Juice (concentrate), chopped, raw, puree, ketchup, soup	Juice (concentrate), chopped, raw, puree, ketchup, soup	
	Root vegetables		Carrot juice (concentrate), carrots, celeriac	Beetroot , carrots, celeriac, parsnip, radish, swede, sweet potato, turnip	Carrots & other root vegetables (turnip, swede, parsnip etc.)
	Other vegetables		Asparagus, dill, parsley, aubergine, peppers, squash (all types), cucumber, avocado, frozen spinach	Artichoke, asparagus, aubergine, avocado, celery, courgette, cucumber, fennel, endive, gherkins, mixed vegetables (canned or frozen), mustard & cress, okra, peppers, pumpkin, spinach (boiled), squash,	Cauliflower, runner beans, leeks etc.
		Asian vegetables	Bamboo shoots, bean sprouts, seaweed	Bamboo shoots, bean sprouts, seaweed	
	Vegetable dishes[2]			Mixed dishes where vegetables are the major component (e.g. vegetable pasta, vegi-burger, vegetable curry/stir-fry)	
Potatoes	Potatoes		Baked/boiled/mashed		

		Boiled/mashed/ Baked[3]		Baked/boiled/canned/mashed (with/without milk/butter)	Baked/boiled/mashed
		Roast potatoes[3]		Roast potatoes (cooked in fat)	Roast potatoes (cooked in fat)
		Chips	Potato fries, chips, deep fried	Potato fries, chips, deep fried potato products	Potato fries, chips, deep fried
Nuts	Nuts		Almonds, hazelnut, Peanuts, roasted & salted, pine kernels, walnut	Nuts & seeds (almond, Bombay mix, brazil nut, cashew, coconut, hazelnut, mixed, peanut, pine nut, pistachio, pumpkin seed, quinoa, sesame seed, sunflower seed, walnut)	Nuts, nut roast & tahini
Pulses & legumes	Soya		Soybean oil, miso soybean paste, soya sauce, soya drink, tofu soy bean curd, soya beans (dried)	Soya beans, soya drink, tofu soya bean curd, soya sauce	Bean curd (e.g. tofu, miso) & soya or similar non-meats
	Beans & peas		Brown beans, green beans & peas	Aduki beans, broad beans, butter beans, chickpeas, cannellini, green beans, haricot, hummus, lentils, mixed, red kidney, runner beans	Peas, sweetcorn, broad beans
	Pulses[4]				Dried peas, beans, lentils, chick peas
	Baked beans[3]			Baked beans canned in tomato sauce	Baked beans canned in tomato sauce
Fruit & berries	Citrus fruits		Orange, lemon, grapefruit, mandarin, lemon juice	Clementine, lemon, lime, mandarin, orange, satsuma, tangerine	Fresh fruit (apple, pear, banana, orange, bunch of grapes etc.)
	Berries		Strawberry	Blackberry, blackcurrant, blueberry, raspberry, redcurrant, strawberry	
	Dried fruit		Apricot, date, fig, prune, raisin	Apricot, banana chips, currant, date, fig, prune, raisin, sultana	
	Other fruit		Apricot, pineapple, peach, fig, kiwi, nectarine, grape, melon	Ackee, apricot, cherry, fruit cocktail/salad, grapefruit, grape, kiwi, mango, melon, nectarine, olive, peach, papaya, phyalis, pineapple, pomegranate	

	Banana	Banana, raw	Banana, raw	
	Nordic fruit	Apple, pear, plum, rhubarb	Apple, pear, plum, rhubarb	
Meat	Poultry	Duck, pheasant, goose, turkey, chicken	Duck, turkey, chicken	Chicken, turkey etc.
	Pork	Bacon, belly, loin, fillet, lard	Bacon, belly, loin, fillet, mince, spare ribs	Red meats (beef, lamb, pork, ham, bacon etc.)
	Beef/veal	Veal, beef, fore rib, beef striploin, beef topside, thick flank, brisket, beef steak, stock (ready)	Beef, fore rib, striploin, topside, thick flank, brisket, steak, mince	
	Lamb	Shoulder, leg, rack	Breast, loin chops, leg, shoulder	
	Mixed meat/ processed meat products	Sausages, wiener, frankfurter, meatballs, burgers	Burgers, black pudding, chicken goujons/nuggets, chicken/turkey roll, corned beef, donner meat, frankfurter, meat loaf, sausages	Sausages, burgers
	Meat dishes[2]		Mixed dishes where meat (beef/pork/lamb/poultry) is the major component (e.g. beef bolognaise, stew, curry, stir-fry)	
	Toppings	Ham(smoked/cooked/boiled), mortadella, spiced meat roll, salt meat, smoked pork fillet, salami, liver pate	Beef slices, ham, meat pate, pepperami, polony, poultry slices, salami, liver pate	
	Offal	Pig's heart, calf's liver, pig's liver	Liver, tongue	Liver, liver pate, kidney, heart
Ice cream/ sweets/ cakes	Ice cream	Ice cream dairy (cream & milk based), lolly	Ice cream (dairy and non-dairy)	
	Chocolate/ cacao	Cacao powder, chocolate (milk, dark, nut)	Cacao powder, chocolate (milk, dark, nut, fruit, filled) & chocolate bars (Bounty, Crème egg ,Kit Kat, Mars, Milky Way, Smarties, Snickers, Twix)	Chocolate (dairy milk or plain, nut, fruit, filled etc.) & chocolate bars (Mars, Twix, Wispa, Bounty, Crème egg etc.)

	Sweets		Boiled sweets, toffees, liquorice, liquorice confectionary, chewy sweets	Boiled sweets, chewy sweets, fruit gums/jellies, fudge, liquorice confectionary, marshmallows, peppermints, toffees	Sweets (peppermints, boiled sweets, toffees etc.)
	Sweet spreads		Chocolate spread (e.g. Nutella), jam, marmalade	Chocolate spread (e.g. Nutella), fruit spread, jam, lemon curd, marmalade, mincemeat	
	Sugar/cakes/ biscuits		Sugar, cakes, cookies & biscuits, honey, icing,	Sugar, cakes, cookies & biscuits, honey, icing, syrup (golden, maple), cereal fruit and nut bars	Sugar, cakes, cookies & biscuits
	Puddings[3]			Fruit pie, crumble, cheesecake, milk pudding, mousse, gateaux	E.g. fruit pie, crumble, cheesecake, milk pudding, mousse, gateaux
Cereal products	Rice		Rice	Brown rice, rice cakes, savoury rice, white rice	Rice
	Pasta		Spaghetti, macaroni	White/wholemeal-based; plain/filled; without sauce, noodles (rice/wheat-based), lasagne	E.g. spaghetti, Pot Noodles, lasagne
	Breakfast products		Frosties, cornflakes, muesli, oats		
		Wholegrain or bran breakfast cereals[3]		All Bran, Bran Flakes, bran cereal, Fruit & Fibre, Fruitbix, Nutri-Grain, Multi-grain start, Puffed wheat, shredded wheat, Weetabix, Wheatflakes	E.g. All Bran, Bran Flakes, Weetabix, Wheatflakes, Fruit & Fibre
		Oat breakfast cereals[3]		Alpen, muesli, oat cereal, porridge, Ready Brek	E.g. porridge, Ready Brek, muesli
		Other breakfast cereals[3]		Coco Pops, Cornflakes, Frosties, Rice Krispies, Special K, Sugar Puffs, Weetos, honey nut cereal, granola	E.g. Cornflakes, Rice Krispies, Special K, Frosties
	Grains, un-refined		Rye, wholemeal, wholegrain breads and bread rolls , rye-seeded crispbread (e.g. ryvita), rye wholegrain flour	Rye, wholemeal, wholegrain, granary, brown breads and bread rolls and bread with added fibre, wholemeal pitta bread, bulgur wheat, oatmeal, bran, rye-seeded/wholemeal/oat crispbread (e.g. ryvita, crackers)	Dark bread (brown/granary, wholemeal)

	Grains, refined		White flour breads and bread rolls , breadcrumbs, wheat crispbreads, wheat/maize flour, dumplings	White flour breads, buns and bread rolls, white pitta bread, breadcrumbs, wheat/maize/rice flour, dumplings, pearl barley, semolina, couscous, wheat crispbreads/crackers	White bread
	Crispbread[4]				Ryvita, crackers etc.
Fats	Oils		Corn, olive, rapeseed, sunflower, thistle, walnut, grapeseed	Hazelnut, olive, sesame, soya, sunflower, vegetable, walnut	
	Margarine		Margarine and fat spreads	Margarine and fat spreads	Cooking fats (fats from fried foods) & spreads
	Savoury sauces, dressings & condiments		Condiments & salad dressings	Gravies and savoury sauces (including pasta and simmer sauces), pickles, chutneys and relishes, condiments & salad dressings	
Fish	Fish	Lean	Flounder, seal, cod, tuna (raw), garfish, plaice, saithe	Catfish, cod, haddock, halibut, lemon sole, plaice, tuna (tinned)	Cod, haddock, plaice, fish fingers etc.
		Oily/fatty	Salmon, mackerel, trout, halibut, herring	Anchovies, kipper, mackerel, orange roughy, salmon, sardines, trout, tuna (raw)	Pilchards, sardines, mackerel, tuna, herring, kippers, trout, salmon etc.
	Shellfish		Crab, lobster, mussels, oysters, prawns	Crab, lobster, mussels, prawn, scampi, scallops, squid	Cockles, crab, mussels, prawns, etc.
	Fish toppings[5]		Caviar (lumpfish roe), mackerel (tinned), sardines (tinned), herrings (raw/ marinated), cod roe (tinned), tuna (tinned)		
		Smoked fish	Salmon, mackerel, halibut, herring		
	Fish dishes[2]			Mixed dishes where fish or seafood is the major component (e.g. fish pie, fish casserole, fish cakes, fish chowder)	
Beverages	Alcohol	Wine	White, rose, red, port	Champagne, white, rose, red, port	

		Beer	Beer, lager, light	Beer, lager, cider, stout	
		Spirits	Spirits, average values	Spirits	
	Tea		Tea, ready to drink	Tea (regular and herbal) with/without milk	Tea, ready to drink
	Herbal tea[4]				Herbal tea
	Coffee		Coffee, ready to drink	Coffee, ready to drink with/without milk	Coffee, ready to drink
	Soft drinks	Soft drinks, sweetened	Sweetened soft drinks, sweetened juice (from cordial) made up, sparkling mineral water	Sweetened soft drinks, sweetened juice (from cordial) made up	Cola (all)
		Soft drinks, light	Soft drinks with no added sugar, juice from cordial made up with no added sugar	Soft drinks with no added sugar, juice from cordial made up with no added sugar	
	Water		Water	Water	
	Juice		Juice from concentrate (sweetened & unsweetened), applesauce	Juice from concentrate, unsweetened	Tinned juice (including łtomato juice) & pure juice not in tin
Dairy products	Light dairy products	Skimmed milk	Butter milk, semi & semi-skimmed milk	Semi & semi-skimmed milk	Milk (all)
		Sweetened/ sugary milk	Chocolate milk	Chocolate milk, Horlicks, Ovaltine	
	Fatty dairy products	Sour dairy products[5]	Junket, sour cream, crème fraiche, sour whole milk	Sour cream, crème fraiche, cream, whipped cream, whole milk & processed milk (dried and & evaporated whole milk)[6]	
		Non-sour dairy products[5]	Cream, whipped cream, whole milk		
	Yoghurt		Ymer, natural yogurt, fruit yogurt, low fat yogurt	Greek yogurt, natural yogurt, fruit yogurt, low fat yogurt, tzatziki	
	Butter		Butter, salted	Butter, spreadable	
	Cheeses	Soft cheeses	Brie, camembert, danablu, Roquefort	Brie, feta, goat's cheese, mozzarella, ricotta, stilton	Cheeses (all)

		Fresh cheeses	Cream cheese, cottage cheese, quark, smoked cheese, processed cheese	Cream cheese, cottage cheese, fromage frais, processed cheese	
		Hard cheeses	Firm cheese (Danbo), Havarti, parmesan	Cheddar (all), Cheshire, Derby, double Gloucester, Edam, Emmental, Gouda, Lancashire, Leicester, parmesan, Red Windsor, Wensleydale	
Snacks	Snacks		Potato crisps, popcorn, pork scratchings	Crisps (potato-, corn-, wheat-, rice), popcorn, pork scratchings, pretzels	Crisps
Eggs	Eggs		Egg yolk, whole egg (boiled or fried), egg dish (e.g. omelette)	Eggs (boiled, poached, fried, baked), mixed dishes where egg is the major component (e.g. scrambled eggs)	Eggs, quiche
Pizza[3]				Pizza	Pizza
Pastries/ Savouries[3]				Puff/filo/shortcrust pastry, sausage roll, pasty, pakoras, pie, savoury pancake, samosa, savoury scroll, vegetable roll, Yorkshire pudding	Pasty, pie (pork pie, steak/meat pie etc.)
Soup[2]				Homemade, prepared/ready to eat soup, canned condensed soup, dry soup mix	

[1] Note that for the ALSPAC dietary data the food descriptions are the descriptions used in the FFQ for each of the questions concerning consumption of that food group and not examples of the food items combined to create that food group as is the case with the DNBC and CARE data where much more detailed dietary data were collected. [2] CARE food group only. [3] CARE & ALSPAC food group only. [4] ALSPAC food group only. [5] DNBC food group only. [6] Note that the fatty dairy subgroups have been combined due to too few observations in CARE data to keep separate.

3.10.1.2 Principal component analysis

As evidenced in Chapter 2; of the *a posterior* methods used to estimate dietary patterns, principal component analysis (PCA) is one of the most commonly used tool to estimate dietary patterns from FFQ data. It is a data reduction approach which aims to reduce a large set of inter-correlated variables into a smaller set of uncorrelated variables or principal components which should still explain the majority of the variance in the original set of variables. It does this by forming linear combinations of the original dietary variables, and the coefficients defining these linear combinations are called factor loadings and are the correlations of each food item with that component (Northstone et al., 2008). The number of components to retain is usually determined using i) a scree plot of eigenvalues (determined by the elbow in the plot), ii) eigenvalues above 1 and iii) interpretability of the components. In order to improve interpretation of PCA results, post estimation rotation of the components is often done. The goal of rotation is to make the patterns of the factor loadings clearer. There are two types of rotation, orthogonal or oblique, the former presumes the components are uncorrelated and the latter that they are correlated (Brown, 2009). The predominant method used when defining dietary patterns is orthogonal varimax rotation. Once the number of components to retain has been determined, scores for each component are derived and can be used to assess associations between the different components and health outcomes (Hu, 2002).

Other data transformation methods are available to derive dietary components such as cluster analysis and latent class analysis (LCA), of which the latter is a more novel approach that considers dietary patterns as latent variables (Sotres-Alvarez et al., 2010). As opposed to PCA, where highly correlated food items are grouped together into components and participants have scores for each component, in cluster analysis and LCA individuals are grouped into separate components with similar food intakes in each group.

3.10.1.3 Standardisation and energy adjustment of dietary data

Standardisation of dietary data prior to dietary pattern analysis is sometimes done. This approach however is not needed if the PCA is based on the correlation matrix (standardised factor loadings) as opposed to the covariance matrix.

In addition, some studies energy adjusted dietary data beforehand. There are several ways of energy adjusting dietary data, including the use of nutrient densities, multi-variate techniques and the residual method; of which the latter appears to be the most widely used technique when it comes to dietary pattern analyses and it was therefore deemed reasonable for use in this thesis. Using the residual method, energy adjusted dietary data are computed as the residuals (the difference between the observed and the fitted values) from regression models with total energy intake as the predictor or independent variable and the food item as the outcome or dependent variable. This then gives a measure of dietary intake that is uncorrelated with total energy intake (Willett, 2013).

Full details of the dietary pattern analysis for each cohort are provided in the individual analysis chapters (Chapter 6, 7 & 8). Rasmussen et al. (2014) used PCA with varimax rotation on residually energy adjusted dietary data to derive the dietary patterns in the DNBC which have been assessed in relation to offspring growth outcomes in Chapter 8. To better enable comparison between cohorts; the same approach has been used to evaluate dietary patterns in both the CARE as well as the ALSPAC cohorts.

3.10.2 Linear regression

Linear regression is a measure used to describe linear relationships. It is used to quantify an association between two variables and allows us to predict the values of one variable (the outcome) based on the value of another (the predictor). It is only applicable when the outcome is continuous but the predictors however can be both categorical and continuous variables. Results from a regression model are only valid if certain conditions have been met. These conditions are mainly concerned with the residuals generated from the model (i.e. the distance between the observed and the fitted values). For the model to be reliable, the residuals need to come from a normal distribution for every value of the predictor variable. This can be assessed by plotting a histogram of the residuals. In addition, variance of the outcome should be the same at each value of the predictor and this can be checked with scatterplots of the residuals vs. predictor variables or the residuals vs. fitted values.

For all analyses where the outcome is a continuous measure, linear regression has been used and plots of the residuals have been generated to assess whether model conditions have been met.

3.10.3 Logistic regression

Logistic regression is used when the outcome of interest is of a binary nature. As opposed to linear regression, there are no assumptions concerning the residuals that need to be met. Instead model diagnostics can be assessed using the Hosmer-Lemeshow (H-L) measure of model fit (Hosmer DW, 2013)

Logistic regression has been used in all analyses of this thesis where the outcomes of interest are binary, these include HBW, LBW, SGA, LWFA and LHFA and for all models, the model fit has been assessed using the Hosmer-Lemeshow goodness of fit test.

3.10.4 Confounders, mediators and effect modifiers

A confounder is a variable that is a predictor of both the exposure and the outcome. It can mask an actual association or falsely create an apparent association between the exposure and outcome when no real association between them exists and it is therefore important to adjust for any confounding factors. Potential confounders in the link between maternal dietary patterns and offspring body composition were identified *a priori* from the literature reviewed in Chapter 2. In order to get the most unbiased estimates, where available these confounders have been adjusted for in all regression models, regardless of their significance levels and their ability to change the overall risk estimate in the particular datasets. However efforts have been made to avoid collinearity which happens when you include covariates that essentially explain the same information in the same models. For example, for the CARE dataset, socio-economic status and educational status were highly correlated and therefore only one of them was included in the models.

In addition, thoughts have been given to variables which could act as mediators. These are variables which are on the causal pathway between the exposure and the outcome and were initially excluded from all models. For example birth weight can be predicted by maternal diet but has in turn the potential to act as a predictor of child body composition, examples of which can be found in the literature review chapter. Consideration has also been given to variables which could act as effect modifiers of the effect of maternal diet on offspring body composition. For example breastfeeding status has been recognised as a possible “programmer” of child growth (Singhal and Lanigan, 2007b) and it was therefore assessed as an effect modifier by including an interaction term in the confounder adjusted models.

All three cohorts had comprehensive data on covariates obtained from questionnaires given at enrolment and during pregnancy. For all cohorts these included: alcohol intake, energy intake, dietary supplements, smoking status, pre-pregnancy weight, maternal height, parity, maternal age, maternal socio-economic status (SES), marital status and gestation. ALSPAC & DNBC also had data on gestational weight gain, paternal height and breastfeeding patterns.

3.10.5 Sensitivity analyses

Separate sensitivity analyses were performed dependent upon the exposure of interest and have been listed in the analysis chapters.

3.10.5.1 Handling missing data: multiple imputation

Both the ALSPAC as well as the DNBC dataset suffered from missing data on several important variables including breastfeeding status, gestational weight gain and paternal height. Generally speaking there are three different types of missing data, missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR) (Donders et al., 2006). If data are MCAR it is unlikely that missingness will lead to biased results as the missingness is not due to any subject characteristics (observed or unobserved) and a complete-case analysis should suffice. However if data are MNAR, where the missingness is likely related to some unobserved participant characteristic or the missing value itself, then the participants with missing data are likely to be different from the source population which in turn will lead to biased estimates. Finally data can be MAR, which is the most common form of missingness in epidemiological research, and occurs when missingness is due to observed participant characteristics. When this is the case, a complete-case analysis will no longer be based on a random sample of the source population (as with MNAR) and simple methods for dealing with missing data, such as the indicator method and overall mean imputation, might also led to biased results (Donders et al., 2006). Instead more sophisticated methods such as multiple imputation (MI) can be used. Using this technique, missing data for a participant are imputed with a value that is predicted using the participant’s other known characteristics (Donders et al., 2006). But rather than just doing this once as with single imputation, this is performed multiple times and an overall average of those values are taken as the new imputed value. Drawing inferences from MI involve three separate steps (Yuan, 2000):

1) The missing data are filled in multiple times to generate multiple complete data sets.

2) The complete data sets are analysed by using standard procedures.
3) The results from the multiple complete data sets are combined for the inference.

It is not possible to assess whether data are MAR as that would require a knowledge of the missing values (Schafer and Olsen, 1998). Hence it is often unclear whether MI is an appropriate technique to use, and often missing values will occur due to a variety of reasons, not just a single one. However, at present there is no simple way to ignore this assumption and MI is still a preferred technique to that of less sophisticated methods and even if MAR seems unrealistic, if a range of covariates which are associated with the missing data are included in the imputation process (step 1), it is unlikely MI will lead to biased results (Schafer and Olsen, 1998).

In order to explore whether missing data could have led to biased estimates, multiple imputation was performed to impute missing values for variables included in the main analysis models for the final sample of mother-child pairs (see Appendix C: Stata code for multiple imputation analysis in ALSPAC). To allow for categorical variables, the fully conditional specification (FCS) method (van Buuren, 2007) was used to impute missing data using a regression method to impute missing values for continuous variables and a logistic regression method to impute missing values for categorical variables. Five imputation datasets were generated, a number which has been suggested sufficient when only a small amount of data are missing (Carpenter JR, 2007). All variables included in the main adjusted analyses, as well as exposures and outcomes, were included in the imputation procedure. Regression analyses were carried out on each dataset and then averaged using Rubin's rules (Rubin, 1987).

4 Maternal diet during pregnancy and offspring size at birth: alcohol in focus

This chapter commences the investigation of the relationship between maternal diet in pregnancy, with alcohol in focus, and offspring size at birth.

Work from this chapter has formed the basis of 1 peer-reviewed paper (Nykjaer et al., 2014), and two conference presentations.

4.1 Chapter overview

There is a lack of consensus in the evidence regarding low maternal alcohol consumption and birth outcomes. Using data from the CARE birth cohort, this study aimed to investigate the association between alcohol intake prior to and during pregnancy with offspring size at birth and to examine the effect of timing of exposure on this relationship.

Questionnaires assessed alcohol consumption prior to pregnancy and for the 3 trimesters separately. Frequency of alcohol consumption was split into categories of intake (≤2 units/week & >2 units/week) including a non-drinking category as the referent. This was related to size at birth, adjusting for confounders including salivary cotinine as a biomarker of smoking status.

Nearly two-thirds of women prior to pregnancy and over half in the 1st trimester reported alcohol intakes above the Department of Health (UK) recommendation of no more than 2 units/week. Associations with offspring size at birth were strongest for intakes above 2 units/week compared to non-drinkers in the periods prior to pregnancy and trimester 1 & 2. Even women who adhered to the recommendations in the first trimester were at a significantly higher risk of having babies born with lower birth weight and birth centile compared to non-drinkers, after adjusting for confounders (P<0.05).

These findings suggest that women should be advised to abstain from alcohol when planning to conceive and throughout pregnancy.

4.2 Introduction

Alcohol was confirmed as a teratogen in the late 1970s after observations made in France and the US in infants born to alcoholic mothers (Lemoine et al., 1968; Ulleland, 1972). Evidence regarding the damaging effects of heavy drinking in pregnancy is now well established. There is however, a lack of consensus regarding the impact of low intakes on offspring size at birth, with studies reporting a wide range and even a protective effect of low intakes in reviews of the evidence (Jacobsen et al., 1993; Spohr, 1996; Institute, 1999; Gray, 2006; Henderson, J. et al., 2007a; Henderson, J. et al., 2007b; Patra et al., 2011; O'Leary, C.M., 2012). This is reflected in the different country-level policy regarding alcohol consumption during pregnancy and highlighted in a review by O’Leary et al (2007) on alcohol policies in English-speaking countries (O'Leary, C.M. et al., 2007). Some, such as the US, recommend abstinence (Gynecologists, 2011). Others advise abstinence but state that small amounts of alcohol are unlikely to cause harm (Policies, 2009). In the UK, the Department of Health (DH) recommends that pregnant women and women trying to conceive should avoid alcohol altogether and never drink more than 1-2 units once or twice a week (Health, 2008). The National Institute of Health and Clinical Excellence (NICE) additionally emphasises the message to avoid drinking alcohol in the first 3 months of pregnancy as this may be associated with an increased risk of miscarriage (NICE, 2010).

According to the UK Health Survey 2011, 52% of women of childbearing age who drink exceed the daily limit of 2-3 units per day and 25% drink more than twice the recommendations (Fat LN, 2011). Results from the most recent UK Infant Feeding Survey (IFS) which included data from over 15,000 women, showed that 40% drank alcohol during pregnancy but only 3% drank more than 2 units per week (Centre, 2012).

Data suggest that over 40% of pregnancies in the UK are unplanned (Rudd, 2013; Association, 2008). With such high rates of unplanned pregnancies and excess drinking, early pregnancy is likely to be the period of highest intake for women who are unaware of their pregnancy and this could put them and their unborn baby at risk.

Alcohol crosses the placenta and results in nearly equal concentrations in the mother and fetus. The mechanisms whereby alcohol affects fetal growth and development are complex as these are staged processes, and the sensitivity of the fetus to alcohol will likely depend on the timing of the exposure (Gray, 2006). Few studies have taken into account the effect of timing of alcohol exposure on birth outcomes. Of those looking at alcohol consumption pre-pregnancy and for all the trimesters separately results were conflicting as to which period of exposure is most sensitive and some found an association between alcohol intake and offspring size at birth all at different levels of exposure whilst others suggested no association even at high levels of intake (O'Keeffe, 2013; Chiaffarino et al., 2006; O'Leary, C. et al., 2009).

The aims of this study were to investigate the relationship between maternal alcohol intake prior to and during pregnancy and offspring size at birth, and to assess whether these relationships differed by timing of exposure during pregnancy.

4.3 Methods

The Caffeine And Reproductive Health (CARE) Study is a region(s) based prospective birth cohort which was set up to examine the association between maternal caffeine intake and birth outcomes (CARE, 2008). Details of the CARE study, including design, setting, dietary assessment, outcome measures and assessment of participant characteristics can be found in Chapter 3.

4.3.1 Assessment of alcohol consumption

Alcohol intake was assessed throughout pregnancy using a food frequency approach adapted from the UK Women's Cohort Study administered at enrolment (12-18 weeks' gestation), week 28 and postpartum (weeks 46-50) (Cade et al., 2004). These assessed consumption 4 weeks prior to pregnancy through to week 12 of gestation, weeks 13-28 and weeks 29-40 respectively. Participants were asked how often (never, less than once/month, 1-3/month, once/week, 2-4/week, 5-6/week, once/day, 2-3/ day, 4-5/day and >6/day) they consumed different types of alcohol (wine, beer/lager/stout, cider, port/sherry/liqueurs, vodka kick and spirits). Frequency of alcohol consumption derived from the questionnaires was converted to times per week which was then multiplied by the units of alcohol in each of the alcoholic beverages listed on the questionnaire to get weekly consumption in units for each of the time periods. For wine, the units of alcohol per portion for each type of alcoholic beverage was 2.3 for beer & cider 2.0, port & spirits 1.0 and vodka kick 1.5. This is in accordance with the conversion factors used since 2006 in The Health Survey of England, one unit of alcohol equating to 10 ml by volume or 8 g by weight (Fat LN, 2011).

4.3.2 Statistical power calculation

Comparing birth weight between non-drinkers and drinkers and the standard deviation of birth weight identified in the study (SD=576 g), the study had 85% power to detect a difference of just over -100 g in birth weight for a two-sided t-test at P<0.05 in trimester 1.

4.3.3 Statistical analysis

Analysis was undertaken using the continuous weekly alcohol variable split into categories of intake based on the Department of Health (2008) recommendations of no more than 2 units/week with the inclusion of a non-drinking category which was used as the reference group (0 units/week, ≤2 units/week and >2 units/week).

Univariable analyses were performed using oneway ANOVA for normally distributed outcomes and the Kruskal-Wallis test otherwise. The chi-square test was used for categorical outcomes.

Data were further analysed using multivariable linear regression for continuous outcomes and multivariable logistic regression for binary outcomes. Maternal pre-pregnancy weight, height, parity, ethnicity, gestation and baby's sex were taken into account in the definition for customised birth centile and were adjusted for in the model for birth weight. Further statistical adjustment was made, based on a priori knowledge from literature, for maternal age, salivary cotinine levels, caffeine intake and maternal education (as a proxy for socioeconomic status). Because of the possible correlation between alcohol consumption and energy intake, energy intake obtained from the 24hr recalls was included in the model, as it was important to distinguish between the separate effects of alcohol and energy intake on birth outcomes (Willet, 2013). Extreme values for energy intake (1% highest and 1% lowest) were excluded based on the method proposed by Meltzer et al. (2007) (Meltzer et al., 2008). The robustness of the results to excluding women with conditions known to predispose to adverse birth outcomes, including previous low birth weight (LBW) baby, gestational diabetes and gestational hypertension, as well as excluding "risky drinkers" for women of childbearing age (defined by the Centers for Disease Control as more than 7 US drinks per week corresponding to 10 UK units (Prevention, 2004)) was also assessed.

4.4 Results

A total of 1303 women were recruited, and of these 1294 had data available on birth outcomes. Five women had terminations and were therefore excluded from this analysis. An additional 25 women were excluded due to extreme energy intakes (the 1% highest and 1% lowest intakes).

4.4.1 Alcohol intake

Of the remaining 1264 women, 1153 (91%), 1135 (90%), 793 (66%) and 377 (30%) women completed the questions on alcohol intake pre-pregnancy, 1st trimester, 2nd trimester and 3rd trimester respectively (Table 9). Alcohol intake before pregnancy and in the first trimester were significantly higher (P<0.0001) than in the 2nd and 3rd trimesters (11.2, 4.0, 1.8 and 1.9 units/week respectively). The prevalence of women consuming more than the recommended 2 units per week were highest before pregnancy (74%) and in the 1st trimester (53%) with mean intakes for women reaching 15.1 units (95% CI: 14.1, 16.1) and 7.2 units (95% CI: 6.6, 7.9) per week respectively. The prevalence of "risky drinkers" was relatively low at 11%, 2% and 3% for trimester 1, 2 and 3, but much higher before pregnancy with 38% of women consuming more than 10 units/week.

Table 9. Self-reported alcohol intake among pregnant women in the CARE study

Characteristic	N (% total sample)	Mean	95% CI
Alcohol intake (units/week)[a]:			
4 weeks before pregnancy	1153 (100.0)	11.2	10.4, 12.1
First trimester	1135 (98.4)	4.0	3.6, 4.4
Second trimester	793 (68.8)	1.8	1.6, 2.0
Third trimester	377 (32.7)	1.9	1.5, 2.3
Categories of intake 4 weeks before pregnancy[b]			
Non-drinkers	157 (13.6)	0	0
<2 units/week	148 (12.8)	0.9	0.9, 1.1
>2 units/week	848 (73.6)	15.1	14.1, 16.1
Categories of intake trimester 1			
Non-drinkers	243 (21.4)	0	0
<2 units/week	292 (25.7)	0.8	0.7, 0.8
>2 units/week	600 (52.9)	7.2	6.6, 7.9
Categories of intake trimester 2			
Non-drinkers	291 (36.7)	0	0
<2 units/week	278 (35.1)	0.8	0.8, 0.9
>2 units/week	224 (28.3)	5.4	4.8, 5.9
Categories of intake trimester 3			
Non-drinkers	193 (51.2)	0	0
<2 units/week	80 (21.2)	0.9	0.8, 1.0
>2 units/week	104 (27.6)	6.3	5.2, 7.3

[a] 1 unit of alcohol is 10 ml by volume or 8 g by weight of pure alcohol.
[b] Categories based on the DH (2008) weekly recommendations of no more than 2 units/week(Health, 2008).

4.4.2 Characteristics of women according to categories of alcohol intake

Table 10 shows the characteristics of participants according to alcohol consumption. Women with alcohol intakes higher than 2 units per week were more likely to be older, have a university degree, be of European origin and less likely to live in an area within the most deprived IMD quartile. These characteristics were consistent across all trimesters. In trimester 1 however, women in the high consumption category were also more likely to have a higher total energy intake compared to the other two categories and have no children. Apart from differences in energy intake, the same differences between the women as seen in trimester 1 were also true for the 4 weeks before pregnancy (results not shown).

Table 10. Characteristics of mothers by alcohol intake during pregnancy reported in three questionnaires[a]

	First trimester (n=1135)				**Second trimester (n=808)**				**Third trimester (n=384)**			
	Non-drinkers (n=243)	**<2 units/wk (n=298)**	**>2 units/wk (n=594)**	P^{b}	**Non-drinkers (n=300)**	**<2 units/wk (n=282)**	**>2 units/wk (n=226)**	P^{b}	**Non-drinkers (n=197)**	**<2 units/wk (n=82)**	**>2 units/wk (n= 105)**	P^{b}
Age (years) mean (95% CI)	29.4 (28.7, 30.1)	29.5 (28.9, 30.1)	30.5 (30.1, 30.9)	0.002	28.9 (28.3, 29.5)	30.7 (30.2, 31.3)	31.8 (31.2, 32.3)	<0.0001	28.5 (27.8, 29.3)	30.8 (29.9, 31.7)	30.7 (29.8, 31.6)	0.0005
Pre-pregnancy BMI (kg/m^2) mean (95% CI)	25.0 (24.4, 25.7)	24.7 (24.1, 25.3)	24.5 (24.1, 24.9)	0.5	25.1 (24.4, 25.8)	24.5 (23.9, 25.0)	23.9 (23.3, 24.4)	0.1	25.5 (24.6, 26.4)	24.0 (23.0, 25.0)	23.9 (23.2, 24.8)	0.1
Total energy intake (kcal) mean (95% CI)	2060 (1778, 2136)	2079 (2012, 2146)	2162 (2111, 2213)	0.04	2075 (2007, 2144)	2169 (2099, 2239)	2181 (2097, 2264)	0.08	2080 (1990, 2170)	2142 (2013, 2277)	2156 (2036, 2276)	0.5
Caffeine intake (mg/day) mean (95% CI)	176.1 (152.7, 199.4)	174.2 (153.3, 195.1)	202.0 (186.3, 217.8)	0.06	163.0 (139.2, 186.8)	158.0 (138.8, 177.3)	175.7 (155.8, 195.6)	0.009	206.1 (171.4, 240.9)	223.3 (170.8, 275.7)	189.4 (158.9, 219.8)	0.4
Smoker at 12 weeks % (n)[c]	17.4(40)	18.3(53)	14.9(85)	0.6	14.6(41)	12.4(33)	9.6 (21)	0.2	22.7(42)	18.8 (15)	11.9(12)	0.2
IMD most deprived quartile % (n)	37.5(87)	32.7(93)	23.3(134)	0.0001	32.7(91)	21.4(58)	16.3 (35)	0.0001	34.1(63)	25.6(20)	15.5(15)	0.003
University degree % (n)	34.6(84)	39.3(117)	43.6(259)	0.05	35.1(102)	49.1(137)	51.6(115)	0.0002	28.5(55)	40.0(32)	50.9(53)	0.0001
European origin % (n)	85.5(206)	94.9(283)	98.2(582)	0.0001	92.0(266)	96.8(270)	99.1(220)	0.001	94.8(181)	96.3(77)	99.0(102)	0.4
Primigravida % (n)	36.6(89)	43.7(119)	53.8(317)	0.0001	52.4(152)	49.8(138)	47.9(107)	0.6	52.1(100)	47.5(38)	56.7(59)	0.5
Preterm labour % (n)	2.1(5)	6.0(18)	4.7(28)	0.08	5.2(15)	3.9(11)	4.5(10)	0.8	7.3(14)	7.5(6)	5.8(6)	0.9
Pre-eclampsia % (n)	5.8(14)	5.1(15)	4.0(28)	0.8	5.9(17)	7.3(20)	2.3(5)	0.05	7.5(14)	5.1(4)	2.9(3)	0.3
Past history of miscarriage % (n)	26.3(63)	22.4(66)	22.3(133)	0.5	27.2(78)	23.1(64)	22.1(49)	0.3	23.2(44)	17.5(14)	23.5(24)	0.5

[a] Split of alcohol intake is based on the DH (2008) weekly recommendations of no more than 2 units/week(Health, 2008). [b] P-value using one-way ANOVA for normally distributed and Kruskal-Wallis for non-normally distributed continuous variables, and x2-test & Fisher's exact test for categorical variables. Significant difference at p<0.05. [c] Smoking status based on salivary cotinine concentrations: non-smoker <1 ng/ml, passive smoker 1-5 ng/ml, current smoker >5 ng/ml. Where numbers do not add up it is due to a small proportion of missing data.

4.4.3 Birth outcomes

Of the 1264 women with information on birth outcomes, 166 (13.1%) babies weighed less than the 10th centile and fifty-seven (4.4%) were low birth weight (<2500g).

4.4.4 Relationship between alcohol intake and size at birth

There was a strong association between alcohol intake before pregnancy and birth weight and birth centile after adjustments for maternal pre-pregnancy weight, height, parity, ethnicity, gestation, baby's sex, maternal age, salivary cotinine levels, caffeine intake and maternal education (Table 11). Women who adhered to the guidelines were not at increased risk, but compared to non-drinkers, alcohol intakes of >2 units/week were associated with a -7.7 (95% CI: -12.8, -2.6) decrease in customised birth centile (adjusted P_{trend}=0.009).

For consumption during pregnancy, after adjustments, alcohol consumption was associated with about a 100 g reduction in birth weight for women consuming >2 units/week in trimester 1 (P_{trend}=0.007). Compared to non-drinkers, alcohol intakes of <2 units/week and >2 units/week in trimester 1 were associated with an adjusted -5.8 (95%CI: -10.8, -0.7) and a -8.2 (95% CI: -12.6, -3.7) decrease in customised birth centile respectively (P_{trend}=0.002). The adjusted odds ratios for SGA were 1.7 (95%CI: 0.9, 3.1) for intakes <2 units/week and 2.0 (95%CI: 1.2, 3.4) for intakes >2 units/week in trimester 1 (P_{trend}=0.03) compared to non-drinkers; with the H-L goodness-of-fit test statistic indicating an acceptable model fit (P=0.55). These associations were attenuated in trimester 2 & 3.

Table 11. The relationship between maternal alcohol intake 4 weeks before pregnancy and size at birth (n=1152)

	Unadjusted change (95% CI)	**P[a]**	**Adjusted change[b] (95% CI)**	**P[a]**
Birth weight (g)				
Non-drinkers	0.0	0.9	0.0	0.03
< 2 units/week	-14.6 (-147.4, 118.1)		-70.2 (-167.4, 26.9)	
>2 units/week	-23.2 (-123.6, 77.1)		-105.7 (-183.5, -27.9)	
Customised birth centile[c]				
Non-drinkers	0.0	0.1	0.0	0.009
< 2 units/week	-2.8 (-9.4, 3.9)		-4.2 (-10.9, 2.4)	
>2 units/week	-4.9 (-9.9, 0.1)		-7.7 (-12.8, -2.6)	
SGA (<10th centile)[c]	**Unadjusted OR (95% CI)**	**P[a]**	**Adjusted OR[b] (95% CI)**	**P[a]**

Non-drinkers	1.0	0.5	1.0	0.2
< 2 units/week	1.4 (0.7, 2.7)		1.7 (0.8, 3.5)	
>2 units/week	1.4 (0.8, 2.3)		1.8 (0.9, 3.2)	
Low birth weight (≤2500 g)				
Non-drinkers	1.0	0.5	1.0	0.4
< 2 units/week	0.6 (0.2, 1.7)		0.4 (0.1, 2.7)	
>2 units/week	0.9 (0.4, 2.2)		1.1 (0.2, 6.1)	

[a] P for trend for categories of alcohol intake. [b] Adjusted for maternal pre-pregnancy weight, height, age, parity, ethnicity, salivary cotinine levels, caffeine intake, education, energy intake, gestation and baby's sex in multivariable linear regression for continuous outcomes and multivariable logistic regression for categorical outcomes. [c] Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation and baby's sex.

Table 12. The relationship between maternal alcohol intake during pregnancy and size at birth

	Trimester 1 (n=1135)				**Trimester 2 (n=793)**				**Trimester 3 (n=377)**			
	Unadjusted change		**Adjusted change[b]**		**Unadjusted change**		**Adjusted change[b]**		**Unadjusted change**		**Adjusted change[b]**	
	(95% CI)	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**
Birth weight (g)												
Non-drinkers	0.0	0.02	0.0	0.007	0.0	0.5	0.0	0.04	0.0	0.6	0.0	0.6
< 2 units/week	-124.8 (-225.4, -24.3)		-98.5 (-170.9, -26.1)		51.3 (-42.5,145.0)		-37.6 (-108.1,32.8)		4.2 (-162.4,170.7)		-34.5 (-153.1, 84.1)	
>2 units/week	-105.9 (-193.9, -17.9)		-100.4 (-165.8, -34.9)		12.9 (-56.5,112.2)		-99.6 (-175.8, -22.3)		73.7 (-78.6, 226.1)		-50.4 (-161.2, -60.3)	
Customised birth centile[c]												
Non-drinkers	0.0	0.01	0.0	0.002	0.0	0.5	0.0	0.06	0.0	0.8	0.0	0.7
< 2 units/week	-4.1 (-9.1, -0.9)		-5.8 (-10.8, -0.7)		-1.4 (-6.3, 3.5)		-3.6 (-8.6, 1.4)		-1.4 (-9.4, 6.6)		-3.1 (-11.1, 4.9)	
>2 units/week	-6.7 (-11.1, -2.3)		-8.2 (-12.6, -3.7)		-2.9 (-8.2, 2.2)		-6.4 (-11.8, -1.1)		1.2 (-6.1, 8.5)		-1.8 (-9.3, 5.7)	
	Unadjusted OR		**Adjusted OR[b]**		**Unadjusted OR**		**Adjusted OR[b]**		**Unadjusted OR**		**Adjusted OR[b]**	
	(95% CI)	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**
SGA (<10th centile)[c]												
Non-drinkers	1.0	0.08	1.0	0.03	1.0	0.2	1.0	0.2	1.0	0.9	1.0	0.7
< 2 units/week	1.4 (0.8, 2.5)		1.7 (0.9, 3.1)		0.7 (0.4, 1.0)		0.8 (0.5, 1.3)		0.9 (0.5, 1.5)		0.9 (0.5, 1.6)	
>2 units/week	1.7 (1.1, 2.8)		2.0 (1.2, 3.4)		0.9 (0.6, 1.5)		1.2 (0.8, 2.1)		0.9 (0.6, 1.6)		1.2 (0.7, 2.1)	
Low birth weight (≤2500 g)												
Non-drinkers	1.0	0.20	1.0	0.8	1.0	0.4	1.0	0.7	1.0	0.7	1.0	0.7

< 2 units/week	0.4 (0.2, 1.0)	1.6 (0.3, 7.4)	1.4 (0.7, 2.8)	0.7 (0.2, 2.9)	1.1 (0.5, 2.4)	0.3 (0.02, 4.1)
>2 units/week	0.6 (0.2, 1.3)	1.6 (0.4, 6.4)	1.6 (0.7, 3.4)	1.5 (0.3, 8.4)	1.4 (0.6, 3.2)	1.8 (0.1, 29.8)

[a] P for trend for categories of alcohol intake in a multivariable linear regression for continuous outcomes and a multivariable logistic regression for categorical outcomes. [b] Adjusted for maternal pre-pregnancy weight, height, age, parity, ethnicity, salivary cotinine levels, caffeine intake, education, energy intake, gestation and baby's sex in a multivariable linear regression for continuous outcomes and a multivariable logistic regression for categorical outcomes. [c] Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation and baby's sex.

4.4.5 Sensitivity analysis

Including total energy intake in the model further strengthened the association between maternal alcohol intakes during pregnancy and offspring size at birth; however it did not influence results for intakes before pregnancy.

Excluding women with high risk pregnancies (n=182) and “risky drinkers” did not alter the results although the confidence intervals became wider due to the reduction in numbers (results not shown).

4.5 Discussion

This is one of very few prospective studies (O'Keeffe, 2013; Chiaffarino et al., 2006; O'Leary et al., 2009) (Feldman et al., 2012; Shu et al., 1995) and the first in a British cohort which has looked at alcohol exposure pre-pregnancy, and in each of the trimesters separately, and their association with offspring size at birth. Maternal alcohol intake during the first trimester was found to have the strongest association with fetal growth. Women who adhered to guidelines in this period were still at increased risk of adverse birth outcomes even after adjustment for known risk factors. Maternal alcohol intakes which exceeded the recommendations in the period leading up to pregnancy were also found to be associated with fetal growth, suggesting that the peri-conceptual period could be particularly sensitive to the effects of alcohol on the fetus. These results highlight the need for endorsing the abstinence only message. It further illuminates how timing of exposure is important in the association of alcohol with fetal growth, with the first trimester being the most vulnerable period.

4.5.1 Alcohol intake and maternal characteristics

As expected, intakes of alcohol were highest in the 4 weeks before pregnancy with decreasing levels observed as pregnancy progressed. The proportion of women drinking during pregnancy (79%, 63% and 49% for trimester 1, 2 & 3 respectively) was considerable higher than results from the IFS (Centre, 2012). IFS data however were collected postpartum and is therefore subject to underreporting. The characteristics of drinking mothers in this study are consistent with those observed in the IFS where mothers aged 35 or over, from managerial and professional occupations and from a White ethnic background were more likely to drink during pregnancy (Centre, 2012). Despite the high prevalence of drinking in this cohort, very few women were considered risky drinkers. The low level of intake could in part be explained by underreporting, a common phenomenon in alcohol assessment (Gray, 2006). Reported alcohol consumption in surveys only accounts for approximately 60% of total alcohol sales and a recent study found evidence that excess alcohol drinking in the UK may be higher than previously thought (Boniface and Shelton, 2013). The actual level of intake may therefore be higher than reported, and associations with offspring size at birth could be with higher levels of intake.

4.5.2 Timing of exposure and offspring size at birth

We found consistently adverse associations between intakes of alcohol above 2 units/week prior to pregnancy and in the 1st and 2nd trimester and birth weight. In a prospective US cohort study, a reduction in birth weight was found in women drinking more than 2 units/week across all trimesters (Shu et al., 1995). The numbers however were small once split into categories of intake and the reduction was not significant with very wide confidence intervals.

We found a significant two-fold increase in the odds of having babies born SGA in mothers drinking more than 2 units/week compared to non-drinkers in trimester 1. O'Leary et al (2009) reported significantly increased odds of having infants born SGA by women drinking up to 60g alcohol/week (7.5 UK units) 3 months prior to pregnancy, an association however, which was not observed at higher levels of alcohol or during pregnancy (O'Leary et al., 2009). Two studies (Chiaffarino et al., 2006; Feldman et al., 2012) found an elevated risk of having a baby born with SGA in drinking mothers, but the threshold of intake was much higher than observed in this study. Chiaffarino et al. (2006) reported significantly increased odds of having a baby born with SGA at daily intakes above 3 units compared to abstainers across all trimesters and pre-pregnancy, but the association was strongest for intakes in trimester 1 (Chiaffarino et al., 2006). Feldman et al. (2012) found a dose-response relationship with a 16% increase for reduced birth weight for every 1 drink increase per day in the second half of trimester 1 and, for all of trimester 2 (Feldman et al., 2012).

The differences between this study's findings and those of other studies are partly due to heterogeneity between studies; in particular, this study looked at very low intakes of alcohol. Where studies have found similar associations, this has been in relation to a much higher threshold of intake.

Studies were reviewed which have accounted for timing of exposure, but the methodologies differed greatly. None used the same method of alcohol assessment. In addition, the period before pregnancy was not specified in some studies and for others, numbers were very small in the higher categories of intake limiting their power to detect a true association (Chiaffarino et al., 2006; O'Leary et al., 2009; Shu et al., 1995). Moreover, choice of confounders was also highly inconsistent across studies; in this study for example, adjustments were made for cotinine levels and energy intake both of which have not been adjusted for in previous research. Additionally, inconsistency in findings between countries may be a reflection of differences in drinking patterns. Finally, differences could also be due to polymorphisms linked to the metabolism of alcohol (Jones, 2011) which may vary between populations. This heterogeneity makes it hard to compare results.

4.5.3 Strengths & limitations

Alcohol intake was averaged to weekly consumption and then split into categories. This was done so as to better reflect the current UK guidelines on alcohol consumption for pregnant women and women trying to conceive and to make results more applicable in a public health context. Although this prevented an investigation into patterns of intake, such as binge drinking, the number of risky drinkers was very low and there would have been little power to detect a true association. Furthermore, the categories included a non-drinking referent and compared low levels of drinking which is appropriate in a moderate-to low drinking population. Units and their alcohol content were clearly defined in this study. Serving sizes and alcohol content of drinks, however, may differ between mothers. The calculation of alcoholic content of beverages was in line with the alcoholic profile of beers, wine and spirits at the time of data collection, a detail often left out in other studies (Feldman et al., 2012). This is important to prevent exposure misclassification which may obscure any relationship with birth outcomes as the alcohol profile of beverages is known to change over time (Fat LN, 2011).

A major strength of this study is the objective measurement of smoking, one of the biggest confounders in the relationship between alcohol and adverse birth outcomes, by using cotinine as a biomarker.

Considering timing of exposure is important so variation in alcohol consumption throughout pregnancy can be identified. Moreover, the timing of exposure will affect birth outcomes differently as fetal development is a staged process and according to Day & Richardson (2004) for this reason, drinking measures should be at least trimester specific (Day and Richardson, 2004). A major strength of this study was the assessment of intake at three time points covering several windows of exposure. Recent reviews have shown that many studies fail to account for timing of exposure which is likely one of the causes of the contradictory evidence surrounding alcohol intake and birth outcomes (Henderson et al., 2007a; Patra et al., 2011; O'Leary and Bower, 2012).

This study was designed for the assessment of caffeine intake not alcohol consumption. However, the questionnaire was validated with reference to caffeine intake (Boylan et al., 2008) and is comparable to other methods used in the assessment of alcohol. Despite intakes being self-reported and thus presenting the issue of under-reporting, alcohol exposure was assessed prospectively in trimester 1 & 2 reducing the potential for differential measurement (recall) bias. Ideally, alcohol intake should have been validated using a biomarker, but as yet, there are no biomarkers which can adequately assess low alcohol intakes and identify patterns of intake (Bearer et al., 2004).

Another limitation is the low sample size observed in the 3rd trimester. However, little difference was found between the controls that completed follow-up compared to those who did not, apart from women who stayed in the study were less likely to live in a deprived area (22% compared to 29% in non-completers, data not shown).

Despite the limitations discussed the potential risk to the fetus presented by even low maternal alcohol intakes prior to and during pregnancy warrants further investigation. Future studies should also take into account timing of exposure, including the period leading up to pregnancy. Maternal alcohol consumption usually decreases throughout pregnancy, as shown in this study, and therefore, averaging exposure measured at one time point in pregnancy to reflect exposure across the whole of pregnancy may obscure any true associations.

4.6 Conclusion

This analysis of prospectively-collected data of a British cohort has demonstrated that low levels of maternal alcohol consumption, in particular in the first trimester, has a negative association with fetal growth and greatly increases the odds for having babies born SGA. Pregnant women and women planning to become pregnant should be advised to abstain from drinking as even those women who adhered to the UK guidelines of 1-2 units once or twice a week in the first trimester were at risk of having babies with reduced birth weight when compared to mothers who abstain from alcohol.

5 Maternal diet during pregnancy and offspring size at birth: fatty fish in focus

Work from this chapter has been presented (poster) at one conference and submitted to a journal for publication and has been accepted upon revision.

5.1 Chapter overview

Essential fatty acids are vital for fetal growth and development. Fish, in particular fatty fish, are important sources of essential fatty acids. Evidence regarding the relationship between maternal fatty fish consumption and birth outcomes is inconsistent and has yet to be examined in an observational setting of a UK pregnant population. This study aimed to investigate the association between fatty fish consumption before and during pregnancy with offspring size at birth in the CARE study, a British prospective birth cohort.

Dietary data were available for 1208 pregnant women to assess preconception and trimester-specific fish consumption using self-reported dietary questionnaires. Additional dietary data from multiple 24 hour recalls during pregnancy were used to estimate an average fatty fish portion size. Intake was classified as ≤2 portions/week and >2 portions/week with a no fish category as referent. Following exclusion of women taking cod liver oil and/or omega-3 supplements, this was related to size at birth, adjusting for confounders including salivary cotinine as a biomarker of smoking status.

Over 40% of women reported no fatty fish consumption prior to and throughout pregnancy. Mean intakes were considerably lower than the recommended two portions/week, with the lowest intake observed in the 1st trimester (106 g/week, 95% CI: 98.9, 112.9). No association was observed between intake of fatty fish before pregnancy or during other pregnancy trimesters with size at birth.

There was a low prevalence of fish consumption in this inner-city UK population. Consumption of fatty fish prior to and/or during pregnancy did not influence size at birth, when taking into account known confounders.

5.2 Introduction

Recent public health research has focused on the role of fatty acids, in particular the omega-6 and omega-3 long chain polyunsaturated fatty acids (LCPUFA), which are derived from their respective precursors, linoleic (LA) and linolenic (LNA) acids. These are vital for the development of cell membranes and new tissues (Hornstra, 2000; Simopoulos AP, 1999; McGregor JA, 2001) and are classified as essential fatty acids (EFA) as they can only be derived from the maternal diet. During pregnancy the most biologically active LCPUFAs, docosahexaenoic acid (DHA) and arachidonic acid (AA) have been shown to have beneficial effects (Jaclyn M, 2010), particularly on the development of the fetal brain and retina (Simopoulos AP, 1999). These EFA cannot be synthesised in the human body (Hornstra, 2000; McGregor JA, 2001;(Oken E, B., MB, 2010) and the conversion rate of precursor to LCPUFA derivative within the fetus is limited (Makrides M, N.M., Simmer K, Pater J, Gibson R, 1995). Consequently the fetus is heavily dependent on the maternal diet for EFA through transport across the placenta (Williamson, 2006; Makrides M, N.M., Simmer K, Pater J, Gibson R, 1995; Hanebutt FL, 2008). Additionally, as the EFA status of the mother has been found to decline during pregnancy (Hornstra, 2000; Makrides M, G., RA, 2000), a dietary source is paramount for meeting the demand for maternal-fetal exchange.

Fish are an important source of essential LCPUFAs. However, the extent to which maternal fish intake plays a role in offspring size at birth is unclear. Findings from some birth cohorts suggest a positive association between total fish intake and birth weight (Guldner L, 2007; Muthayya et al., 2009; Rogers I, 2004; Ramon et al., 2009; Brantsaeter et al., 2012), LBW (Muthayya S, 2009; Brantsaeter et al., 2012). However, negative associations have also been found (Guldner L, 2007; Ramon et al., 2009; Oken E, K.K., Olsen SF, et al, 2004; Mendez MA, 2010) and in some cases no association with size at birth has been evident (Drouillet et al., 2009; Mohanty et al., 2015) Mendez MA, 2010; Mohanty et al., 2015; Guldner L, 2007; Heppe et al., 2011). A recent meta-analysis of 19 European birth cohorts assessing birth weight and length of gestation in relation to maternal total fish intake during pregnancy concluded that there was a small but significant increase in birth weight in babies born to mothers who consumed fish during pregnancy compared to non-consumers (Leventakou et al., 2014)

It has been hypothesised that adverse associations may be due to contaminants in fish including mercury and persistent organic pollutants (POPs). Fatty fish is a known source of these contaminants, particularly in larger fish species (Halldorsson TI, 2007).

However, studies that have focused on differentiating between types of fish consumed including lean, fatty and shellfish in relation to birth outcomes have been inconclusive (Mendez MA, 2010; Mohanty et al., 2015; Ramon R, 2009; Brantsaeter et al., 2012; Guldner L, 2007) although there may be a trend toward a negative association between fatty fish and fetal growth (Halldorsson TI, 2007; Ramon R, 2009).

The current advice in the UK is to consume at least two portions of fish/week (~140 g/portion), one of which should be fatty fish (Nutrition, 2004). This recommendation also applies to pregnant women and women trying to conceive but with an upper limit of maximum two portions of fatty fish/week. Pregnant women and women trying to conceive are also advised to avoid consumption of larger species such as marlin, swordfish and shark (Nutrition, 2004). Despite the guideline stating that up to 2 portions of fish/week does not present any harm, many Western pregnant women consume limited amounts of fish (Cetin I, 2008; Bloomingdale A, 2010; Oken E, B., MB, 2010) with low intakes of LCPUFA which could be potentially detrimental to fetal development.

Using data from the CARE study, a prospective UK-based birth cohort, this study aimed to investigate the association between maternal fatty fish intake before and during pregnancy with offspring size at birth.

5.3 Methods

The Caffeine And Reproductive Health (CARE) Study is a region(s) based prospective birth cohort which was set up to examine the association between maternal caffeine intake and birth outcomes (CARE, 2008). Details of the CARE study, including design, setting, outcome measures and assessment of participant characteristics can be found in Chapter 3.

5.3.1 Assessment of maternal fatty fish Intake

5.3.1.1 Recall Data

Rather than using the Scientific Advisory Committee on Nutrition (SACN) estimate of 140 grams (g) per portion of fatty fish, which is based on data from a non-pregnant population (the National Diet and Nutrition Survey) estimates were derived of the average portion size of fatty fish from 24 hour dietary recalls administered by research midwives at 14-18 weeks and 28 weeks gestation. A total of 1276 women reported dietary information by recall at week 16, and 601 women at week 28. Of these women, 162 (12.7%) and 70 (11.6%) reported intakes of any fatty fish at the first and second recall respectively. Reported canned tuna intake was removed from the analysis as evidence suggests this should not be classified as fatty fish (SACN, 2004). Combining both sets of recall data together, a total of 106 women reported fatty fish intake. The amount of fish consumed in grams at each meal was used to obtain an average value of 101 g (min: 10 g, max: 300 g) per portion of fish.

5.3.1.2 Self-reported questionnaires

Fatty fish consumption was ascertained prior to and throughout pregnancy using a frequency type self-reported questionnaire adapted from the UK Women's Cohort Study (Cade et al., 2004) and administered at enrolment (12–18 weeks gestation), week 28 and postpartum (weeks 46-50). Participants were asked how often (never; less than once/month; 1–3 times/month; once/week; 2–4 times/week; 5–6 times/week; once/day; 2–3 times/day; 4–5 times/day and >6 times/day) they consumed fatty fish (examples given were: salmon, tuna (fresh only), herring, kipper, mackerel, pilchards, sprats and swordfish).No examples of what constitutes a portion were given in the questionnaire. Frequency of fish consumption derived from the questionnaires was converted to times per week, which was then multiplied by the portion estimate of fish (101 g) obtained from the recall data (see above) in order to get weekly consumption in grams for each of the trimesters.

5.3.1.3 Statistical power calculation

Comparing mothers consuming >2 portions/week to non-consumers, the study had 80% power to detect an odds ratio of approximately 0.4 for SGA. The equivalent test for linear trend including the intermediate category half way between these extremes would have 90% power. Similarly, comparing the birth weight of babies born to mothers consuming >2 portions of fish/week with non-consumers, assuming the SD to be approximately 500 g, this study had 85% power to detect a difference of 150 g in birth weight at $p<0.05$.

5.3.2 Statistical Analysis

Analysis was conducted using the continuous weekly fish variable assigned into three categories of intake based on the current UK guidelines of no more than 2 portions of fatty fish per week (Nutrition, 2004) with the addition of a "no fish" category which was used as the referent group: no fish, ≤2 portions/week and >2 portions/week.

Univariable analyses were performed using one-way ANOVA for normally distributed variables, Kruskal-Wallis for non-parametric variables and chi-squared test for categorical outcomes. Multivariable linear and logistic regression models were used to assess the association between maternal fatty fish intake and continuous and dichotomous birth outcomes respectively. Maternal pre-pregnancy weight, height, ethnicity, parity, gestation and neonatal sex were accounted for when calculating the SGA variable and were adjusted for in the birth weight models. Covariates adjusted for in all models were selected based on a priori knowledge from the literature and included maternal age, salivary cotinine levels, self-reported caffeine intake and alcohol consumption and university degree status as a marker for socioeconomic status.

In order to separate the effect of fatty fish from supplements as opposed to dietary sources on birth outcomes, women taking any cod liver oil and/or omega-3 supplements were removed from the analysis. Women with extreme values for energy intake (highest 1% and lowest 1%), obtained from the 24 hour recall data, were excluded due to possible bias with self-reported dietary intake, as proposed by Meltzer et al. (2008).

Sensitivity analyses were conducted taking into account previous high-risk pregnancies (including a previous low LBW baby, gestational diabetes and gestational hypertension) and total energy intake during pregnancy.

5.4 Results

A total of 1303 pregnant women in Leeds were enrolled into the CARE study. Of these, nine were lost to follow-up, five terminated pregnancies and others were excluded due to stillbirth (n=6), neonatal death (n=3) and late miscarriage (n=10). Following exclusions of women taking cod liver oil and/or omega-3 supplements (n=37) as well as those with extreme energy intakes (n=25) left 1208 mothers with data available on birth outcomes.

5.4.1 Types of fatty fish consumed (24-hour recall)

The average portion of fatty fish was 101 g. Of the 106 women consuming fatty fish in the 24 hour recall data, 52 (49.1%) women ate salmon, 25 (23.6%) ate raw tuna and 14 (13.2%) ate mackerel. Other types of fatty fish included anchovies (4.7%), sardines (6.6%), trout (5.7%) and orange roughy (0.9%). Fatty fish consumption accounted for 4.8% of the total energy intake (results not shown).

5.4.2 Frequency of fatty fish consumption (questionnaire)

Of the 1208 women with birth outcome data, 1116 (92.4%) women had information available on frequency of fatty fish intake before pregnancy, 1114 (92.2%) in the 1st trimester, 812 (67.2%) in the 2nd trimester and 409 (33.9%) in the 3rd trimester (Table 13). For those women who reported consuming any fatty fish, intake before pregnancy (123.5 g/week) was significantly higher ($p<0.0001$) than trimester 1 & 2 (106.4 and 107.4 g/week respectively) but slightly lower than the mean intake in the 3rd trimester (136.5 g/week). The proportion of women reporting any fish intake, however, decreased throughout pregnancy with the lowest proportion observed in trimester 3 (43.3%).The prevalence of women consuming within the recommended guidelines of no more than 2 portions of fatty fish per week was highest in trimester 1 (47.0%) and in the 2nd trimester (48.8%), with mean intakes for women reaching 64.3 g (95% CI 61.0 to 67.7) and 71.3 g (95% CI 66.6 to 75.7) per week, respectively.

Table 13. Self-reported fatty fish intake across pregnancy

	N (%)	**Mean (g)**	**95% CI**
Fish intake (g/week) (consumers only):			
4 weeks before pregnancy (n=1166)	648 (58.1)	123.5	115.1, 131.9
First trimester (n=1114)	652 (58.5)	106.4	98.9, 112.9
Second trimester (n=812)	466 (57.4)	107.4	98.2, 116.6
Third trimester (n=409)	177 (43.3)	136.5	118.8, 154.1
Categories of intake 4 weeks before pregnancy*			
No fish	468 (41.9)	0	0
≤2 portions/week	491 (44.0)	67.6	64.8, 70.5
>2 portions/week	157(14.1)	298.1	286.7, 309.6
Categories of intake trimester 1			
No fish	462 (41.47)	0	0
≤2 portions/week	524 (47.0)	64.3	61.0, 67.7
>2 portions/week	128 (11.5)	278.9	267.1, 290.7
Categories of intake trimester 2			
No fish	346 (42.6)	0	0
≤2 portions/week	396 (48.8)	71.3	66.6, 75.7
>2 portions/week	70 (8.6)	311.8	291.9, 331.7
Categories of intake trimester 3			
No fish	232 (56.7)	0	0
≤2 portions/week	131 (32.0)	75.4	70.4, 80.4
>2 portions/week	46 (11.3)	310.5	279.0, 341.9

[a] Categories based on the UK recommendations of no more than 2 portions of fatty fish/week(Nutrition, 2004). One portion of fish is 101g.

5.4.3 Maternal characteristics according to categories of fish intake

Table 14 shows characteristics of participants according to maternal fish intake in each trimester. Women who consumed fish during pregnancy were more likely to be older, have a university degree, to consume alcohol, were less likely to smoke and less likely to live in an area within the most deprived Index of Multiple Deprivation (IMD) quartile. These characteristics were consistent across all trimesters and the four weeks leading up to pregnancy (results not shown). Women consuming fish in trimester 1 & 2 were also more likely to have a lower BMI, and those consuming fish in trimester 1 were shown to have a lower caffeine intake than non-fish consumers.

Table 14. Characteristics of mothers by fatty fish intake reported during pregnancy in three questionnaires

	Trimester 1 (n=1114)				**Trimester 2 (n=812)**				**Trimester 3 (n=409)**			
	No fish (n=462)	**≤2 portions/ week (n=524)**	**>2 portions/ week (n=128)**	***P***[a]	**No fish (n=346)**	**≤2 portions/ week (n=396)**	**>2 portions/ week (n=70)**	***P***[a]	**No fish (n=232)**	**≤2 portions/ week (n=131)**	**>2 portions/ week (n=46)**	***P***[a]
Age (years) mean (SD)	28.5(5.6)	30.8(4.4)	31.7(4.6)	0.0001	29.0(5.2)	31.0(4.5)	31.1(4.0)	0.0001	28.3(5.0)	31.0(4.2)	31.3(4.8)	0.0001
Pre-pregnancy BMI (kg/m^2) mean (SD)	25.1(5.3)	24.4(4.3)	23.9(5.3)	0.01	25.0(5.0)	24.3(4.9)	23.7(3.9)	0.04	25.3(5.4)	24.3(5.5)	24.2(3.7)	0.1
Total energy intake (kcal) mean (SD)	2109.4 (595.6)	2111.5 (614.3)	2183.5 (670.8)	0.8	2119.5 (582.2)	2165.7 (614.3)	2188.8 (625.6)	0.5	2148.1 (610.7)	2106.3 (608.1)	2145.5 (648.8)	0.9
Caffeine intake (mg/day) mean (SD)	223.3 (225.4)	159.9 (151.3)	190.6 (177.6)	0.0001	187.3 (218.9)	149.6 (130.9)	172.2 (203.3)	0.8	233.6 (257.1)	174.3 (141.1)	217.9 (242.6)	0.6
Alcohol intake: % non-drinkers (n)	28.3(127)	16.4(84)	20.0(24)	0.0001	44.7(139)	30.6(117)	34.4(22)	0.0003	60.3(123)	37.0(44)	40.0(14)	0.0001
Smoker at 12 weeks % (n)[b]	60.9(266)	81.1(411)	74.8(92)	0.0001	62.6(206)	80.5(310)	83.6(56)	0.0001	57.0(126)	79.8(103)	71.1(32)	0.0001
IMD most deprived quartile % (n)	41.1(182)	21.7(109)	19.1(24)	0.0001	36.3(120)	17.2(66)	16.4(11)	0.0001	36.1(79)	19.5(25)	21.7(10)	0.0001
University degree % (n)	24.5(113)	50.4(264)	56.3(72)	<0.0001	30.1(104)	52.3(207)	65.7(46)	<0.0001	25.0(58)	57.3(75)	47.8(22)	<0.0001
European origin % (n)	94.8(437)	93.5(489)	94.5(121)	0.7	96.0(332)	96.2(379)	91.4(64)	0.2	97.0(225)	97.7(126)	91.3(42)	0.1
Primigravida % (n)	45.3(209)	51.1(267)	40.9(52)	0.06	49.3(170)	51.5(204)	49.3(34)	0.8	51.1(118)	55.0(72)	50.0(23)	0.7
Baby's gender: % male (n)	52.6(243)	49.1(257)	43.8(56)	0.2	51.5(178)	46.2(183)	50.0(35)	0.4	51.3(119)	47.3(62)	58.7(27)	0.4
Gestational hypertension % (n)	5.9(27)	4.5(23)	5.6(7)	0.6	5.1(17)	6.6(26)	1.4(1)	0.2	6.2(14)	5.4(7)	4.4(2)	0.9
Past history of miscarriage % (n)	22.4(102)	22.9(119)	27.8(35)	0.4	22.5(77)	23.9(94)	32.4(22)	0.2	22.7(52)	20.6(27)	20.0(9)	0.9

[a] P-value using one-way ANOVA and Kruskal-Wallis for normally and non-normally distributed continuous variables respectively, and x2-test & Fisher's exact test for categorical variables. Significant difference at p<0.05. [b] Smoking status based on salivary cotinine concentrations: non-smoker <1 ng/ml, passive smoker 1-5 ng/ml, current smoker >5 ng/ml. Where numbers do not add up it is due to a small proportion of missing data. SD, standard deviation; BMI, body mass index; IMD, Index of Multiple Deprivation.

5.4.4 Pregnancy Outcomes

Of the 1208 women with information on birth outcomes, 153 (12.7%) babies were born SGA (<10th centile) and 46 (3.8%) were LBW (<2500 g). The mean birth weight of the total sample was 3446 g (SD=537 g).

5.4.5 Relationship between fish intake before pregnancy and birth outcomes

There was no significant association between fatty fish intake before pregnancy and size at birth (Table 15).

Table 15. The relationship between maternal fatty fish intake 4 weeks before pregnancy and size at birth

	Unadjusted change (95% CI)	P[a]	Adjusted change[b] (95% CI)	P[a]
Birth weight (g)	(n=1,116)		(n=1,029)	
No fish	0	0.3	0	0.7
≤2 portions/week	45.8 (-23.3, 115.0)		-17.9 (-75.3, 39.5)	
>2 portions/week	71.6 (-27.1, 170.3)		-35.7 (-115.6, 44.1)	
	Unadjusted OR (95% CI)	**P[a]**	**Adjusted OR[b] (95% CI)**	**P[a]**
SGA (<10th centile)[c]	(n=1,116)		(n=1,048)	
No fish	1	0.3	1	0.6
≤2 portions/week	0.7 (0.5, 1.1)		1.0 (0.6, 1.5)	
>2 portions/week	1.0 (0.6, 1.6)		1.3 (0.8, 2.3)	
Low birth weight (≤2500 g)	(n=1,116)		(n=1,029)	
No fish	1	0.8	1	0.3
≤2 portions/week	0.9 (0.5, 1.7)		1.9 (0.7, 5.3)	
>2 portions/week	0.7 (0.3, 1.9)		3.1 (0.8, 12.7)	

[a] P for trend for categories of fish intake. [b] Adjusted for maternal pre-pregnancy weight, height, age, parity, ethnicity, salivary cotinine levels, caffeine intake, alcohol intake, education, gestation and baby's sex in multivariable linear regression for continuous outcome and multivariable logistic regression for categorical outcomes. [c] Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation and baby's sex.

5.4.6 Relationship between fish intake and size at birth

When comparing babies born to mothers consuming no fatty fish in trimester 1, mothers consuming up to two portions of fatty fish/week had babies weighing 58.4 g less (95% CI: -115.1, -1.5) although there was no linear trend (P_{trend}=0.1). There was no evidence of any relationship between fatty fish intake in the second or third trimester and size at birth expressed as birth weight (g), SGA (<10th centile) or low birth weight (table 15).

5.4.7 Sensitivity analysis

Adding total energy intake to the regression models did not affect the results. Similarly, including an indicator for high risk pregnancies as a possible moderator (n=175) did not significantly alter the results (results not shown).

Table 16. The relationship between maternal fatty fish intake during pregnancy and size at birth

	Trimester 1				**Trimester 2**				**Trimester 3**			
	Unadjusted change		**Adjusted change[b]**		**Unadjusted change**		**Adjusted change[b]**		**Unadjusted change**		**Adjusted change[b]**	
	(95% CI)	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**
Birth weight (g)	(n=1,114)		(n=1,028)		(n=812)		(n=751)		(n=409)		(n=387)	
No fish	0	0.3	0	0.1	0	0.2	0	0.3	0	0.3	0	0.8
≤2 portions/week	30.4 (-37.9, 98.7)		-58.4 (-115.1, -1.7)		75.3 (-6.5, 157.1)		-47.3 (-113.0, 18.4)		109.6 (-25.4, 244.6)		-35.6 (-139.9,68.7)	
>2 portions/week	87.7 (-19.2,194.6)		-64.0 (-151.1, 23.1)		42.3 (-103.4,188.1)		-71.4 (-185.8,43.13)		52.6 (-146.8, 251.9)		-21.8 (-169.0,125.4)	
	Unadjusted OR		**Adjusted OR[b]**		**Unadjusted OR**		**Adjusted OR[b]**		**Unadjusted OR**		**Adjusted OR[b]**	
	(95% CI)	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**	**(95% CI)**	**P[a]**
SGA (<10th centile)[c]	(n=1,114)		(n=1,046)		(n=812)		(n=763)		(n=409)		(n=389)	
No fish	1	0.2	1	0.3	1	0.6	1	0.6	1	0.9	1	0.8
≤2 portions/week	0.9 (0.6, 1.2)		1.2 (0.8, 1.8)		0.8 (0.6, 1.2)		1.1 (0.4, 1.7)		0.9 (0.6, 1.5)		1.1 (0.7, 1.9)	
>2 portions/week	0.5 (0.3, 1.0)		0.7 (0.4, 1.5)		1.0 (0.5, 1.9)		1.5 (0.7, 3.0)		1.0 (0.5, 2.0)		1.2 (0.6, 2.5)	
Low birth weight (≤2500 g)	(n=1,114)		(n=1,028)		(n=812)		(n=751)		(n=409)		(n=387)	
No fish	1	0.3	1	0.4	1	0.3	1	0.2	1	0.5	1	0.2
≤2 portions/week	0.8 (0.4, 1.5)		2.0 (0.7, 5.6)		0.6 (0.3, 1.2)		3.0 (0.9, 9.7)		0.7 (0.3, 1.4)		2.4 (0.6, 9.7)	
>2 portions/week	0.3 (0.1, 1.3)		1.2 (0.2, 7.4)		0.6 (0.2, 2.2)		1.5 (0.3, 8.1)		1.0 (0.4, 2.7)		5.5 (0.9, 31.9)	

[a] P for trend for categories of maternal fish intake in linear and logistic regression models for continuous and dichotomous outcomes respectively. [b] Adjusted for maternal pre-pregnancy weight, height, age, parity, ethnicity, salivary cotinine levels, caffeine intake, alcohol intake, education, gestation and baby's sex in multivariable linear regression for continuous outcome and multivariable logistic regression for categorical outcomes. [c] Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation and baby's sex. LBW, low birth weight; n, number; OR, odds ratio; SGA, small for gestation age.

5.5 Discussion

This is the first British prospective birth cohort study to assess maternal fatty fish intake prior to and throughout each of the trimesters separately in relation to offspring size at birth.

The results showed the majority of pregnant women consuming considerably less than the recommended two portions of fatty fish per week prior to and throughout pregnancy and a trend towards a decreased fish consumption with the progression of pregnancy. Overall there was no statistically significant association between maternal fatty fish intake and offspring size at birth, when taking into account known confounders.

5.5.1 Fish intake and maternal characteristics

Maternal fatty fish intake was highest in the period leading up to pregnancy decreasing as pregnancy progressed with the proportion of non-consumers increasing. The mean weekly intakes (124 g, 106 g, 107 g and 137 g/week for the period before pregnancy, trimester 1, 2 & 3 respectively) were considerably lower than the mean of 190 g of fatty fish/week reported in a UK national survey of women (non-pregnant women aged 19-64) carried out around the same time (Henderson, L. et al., 2002) and noticeably lower than the UK guidelines of up to two portions of 140 g fatty fish/week. The proportion of women in this study not consuming any fatty fish in the 3rd trimester (56.7 %) was slightly higher compared to results from the Avon Longitudinal Study of Parents and Children (ALSPAC) which showed in their study of fish intake in pregnancy and birth weight that 42.6% of pregnant women (n=11511) reported never or rarely consumed any fatty fish in the 3rd trimester (Rogers I, 2004). Compared to other non UK studies assessing fatty fish intakes in Western pregnant women, the proportion not consuming any fatty fish were 33% during the 1st trimester in a Dutch birth cohort (n=3380) (Heppe et al., 2011), 11% during the 2nd trimester in a large Norwegian birth cohort (n= 62099) (Brantsaeter et al., 2012) and 24% reported consuming <0.2 portions of fatty fish/month before pregnancy in a US cohort (Mohanty et al., 2015), all lower than that observed in this cohort. Results from another more recent Danish study (DNBC) however (n=44824) reported a similar proportion of 54% of non-consumers from their assessment of fatty fish intake in the 2nd trimester (Halldorsson TI, 2007). Similarly, results from a Spanish cohort of pregnant women (IMNA) showed 41% of women reporting consuming <1portion of fatty fish/month (Ramon R, 2009). Results from the meta-analysis by Leventakou et al. (2014) of 19 European cohorts (some of which are mentioned above) showed a considerable variation in fatty fish intake between countries; with Italian, Spanish & Portuguese mothers consuming fatty fish more than twice as often as Irish & French mothers. It is however impossible to tell how much more fatty fish the Spanish mothers ate than the Irish, for instance, because the researchers had data only on frequency, not quantity.

Although it is probable that some women simply do not like fish, reasons for low consumption are likely to include perceptions about cost, access to stores that sell fish, and uncertainty about preparation and cooking methods. Furthermore, some women may abstain from fish out of a worry that they and their babies will be harmed by contaminants present in some types of fish, a concern which is highlighted in the current UK guidelines but may actually result in a lack of consumption rather than a lowered intake of fatty fish. The characteristics of the mothers in this study across categories of increased fish consumption are consistent with those observed in other studies where slightly older women, those consuming alcohol and women of higher socioeconomic status and higher education tended to consume higher levels of fish and were less likely to be smokers (Halldorsson TI, 2007; Rogers I, 2004; Heppe et al., 2011; Brantsaeter et al., 2012; Oken E, 2004; Muthayya S, 2009; Drouillet et al., 2009)

5.5.2 Interpretation of main findings

We did not find any association between maternal fatty fish intake before and during pregnancy with offspring size at birth.

In the ALSPAC study, Rogers et al. (2004) used n-3 fatty acids as a marker of fish consumption and found no association with LBW or intrauterine growth retardation once they adjusted for confounders (Rogers I, 2004). Despite having data on type of fish consumed they did not relate this to birth outcomes but focused instead on n-3 fatty acid intake from fish as well as frequency of total fish consumption making it impossible to draw direct comparisons to this study. Other studies have reported a similar lack of association between maternal fatty fish intake and birth outcomes (Brantsaeter et al., 2012; Mendez MA, 2010; Mohanty et al., 2015; Ramon R, 2009). In their meta-analysis Leventakou et al. (2014) in addition to assessing total fish intake, also assessed types of fish (fatty, lean and seafood) in relation to birth outcomes and similarly to results from this study, they found no association between fatty fish and LBW. Where lean fish and shellfish had no significant associations with any birth outcomes, they did observe a positive association between fatty fish and birth weight, albeit a small one at 2.38 g (95% CI: 0.51, 4.25) for every 1 unit (times/week) increment. The authors stipulated that the n-3 LCPUFA content in fatty fish could be the contributing factor behind the overall positive association they found between total fish intake and birth weight (Leventakou et al., 2014). Contrary to this, Halldorson et al. (2007) reported a reduction of 27.5 g in birth weight of babies born to mothers consuming fatty fish more than four times/month compared to non-consumers as well as an increased risk of having babies born SGA (Halldorsson TI, 2007).

Differences in findings are partly due to heterogeneity between studies. In particular what constitutes a portion of fish varies from study to study and has been shown to range from 85 g to 200 g depending on the type of fish as well as the country of the study (Guldner L, 2007; Mohanty et al., 2015; Leventakou et al., 2014). In addition, categories of intake differ from study to study with some choosing very high or low categories of intake. We chose to assess intake from a more public health relevant context but this resulted in very small numbers in the high consumption category (>2 portions/week) which limited the power to detect a true association. Furthermore, it is unclear whether timing of exposure has any effect on outcomes and to this author's knowledge; no study to date has looked at all trimester specific fatty fish intakes in relation to size at birth. Of the studies which have assessed intake in more than one trimester and/or prior to pregnancy (Drouillet et al., 2009; Muthayya S, 2009; Oken E, 2004; Olsen SF, 2006), one found a positive association with size at birth in overweight women for intakes before pregnancy but not in the final period of pregnancy (Drouillet et al., 2009). Another found an increased risk of LBW babies in women reporting no fish consumption in the third trimester, but not in trimester 1 (Muthayya S, 2009). Finally one study found a negative association with size at birth and fish intake reported in the 1st trimester but not in the 2nd trimester (Oken E, 2004). None of these studies however looked at types of fish consumed. Moreover, the choice of confounders tend to be inconsistent across studies and since not only in the present study, but also in other studies, high fish consumption has been shown to be strongly related to a higher education level and more healthy lifestyle habits any positive associations between fish consumption and birth outcomes may be partly due to residual confounding by lifestyle-related characteristics if studies have failed to take these into account in their analysis. Additionally, discrepancies in findings between countries may be a reflection of differences in dietary patterns. This heterogeneity makes it hard to compare results.

5.5.3 Strengths

As a unique feature of this study there were two sources of dietary intake available which allowed for the derivation of a study specific estimation of a portion of fatty fish rather than using the SACN estimation of 140 g/portion (Nutrition, 2004). This may have given a truer picture of actual intake of fatty fish within a cohort of British pregnant women. Fish intake was averaged to weekly consumption and then divided into categories. This was done so as to better reflect the current UK guidelines on fish consumption for pregnant women and women trying to conceive, and to make the results more applicable in a public health context.

Maternal fish intake was assessed at three time points covering a wide window of exposure and taking into account variations across trimesters. Furthermore, only self-reported fatty fish intake was accounted for in the questionnaire. Therefore the relationship with fatty fish could be assessed, as previous studies have combined types of fish such as lean fish, shellfish and molluscs in their overall analysis, biasing the true effect. Of the studies that have identified associations in relation to fatty fish, Halldorsson et al. (2007) found a negative association with size at birth (Halldorsson TI, 2007) and Ramon et al. (2009) found that consumption of larger fatty fish ≥ twice/week (such as swordfish) compared to <once/month was associated with a higher risk of SGA, however the P for trend across categories of intake was not significant (Ramon R, 2009). Women in these cohorts were high fish consumers however. Other studies have not specifically identified fatty fish within their analysis and therefore findings cannot be explicitly compared.

In this study information was available for a wide range of confounders. The objective measurement of salivary cotinine samples meant that smoking, a significant confounder in relation to maternal fish intake and birth outcomes, was assessed accurately with a biomarker.

5.5.4 Limitations

The questionnaires used in this study were originally designed to assess caffeine intake in pregnancy and not dietary fish consumption. However, the questionnaire was validated with reference to caffeine intake (Boylan et al., 2008); and other food related questions were comparable to other methods used in the assessment of fish. Despite intakes being self-reported and thus presenting the issue of under-reporting, fish consumption was assessed prospectively in trimesters 1 and 2, reducing the potential for differential measurement (recall) bias.

An explanation for insignificant findings with fish intake and offspring size at birth could be due to the number of women included in the analysis (n=1208) compared to other large cohorts (Halldorsson TI, 2007; Oken E, 2004; Olsen SF, 2006; Guldner L, 2007; Rogers I, 2004) as well as the low consumption of fish reported in this cohort. We had limited power to detect small associations due to the low numbers in the high consumption category, especially in trimester 3 (n=409). However, previous studies with smaller cohorts have detected associations in relation to fish intake (Mendez MA, 2010; Ramon R, 2009; Drouillet et al., 2009; Guldner L, 2007), although these women consumed high intakes of fish due to their Mediterranean diets.

A major weakness within this cohort was the lack of objective measurement of self-reported fish consumption. This could have been validated using a biomarker, such as erythrocytes concentrations of n-3 fatty acids, to indicate accurate fish intake during pregnancy, which has been addressed in previous studies (Oken E, 2004; Ramon R, 2009; Mendez MA, 2010; Halldorsson TI, 2007).

5.6 Conclusion

Overall, results from the CARE cohort provided no evidence that fatty fish intake of ≥2 times per week is associated with size at birth.

Ideally, trials and cohort studies focusing on types of fish as well as timing of exposure are needed to help improve the understanding of the relationship between maternal fish intake during pregnancy and birth outcomes. This will ultimately provide a definitive guideline for healthcare professionals to assist pregnant mothers on dietary and/or supplementary intake during pregnancy to reduce adverse fetal outcomes.

6 Maternal dietary patterns in pregnancy and offspring size at birth in a cohort of British women: the CARE study

6.1 Chapter overview

This chapter commences the investigation of the relationship between maternal dietary patterns during pregnancy and offspring size at birth.

The aim of this analysis was to investigate the associations between maternal dietary patterns during pregnancy and offspring size at birth using data from a prospective cohort of 1,109 pregnant women aged 18-45 years in Leeds, UK, The Caffeine and Reproductive Health study (CARE). Dietary intake was reported in a 24-hour recall administered by a research midwife at 14-18 weeks gestation. The 1,770 food items from the recalls were aggregated into 73 food groups and principal component analysis was used to derive dietary patterns. Information on delivery details was obtained from hospital maternity records.

Four dietary patterns were derived and identified as: ‘fruit & wholegrains’, ‘traditional meat & vegetables’, ‘vegetables & oils’ and ‘cheese, pasta & sauce’. Only the first component, characterised by high positive correlations with fruits, Nordic fruits in particular, and unrefined grains as well as wholegrain and bran breakfast cereal and negative correlations with refined grains, was found to be significantly associated with offspring size at birth, and only so for mothers who entered pregnancy with a healthy BMI (<25 kg/m^2). Mothers who scored highly on this dietary pattern were more likely to be older, have a lower pre-pregnancy BMI, have a university degree, be nulliparous, take dietary supplements in the 1st trimester, be vegetarian, and have a higher alcohol intake and a lower caffeine intake than those in the lower quintile scores. They were less likely to be smokers in the 1st trimester and to live in the most deprived area.

Positive significant association between a ‘fruit & wholegrains’ dietary pattern and birth weight as well as birth weight centile was found in unadjusted analyses, however once adjustments were made for pre-pregnancy BMI, age, parity, ethnicity, salivary cotinine levels, educational status, caffeine intake, trimester 1 alcohol intake, gestation & infant’s sex, significance was lost. There was however a significant interaction observed between the ‘fruit & wholegrains’ and maternal pre-pregnancy BMI on offspring risk of being SGA (P=0.03). For every 1 unit increase in the ‘fruit & wholegrains’ dietary pattern score, mothers with a pre-pregnancy BMI <25 (kg/m2) had 20% lower odds of having an infant born SGA (95% CI: 0.66, 0.96, P=0.01).

6.2 Introduction

Chapter 1 outlined maternal nutrition as one of the key determinants of offspring growth and later health. In Chapter 4 and Chapter 5 the association between maternal alcohol intake and fatty fish consumption prior to and during pregnancy and offspring size at birth was explored; providing further support on the evidence of alcohol as a teratogen, even in low amounts in the first trimester of pregnancy. The evidence for fatty fish intake however was inconclusive. As nutrients are not consumed in isolation, and intakes are often highly correlated, it can be difficult to identify a true association between single foods such as fatty fish and fetal growth (Hu, 2002). This may be resolved by the use of dietary patterns that encompass multiple dietary components. As highlighted in Chapter 2, there has been an increased interest in this area of research, evidenced by the recentness of the publications reviewed. The literature review identified 18 studies which assessed maternal dietary patterns in relation to size at birth all with varying results; although findings were somewhat in agreement with the hypothesis that optimal perinatal nutrition, gained from a healthy maternal dietary pattern consistent with general dietary guidelines for healthy eating, leads to favourable pregnancy outcomes in terms of size at birth. The evidence appeared to be most convincing for birth weight (expressed in grams as well as FGR and SGA), with the alternative healthy eating index (AHEI) showing the strongest association, where results from one Spanish prospective birth cohort (INMA) showed that mothers with a dietary pattern that scored highly on the AHEI had offspring with up to 126 g higher birth weight compared to mothers with lower scores as well as the greatest reduction in risk of FGR for birth weight (76 % reduced odds) (Rodriguez-Bernal et al., 2010). Evidence for more unhealthy dietary patterns, characterised by high intakes of processed food, refined grains and sugary foods and drinks was less uniform. Several methodological issues were identified in the studies reviewed in regards to exposure and outcome measures, dietary pattern analysis as well as statistical analysis, in particular the sometimes poor and inconsistent consideration of confounders. Studies were based in a variety of countries with the majority using data from large European birth cohorts. Only one study used data from a UK cohort. Northstone et al. (2008) found a positive association between a ‘health conscious’ dietary pattern, characterised by high intakes of salad, fruit, rice, pasta, breakfast cereals, fish, eggs, pulses, fruit juices, poultry and non-white bread, and birth weight . However they did not assess confounding as this would have influenced the purpose of their main analysis which was to examine the effect of the timing of energy adjustment on maternal dietary patterns and their association with health outcomes, in this case birth weight (Northstone et al., 2008). The association between maternal dietary patterns during pregnancy and offspring size at birth has therefore yet to be explored in a UK sample of low risk pregnant women where important confounders such as maternal smoking, age and pre-pregnancy BMI have been taken into account.

6.2.1 Aim & objectives

The main aim of this chapter was to explore the relationship between maternal dietary patterns in pregnancy and offspring size at birth using data from a low risk UK sample of pregnant women. The following objectives were addressed:

1. Characterise dietary patterns in a British cohort of low-risk pregnant women
2. Investigate associations between maternal dietary patterns in pregnancy and size at birth
3. Explore the role of maternal pre-pregnancy BMI status as an effect modifier in the association investigated in objective 2.

6.3 Methods

The Caffeine And Reproductive Health (CARE) Study is a region(s) based prospective birth cohort which was set up to examine the association between maternal caffeine intake and birth outcomes (CARE, 2008). Details of the CARE study, including design, setting, dietary assessment, outcome measures and assessment of participant characteristics can be found in Chapter 3. Below are details of the study sample available for analysis, power calculation and statistical methods including details of the dietary pattern analysis.

6.3.1 Mother-offspring pairs available for analysis

Figure 12 shows the participant flow chart. Of the 1,270 live births, 1,244 mothers had 24 hour recall data available from the 2nd trimester. After excluding extreme energy intakes (highest and lowest 1%, equivalent to < 919 kcal/day and >4486 kcal/day) and restricting analyses to term births (37-42 weeks gestation) the final dataset contained 1,109 mother-offspring pairs (for details on exclusion criteria see Chapter 3).

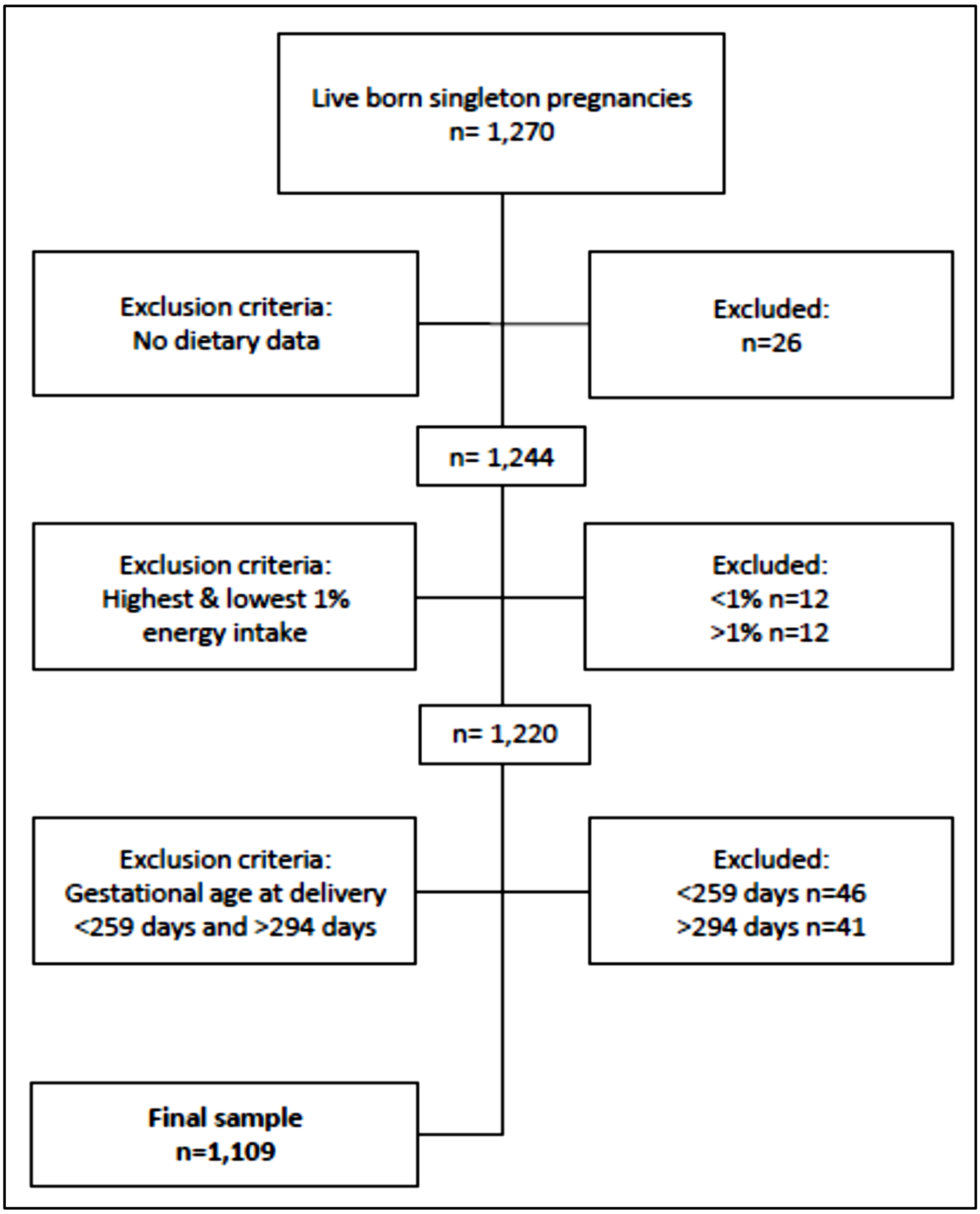


Figure 12. CARE study participant flowchart

6.3.2 Statistical power calculation

Comparing the birth weight (g) of babies born to mothers in the lowest quintile category of the first component (the one explaining the highest proportion of variance in the dietary data) resulting from the PCA with those in the highest quintile category, and using the SD of 476 g of birth weight for the total sample, this study had 85% power to detect a difference of 135 g in birth weight for a two sample t test at $p<0.05$.

6.3.3 Statistical analysis

6.3.3.1 PCA

Prior to performing the PCA, the 73 food items (see Chapter 3,Table 8), expressed as grams per day, were energy adjusted using the residual method as detailed in Chapter 3, section 3.10.1.3. The PCA was based on the correlation matrix (Manly, 2004), and the choice of components to retain was assessed using the scree plot (Cattell, 1966), percentage of variance explained by components and their interpretability. As can be seen from figure 2 below, the elbow in the scree plot (identified by the red arrow) indicated that the appropriate number of components to retain was around 4 and in addition these all had eigenvalues above 1, a criteria often used to aid in the decision on number of components to retain in PCA analysis.

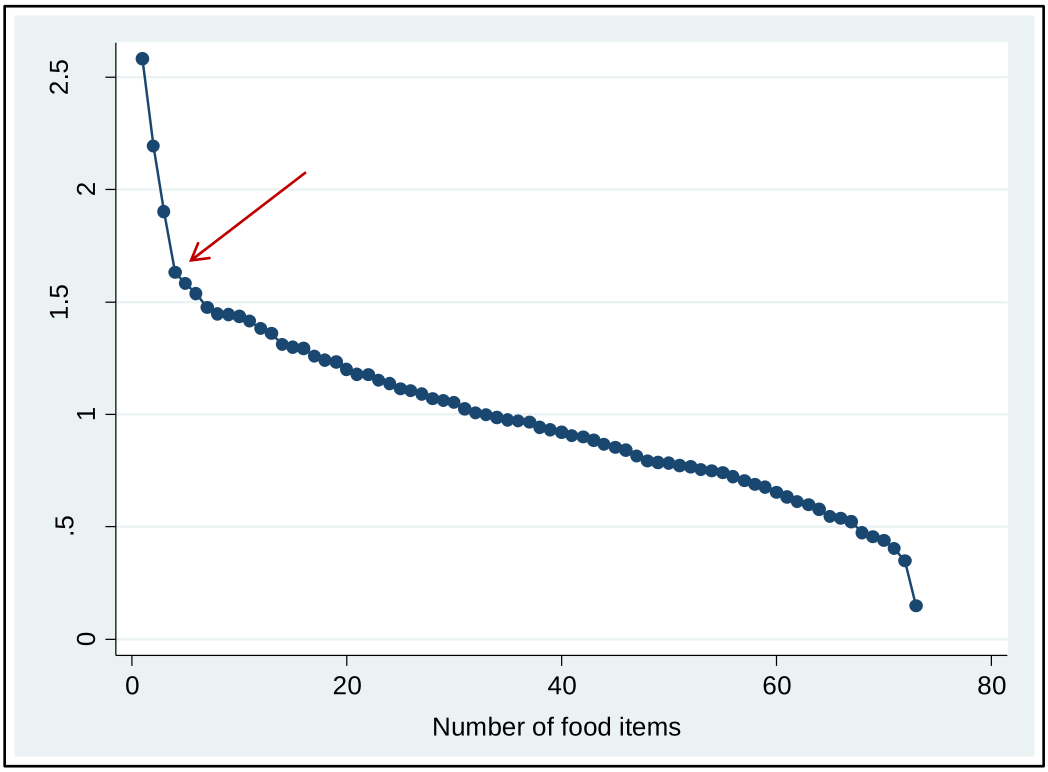


Figure 13. Scree plot of eigenvalues from PCA on 73 energy adjusted food groups

The components were then rotated using varimax rotation, a standard method for clarifying the components without changing the data (Kline, 1994), and scores for each participant for each component were predicted and further categorised into quintiles for inclusion in regression models to allow for any non-linearity.

6.3.3.2 Univariable analyses

Characteristics of mothers across quintile categories of dietary pattern scores were assessed in univariable analyses using the one-way analysis of variance (ANOVA) for normally distributed continuous outcome variables and the Kruskal-Wallis test for non-normally distributed continuous and ordinal outcome variables and the $\chi 2$ or Fisher's exact test for nominal categorical outcome variables. Comparisons of included and excluded mothers were done using the two sample t-test for normally distributed variables and the Mann-Whitney U-test for non-normally distributed continuous and ordinal variables and the $\chi 2$ test for nominal categorical variables.

6.3.3.3 Regression analyses

Regression analyses were undertaken using both the continuous dietary pattern score as the predictor as well as the categories defined by the quintiles of dietary pattern score with the lowest quintile score as the referent. Any association with continuous outcomes (birth weight (g) and birth centile) and dichotomous outcomes (SGA & LGA) were assessed in univariable and multivariable linear and logistic regression models respectively. There were too few observations for LBW within strata of dietary patterns quintile scores to investigate any relationship. Covariates were selected based on a predefined list of confounders gathered from a review of the literature in this research area, and determined a priori. The CARE study had data available on the following covariates which were considered as confounders and expressed as: BMI (kg/m^2), ethnicity (Caucasian/ Other), maternal age (years), parity (nulli/multiparous), educational level as an indicator of socioeconomic status (university degree/no degree), smoking status (non-smoker, cotinine < 5 ng/ml; passive/occasional smoker, cotinine 1-5 ng/ml; smoker, cotinine >5 ng/ml) and gestation (weeks). Dietary supplement use in the 1st trimester (yes/no) was additionally assessed as a possible confounder by including it in the models. Infant's sex (male/female) was adjusted for in all models as it is likely to influence size at birth. Spearman's correlation was used to assess relationships between confounders in order to identify any collinearity and avoid over-adjustment in models. The test identified no close associations between the selected variables and they were therefore all entered into multivariate models (except for when the outcomes were birth weight centile/SGA/LGA where gestational age, maternal height, weight, ethnicity, parity, and infant's sex were already taken into account). Test for linearity were done by fitting a linear trend over the categories of dietary pattern exposure scores in unadjusted and fully adjusted models.

6.3.3.4 Effect modification

It has been recognised in previous research that maternal BMI could act as a possible modifier of the effect of maternal diet on offspring size at birth. Effect modification was therefore assessed by adding an interaction term between the dietary pattern exposure and maternal pre-pregnancy BMI (kg/m^2). Originally, World Health Organisation cut-off points of BMI were applied to group mothers; underweight BMI <18.5, healthy weight BMI 18.5-24.9, overweight BMI 25.0-29.9, obese BMI ≥30 kg/m2. However due to insufficient numbers in the lower and higher categories, for this analysis, some BMI categories were therefore merged to improve robustness of results, comparing women who reported a healthy pre-pregnancy BMI at enrolment (<25 kg/m^2) to those who were classed as overweight or obese (≥25 kg/m^2).

6.3.3.5 Sensitivity analyses

The robustness of results was assessed by excluding mothers with gestational hypertension (n=54) but not gestational diabetes as there were only three mothers in the study sample with this condition.

6.4 Results

The final study sample consisted of 1,109 pregnant women and their offspring, representing 85% of the original cohort. A comparison analysis between the study sample and excluded mothers (n=194) (see Table 17 below) revealed that included mothers were significantly less likely to be smokers in the 1st trimester (16% vs. 25%), be nulliparous (45% vs. 56%) and live in an area within the most deprived IMD quartile (29% vs. 37%) compared to excluded mothers. As expected due to the energy exclusion criteria, there was a significant difference in energy intake (kcal/day). Mothers did not differ in terms of age, BMI, ethnicity and other covariates adjusted for in multivariable analyses. The mean maternal age of the study sample was 29.9 years (SD 5.2) with a mean pre-pregnancy BMI (kg/m^2) of 24.6 (SD 4.8).

Table 17. Characteristics of CARE study mothers included in dietary pattern analysis vs. excluded mothers[a]

	Included (n=1,109)	Excluded (n=194)	*P*[b]
Age (years), mean (95% CI)	29.9 (29.6, 30.2)	29.5 (28.8, 30.3)	0.3
Pre-pregnancy BMI (kg/m^2), mean (95% CI)	24.6 (24.3, 24.9)	24.8 (24.1, 25.4)	0.7
Energy intake (kcal/d), mean (95% CI)	2099.9 (2964.6, 2135.1)	2222.7 (2037.6, 2407.7)	0.04
Alcohol intake (units/d), median (IQR)	0.26 (004, 0.80)	0.26 (0.04, 0.80)	0.08

Caffeine intake (mg/d), median (IQR)	136.84 (62.80, 245.55)	149.58 (78.41, 259.61)	0.1
Smoker at 12 weeks[c], n (%)	170 (16.0)	47 (25.1)	0.0009
IMD most deprived quartile, n (%)	311 (29.0)	68 (37.0)	0.01
University degree, n (%)	441 (39.8)	65 (33.5)	0.1
Caucasian, n (%)	1,042 (94.0)	174 (90.6)	0.08
Nulliparous, n (%)	501 (45.3)	96 (55.8)	0.01
Past history of miscarriage, n (%)	832 (76.1)	140 (74.9)	0.7
Vegetarian, n (%)	99 (9.2)	17 (9.2)	0.98
Gestational diabetes, n (%)	3 (0.3)	4 (2.2)	0.01
Gestational hypertension, n (%)	54 (5.0)	7 (3.8)	0.5

[a]Where numbers do not add up this is due to a small proportion of missing data. [b]P value using two sample t-test for normally distributed and Mann-Whitney U-test test for non-normally distributed continuous and ordinal variables and the χ2 or Fisher's exact test for nominal categorical variables. Significant difference at P<0.05. [c]Measured using salivary cotinine levels (>5 ng/ml). BMI, body mass index; CI, confidence interval; IQR, interquartile range; n, number

6.4.1 Maternal dietary patterns

Four dietary patterns were derived from the PCA, explaining 11.4% of the variance in the dietary data. Table 18 presents factor correlations for the foods associated with each pattern. The higher the factor correlation for a food, the stronger the association of that food with that pattern. Negative factor correlations indicate that non-use of a food was associated with the pattern. The components have been labelled according to the food items with the highest factor correlations. The first component, labelled 'fruit & wholegrains', had high positive correlations with fruits, Nordic fruits in particular, and unrefined grains as well as wholegrain and bran breakfast cereal and negative correlations with refined grains. The second component was labelled "traditional meat & vegetable', because of its reflection of a traditional British diet of two vegetables (cabbage and root vegetables) and one meat (pork), it also had high loadings for all potatoes but chips. The third component was characterised by high correlations with onions, tomatoes and 'other vegetables' as well as oils and it was labelled 'vegetables & oils'. Finally, the fourth component 'cheese, pasta & sauce' correlated positively with hard cheese, pasta and condiments/dressing/sauce as well as butter and negatively with chips and ice cream.

Table 18. Factor correlations of the 73 food groups* in the four dietary components obtained using PCA on energy adjusted data (N=1,109)

Food item	**Fruit & wholegrains**	**Traditional meat & vegetables**	**Vegetables & oils**	**Cheese, pasta & sauce**
% variance explained	3.1	3.0	3.0	2.3
Vegetables				
Asian vegetables	0.064	-0.046	0.063	-0.130
Cabbage	-0.020	**0.437**	-0.018	0.002
Corn	0.074	-0.011	0.108	-0.094
Mushroom	-0.073	0.041	0.138	0.119
Onion	-0.007	0.058	**0.422**	-0.032
Root vegetables	0.056	**0.444**	0.036	-0.016
Salad	0.126	-0.050	0.115	0.006
Tomato	-0.021	-0.082	**0.332**	0.151
Other vegetables	0.114	-0.046	**0.288**	0.072
Vegetable dishes	0.064	-0.052	-0.024	-0.043
Potatoes				
Baked/boiled/ mashed	0.062	**0.309**	-0.026	0.026
Chips	-0.134	-0.131	-0.131	**-0.244**
Roast potatoes	-0.057	**0.377**	-0.019	-0.025
Nuts				
Nuts & seeds	0.073	-0.048	0.088	0.039
Pulses/legumes				
Baked beans	0.007	0.013	-0.117	-0.067
Legumes	0.110	0.129	0.048	-0.155
Soya	0.046	-0.040	0.140	-0.139
Fruit & Berries				
Banana	**0.276**	-0.037	-0.007	-0.011
Berries	0.086	0.054	-0.025	0.104
Citrus fruit	0.192	0.016	-0.039	0.025
Dried fruit	0.143	-0.037	0.082	0.004
Nordic fruit	**0.289**	-0.011	0.018	-0.145
Other fruit	0.142	0.016	0.053	-0.100
Meat				
Beef	-0.082	0.114	0.163	0.060
Lamb	-0.009	0.136	0.023	-0.070
Meat toppings	-0.053	0.002	-0.081	0.181
Meat dishes	-0.051	-0.155	0.052	-0.095
Processed meat	-0.101	-0.006	-0.121	-0.106
Offal	-0.068	-0.011	**0.322**	-0.103
Pork	-0.159	**0.257**	0.037	0.005
Poultry	0.008	0.096	0.080	-0.085
Ice cream/sweets/ cakes				
Chocolate	0.027	-0.057	-0.058	-0.066

Ice cream	0.026	0.055	0.090	**-0.234**
Sugar/cakes/ biscuits	0.092	0.000	-0.026	0.095
Puddings	-0.044	0.088	-0.039	-0.020
Sweets	0.015	0.046	-0.030	0.067
Sweet spreads	0.089	-0.013	0.018	-0.018
Cereal products				
Refined grains	**-0.237**	-0.168	0.007	0.142
Unrefined grains	**0.314**	0.030	-0.008	0.098
Oat breakfast cereal	0.128	-0.019	-0.031	-0.030
Wholegrain/bran breakfast cereal	**0.243**	0.007	-0.100	0.068
Other breakfast cereal	-0.016	0.062	0.030	-0.179
Pasta	0.005	-0.089	0.159	**0.298**
Rice	0.027	-0.107	0.159	-0.193
Fats				
Butter	-0.066	-0.027	-0.005	**0.230**
Condiments/ dressing/sauce	-0.011	0.146	0.003	**0.283**
Margarine	-0.045	-0.010	-0.089	-0.041
Oil	-0.006	0.008	**0.392**	-0.020
Fish				
Lean	0.082	-0.032	-0.062	-0.106
Oily/fatty	0.127	0.013	0.029	0.021
Shellfish	-0.036	0.014	0.122	-0.100
Fish dishes	0.048	-0.090	-0.061	-0.050
Beverages				
Beer	-0.104	-0.006	0.004	-0.141
Coffee	-0.146	-0.013	-0.042	0.067
Juice	0.107	0.044	-0.029	0.002
Soft drink-diet	-0.025	0.018	-0.098	0.093
Soft drink-sugar	-0.157	-0.038	0.036	-0.152
Spirits	-0.065	-0.001	0.014	0.062
Tea	0.006	0.096	-0.040	0.078
Water	**0.292**	-0.005	0.064	0.078
Wine	-0.100	0.036	0.069	0.164
Dairy products				
Fresh cheese	0.092	-0.024	-0.001	0.032
Hard cheese	0.052	-0.075	-0.062	**0.354**
Soft cheese	0.001	0.014	0.141	0.167
Sweetened milk	0.004	-0.052	0.011	0.030
Full fat milk	-0.134	-0.035	0.002	-0.066
Low fat milk	0.183	0.112	-0.076	-0.021
Yoghurt	**0.256**	-0.090	-0.083	0.005
Snacks				
Snack	-0.078	-0.042	-0.043	0.089

Eggs				
Egg	-0.093	0.033	0.082	0.022
Pizza				
Pizza	-0.057	-0.100	-0.062	-0.014
Pastries/savouries				
Pastries/savouries	-0.080	0.139	-0.060	-0.045
Soup				
Soup	0.060	-0.042	-0.068	0.046

*For a description of each food group please see Table 8.
Factor correlations above 0.2 are shown in bold.

In order to facilitate interpretation, the 73 food items entered into the PCA were aggregated into 14 main food groups as described: vegetables (including vegetable dishes), potatoes, nuts, fruit, meat (including meat dishes), ice cream/sweets/cakes, cereals, fats, fish (including fish dishes), beverages, dairy, snacks, eggs and pulses/legumes with the addition of the three CARE specific food groups: pizza, pastries/savouries and soup. Table 19 presents the average daily intake of the food groups, total energy intake, macronutrients as well as selected micronutrients across dietary pattern quintiles. Intakes of macronutrients were calculated as percentage energy by multiplying the daily intakes in grams of each macronutrient with its caloric value per gram (4 kcal/g for carbohydrates and protein and 9 kcal/g for fat) and dividing by the energy intake and multiplying by 100. For the ‘fruit & wholegrains’ component higher scores implied higher intakes of vegetables, legumes, fruit, cereal products, fish, beverages, ice cream/sweets/cakes and dairy. Mothers in the highest quintile had a median fruit intake of 240 g compared to a median of 0 in the lowest quintile category; they also had a lower intake of meat (36 g in the highest quintile vs. 140 g in the lowest), potatoes and snacks. In terms of nutrients, higher scores for this component implied higher intakes for all but fats and there was no clear trend for energy intake although mothers in the highest quintile had a lower energy intake than mothers in the lowest quintile (2176 kcal/day vs. 2254 kcal/day). As for the second component, ‘traditional meat & vegetables’ higher scores resulted in higher intakes of vegetables, potatoes, legumes, meat, ice cream/sweets/cakes, fats, beverages and pastries whereas mothers with lower scores had higher intakes of cereal products. There was no clear trend for intakes of fruit or dairy nor any of the nutrients although, similarly to the ‘fruit & wholegrains’ component, energy intake was lower for mothers in the highest compared to the lowest quintile, however intakes in between were lower than that of the highest quintile scores. The third component was characterised by higher intakes of vegetables, fruit, meat, cereal, fats and fish and lower intakes of potatoes, legumes and beverages in the higher quintile categories. There was no clear trend for any of the nutrients apart from protein where mothers with higher scores had higher % energy from protein. Higher scores for the final component, ‘cheese, pasta & sauce’, implied higher intakes of vegetables, fruit, cereal products, fats and beverages and lower intakes of potatoes, legumes, meat and fish but with no trend for the remaining foods and nutrients. For clarity, the highest and lowest intakes across all dietary patterns have been highlighted in bold in the table below.

Table 19. Average daily intake of energy, selected nutrients and main food groups* (g/day) across dietary pattern quintile scores based on a 24-hour dietary recall at 14-18 weeks of pregnancy in the CARE study (N=1,109)

	Fruit & wholegrains				
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Nutrients	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Energy intake (kcal/d)	2254.1 (2175.9, 2332.2)	2009.2 (1924.8, 2093.5)	2022.8 (1947, 2098.7)	2037.2 (1963.6, 2110.8)	2176.4 (2097.6, 2255.2)
Fats (% energy)	**38.6 (37.6, 39.6)**	37.1 (36.1, 38.1)	36.1 (35.1, 37.1)	34.9 (33.9, 35.9)	**32.0 (30.9, 33.1)**
Carbohydrates (% energy)	**49.2 (47.9, 50.4)**	51.1 (49.9, 52.3)	51.9 (50.7, 53.2)	52.4 (51.4, 53.5)	**55.9 (54.6, 57.1)**
NSP** (g/d)	**10.5 (9.9, 11.1)**	11.1 (10.4, 11.7)	13.2 (12.6, 13.9)	15.7 (14.9, 16.5)	**20.0 (19.0, 21.0)**
Protein (% energy)	14.4 (13.8, 14.9)	14.5 (13.9, 15.1)	14.7 (14.1, 15.2)	15.6 (15.1, 16.2)	15.4 (14.9, 15.9)
Folate (µg/d)	**211.3 (199.2, 223.5)**	214.6 (201.0, 228.1)	250.6 (237.1, 264.1)	274.5 (261.9, 287.1)	**330.2 (313.0, 347.5)**
Calcium (mg/d)	886.4 (829.1, 943.6)	**817.0 (764.7, 869.4)**	882.8 (829.8, 935.9)	949.9 (894.2, 1005.6)	1109.2 (1051.6, 1166.9)
Iron (mg/d)	10.4 (9.9, 10.9)	**10.0 (9.4, 10.6)**	10.9 (10.4, 11.5)	12.0 (11.3, 12.6)	**14.0 (13.2, 14.7)**
Main food groups	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables & vegetable dishes	40 (0, 169)	65 (0, 166)	105 (20, 215)	124.5 (20, 201)	160 (68, 275)
Potatoes	100 (0, 165)	35 (0, 165)	59 (0, 165)	0 (0, 120)	0 (0, 160)
Nuts	0	0	0	0	0
Legumes/pulses	0	0	0 (0, 60)	0 (0, 50)	0 (0, 70)
Fruit	**0**	0 (0, 100)	50 (0, 135)	137 (48, 240)	**240 (140, 374)**
Meat & meat dishes	**140 (46, 250)**	102.5 (36, 190)	100 (0, 172)	85 (0, 165)	**36 (0, 135)**
Ice cream/ sweets/cakes	49.5 (4, 90)	51 (12, 109.5)	56.5 (2, 102)	57.1 (23, 97)	60 (20, 116)
Cereal products	144 (84, 224)	135.5 (72, 220)	133.5 (93, 242)	157 (90, 250)	193 (131, 288)
Fats	29.5 (14, 65)	23.5 (10, 55)	29 (12, 60)	30 (10, 61)	27 (12, 50)
Fish	0	0	0	0 (0, 45)	**0 (0, 82)**
Beverages	1459.5 (1020, 1980)	1356 (1030, 1863)	1635 (1220, 2208)	1647.5 (1210, 2085)	**1800 (1280, 2382)**
Dairy products	**130 (20, 293)**	150 (40, 290)	173 (75, 340)	238 (100, 395)	**311 (195, 469)**
Snacks	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 28)
Eggs	0	0	0	0	0
Pizza	0	0	0	0	0
Pastries	0	0 (0, 21)	0	0	0
Soup	0	0	0	0	0

Traditional meat & vegetables

	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Nutrients	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Energy intake (kcal/d)	2313.6 (2242.8, 2384.4)	2013.6 (1933.1, 2094.1)	1986.3 (1905.3, 2067.4)	2019 (1943.8, 2094.2)	2167.1 (2087.3, 2247)
Fats (% energy)	37.0 (36.1, 37.9)	35.7 (34.7, 36.7)	35.0 (33.8, 36.1)	36.0 (34.8, 37.2)	35.1 (34, 36.1)
Carbohydrates (% energy)	52.1 (51.1, 53.2)	53.4 (52.2, 54.6)	52.6 (51.3, 53.9)	51.2 (49.8, 52.6)	51.1 (49.9, 52.3)
NSP** (g/d)	13.5 (12.8, 14.2)	12.2 (11.4, 13.1)	13.1 (12.2, 14.0)	14.6 (13.7, 15.4)	17.2 (16.3, 18.1)
Protein (% energy)	**13.6 (13.2, 14.0)**	13.7 (13.3, 14.2)	15.2 (14.6, 15.8)	15.5 (15.0, 16.0)	**16.6 (16.0, 17.2)**
Folate (µg/d)	229.1 (216.3, 241.9)	222.3 (207.3, 237.4)	232.5 (220.2, 244.9)	267.9 (253.8, 281.9)	329.4 (313.3, 345.4)
Calcium (mg/d)	1008.3 (950.7, 1066)	890.5 (833.7, 947.4)	888.9 (831.9, 945.9)	919.0 (862.9, 975.2)	937.7 (883.0, 992.4)
Iron (mg/d)	11.4 (10.9, 12)	10.6 (9.9, 11.3)	10.9 (10.3, 11.5)	11.6 (11, 12.2)	12.8 (12.1, 13.5)
Food item	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables & vegetable dishes	55 (0, 175)	60 (0, 170)	70 (0, 185)	111 (20, 200)	185 (120, 273)
Potatoes	**0 (0, 110)**	0 (0, 100)	0 (0, 120)	60 (0, 175)	**170 (90, 240)**
Nuts	0	0	0	0	0
Legumes/ pulses	0	0	0 (0, 20)	0 (0, 70)	0 (0, 70)
Fruit	50 (0, 177)	100 (0, 180)	70 (0, 200)	61.5 (0, 210)	100 (0, 200)
Meat & meat dishes	100 (0, 281)	65.5 (0, 180)	82 (0, 150)	90 (0, 155)	130 (53, 190)
Ice cream/ sweets/cakes	52 (18, 92)	52 (20, 107)	54 (14, 102.5)	56 (15, 100)	**70 (24, 125)**
Cereal products	207 (122, 326)	161 (96, 291)	160 (102, 237)	140 (87, 215)	108 (72, 176)
Fats	25 (10, 43)	22 (10, 47)	23 (10, 54)	27 (10, 59)	51 (19, 86)
Fish	0	0	0	0	0
Beverages	1525 (1175, 2000)	1468 (1180, 2028)	1542.5 (1070, 2073)	1648 (1106, 2164)	1696 (1250, 2220)
Dairy products	195 (45, 385)	180 (60, 300)	194 (60, 329.5)	212.5 (120, 413)	200 (70, 365)
Snacks	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 30)	**0 (0, 27)**
Eggs	0	0	0	0	0
Pizza	0	0	0	0	0
Pastries	0	0	0	0	**0 (0, 63)**
Soup	0	0	0	0	0

			Vegetables & oils		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Nutrients	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Energy intake (kcal/d)	**2378.1 (2298.1, 2458.2)**	1998.6 (1927, 2070.1)	**1970.1 (1896.5, 2043.7)**	1988 (1908.6, 2067.5)	2164.8 (2086.9, 2242.6)
Fats (% energy)	36.4 (35.4, 37.5)	36.1 (35.1, 37.2)	35.5 (34.5, 36.5)	34.9 (33.8, 36)	35.8 (34.7, 37.0)
Carbohydrates (% energy)	52.6 (51.4, 53.8)	52.6 (51.4, 53.8)	52.9 (51.7, 54.1)	51.7 (50.4, 53)	50.7 (49.3, 52.0)
NSP** (g/d)	15.5 (14.6, 16.4)	12.9 (12.1, 13.7)	12.9 (12.1, 13.7)	13.2 (12.4, 14.1)	16.0 (15.1, 16.9)
Protein (% energy)	13.8 (13.4, 14.2)	14.1 (13.6, 14.6)	14.6 (14.0, 15.1)	16.0 (15.3, 16.6)	16.1 (15.6, 16.7)
Folate (µg/d)	268.5 (251.7, 285.4)	239.1 (224.8, 253.3)	245.6 (231.5, 259.8)	243.3 (228.4, 258.2)	284.5 (270.3, 298.7)
Calcium (mg/d)	1116.6	946.1	852.8	827.0	902.0

	(1056.9, 1176.3)	(887.1, 1005)	(798.3, 907.2)	(775.5, 878.5)	(851.8, 952.2)
Iron (mg/d)	12.1 (11.4, 12.9)	10.6 (10, 11.2)	10.7 (10.2, 11.3)	10.8 (10.2, 11.4)	13.1 (12.4, 13.7)
Food item	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables & vegetable dishes	**19 (0, 90)**	42 (0, 126)	90 (20, 160)	127 (50, 207)	**255 (168, 380)**
Potatoes	120 (0, 175)	37.5 (0, 165)	80 (0, 165)	0 (0, 120)	0 (0, 120)
Nuts	0	0	0	0	0
Legumes/ pulses	**0 (0, 90)**	0 (0, 35)	0 (0, 40)	0	0 (0, 50)
Fruit	15.5 (0, 160)	57 (0, 180)	80 (0, 200)	100 (0, 200)	100 (0, 214)
Meat & meat dishes	79 (0, 172)	53.5 (0, 150)	100 (0, 180)	130 (40, 220)	114 (0, 200)
Ice cream/ sweets/cakes	66.5 (30, 128)	53.5 (17, 110)	**43 (10.5, 106)**	52.5 (12, 100)	56 (18, 94)
Cereal products	133 (81, 195)	132 (78, 199)	132.5 (95, 196)	175.5 (93, 300)	240 (136, 333)
Fats	29.5 (14, 55)	24 (12, 60)	24 (10, 47)	30.5 (10, 67)	31 (14, 60)
Fish	0	0	0	0	0 (0, 15)
Beverages	1587 (1180, 2246)	1515 (1112, 1975)	1557.5 (1100, 2085)	1542.5 (1110, 2020)	**1263 (1643, 2272)**
Dairy products	257.5 (100, 453)	191.5 (60, 380)	180 (60, 350)	180 (60, 323)	200 (60, 332)
Snacks	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 30)
Eggs	0	0	0	0	0
Pizza	0	0	0	0	0
Pastries	0 (0, 21)	0 (0, 30)	0	0	0
Soup	0	0	0	0	0

			Cheese, pasta & sauce		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Nutrients	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Energy intake (kcal/d)	2265.7 (2190.2, 2341.2)	2011.7 (1931.4, 2092)	1961.2 (1887.4, 2034.9)	1996.5 (1918.9, 2074.0)	2265.1 (2186.3, 2344.0)
Fats (% energy)	35.0 (33.9, 36)	34.1 (33.0, 35.2)	35.5 (34.4, 36.6)	37.0 (36.0, 38.0)	37.2 (36.2, 38.3)
Carbohydrates (% energy)	53.0 (51.7, 54.2)	54.3 (53.0, 55.6)	52.9 (51.6, 54.1)	50.4 (49.2, 51.6)	50.0 (48.8, 51.2)
NSP** (g/d)	14.8 (13.8, 15.8)	13.4 (12.5, 14.3)	13.4 (12.5, 14.2)	13.3 (12.5, 14.2)	13.3 (12.5, 14.0)
Protein (% energy)	14.6 (14.1, 15.2)	14.7 (14.1, 15.3)	14.7 (14.2, 15.2)	15.4 (14.8, 16.0)	15.1 (14.7, 15.6)
Folate (μg/d)	262.8 (247.6, 278.0)	245.2 (229.2, 261.3)	244.6 (230.0, 259.2)	245.6 (231.9, 259.2)	282.8 (267.6, 298.0)
Calcium (mg/d)	887.4 (836.8, 937.9)	832.9 (773.5, 892.2)	868.1 (818.1, 918.2)	931.0 (876.3, 985.6)	**1126.1 (1065.9, 1186.2)**
Iron (mg/d)	11.7 (11.2, 12.3)	11.3 (10.5, 12.1)	11.2 (10.5, 11.8)	10.8 (10.3, 11.4)	12.3 (11.7, 12.9)
Food item	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables & vegetable dishes	80 (0, 190)	70 (0, 200)	100 (20, 201)	113.5 (20, 210)	137 (46, 248)
Potatoes	120 (0, 170)	95 (0, 165)	47.5 (0, 165)	0 (0, 120)	0 (0, 120)
Nuts	0	0	0	0	0
Legumes/ pulses	0 (0, 90)	0 (0, 60)	0 (0, 40)	0	0
Fruit	87 (0, 240)	40 (0, 178)	82.5 (0, 183)	72.5 (0, 197)	100 (0, 190)
Meat & meat dishes	130 (20, 260)	103.5 (0, 199)	93 (0, 173)	98 (0, 172)	50 (0, 136)
Ice cream/ sweets/cakes	65.5 (20, 129)	50 (12, 97)	52 (16, 89)	58.6 (22, 104)	56 (20, 103.7)

Cereal products	128.5 (72, 207)	132.5 (84, 230)	137.5 (80, 208)	154 (102, 220)	**242 (144, 350)**
Fats	**19.5 (5, 35)**	20 (7, 45)	25 (10, 50)	36.5 (15, 73)	**54 (24, 121)**
Fish	0 (0, 45)	0	0	0	0
Beverages	1478 (1070, 1998)	1545 (1090, 2085)	1520 (1163, 2060)	1587 (1160, 2180)	1702 (1270, 2310)
Dairy products	200 (60, 396)	180 (40, 340)	200 (70, 370)	181 (60, 340)	240 (120, 380)
Snacks	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 30)	0 (0, 30)
Eggs	0	0	0	0	0
Pizza	0	0	0	0	0
Pastries	0	0	0	0	0
Soup	0	0	0	0	0

*For a description of each food group please see Table 8. **Defined by the Englyst method. The highest and lowest average value for each food group and nutrient across all dietary patterns are shown in bold. CI, confidence interval; IQR, interquartile range; NSP, non-starch polysaccharides; Q, quintile.

6.4.2 Characteristics of mothers across quintile categories of dietary patterns scores

Characteristics of participants in the CARE study across quintile categories of the four dietary pattern scores can be found in Table 20. Mothers who scored highly on the first component were significantly more likely to be older, have a lower pre-pregnancy BMI, have a university degree, be nulliparous, take dietary supplements in the 1st trimester, be vegetarian, and have a higher alcohol intake and a lower caffeine intake than those in the lower quintile scores. They were less likely to be smokers in the 1st trimester and to live in the most deprived area. Those in the higher quintile categories of the ‘traditional meat & vegetables’ component were significantly older than mothers in the lower categories. No other significant differences in participant characteristics were found for this component. As for the third component, ’vegetables & oils’, mothers in the highest quintile category were similarly to those scoring highly on the first component, more likely to be older, have a lower pre-pregnancy BMI, have a university degree, be vegetarian and have a lower caffeine intake. They were also less likely to be smokers in the 1st trimester and to be Caucasian. Mothers who scored highly on the fourth component were significantly more likely to be older, to have a university degree and have a higher alcohol intake throughout pregnancy.

Table 20. CARE study sample characteristics according to quintile categories of dietary pattern scores (n=1,109)[a]

	Fruit & wholegrains						**Traditional meat & vegetables**					
	Q1 (n=222)	**Q2 (n=222)**	**Q3 (n=222)**	**Q4 (n=222)**	**Q5 (n=221)**	***P*[b]**	**Q1 (n=222)**	**Q2 (n=222)**	**Q3 (n=222)**	**Q4 (n=222)**	**Q5 (n=221)**	***P*[b]**
Age of mother (years), mean (SD)	27.8 (5.9)	29.1 (5.8)	30.0 (4.7)	31.0 (4.8)	31.6 (3.6)	<0.0001	29.1 (5.2)	29.4 (5.7)	30.0 (5.1)	30.6 (4.8)	30.4 (5.0)	0.01
Pre-pregnancy BMI (kg/m^2), mean (SD)	25.3 (5.3)	25.3 (5.1)	24.7 (4.8)	24.2 (4.0)	23.6 (4.7)	0.0003	24.5 (4.4)	24.5 (4.9)	25.2 (5.3)	24.6 (4.7)	24.3 (4.8)	0.3
Caucasian, n (%)	215 (96.9)	207 (93.2)	204 (91.9)	209 (94.1)	207 (94.1)	0.3	202 (91.0)	209 (94.1)	209 (94.1)	212 (95.5)	210 (95.5)	0.3
Smoker at 12 weeks, n (%)[c]	82 (39.4)	46 (21.4)	27 (12.7)	10 (4.7)	5 (2.4)	0.0001	36 (17.1)	39 (18.2)	34 (16.1)	32 (15.0)	29 (13.7)	0.5
University degree, n (%)	33 (14.9)	53 (23.9)	93 (41.9)	118 (53.2)	144 (65.2)	<0.0001	82 (36.9)	89 (40.1)	87 (39.2)	96 (43.2)	87 (39.4)	0.8
IMD most deprived quartile, n (%)	98 (45.4)	70 (32.3)	49 (23.0)	58 (27.1)	36 (17.1)	<0.0001	74(34.4)	66 (31.1)	62 (29.1)	55 (25.1)	54 (25.5)	0.09
Nulliparous, n (%)	86 (39.1)	97 (43.9)	93 (42.1)	97 (43.7)	128 (57.9)	0.001	121 (55.0)	125 (56.6)	120 (54.3)	118 (53.2)	120 (54.3)	0.9
Dietary supplements in 1st trimester, n (%)	162 (73.6)	174 (79.1)	182 (82.7)	181 (82.7)	197 (90.4)	<0.0001	184 (83.6)	176 (79.6)	177 (80.8)	179 (80.6)	180 (83.7)	0.7
Vegetarian, n (%)	8 (3.7)	9 (4.2)	19 (8.7)	25 (11.8)	38 (17.8)	<0.0001	23 (10.7)	19 (8.8)	21 (9.9)	22 (10.4)	14 (6.5)	0.6
Gestational hypertension, n (%)	12 (5.5)	17 (7.9)	9 (4.1)	11 (5.0)	5 (2.3)	0.1	11 (5.1)	8 (3.7)	15 (6.9)	11 (5.0)	9 (4.1)	0.6
Previous miscarriage, n (%)	61 (27.5)	52 (23.4)	56 (25.2)	50 (22.5)	44 (19.9)	0.4	57 (25.7)	53 (23.9)	51 (23.0)	48 (21.6)	54 (24.4)	0.9
Alcohol intake (>2 units/wk), n (%)	100 (51.3)	93 (47.0)	99 (48.3)	106 (54.1)	131 (63.3)	0.004	105 (51.2)	97 (50.8)	113 (57.1)	101 (49.3)	113 (55.9)	0.7
Caffeine intake (mg/d), median (IQR)	214.6 (93.4, 354.2)	171.1 (71.2, 276.0)	135.3 (63.3, 226.7)	130.3 (51.8, 223.5)	82.1 (39.0, 163.7)	0.0001	131.6 (65.9, 230.7)	148.3 (60.5, 266.3)	136.1 (56.7, 250.7)	140.1 (63.9, 251.9)	130.8 (65.0, 219.8)	0.7
Neonatal characteristics												
Birth weight (g), mean (SD)	3476.8 (527.2)	3432.7 (454.2)	3457.7 (493.1)	3514.2 (449.6)	3532.5 (447.4)	0.16	3539.5 (499.8)	3441.2 (445.7)	3466.6 (469.7)	3506.0 (482.6)	3460.3 (477.6)	0.19
Child sex (male), n (%)	103 (46.4)	122 (55.0)	103 (46.4)	114 (51.4)	116 (52.5)	0.3	108 (48.7)	110 (49.6)	117 (52.7)	115 (51.8)	108 (48.9)	0.9

Table 19 continued. CARE study sample characteristics according to quintile categories of dietary pattern scores (n=1,109)[a]

	Vegetable & oils						Cheese, pasta & sauces					
	Q1 (n=222)	**Q2 (n=222)**	**Q3 (n=222)**	**Q4 (n=222)**	**Q5 (n=221)**	***P*[b]**	**Q1 (n=222)**	**Q2 (n=222)**	**Q3 (n=222)**	**Q4 (n=222)**	**Q5 (n=221)**	***P*[b]**
Age of mother (years), mean (SD)	28.8 (5.4)	29.5 (5.4)	29.6 (5.3)	30.6 (4.9)	31.0 (4.6)	<0.0001	28.8 (5.3)	29.5 (5.6)	30.0 (5.2)	30.6 (5.0)	30.6 (4.5)	0.0007
Pre-pregnancy BMI (kg/m^2), mean (SD)	24.2 (4.8)	24.9 (5.0)	25.1 (4.9)	25.2 (5.3)	23.8 (3.9)	0.01	24.7 (5.1)	24.8 (5.0)	24.6 (4.5)	24.7 (4.9)	24.3 (4.7)	0.9
Caucasian, n (%)	219 (98.7)	212 (95.5)	213 (96.0)	206 (93.2)	192 (86.9)	<0.0001	206 (93.2)	205 (92.3)	204 (91.9)	212 (95.5)	215 (97.3)	0.08
Smoking in pregnancy, n (%)[c]	61 (28.8)	38 (18.3)	36 (17.1)	20 (9.3)	15 (7.0)	0.0001	36 (17.0)	39 (18.7)	34 (16.3)	29 (12.4)	32 (15.0)	0.4
University degree, n (%)	70 (31.5)	69 (31.1)	88 (39.6)	93 (41.9)	121 (54.8)	<0.0001	80 (36.0)	69 (31.1)	92 (41.1)	94 (42.3)	106 (48.0)	0.004
IMD most deprived quartile, n (%)	73 (34.0)	64 (29.0)	67 (31.6)	58 (27.0)	49 (22.8)	0.2	72 (34.1)	60 (28.2)	73 (33.8)	56 (25.8)	50 (23.4)	0.18
Nulliparous, n (%)	100 (45.3)	109 (49.1)	89 (40.1)	100 (45.5)	103 (46.8)	0.4	107 (48.6)	99 (44.6)	102 (46.2)	99 (44.5)	94 (42.7)	0.8
Dietary supplements in the 1st trimester questionnaire, n (%)	176 (79.6)	183 (83.2)	170 (78.3)	174 (79.8)	193 (87.3)	0.1	180 (82.2)	167 (75.2)	179 (82.9)	184 (84.0)	186 (84.2)	0.09
Vegetarian, n (%)	17 (7.8)	13 (6.1)	18 (8.5)	18 (8.5)	33 (15.4)	0.01	14 (6.6)	20 (9.2)	19 (8.8)	22 (10.3)	24 (11.3)	0.5
Gestational hypertension, n (%)	11 (5.1)	8 (3.7)	15 (6.9)	11 (5.0)	9 (4.1)	0.6	11 (5.1)	8 (3.7)	15 (6.9)	11 (5.0)	9 (4.1)	0.6
Alcohol intake (>2 units/wk), n (%)	106 (52.2)	109 (53.4)	103 (51.5)	100 (50.8)	111 (56.4)	0.8	95 (47.3)	98 (50.8)	106 (52.0)	106 (52.0)	124 (61.7)	0.02
Caffeine intake (mg/d), median (IQR)	166.0 (79.7, 305.2)	161.7 (73.9, 262.0)	128.1 (54.0, 239.6)	125.3 (62.2, 207.8)	119.7 (53.3, 228.5)	0.0003	119.2 (53.9, 232.1)	120.6 (62.7, 239.6)	153.5 (71.2, 258.5)	127.4 (60.5, 230.1)	158.3 (69.6, 261.0)	0.2
Neonatal characteristics												
Birth weight (g), mean (SD)	3468.7 (485.8)	3483.1 (513.9)	3500.0 (433.9)	3506.8 (461.7)	3454.9 (482.8)	0.8	3459.2 (469.4)	3485.0 (482.0)	3446.5 (475.3)	3482.3 (481.6)	3540.8 (469.7)	0.3
Child sex (% male)	111 (50.0)	126 (56.8)	105 (47.3)	106 (47.8)	110 (49.8)	0.3	113 (50.9)	106 (47.8)	115 (51.8)	104 (46.9)	120 (54.3)	0.5

[a]Where numbers do not add up this is due to a small proportion of missing data. [b]P value using ANOVA for normally distributed and the Kruskal-Wallis test for non-normally distributed continuous and ordinal variables and the χ2 or Fisher's exact test for nominal categorical variables. Significant difference at P<0.05. [c]Measured using salivary cotinine levels. BMI, body mass index; d, day; g, gram; IMD, Index of Multiple Deprivation; IQR, interquartile range; SD, standard deviation; wk, week.

6.4.3 Offspring characteristics

All mothers had information available on offspring size at birth, gestation and infant's sex. Mean birth weight of the study sample was 3.48 kg (SD 476 g) with a mean gestation of 40 weeks (SD 1.2 weeks) and 17 babies (1.5 %) weighing less than 2.5 kg. Twelve percent (n=130) of infants were classed as SGA (<10th centile) and 10% (n=111) as LGA (>90th centile). Fifty percent of infants were male.

6.4.4 Relationship between maternal dietary patterns and birth weight

Table 20 shows the crude and adjusted associations between size at birth expressed as birth weight and customised birth centile and maternal dietary patterns in pregnancy. The 'fruit & wholegrains' dietary pattern was found to be significantly associated with both birth weight in grams and birth weight measured on the customised birth centile. The unadjusted change in birth weight (g) per 1 unit increase in the 'fruit & wholegrains' dietary pattern score was 22.1 g (95% CI: 3.44, 40.76 *P*=0.02). A rather modest increase; however there is a clinical importance for even small increases in birth weight as any extra weight would make a difference in the perinatal morbidity and mortality in an already small baby. Adjusting for maternal pre-pregnancy BMI, age, parity, ethnicity, salivary cotinine levels, educational status, caffeine intake, trimester 1 alcohol intake, gestation and infant's sex however attenuated this relationship and it was no longer significant (adjusted change 15.5 g, 95% CI -4.30, 35.25, *P*=0.10) (Table 21).

Considering birth centile as an outcome, the unadjusted change per 1 unit increase in the 'fruit & wholegrains' dietary pattern score was 2.1 centile points (95% CI: 0.91, 3.18, *P*<0.0001). However when adjusting for salivary cotinine levels, educational status, caffeine intake and trimester 1 alcohol intake, the relationship was attenuated and rendered non significant (0.73 centile points; 95% CI: -0.65, 2.10, *P*=0.3). In unadjusted analyses, compared to mothers in the lowest 'fruit & wholegrains' quintile score, mothers in the highest quintile score had infants with a 7.94 higher birth centile (95% CI: 2.56, 13.31, *P*=0.004, P_{trend}=0.009). The adjusted relationship however was not significant (2.46 centile point; 95% CI: -3.96, 8.87, P_{trend}=0.1).

The 'cheese, pasta & sauces' dietary component was found to have a similar association with birth weight in unadjusted analyses to that of the 'fruit & wholegrains' dietary pattern with a change of just over 22 g in birth weight for every 1 unit increase in the component score (95% CI: 0.59, 43.88, *P*=0.04). The effect estimates however were not significant once adjustments for confounders were made (Table 21).

There was no evidence of a relationship between the ‘traditional meat & vegetables’ dietary pattern or the ‘vegetables & oils’ dietary pattern and birth weight.

Table 21. The relationship between maternal dietary patterns in pregnancy and birth weight and birth centile in the CARE study

	Birth weight (g)				**Customised birth centile**^{a}			
	Crude β (95% CI) n=1,109	P^b	Adjusted β^c (95% CI) n=940	P^b	Crude β (95% CI) n=1,109	P^b	Adjusted β^d (95% CI) n=958	P^b
Fruit & wholegrains								
Continuous score	22.10 (3.44, 40.76)	0.02	15.48 (-4.30, 35.25)	0.1	2.05 (0.91, 3.18)	<0.0001	0.73 (-0.65, 2.10)	0.3
Q1	0	0.17	0	0.1	0	0.009	0	0.1
Q2	-44.09 (-132.62, 44.43)		-66.75 (-151.05, 17.55)		-0.85 (-6.22, 4.52)		-4.95 (-10.86, 0.95)	
Q3	-19.11 (-107.63, 69.41)		-26.97 (-113.66, 59.71)		4.29 (-1.08, 9.66)		-0.64 (-6.70, 5.42)	
Q4	37.37 (-51.15, 125.90)		-17.34 (-107.36, 72.68)		4.08 (-1.29, 9.45)		-2.50 (-8.82, 3.81)	
Q5	55.69 (-32.93, 144.32)		48.44 (-44.1, 140.90)		7.94 (2.56,13.31)		2.46 (-3.96, 8.87)	
Traditional meat & vegetables								
Continuous score	-6.39 (-25.34, 12.57)	0.5	-13.03 (-30.38, 4.31)	0.14	-0.65 (-1.80, 0.50)	0.27	-0.81 (-2.01, 0.39)	0.2
Q1	0	0.19	0	0.2	0	0.24	0	0.3
Q2	-98.37 (-186.91, -9.83)		-76.25 (-158.08, 5.59)		-5.99 (-11.38,-0.61)		-5.07 (-10.86, 0.72)	
Q3	-72.94 (-161.48, 15.60)		-60.17 (-141.91, 21.56)		-4.69 (-10.07, 0.70)		-4.36 (-10.11, 1.40)	
Q4	-33.57 (-122.11, 54.97)		-41.63 (-122.75, 39.49)		-3.94 (-9.33, 1.45)		-4.48 (-10.19, 1.23)	
Q5	-79.26 (-167.90, 9.38)		-91.12 (-172.91, -9.32)		-4.65 (-10.05, 0.74)		-5.40 (-11.13, 0.33)	
Vegetables & oils								
Continuous score	-6.13 (-25.09, 12.84)	0.5	-7.15 (-24.87, 1057)	0.4	0.25 (-0.90, 1.41)	0.67	-0.52 (-1.77, 0.73)	0.4
Q1	0	0.8	0	0.8	0	0.76	0	0.7
Q2	14.44 (-74.28, 103.15)		20.16 (-61.89, 102.22)		1.88 (-3.52, 7.28)		-0.32 (-6.09, 5.44)	
Q3	31.33 (-57.38, 120.05)		-22.02 (-104.13, 60.09)		1.78 (-3.62, 7.18)		-2.59 (-8.37, 3.20)	
Q4	38.11 (-50.60, 126.83)		2.97 (-79.95, 85.89)		3.74 (-1.66, 9.14)		0.05 (-5.77, 5.87)	
Q5	-13.77 (-102.58, 75.05)		-25.52 (-108.96, 57.91)		1.89 (-3.52, 7.29)		-3.25 (-9.10, 2.60)	
Cheese, pasta & sauces								
Continuous score	22.23 (0.59, 43.88)	0.04	8.99 (-11.39, 29.37)	0.4	0.70 (-0.62, 2.02)	0.3	0.45 (-0.99, 1.88)	0.5
Q1	0	0.27	0	0.6	0	0.4	0	0.4

Q2	25.82	46.69	0.68	1.70
	(-62.76, 114.40)	(-36.11, 129.50)	(-4.72, 6.07)	(-4.12, 7.51)
Q3	-12.75	17.56	0.56	0.40
	(-101.33, 75.83)	(-64.53, 99.65)	(-4.84, 5.95)	(-5.38, 6.19)
Q4	23.10	0.66	-2.08	-2.37
	(-65.48, 111.68)	(-80.59, 81.91)	(-7.48, 3.31)	(-8.08, 3.35)
Q5	81.63	49.48	3.27	3.08
	(-7.06, 170.31)	(-33.02, 131.99)	(-2.13, 8.67)	(-2.71, 8.88)

β:where the predictor is continuous β refers to the change in the outcome for every 1 unit increase in the predictor. Where the predictor is categorical it is the difference in the outcome between one category (e.g. Q2) and the ref category (Q1).[a]Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation & infant's sex. [b]P for trend across dietary pattern quintiles. [C]Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, salivary cotinine levels, educational status, caffeine intake, trimester 1 alcohol intake, gestation & infant's sex in multivariable linear regression models. [d]Adjusted for maternal age, salivary cotinine levels, educational status, caffeine intake and trimester 1 alcohol intake in multivariable linear regression models. CI, confidence interval; Q, quintile.

6.4.5 Relationship between maternal dietary patterns, small for gestational age and large for gestational age

Table 22 presents crude and adjusted odd ratios (OR) of having a SGA or LGA baby across the four dietary patterns. In unadjusted analyses, the 'fruit & wholegrains' component was found to have a protective effect against SGA. For every 1 unit increase in that component, mothers were 19% less likely to have an infant born SGA (95% CI: 0.71, 0.92, *P*=0.002). Adjusting for maternal age, salivary cotinine levels, educational status, caffeine intake and trimester 1 alcohol intake attenuated this association (OR: 0.88; 95% CI: 0.75, 1.02, *P*=0.09). Similarly, compared to mothers in the lowest 'fruit & wholegrains' quintile score, mothers in the highest quintile score had 60% lower odds (95% CI: 0.21, 0.76, P=0.005, P_{trend}=0.02) of having an infant born SGA. However, the adjusted association was not significant (OR: 0.53, 95% CI: 0.25, 1.11, P_{trend}=0.1). For both models, the H-L goodness-of-fit test statistic indicated an acceptable model fit (*P*=0.61 & *P*=0.52 respectively) No other dietary pattern had a significant relationship with SGA in either crude or adjusted analyses (Table 22).

In terms of LGA, after adjusting for maternal age, salivary cotinine levels, educational status, caffeine intake and trimester 1 alcohol intake, compared to mothers in the lowest quintile score, mothers in the second and fourth quintile categories of the 'fruit & wholegrains' dietary pattern appeared to have lower odds, 53% (95% CI: 0.23, 0.93, *P*=0.03) and 60% (95% CI: 0.19, 0.83, *P*=0.01) respectively, of having infants born LGA, however the P for trend was not significant (P_{trend}=0.09). And again the H-L goodness-of-fit test statistic indicated an acceptable model fit (*P*=0.69). No other dietary pattern was shown to have a significant association with LGA (Table 22).

Table 22. The relationship between maternal dietary patterns in pregnancy and small for gestational age and large for gestational age in the CARE study (N=1,109)

	SGA (<10th centile)[a]				LGA (>90th centile)[a]			
	Crude OR (95% CI)	*P*[b]	Adjusted OR[c] (95% CI)	*P*[b]	Crude OR (95% CI)	*P*[b]	Adjusted OR[c] (95% CI)	*P*[b]
Fruit & wholegrains								
Continuous score	0.81 (0.71, 0.92)	0.002	0.88 (0.75, 1.02)	0.09	0.99 (0.87, 1.13)	0.88	0.91 (0.78, 1.07)	0.25
Q1	1	0.02	1	0.1	1	0.4	1	0.09
Q2	0.86 (0.51, 1.47)		1.09 (0.61, 1.94)		0.67 (0.35, 1.25)		0.47 (0.23, 0.93)	
Q3	0.93 (0.55, 1.57)		1.26 (0.70, 2.28)		0.91 (0.51, 1.65)		0.60 (0.31, 1.16)	
Q4	0.54 (0.29, 0.94)		0.71 (0.35, 1.42)		0.63 (0.33, 1.19)		0.40 (0.19, 0.83)	
Q5	0.40 (0.21, 0.76)		0.53 (0.25, 1.11)		1.01 (0.56, 1.79)		0.67 (0.34, 1.31)	
Traditional meat & vegetables								
Continuous score	1.03 (0.92, 1.17)	0.58	1.04 (0.92, 1.18)	0.5	1.02 (0.90, 1.16)	0.7	0.99 (0.86, 1.14)	0.89
Q1	1	0.17	1	0.16	1	0.8	1	0.19
Q2	1.00 (0.57, 1.75)		1.07 (0.58, 1.95)		0.70 (0.37, 1.31)		0.87 (0.45, 1.68)	
Q3	0.72 (0.40, 1.32)		0.75 (0.40, 1.42)		0.91 (0.50, 1.66)		1.02 (0.54, 1.93)	
Q4	0.65 (0.35, 1.20)		0.70 (0.36, 1.34)		0.82 (0.45, 1.52)		0.80 (0.54, 1.93)	
Q5	1.26 (0.73, 2.16)		1.42 (0.79, 2.53)		0.96 (0.53, 1.74)		0.88 (0.47, 1.68)	
Vegetables & oils								
Continuous score	1.00 (0.89, 1.13)	0.98	1.06 (0.93, 1.20)	0.37	1.01 (0.89, 1.15)	0.64	0.98 (0.85, 1.14)	0.8
Q1	1	0.49	1	0.9	1	0.64	1	0.67
Q2	0.79 (0.46, 1.37)		0.92 (0.51, 1.65)		1.36 (0.72, 2.54)		1.16 (0.60, 2.23)	
Q3	0.73 (0.42, 1.27)		0.93 (0.51, 1.68)		1.06 (0.55, 2.04)		0.76 (0.38, 1.55)	
Q4	0.60 (0.33, 1.07)		0.76 (0.40, 1.43)		1.48 (0.80, 2.75)		1.18 (0.62, 2.25)	
Q5	0.70 (0.40, 1.22)		0.96 (0.52, 1.76)		1.06 (0.55, 2.05)		0.87 (0.44, 1.72)	
Cheese, pasta & sauces								
Continuous score	1.00 (0.87, 1.15)	0.98	1.01 (0.87, 1.18)	0.8	1.05 (0.90, 1.22)	0.55	1.01 (0.86, 1.20)	0.87
Q1	1	0.34	1	0.2	1	0.82	1	0.67
Q2	0.60 (0.33, 1.10)		0.59 (0.30, 1.13)		1.34 (0.72, 2.48)		1.42 (0.75, 2.71)	
Q3	0.78 (0.44, 1.37)		0.78 (0.42, 1.45)		0.95 (0.49, 1.82)		0.86 (0.43, 1.75)	
Q4	1.08 (0.63, 1.84)		1.20 (0.68, 2.13)		1.17 (0.62, 2.19)		1.11 (0.57, 2.13)	
Q5	0.82 (0.46, 1.44)		0.80 (0.44, 1.48)		1.17 (0.62, 2.20)		1.09 (0.55, 2.14)	

[a] Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation and infant's sex. [b] P for trend across dietary pattern quintiles. [c] Further adjusted for maternal age, salivary cotinine levels, educational status, caffeine intake and trimester 1 alcohol intake in multivariable logistic regression models. CI, confidence interval; OR, odds ratio; Q, quintile.

6.4.6 Sensitivity analyses & effect modification

Including supplement use in the 1st trimester in the model did not alter the results (data not shown). Excluding mothers with gestational hypertension (n=54, 5%) did not alter results notably (data not shown). There was a significant interaction observed between the ‘fruit & wholegrains’ as well as the ‘cheese, pasta & sauces’ dietary patterns and maternal pre-pregnancy BMI on offspring risk of being SGA (*interaction P*=0.03), however for the latter dietary pattern the association was not significant (see Table 23). For every 1 unit increase in the ‘fruit & wholegrains’ dietary pattern score, mothers with a pre-pregnancy BMI <25 (kg/m^2) had 20% lower odds of having an infant born SGA (95% CI: 0.66, 0.96, *P*=0.01). Excluding mothers with a BMI <18.5 (n=32) did not alter this association (OR: 0.80, 95% CI: 0.67, 0.97; P=0.02) (data not shown).

Table 23 Multivariate[a] regression estimates from stratified analyses for associations between maternal dietary patterns in pregnancy with offspring size at birth with testing for effect modification by maternal pre-pregnancy BMI (kg/m^2)

	Birth weight (g) (n=940)		**Birth centile[b]** (n=942)		**SGA (<10th centile)[b]** (cases/N= 120/942)		**LGA (>90th centile)[b]** (cases/N= 99/942)	
	β (95 % CI)	*P*[c]	*β* (95 % CI)	*P*[c]	OR (95 % CI)	*P*[c]	OR (95 % CI)	*P*[c]
Fruit & wholegrains		0.09		0.2		0.03		0.6
(Per 1 unit increase)								
BMI <25 (kg/m^2)	23.48 (0.37, 46.6)		1.01 (-0.60, 2.62)		0.80 (0.66, 0.96)	(0.01)	0.91 (0.75, 1.11)	
BMI ≥25 (kg/m^2)	-9.42 (-42.80, 23.45)		-0.60 (-2.93, 1.73)		1.09 (0.85, 1.39)		0.85 (0.64, 1.11)	
Traditional meat & vegetables		0.7		0.9		0.25		0.9
(Per 1 unit increase)								
BMI <25 (kg/m^2)	-14.35 (-35.95, 7.26)		-0.90 (-2.42, 0.62)		1.12 (0.96, 1.30)		1.00 (0.84, 1.19)	
BMI ≥25 (kg/m^2)	-7.85 (-37.83, 22.12)		-0.71 (-2.82, 1.39)		0.95 (0.75, 1.19)		0.98 (0.77, 1.25)	
Vegetables & oils		0.5		0.9		0.19		0.1
(Per 1 unit increase)								
BMI <25 (kg/m^2)	-3.96 (-24.97, 17.04)		-0.53 (-2.00, 0.94)		1.11 (0.97, 1.27)		1.05 (0.90, 1.22)	
BMI ≥25 (kg/m^2)	-16.44 (-50.59, 16.70)		-0.62 (-2.97, 1.74)		0.90 (0.68, 1.19)		0.78 (0.56, 1.08)	
Cheese, pasta & sauces		0.4		0.3		0.03		0.65
(Per 1 unit increase)								
BMI <25 (kg/m^2)	3.16 (-21.63, 27.45)		-0.12 (-1.85, 1.62)		1.15 (0.95, 1.38)		1.03 (0.84, 1.26)	
BMI ≥25 (kg/m^2)	23.16 (-13.69, 60.00)		1.44 (-1.14, 4.03)		0.80 (0.62, 1.04)		0.95 (0.70, 1.28)	

β refers to the change in the outcome for every 1 unit increase in the predictor. [a]Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, salivary cotinine levels, educational status, caffeine intake, trimester 1 alcohol intake, gestation and infant's sex in multivariable linear regression models. [C]Interaction P value, testing the null hypotheses that associations do not differ by maternal pre-pregnancy BMI [b]Takes into account maternal pre-pregnancy weight, height, parity, ethnicity, gestation and infant's sex and further adjusted for maternal age, salivary cotinine levels, educational status, caffeine intake & trimester 1 alcohol intake. BMI, body mass index; CI, confidence interval; OR, odds ratio.

6.5 Discussion

The aim of this chapter was to assess whether there was evidence of any link between maternal dietary patterns in pregnancy and size at birth in a low risk pregnant British population. In this analysis of 1,109 mothers of singletons delivered at term (37-42 weeks gestation) there was no significant association between maternal dietary patterns during the second trimester of pregnancy and size at birth, when taking into account known confounders. However, a significant interaction between maternal pre-pregnancy BMI status and a ‘fruit and wholegrains’ dietary pattern on offspring risk of being SGA was observed whereby mothers with higher ‘fruit & wholegrains’ dietary pattern scores who entered pregnancy with a ‘healthy’ BMI (<25 kg/m^2) had 20 % lower odds of having a SGA baby.

This is the first time this association has been explored in a UK population whilst taking into account important confounders such as maternal smoking, age and pre-pregnancy BMI.

6.5.1 Dietary patterns in pregnancy & maternal characteristics

There was no clear ‘unhealthy’ dietary pattern, high in foods such as processed meats, refined grains and sugar-sweetened beverages (SSB) as evidenced in other studies, although the ‘cheese, pasta & sauce’ dietary pattern exhibited the least healthy traits with the highest intake of fats and energy and the lowest intakes of fruit, vegetables and legumes as well as folate and iron for mothers within the higher quintile scores compared to the other three dietary patterns. Similarly to some of the studies reviewed in Chapter 2 (Coelho Nde et al., 2015; Northstone et al., 2008; Thompson et al., 2010; Wolff and Wolff, 1995) a ‘traditional’ dietary pattern to the study setting, the ‘traditional meat & vegetables’, was also observed. The ‘fruit and wholegrains’ dietary pattern appeared to be similar to dietary patterns or scores considered healthy observed in other studies (Coelho Nde et al., 2015; Colon-Ramos et al., 2015; Hillesund et al., 2014; Knudsen et al., 2008; Northstone et al., 2008; Poon et al., 2013; Rifas-Shiman et al., 2009; Rodriguez-Bernal et al., 2010; Shapiro et al., 2016; Wolff and Wolff, 1995; Saunders et al., 2014) and was considered to be the dietary pattern that adhered best to dietary guidelines for pregnant women and for the population in general with the highest intakes of fruit, fish, beverages (mainly due to high intakes of water (900 g/d)), dairy (driven by high intakes of yoghurt and low-fat milk (160g/d)), iron (14 mg/d), folate (330 µg/d) and NSP (20 g/d) as well as % dietary energy from carbohydrates (56%) and the lowest intakes of % dietary energy from fat (32%) and meat (36 g/d) for mothers within the highest quintile scores compared to the highest quintile scores of the other three dietary patterns. Despite this, mothers still did not meet the recommended intake of two portions of fish per week (~280 g/wk), however as outlined in Chapter 5, similar low intakes of fish have been observed in other pregnant populations. The combined median intake of fruit and vegetables in the highest quintile score of the 'fruit and wholegrains' pattern was 422 g (IQR: 273, 554) so above the UK recommendations of 5 portions per day (~400 g/d). As for caffeine and alcohol, intakes of the former were well below the recommended cut-off of no more than 200 mg/d whereas intakes of the latter were quite high with 63% of mothers in the highest quintile score consuming more than 2 units per week in the first trimester. As stated in Chapter 4, similar observations have been made in other studies, where mothers who follow a healthier dietary pattern tend to drink more. However, as outlined in the alcohol analysis chapter, the proportion of risky drinkers (>10 units/week) within this cohort was low. Characteristics of mothers who adhered to a healthier pattern such as the 'fruit and wholegrains' were in agreement with those observed for prudent or health conscious dietary patterns of pregnant women observed in the studies reviewed in Chapter 2, where mothers were less likely to smoke, have a low SES and more likely to be older, have a lower pre-pregnancy BMI, have a university degree, be nulliparous and take dietary supplements.

6.5.2 Interpretation of main findings

Overall there only appeared to be evidence of an association between the 'fruit & wholegrains' dietary pattern and offspring size at birth expressed as birth weight, birth weight centile and SGA (<10th centile), however once adjustment were made for important confounders, this was only evident for mothers who entered pregnancy with a healthy BMI (<25 kg/m^2) who had 20% lower odds of having a baby born SGA. Whereas no protective association appeared for mothers with higher 'fruit & wholegrains' scores who entered pregnancy overweight or obese (BMI≥25 kg/m^2), suggesting that any positive effects of a healthy dietary pattern was forfeited when mothers entered pregnancy overweight or obese. Saunders at al. (2014) found a similar significant interaction between maternal pre-pregnancy BMI and the MD score (characterised by high consumption of fruit, vegetables, legumes and grains, moderate consumption of fish, dairy products and alcohol, and low meat intake) on offspring risk of FGR in their cohort of 728 French-Caribbean mothers however the 20% reduction in risk for offspring born to mothers with a BMI <25 kg/m^2 was non-significant (95%: CI 0.7, 1.1). Other studies have found similar positive associations between a healthy maternal dietary pattern and offspring size at birth, regardless of maternal pre-pregnancy BMI status. These studies often consisted of larger samples (Knudsen et al., 2008; Northstone et al., 2008) or used the dietary exposure as a continuous measure rather than categorising it and thus had better power to detect changes in offspring size at birth. Due to the rather small sample size of this cohort and consequently lower numbers in the dietary pattern quintiles, this study had limited power to detect smaller changes in birth weight. And although a positive trend for ‘fruit & wholegrains’ was observed, there is still the possibility of type I error due to multiple testing.

6.5.3 Strengths & limitations

Consideration has been given to the strengths and limitations concerning the study sample, dietary assessment, dietary pattern analysis, outcome measures and residual confounding within this study in the sections below.

6.5.3.1 Study sample

The sample used for this analysis consisted of a relatively large cohort (N=1,109) of low risk pregnant women representing 85% of the original cohort. The comparison analysis between the study sample and excluded mothers revealed that included mothers were significantly less likely to be smokers in the 1st trimester, be nulliparous and live in an area within the most deprived IMD quartile compared to excluded mothers. Indicating that the sample may not be representative of a British pregnant population and therefore the external validity and generalisability of the findings of the study sample to the general population should be questioned; however, that is not to say that the internal validity of the findings was affected. Furthermore, the prevalence of LBW babies (<2,500 g) in this sample (1.5 %) was much lower than the National UK (7.2%) and the Yorkshire & Humber region average (7.8%) for 2007 (Office for National Statistics, 2007), the time of the study period, most likely a result of including term births only. But even for the original cohort, the percentage of LBW was lower (4.4%) in comparison to the national average raising the possibility that women who are more likely to have LBW babies were less likely to participate in this study.

6.5.3.2 Dietary assessment

As highlighted in Chapter 2, dietary assessment is prone to measurement error. Diet in this cohort was assessed using a 24 hour recall recorded by a midwife where mothers were asked to report all the food and drink they had consumed in a 24 hour period (12 midnight to 12 midnight) including portion sizes and drink amounts. Despite being interviewer administered, this type of measure is still prone to recall bias as you are reliant on the participant's memory as well as honesty (Margetts and Nelson, 1997). Although a less common approach when it comes to dietary pattern analysis, possibly due to the time consuming task of having to code as well as allocate thousands of foods to overall food groups before applying any dietary pattern analysis techniques, 24 hour recalls are a useful tool for capturing total diet and more likely to yield real life result, as opposed to a FFQ which is only as good as its foods listed and may therefore not capture total diet. Diet was only assessed at one time point and does therefore not reflect dietary intake throughout pregnancy however previous studies which have assessed dietary change in pregnancy have found little variation in pregnant women's eating habits across trimesters (Rifas-Shiman et al., 2006; Crozier et al., 2009).

Despite the rather large sample, this method is prone to within-person day to day variation and hence extreme values are more common which may give certain foods undue influence. Attempts to remove the extraneous effect of food data with large variances were done by excluding mothers with extreme energy intakes at either end of the spectrum (1% highest and lowest) and in addition, the PCA was based on the standardised factor loadings from the correlation matrix.

6.5.3.3 Dietary pattern analysis

PCA was performed on 73 energy adjusted food groups and choice of factors to retain was based on both the scree plot, percentage of variance explained by components as well as their interpretability. A strength of this study is the use of energy adjusted dietary data. As highlighted in Chapter 2, it is important to demonstrate that any association between maternal dietary patterns and offspring size at birth is independent of caloric intake. The reasoning behind the food grouping has been outlined in Chapter 3. As has been highlighted in Chapter 2 in the review of the evidence, the number and nature of food data entered into a PCA will influence the resulting patterns. The number of food groups used in the PCA was somewhat high compared to that of other studies reviewed which used *a posteriori* techniques to derive dietary patterns. However, the food groups considered for this analysis covered a large range of foods in order to prevent loss of important information. It could be argued that diet variety was lost by aggregating 1,770 food items into 73 food groups despite doing so on the basis of similarity of nutrient composition and comparable usage. Nevertheless, the PCA did show four distinct components. The goal of PCA is essentially to explain as high a proportion of the variance in dietary intake through a smaller set of components, however the four components derived for this cohort only explained 11.4% of the variance in the dietary data which is quite low compared to other studies that have used a similar approach to derive dietary patterns. However given that mothers are unlikely to limit food choices to one pattern exclusively, it was thought more prudent to rely on interpretability of the factors, rather than variance explained.

As shown in the review of the evidence, PCA appears to be the most common technique used to assess dietary patterns in populations but as highlighted in section 2.5.3 it is not without limitations. Despite these limitations and the fact that dietary patterns from PCA are subject to consumption patterns in the population under study and may therefore not be transferable across populations they represent real dietary habits and patterns of food choice and are therefore of direct relevance to the formulation of future public health messages.

6.5.3.4 Outcome measures

A strength of this analysis was the use of a customised birth weight centile, which takes into account gestational age, maternal height, weight, ethnicity and parity, and neonatal birth weight and sex.

6.5.3.5 Residual confounding

Because this is not a RCT, there is a possibility that residual confounding may be contributing to the apparent association between mothers who scored highly on the ‘fruit & wholegrains’ dietary pattern and offspring lowered risk of being SGA. Although we adjusted for many relevant confounders, including the use of an objective biomarker for smoking status which is less liable to bias from self-report; no data were available on GWG and therefore we could not assess its potential role as a mediator of the association. Shapiro et al. (2016) however assessed its potential mediating role in sensitivity analyses in their cohort of 1,079 pregnant mothers and found no strong evidence of mediation on the association between the HEI-2010 and neonatal adiposity. Of the other studies reviewed, GWG was either omitted from analyses or included as a confounder together with multiple other maternal lifestyle factors and therefore its independent role was not assessed.

6.5.4 Implications for research and practice

Further research is needed to explore the role of maternal dietary patterns during pregnancy and offspring size at birth. Despite its relatively large sample size, this analysis was not powered to detect small changes in birth weight which may be of importance in terms of future health and therefore similar investigations should be performed in a larger setting. The suggestive trend of a positive association with a more health conscious dietary pattern during pregnancy and offspring size at birth for mothers entering pregnancy with a healthy BMI (<25 kg/m^2) is supportive of current dietary guidelines for pregnant women, which aim to ensure optimal health for both the mother and the baby. It appears that for mothers entering pregnancy overweight or obese, any positive effects of a more healthy diet is lost further highlighting the importance of pre-pregnancy weight management to ensure a healthy baby/pregnancy.

6.6 Conclusion

In this analysis of a UK sample of 1,109 pregnant mothers, four distinct dietary patterns were defined using PCA on 24 hr recall food data collected in the second trimester of pregnancy. Of these dietary patterns only the first component, the ‘fruit & wholegrains’ appeared to have a positive association with offspring size at birth (SGA) and only so for mothers entering pregnancy with a healthy BMI. This component, characterised by high positive correlations with fruits, Nordic fruits in particular, and unrefined grains as well as wholegrain and bran breakfast cereal and negative correlations with refined grains, appeared to conform best with current dietary guidelines for pregnant women in the UK. It is important to reiterate however that despite the suggestive protective effects of a healthier dietary pattern, this study is observational so causality cannot be inferred from the findings. In addition, this analysis was based on one 24 hour recall data and it could be argued that despite the rather large sample size, it is not a useful measure of habitual diet in a smaller population and therefore a less suitable approach for assessing patterns in intake than say data from FFQs. In addition this study was not sufficiently powered to detect smaller changes in offspring size at birth and further exploration of this association in a larger sample is warranted.

In the next chapter, the investigation commenced in this chapter will be explored in a larger dataset of British pregnant women and will be further extended to assess the potential impact of maternal dietary patterns during pregnancy on not only offspring size at birth but later child growth outcomes.

7 Maternal dietary patterns in pregnancy and offspring growth outcomes: the ASLPAC study

Chapters 4 and 5 explored the relationship between the single foods alcohol and fatty fish and offspring size at birth using data from a British prospective cohort of low risk pregnant women. Chapter 6 extended this approach by looking at diet from a more holistic perspective in relation to size at birth within the same cohort. Following on from that, this chapter evaluates the relationship with more long-term growth outcomes through analysis of data from the ALSPAC cohort. This includes offspring weight and height measured at age 7.5 years.

7.1 Chapter overview

The aim of this analysis was to investigate the associations between maternal dietary patterns during pregnancy and offspring size at birth and 7.5 years using data from a British prospective birth cohort, the ALSPAC study in Bristol, of 6,756 mother-offspring pairs. Dietary intake was reported in a self-administered FFQ at 32 weeks gestation. Principal component analysis was done on 44 energy adjusted food group. Information on delivery details was obtained from hospital maternity records. Child height and weight was measured by trained staff at 7.5 years follow-up. Offspring growth was expressed as age specific weight (WFA) and height (HFA) Z-scores using the World Health Organisation growth reference. Z-score cut-off points of <2 SD were used to classify low weight-for-age (LWFA) and low height-for-age (LHFA) at 7.5 years. These were related to dietary patterns expressed as quintile scores in multivariable regression models, taking into account known confounders and assessing possible mediation by birth weight and gestational weight gain as well as effect modification by breastfeeding and pre-pregnancy BMI status.

Two dietary patterns were derived and identified as: ‘modern health conscious’ and ‘traditional health conscious’. The first component was characterised by high correlations with nuts, soya & pulses, fresh fruit, rice, pasta, dark bread and juice and negative correlations with chips and roast potatoes, processed meat and white bread. The second component was characterised by high correlations with cabbage, root vegetables, other green vegetables, beans and peas, poultry and red meat.

In adjusted analyses, compared to those in the lowest quintile score, mothers in the highest ‘modern health conscious’ dietary pattern quintile had babies born with higher birth weight (45 g, 95% CI: 9, 81; P_{trend}=0.03) and birth length (0.20 cm, 95% CI: 0.01, 0.39; $_{Ptrend=}$0.002). Compared to mothers in the lowest quintile score, mothers in the highest quintile score of the ‘traditional meat & vegetables’ dietary pattern had infants born with slightly higher WFL Z-scores only (adjusted change: 0.15, 95% CI: 0.06, 0.25 P_{trend}=0.02). Further adjustments for GWG did not alter these associations. Neither dietary pattern was associated with offspring HBW nor LBW. There was a borderline significant association between the ‘modern health conscious’ dietary pattern and offspring HFA Z-scores at 7.5 years. In adjusted analyses, compared to those in the lowest quintile score, those in the highest ‘modern health conscious’ dietary pattern quintile had children with slightly higher HFA Z-scores (0.08, 95% CI: -0.01, 0.17; P_{trend}=0.07); which was further strengthened in analyses with missing data imputed (0.10, 95% CI: 0.03, 0.17; P_{trend}=0.003). The ‘traditional meat & vegetables’ dietary pattern appeared to have a protective effect on offspring risk of being LHFA at 7.5 years. However this relationship was lost in the sample with missing data imputed. No significant evidence of mediation by GWG or birth weight was observed.

7.2 Introduction

In chapter 6 the association between maternal dietary patterns during pregnancy and offspring size at birth was explored. Maternal diet may have a direct effect on fetal growth, but could also cause epigenetic changes in the fetus affecting fetal metabolism which could have consequences for later growth or body composition (Wu et al., 2004).

The literature review identified 4 prospective birth cohort studies which had investigated maternal dietary patterns during pregnancy in relation to infant or child growth outcomes, including lean mass, fat mass, BMI, waist circumference and WFL. Of the two studies which used PCA to derive dietary patterns, one found a positive association with child lean mass at 9 years and a ‘prudent’ dietary pattern (Cole et al., 2009), however only adjustments for maternal age and child gender were made so findings should be interpreted with caution. Two studies assessed MD adherence and only one observed a positive modest significant association with offspring waist circumference at 4 years, but not with child BMI or abdominal obesity (Fernandez-Barres et al., 2016). Several methodological issues were identified in the four studies reviewed in regards to exposure measures, dietary pattern analysis as well as statistical analysis, in particular the sometimes poor and inconsistent consideration of confounders (see Chapter 2 section 2.4.3 for a review of studies). Furthermore, sample sizes were much smaller (ranging from 198 to 2,689 participants) than that observed for the studies reporting on size at birth and it is possible that the studies lacked power to detect any significant associations.

7.2.1 Aim & objectives

The main aim of this chapter was to explore the relationship between maternal dietary patterns in pregnancy and offspring size at birth and later child height and weight growth outcomes using data from a large sample of pregnant women in the UK. The following objectives were addressed:

1. Characterise dietary patterns in a British cohort of pregnant women
2. Investigate associations between maternal dietary patterns in pregnancy and size at birth
3. Explore the role of maternal pre-pregnancy BMI status as an effect modifier on the association investigated in objective 2
4. Explore the role of GWG as a mediator of the association investigated in objective 2
5. Investigate associations between maternal dietary patterns in pregnancy and child height and weight
6. Explore the role of breastfeeding status as an effect modifier on the association investigated in objective 5
7. Explore the role(s) of GWG and birth weight as mediators of the association investigated in objective 5

7.3 Methods

ALSPAC is a large prospective birth cohort study set up with the aim to identify features of the environment, genotypes and the interaction between the two which influence the health, development and well-being of children throughout the life course. Details of the ALSPAC study, including design, setting, dietary assessment, outcome measures and assessment of participant characteristics can be found in Chapter 3. Below are details of the study sample available for analysis, power calculation and statistical methods including details of the dietary pattern analysis.

7.3.1 Mother-offspring pairs available for analysis

Only singleton live births (n=13,677) with maternal dietary data (n=11,874) were included. Participants with more than 10 items missing from the FFQ were excluded (n=26) and for those with 10 or fewer items missing (n=1,833) the assumption was made that they never consumed the item and it was given a value of 0. This was necessary in order for the data to be included in the PCA, a method that cannot deal with missing values. Only mothers whose children attended the 7.5 year follow-up were included (n=7,153). In addition, mothers whose babies had a gestational age at delivery of <259 days (37 weeks) (n=318) and >294 days (42 weeks) (n=32), (i.e. three weeks before and two weeks after expected date of delivery), were excluded in order to avoid strata with too few observations and to exclude infants with pathologies that may be irrelevant to the purpose of this analysis. Finally offspring with missing data on height and weight measurements at follow-up were excluded, leaving a final study sample of 6,756 mother-child pairs for analysis. Figure 14 shows a flowchart of the ALSPAC participants included in this analysis.

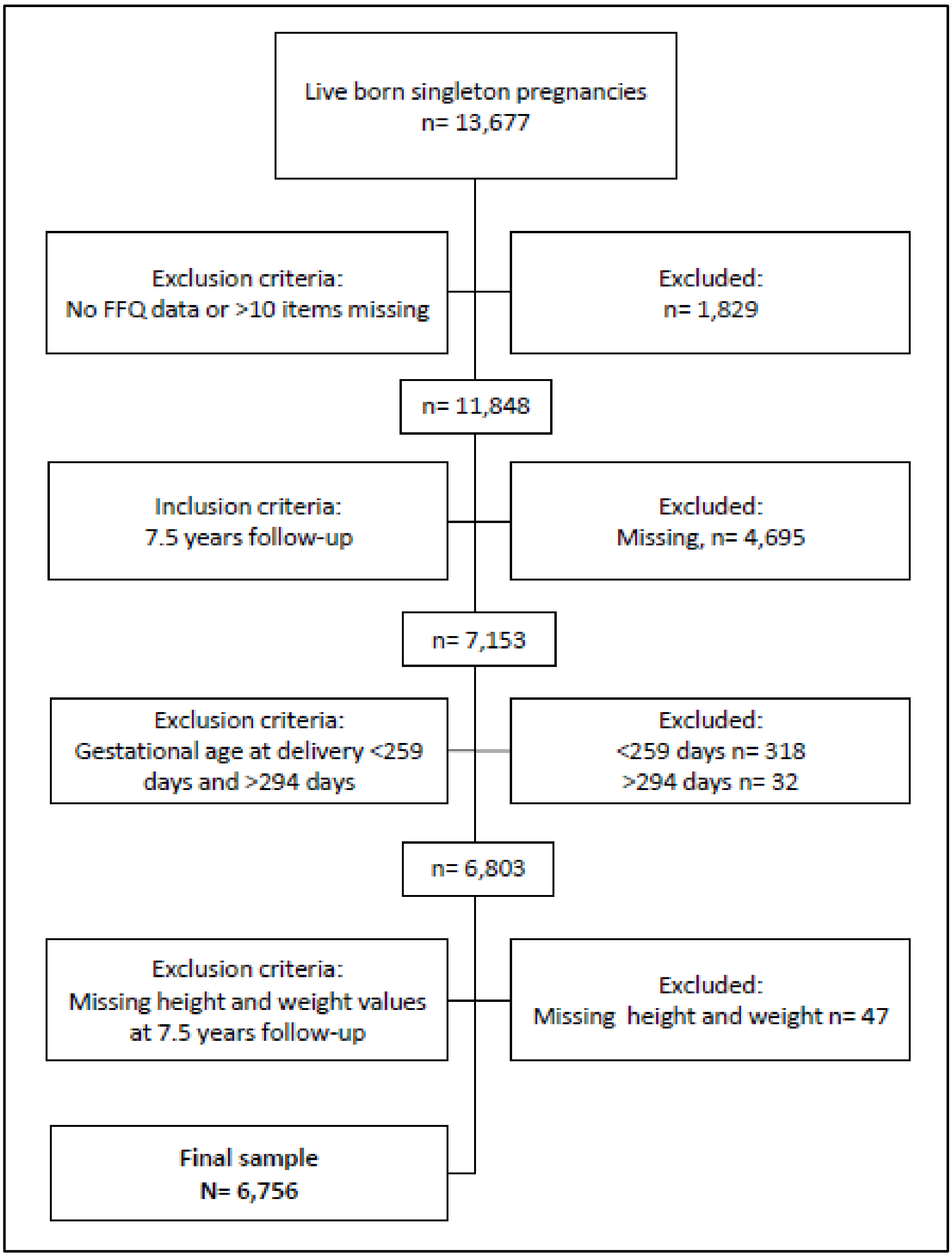


Figure 14. ALSPAC study participant flowchart

7.3.2 Statistical power calculation

Comparing the birth weight (g) of babies born to mothers in the lowest quintile category of the first component (the one explaining the highest proportion of variance in the dietary data) resulting from the PCA with those in the highest quintile category, and using the SD of 466 g of birth weight for the total sample, this study had 85% power to detect a difference of 55 g (around two ounces; representing quite a modest size difference) in birth weight for a two sample t-test at $P<0.05$.

7.3.3 Statistical analysis

7.3.3.1 PCA

Principal component analysis was performed on residually energy adjusted dietary data (please refer to Chapter 3 section 3.10.1.1 for details of the ALSPAC food groups). As with the CARE dietary pattern analysis the PCA was based on the correlation matrix (Manly, 2004) and the choice of components to retain was based on the scree plot (Cattell, 1966), percentage of variance explained by components and their interpretability. As can be seen from Figure 2 below the first bend in the curve (the ‘elbow’ as indicated by the arrow) happens around the second component and because of this as well the relatively high eigenvalues the choice was made to retain two components for further analysis.

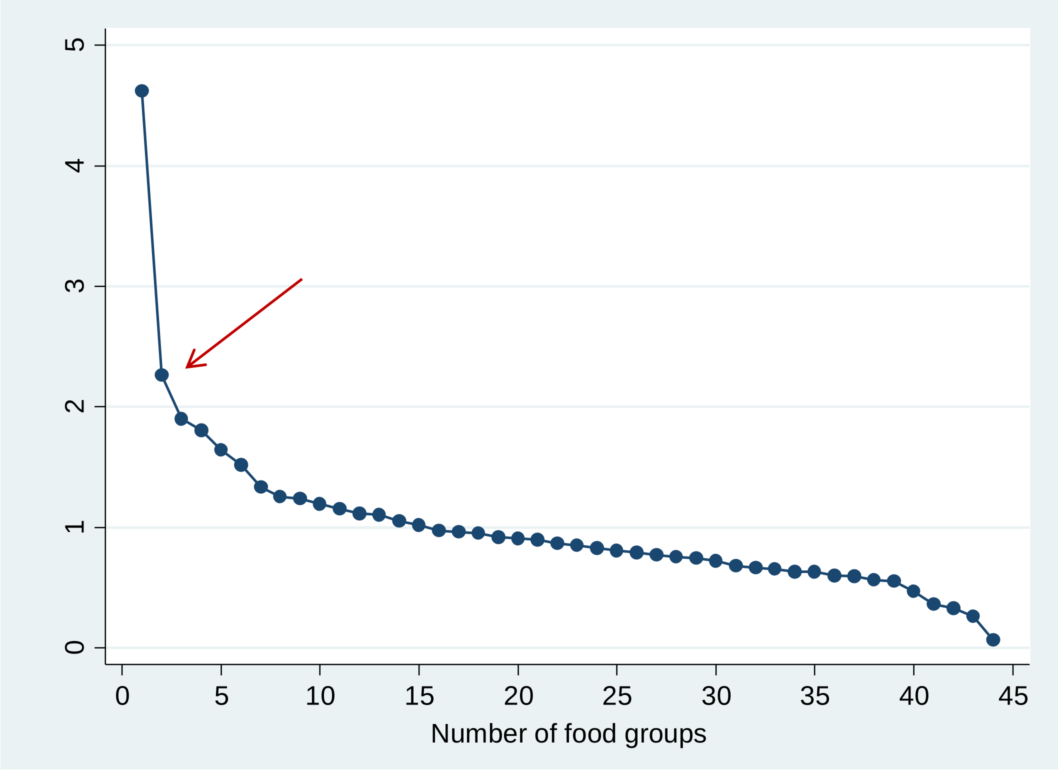


Figure 15. Scree plot of eigenvalues from PCA on 44 energy adjusted food groups

The components were rotated using varimax rotation in order to obtain a simpler structure done by maximising the factor loadings for each component (Kline, 1994). Scores for each participant for each component were then predicted and further categorised into quintiles for inclusion in regression models to allow for any non-linearity.

7.3.3.2 Univariable analysis

Characteristics of mothers across quintile categories of the two dietary pattern scores were assessed in univariable analyses using the one-way analysis of variance (ANOVA) for normally distributed continuous variables and the Kruskal-Wallis test for non-normally distributed continuous and ordinal variables and the χ2 for nominal categorical variables. Mothers in the study sample were compared to excluded mothers using the two sample t-test for normally distributed variables and the Mann-Whitney U-test for non-normally distributed continuous and ordinal variables and the χ2 test for nominal categorical variables.

7.3.3.3 Regression analyses

Regression analyses were undertaken using both the continuous dietary pattern score as the predictor as well as the categories defined by the quintiles of dietary pattern score with the lowest quintile score as the referent. Associations with birth weight (g), birth length, offspring WFL Z-scores at birth and HFA & WFA Z-scores at age 7.5 years were assessed in linear univariable and multivariable regression models. Associations with dichotomous growth outcomes (LBW, HBW, LWFA and LHFA at 7.5 years) were assessed using logistic univariable and multivariable regression models. All offspring size at birth models were adjusted for maternal pre-pregnancy BMI (18.5, 18.6–24.9, 25–29.9, 30–35, >35 in kg/m2; 8.0% missing), age (<20, 20-39, ≥40; 0 % missing), parity (nulli/multiparous; 2 % missing), ethnicity (Caucasian/Other; 0.6 % missing), smoking in pregnancy (smoker/non-smoker; 0.7 % missing), educational qualification (university degree/no degree; 0.3 % missing), gestational age (weeks; 0 % missing) and infant’s sex (0 % missing; with the exception of WFL Z-scores which takes into account infant’s sex). Models for the sex-and-age specific HFA and WFA offspring growth outcomes at 7.5 years were similarly adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification and child height (cm) in the WFA models and paternal height (cm; 28 % missing) in the HFA models. Test for linearity were done by fitting a linear trend over the categories of dietary pattern exposure scores in unadjusted and fully adjusted models.

7.3.3.4 Mediation and effect modification

Covariates thought to be on the causal pathway (birth weight (g; 1 % missing) and gestational weight gain (g; 8 % missing) were initially excluded from the models and were entered in additional models to assess mediation. Breastfeeding status has been recognised as a possible ‘programmer’ of childhood growth (Singhal and Lanigan, 2007a) and it was therefore assessed as an effect modifier by including an interaction term in the confounder adjusted models. In addition maternal BMI was assessed as an effect modifier of the effect of maternal diet on offspring size at birth and similarly to the CARE analysis, stratified analyses were presented for women who reported a healthy pre-pregnancy BMI at enrolment (<25 kg/m2) and those who were classed as overweight or obese (≥25 kg/m2).

7.3.3.5 Sensitivity analyses

In order to explore whether missing data could have led to biased estimates, multiple imputation (MI) was performed to impute missing values for variables (e.g. paternal height had 1,872 missing values) included in the child growth models for the final sample of mother-child pairs (for details on MI see Chapter 3 section 3.10.5.1). In addition, robustness of results were assessed by excluding mothers with gestational diabetes (n=28) as this condition may cause changes in the placenta with the potential for altering nutrient availability for the fetus and thus affecting fetal growth (Desoye and Hauguel-de Mouzon, 2007; Jansson et al., 2006).

7.4 Results

A total of 6,756 mother-child pairs were included in the final analysis representing 47% of the ALSPAC cohort of mothers with singletons alive at 1 year[3]. When comparing characteristics of the included mothers to that of the excluded, mothers in this study sample were more likely to be older, have a higher energy intake, have a university degree (16% vs. 9%), be Caucasian, be vegetarian (6% vs 5%) and breastfeed for more than 6 months (36% vs. 23%). They were less likely to smoke (18% vs. 32%) and as expected due to the exclusion criteria on gestational age they had babies born with a higher birth weight. There were no significant differences in pre-pregnancy BMI (kg/m^2), parity, gestational weight gain and several other covariates (Table 24). The mean maternal age of the study sample was 29 years (SD 4.5) with a mean pre-pregnancy BMI (kg/m^2) of 22.9 (SD 3.7).

Table 24. Characteristics of ALSPAC study mothers included in dietary pattern analysis vs. excluded mothers[a]

	Included (n=6,756)	**Excluded (n=7,748)**	***P[b]***
Age (years), n (%)			<0.0001
≤20	198 (2.9)	802 (11.4)	
>21-39	6,456 (95.6)	6,171 (87.1)	
≥40	102 (1.5)	69 (1.0)	
Pre-pregnancy BMI (kg/m^2), n (%)			0.9
≤ 18.5	267 (4.3)	309 (6.0)	
18.6-24.9	4,699 (75.6)	3,727 (72.7)	
25-29.9	935 (15.0)	783 (15.1)	
30.0-34.9	236 (3.8)	227 (4.4)	
≥35	78 (1.3)	96 (1.9)	
Energy intake (kcal/d), mean (95% CI)	1744.7 (1833.7, 1755.7)	1707.8 (1694.02, 1721.56)	<0.0001
Smoking in pregnancy, n (%)	1,213 (18.1)	2,033 (32.4)	<0.0001
Dietary supplements before 32 weeks gestation, n (% yes)	3,086 (45.8)	219 (46.5)	0.5
University degree, n (%)	1,095 (16.3)	482 (8.7)	<0.0001

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[3] For reporting purposes for child based data, the ALSPAC study group usually work with ‘alive at 1 year’ as the baseline group.

Caucasian, n (%)	6,594 (98.2)	5,259 (96.4)	<0.0001
Nulliparous, n (%)	3,002 (45.4)	2,713 (44.1)	0.3
Past history of miscarriage, n (%)	1,375 (20.8)	1,376 (22.2)	0.05
Vegetarian, n (%)	390 (5.9)	257 (4.8)	0.007
Gestational diabetes, n (%)	47 (0.7)	28 (0.5)	0.4
Gestational hypertension, n (%)	950 (14.3)	978 (14.7)	0.6
Gestational weight gain (g/week), mean (95% CI)	456.2 (452.3, 460.1)	453.0 (448.4, 457.6)	0.9
Birth weight (g), mean (95% CI)	3496.2 (3485.1, 3507.4)	3313.1 (3298.9, 3327.4)	<0.0001
Breast feeding duration, n (%)			<0.0001
Never	1,172 (18.6)	1,540 (32.7)	
<3 months	1,941 (30.8)	1,588 (33.7)	
3-6 months	892 (14.2)	521 (11.1)	
>6 months	2,294 (36.4)	1,065 (22.6)	

[a]Excluded mothers with singletons alive at 1 year. Where numbers do not add up this is due to a small proportion of missing data. [b]P value using two sample t-test for normally distributed and Mann-Whitney U-test for non-normally distributed continuous and ordinal variables and the χ2 test for nominal categorical variables. Significant difference at P<0.05. BMI, body mass index; CI, confidence interval; N, number

7.4.1 Maternal dietary patterns

Two dietary patterns were derived from the PCA explaining 16% of the variance in the dietary data. The components were given names representative of the food groups with the highest correlations (Table 25). The first component was labelled ‘modern health conscious’ because of its high correlations with nuts, soya & pulses, fresh fruit, rice, pasta, dark bread and juice and its negative correlations with chips and roast potatoes, processed meat and white bread. The second component was characterised by high correlations with cabbage, root vegetables, other green vegetables, beans and peas, poultry and red meat and was labelled ‘traditional meat & vegetables’.

Table 25. Factor correlations of the 44 food groups* in the two dietary components obtained using PCA on energy adjusted data (N=6,756)

Food item	**Modern health conscious**	**Traditional meat & vegetables**
% Variance explained	9.8%	5.9%
Vegetables		
Cabbage, Brussel sprouts, kale and other green leafy vegetables	-0.009	**0.412**
Salad	0.192	0.079
Root vegetables	0.044	**0.375**
Other green vegetables	0.047	**0.408**
Potatoes		
Boiled/mashed/baked	-0.011	**0.245**
Roast potatoes	**-0.254**	0.121
Chips	**-0.232**	-0.085

Nuts		
Nuts & tahini	**0.235**	-0.113
Pulses & legumes		
Soya	**0.205**	-0.136
Beans & peas (peas, sweetcorn, broad beans)	-0.040	**0.223**
Pulses	**0.278**	-0.079
Baked beans	-0.082	0.016
Fruit & berries		
Fresh fruit	**0.219**	0.098
Meat		
Poultry	-0.101	**0.314**
Red meats	-0.169	**0.290**
Mixed meat/processed meat products (sausages & burgers)	**-0.201**	0.008
Offal	-0.030	0.075
Ice cream/sweets/cakes		
Chocolate/cacao	-0.099	-0.159
Sweets	-0.090	-0.047
Sugar/cakes/biscuits	-0.147	-0.110
Puddings	0.009	0.025
Cereal products		
Rice	**0.200**	0.089
Pasta	**0.223**	0.047
Oat breakfast cereal	0.137	0.016
Wholegrain or bran breakfast cereal	0.146	0.059
Other breakfast cereal	-0.124	-0.039
Dark bread	**0.261**	-0.031
White bread	**-0.205**	-0.053
Crispbread	0.111	0.010
Fats		
Cooking fats and fat spreads	0.079	-0.102
Fish		
Lean/white	0.046	0.174
Oily/fatty	0.155	0.121
Shellfish	0.057	0.036
Beverages		
Tea	-0.071	0.014
Herbal tea	0.167	-0.037
Coffee	-0.087	0.019
Soft drink- sugar (Cola)	-0.121	-0.055
Juice	**0.201**	0.027
Dairy products		
Milk (all)	-0.053	0.041
Cheeses	0.181	-0.014
Snacks		
Snacks	-0.124	-0.104
Eggs		

Eggs	0.045	0.050
Pizza		
Pizza	0.046	-0.111
Pastries/Savouries		
Pastries/Savouries	-0.191	-0.018

*For a description of each food group please see Table 8
Factor correlations above 0.2 are shown in bold.

To ease interpretation, the 44 food groups were aggregated into 14 main food groups with the addition of the ALSPAC specific food groups ‘pizza’ and ‘pastries/savouries’.

Table 26 presents the average daily intake of the food groups, total energy intake, macronutrients as well as selected micronutrients across the two dietary pattern quintiles. For the ‘modern health conscious’ component higher scores implied higher intakes of vegetables, nuts, legumes, fruit, cereal products, fats and fish. Mothers in the highest quintile had a median fruit intake of 169 g compared to a median of 34 g in the lowest quintile category and similarly for vegetables and cereal products mothers in the highest quintile had a median intake of 148 g and 236 g respectively compared to a median of 81 g and 117 g in the lowest quintile; mothers in the highest quintiles had a lower intake of meat, potatoes, ice cream/sweets/cakes, dairy, snacks, pastries and beverages. In terms of nutrients, higher scores for this component implied higher intakes for all but fats and there was no clear trend for energy intake. As for the second component, ‘traditional meat & vegetables’ higher scores resulted in higher intakes of vegetables, potatoes, legumes, meat, cereal products, fish and dairy. Whereas mothers with lower scores had higher intakes of ice cream/sweets/cakes, fats and snacks. Similarly to the other component there was no clear trend for energy intake, however mothers in the highest quintile category had a higher % energy from protein as well as higher intakes of folate and iron and a lower % energy from fat and carbohydrate.

Table 26. Average daily intake of energy, selected nutrients and main food groups* (g/day) across dietary pattern categories based on a FFQ at 32 weeks of pregnancy in the ALSPAC study (N=6,756)

	Modern health conscious				
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Nutrients	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Energy intake (kcal/d)	**1832.5 (1805.0, 1860.0)**	**1669.4 (1645.0, 1693.9)**	1694.2 (1670.0, 1718.4)	1711.3 (1688.2, 1734.3)	1816.1 (1793.9, 1838.4)
Fats (% energy)	**38.5 (38.3, 38.8)**	37.6 (37.3, 37.8)	36.8 (36.6, 37.1)	36.0 (35.8, 36.3)	36.0 (35.7, 36.2)
Carbohydrates (% energy)	49.1 (48.8, 49.3)	48.9 (48.6, 49,2)	48.8 (48.6, 49.1)	49.1 (48.9, 49.4)	49.4 (49.2, 49.7)
Protein (% energy)	15.0 (14.8, 15.1)	16.1 (16.0, 16.2)	16.8 (16.7, 17.0)	17.3 (17.2, 17.5)	17.1 (17.0, 17.2)
Folate (µg/d)	219.8	224.7 (221.3,	246.6 (243.1,	260.4 (257.0,	295.3 (291.7,

	(216.3, 223.2)	228.2)	250.1)	263.8)	298.9)
Calcium (mg/d)	916.2 (900.6, 931.8)	**888.3 (873.7, 902.8)**	933.0 (918.7, 947.3)	962.7 (949.1, 976.4)	**1046.9 (1032.1, 1061.7)**
Iron (mg/d)	**9.1 (9.0, 9.3)**	9.3 (9.2, 9.5)	10.3 (10.1, 10.5)	11.1 (10.9, 11.2)	**12.8 (12.6, 12.9)**
Main food groups	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	80.8 (55.6, 105.0)	92.1 (63.5, 11.8.3)	105.0 (75.7, 137.1)	118.3 (85.1, 161.5)	148.3 (105.0, 148.3)
Potatoes	**115.4 (93.4, 154.4)**	115.4 (80.3, 126.7)	93.4 (58.3, 119.4)	80.3 (50.9, 119.4)	**58.2 (39.1, 115.0)**
Nuts	**0 (0, 0)**	0 (0.0)	0 (0, 3.7)	0 (0, 3.7)	**3.7 (0, 14.9)**
Legumes/ pulses	59.7 (30.8, 59.7)	59.7 (30.8, 59.7)	59.7 (30.8, 59.7)	59.7 (30.8, 67.8)	**65.1 (39.4, 94.0)**
Fruit	**33.7 (33.7, 92.7)**	92.7 (33.7, 92.7)	92.7 (33.7, 168.6)	92.7 (33.7, 168.6)	**168.6 (92.7, 168.6)**
Meat	59.4 (53.7, 97.7)	59.4 (40.6, 76.6)	59.4 (53.7, 82.0)	59.4 (41.9, 76.6)	53.7 (13.4, 59.4)
Ice cream/ sweets/ cakes	**92.3 (58.2, 138.6)**	77.2 (49.6, 112.4)	71.2 (41.0, 105.3)	63.8 (35.8, 96.9)	**56.6 (32.4, 87.6)**
Cereal products	**116.9 (81.4, 167.2)**	142.6 (96.9, 178.1)	164.9 (128.0, 206.9)	190.4 (155.1, 235.7)	**235.7 (191.2, 279.1)**
Fats	15.4 (7.4, 28.0)	15.4 (10.4, 21.4)	15.4 (14.0, 23.9)	20.0 (14.0, 28.0)	**21.0 (14.0, 28.4)**
Fish	15.6 (9.3, 37.1)	17.8 (9.3, 45.6)	37.1 (17.8, 45.6)	43.3 (17.8, 71.1)	**45.6 (17.8, 71.1)**
Beverages	**1075.7 (760.0, 1409.3)**	942.9 (615.7, 1195.7)	885.7 (597.1, 1178.6)	884.3 (505.7, 1151.4)	**825.7 (570.0, 1151.4)**
Dairy products	398.3 (292.3, 522.6)	378.5 (258.8, 499.6)	390.0 (280.9, 496.7)	380.9 (288.4, 480.4)	**376.6 (269.7, 474.4)**
Snacks	7.7 (7.7, 21.2)	7.7 (1.9, 7.7)	7.7 (1.9, 7.7)	1.9 (0.0, 7.7)	1.9 (0.0, 7.7)
Eggs	7.4 (7.4, 29.7)	7.4 (7.4, 29.7)	29.7 (7.4, 29.7)	29.7 (7.4, 29.7)	29.7 (7.4, 29.7)
Pizza	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)
Pastries	**9.2 (9.2, 36.9)**	9.2 (0.0, 9.2)	9.2 (0.0, 9.2)	0.0 (0.0, 9.2)	**0.0 (0.0, 0.0)**

			Traditional meat & vegetables		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
Nutrients	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**
Energy intake (kcal/d)	1810.7 (1782.6, 1838.8)	1721.6 (1698.0, 1745.2)	1691.3 (1667.9, 1714.7)	1687.2 (1664.0, 1710.3)	1812.8 (1789.1, 1836.4)
Fats (% energy)	38.4 (38.2, 38.7)	37.8 (37.6, 38.1)	36.9 (36.7, 37.1)	36.1 (35.9, 36.4)	**35.7 (35.4,35.9)**
Carbohydrates (% energy)	**50.2 (50.0, 50.5)**	49.2 (49.0, 49.5)	49.0 (48.7,49.2)	48.7 (48.5, 49.0)	**48.2 (47.9, 48.4)**
Protein (% energy)	**14.0 (13.9, 14.1)**	15.5 (15.4, 15.6)	16.7 (16.6, 16.8)	17.6 (17.5, 17.7)	**18.6 (18.5, 18.7)**
Folate (µg/d)	**219.3 (215.5, 223.0)**	230.6 (227.4, 233.9)	241.3 (238.1, 244.5)	253.9 (250.5, 257.3)	**301.7 (298.1, 305.4)**
Calcium (mg/d)	953.0 (936.5, 969.4)	926.5 (912.2, 940.7)	931.6 (917.5, 945.7)	935.0 (920.4, 949.6)	1001.0 (986.5, 1015.6)
Iron (mg/d)	9.7 (9.6, 9.9)	9.9 (9.7, 10.1)	10.3 (10.1, 10.5)	10.7 (10.5, 10.8)	12.0 (11.8, 12.1)
Main food groups	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	**60.9 (38.0, 97.5)**	87.0 (66.6, 118.3)	101.6 (80.8, 118.3)	118.3 (94.1, 157.1)	**178.0 (130.6, 235.8)**
Potatoes	86.0	93.4	93.4	107.6	115.4

	(50.9, 115.4)	(58.2, 115.4)	(58.2, 115.4)	(58.2, 126.7)	(80.3, 148.8)
Nuts	0.0 (0.0, 3.7)	0.0 (0.0, 3.7)	0.0 (0.0, 3.7)	0.0 (0.0, 3.7)	0.0 (0.0, 3.7)
Legumes/ pulses	**47.5** **(21.1, 59.7)**	59.7 (30.8, 59.7)	59.7 (30.8, 59.7)	59.7 (30.8, 67.8)	59.7 (30.8, 76.9)
Fruit	92.7 (33.7, 92.7)	92.7 (33.7, 92.7)	92.7 (33.7, 168.6)	92.7 (92.7, 168.6)	92.7 (92.7, 168.6)
Meat	**38.0** **(19.1, 59.4)**	53.7 (38.0, 59.4)	59.4 (53.7, 76.3)	59.4 (53.7, 97.7)	**81.7** **(53.7, 104.7)**
Ice cream/ sweets/ cakes	90.4 (104.4, 211.2)	76.2 (49.1, 112.2)	67.0 (39.7, 104.1)	63.1 (37.8, 91.9)	61.2 (32.9, 98.1)
Cereal products	161.4 (104.4, 211.2)	163.7 (108.1, 214.9)	170.0 (124.9, 223.4)	170.0 (125.1, 227.1)	183.7 (138.8, 238.7)
Fats	20.4 (14.0, 28.4)	20.0 (14.0, 28.0)	15.4 (14.0, 28.0)	**14.4** **(14.0, 21.4)**	15.4 (14.0, 22.4)
Fish	**15.6** **(6.3, 37.1)**	17.8 (9.3, 45.6)	37.1 (17.8, 49.6)	42.9 (17.8, 71.1)	**45.6** **(17.8, 71.1)**
Beverages	961.4 (617.1, 1302.1)	897.1 (581.4, 1185.7)	885.7 (588.6, 1185.7)	885.7 (600.0, 1178.6)	901.4 (615.7, 1224.3)
Dairy products	380.0 (265.8, 505.5)	379.5 (273.7, 488.4)	385.0 (272.8, 487.0)	378.9 (282.0, 488.8)	**402.2** **(296.6, 510.0)**
Snacks	7.7 (1.9, 21.2)	7.7 (1.9, 7.7)	7.7 (1.9, 7.7)	1.9 (0.0, 7.7)	1.9 (0.0, 7.7)
Eggs	7.4 (7.4, 29.7)	29.7 (7.4, 29.7)	29.7 (7.4, 29.7)	29.7 (7.4, 29.7)	29.7 (7.4, 29.7)
Pizza	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)	16.4 (0.0, 16.4)
Pastries	9.2 (0.0, 9.2)	9.2 (0.0, 9.2)	9.2 (0.0, 9.2)	9.2 (0.0, 9.2)	0.0 (0.0, 9.2)

*For a description of each food group please see Table 8. The highest and lowest average value for each food group and nutrient across all dietary patterns are shown in bold. CI, confidence interval; IQR, interquartile range; Q, quintile.

7.4.2 Characteristics of mothers across quintile categories of dietary patterns scores

Characteristics of participants in the ALSPAC study across quintile categories of the two dietary pattern scores can be found in Table 27. For both components, mothers who scored highly were significantly more likely to be older, have a university degree, to breastfeed for more than 3 months, to have partners who were slightly taller and they were less likely to smoke compared to those in the lower quintile scores. Mothers who scored highly on the first component were also significantly more likely to be Caucasian, be nulliparous, take dietary supplements before 32 weeks gestation, be vegetarian, have a higher alcohol intake, have babies born with a higher birth weight and were less likely to enter pregnancy overweight or obese than those in the lower quintile scores. Those in the higher quintile categories of the ‘traditional meat & vegetables’ component were significantly less likely to be Caucasian, nulliparous, take dietary supplements before 32 weeks gestation, be vegetarian and more likely to have a lower gestational weight gain and to have male infants than mothers in the lower categories.

Table 27. ALSPAC study sample characteristics according to quintile categories of dietary pattern scores (n=6,756)*

	Modern health conscious						**Traditional meat & vegetables**					
	Q1 (n=1,352)	**Q2 (n=1,351)**	**Q3 (n=1,351)**	**Q4 (n=1,351)**	**Q5 (n=1,351)**	***P-valueǂ***	**Q1 (n=1,352)**	**Q2 (n=1,351)**	**Q3 (n=1,351)**	**Q4 (n=1,351)**	**Q5 (n=1,351)**	***P-valueǂ***
Age of mother (years), n (%)						0.0001						0.0001
≤20	103 (7.6)	45 (3.3)	26 (1.9)	15 (1.1)	9 (0.7)		80 (5.9)	44 (3.3)	25 (1.9)	37 (2.7)	12 (0.9)	
>21-39	1,241 (91.8)	1,296 (95.9)	1,299 (96.2)	1,312 (97.1)	1,308 (96.8)		1,262 (93.3)	1,297 (96.0)	1,303 (96.5)	1,285 (95.1)	1,309 (96.9)	
≥40	8 (0.6)	10 (0.7)	26 (1.9)	24 (1.8)	34 (2.5)		10 (0.7)	10 (0.7)	23 (1.7)	29 (2.2)	30 (2.2)	
Pre-pregnancy BMI (kg/m^2), n (%)						0.0001						0.2
≤ 18.5	65 (5.4)	45 (3.6)	53 (4.3)	45 (3.6)	59 (4.6)		77 (6.2)	39 (3.2)	49 (3.9)	52 (4.2)	50 (4.0)	
18.6-24.9	830 (68.7)	912 (73.6)	899 (73.0)	972 (77.5)	1,086 (84.8)		915 (73.6)	927 (75.7)	969 (78.0)	928 (74.7)	690 (76.1)	
25-29.9	230 (19.0)	204 (16.5)	203 (16.5)	188 (15.0)	110 (8.6)		191 (15.4)	187 (15.3)	180 (14.5)	197 (15.9)	180 (14.3)	
30.0-34.9	62 (5.1)	56 (4.5)	60 (4.9)	39 (3.1)	19 (1.5)		50 (4.0)	51 (4.2)	29 (2.3)	51 (4.1)	55 (4.4)	
≥35	21 (1.7)	23 (1.9)	17 (1.4)	11 (0.9)	6 (0.5)		11 (0.9)	20 (1.6)	16 (1.3)	14 (1.1)	17 (1.4)	
Caucasian, n (%)	1,334 (99.2)	1,330 (99.0)	1,318 (98.4)	1,310 (97.5)	1,302 (96.8)	<0.0001	1,319 (98.3)	1,332 (98.9)	1,312 (97.7)	1,324 (98.6)	1,307 (97.4)	0.02
Smoking in 1st trimester, n (%)	455 (34.3)	314 (23.4)	195 (14.5)	126 (9.4)	123 (9.1)	<0.0001	371 (27.7)	261 (19.6)	221 (16.4)	194 (14.4)	166 (12.4)	<0.0001
University degree, n (%)	36 (2.7)	72 (5.33)	151 (11.2)	305 (22.6)	531 (39.4)	<0.0001	161 (12.0)	202 (15.0)	224 (16.6)	226 (16.7)	282 (20.9)	<0.0001
Nulliparous, n (%)	511 (38.8)	563 (42.9)	623 (47.1)	652 (49.0)	653 (49.1)	<0.0001	660 (49.9)	598 (45.4)	611 (45.9)	597 (45.2)	536 (40.5)	<0.0001
Dietary supplements before 32 weeks gestation, n (% yes)	606 (44.9)	624 (46.4)	550 (40.1)	624 (46.4)	682 (50.5)	<0.0001	665 (49.3)	630 (46.8)	592 (44.0)	619 (46.0)	580 (43.1)	0.01
Vegetarian, n (% yes)	7 (0.5)	14 (1.1)	21 (1.6)	65 (4.9)	283 (21.3)	<0.0001	178 (13.4)	84 (6.3)	51 (3.9)	45 (3.4)	32 (2.4)	<0.0001
Breast feeding duration, n (%)						0.0001						0.0001

Never	432 (35.8)	308 (25.0)	238 (18.9)	132 (10.3)	62 (4.7)		323 (26.5)	283 (22.7)	237 (18.7)	174 (13.6)	155 (12.1)	
<3 months	450 (37.3)	450 (36.5)	427 (33.8)	379 (29.5)	235 (17.9)		394 (32.3)	400 (32.0)	380 (30.0)	413 (32.2)	354 (27.6)	
3-6 months	121 (10.0)	174 (14.1)	185 (14.7)	213 (16.6)	199 (15.1)		146 (12.0)	157 (12.6)	189 (14.9)	198 (15.4)	202 (15.7)	
>6 months	205 (17.0)	300 (24.4)	412 (32.7)	559 (43.6)	818 (62.3)		356 (29.2)	409 (32.8)	459 (36.3)	497 (38.8)	573 (44.6)	
Preeclampsia, n (%)	18 (1.3)	15 (1.1)	27 (2.0)	20 (1.5)	17 (1.3)	0.3	16 (1.2)	27 (2.0)	19 (1.4)	20 (1.5)	15 (1.1)	0.3
Gestational diabetes, n (%)	5 (0.4)	6 (0.5)	5 (0.4)	8 (0.6)	4 (0.3)	0.8	8 (0.6)	4 (0.3)	3 (0.2)	4 (0.3)	9 (0.7)	0.1
Gestational weight gain (g/week), mean (SD)	451.1 (165.5)	454.0 (162.7)	456.4 (161.05)	463.8 (155.4)	455.9 (136.3)	0.3	464.9 (164.4)	461.6 (158.6)	454.7 (150.6)	452.2 (154.4)	447.6 (153.6)	0.04
Alcohol intake** (units/day), median (IQR)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 4)	0.0001	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0.17
Paternal height (cm), median (IQR)	175.0 (170.0, 180.0)	177.5 (172.5, 180.0)	177.5 (172.5, 180.0)	177.5 (172.5, 180.0)	177.5 (172.5, 180.0)	0.0001	175.0 (172.5, 180.0)	177.5 (172.5, 18.0)	177.5 (172.5, 18.0)	177.5 (172.5, 18.0)	177.5 (172.5, 18.0)	0.03
Neonatal characteristics												
Birth weight (g), mean (SD)	3,468.2 (460.9)	3498.5 (464.6)	3,482.0 (478.5)	3,517.9 (464.0)	3,514.6 (461.2)	0.03	3.473.8 (473.1)	3,488.1 (467.4)	3,502.2 (474.1)	3,499.2 (453.6)	3,517.8 (461.7)	0.2
Child sex (% male)	668 (49.4)	695 (51.4)	691 (51.2)	671 (49.7)	681 (50.4)	0.8	653 (48.3)	676 (50.0)	657 (48.6)	702 (52.0)	718 (53.2)	0.05

*Where numbers do not add up this is due to a small proportion of missing data. ǂP value using ANOVA for normally distributed and Kruskal-Wallis test for non-normally distributed continuous and ordinal variables and the χ2 or Fisher's exact test for nominal categorical variables. ** Alcohol intake only available for a sub-sample of 3,903 mothers. Significant difference at P<0.05. BMI, body mass index; g, gram; n, number; SD, standard deviation; IQR, interquartile range; Q, quintile.

7.4.3 Offspring anthropometry

Table 28 shows offspring size at birth as well as child height and weight measures at the 7.5 years follow-up. Mean birth weight for the whole sample was just under 3.5 kg with 1 % (n=95) of infants born with LBW and 2 % (n=136) born with HBW. The mean birth length was around 50 cm and the infants had an overall lower mean WFL Z-score at birth compared to the WHO reference population. Boys tended to be significantly longer and heavier than girls at birth. At the 7.5 years follow-up, the average height for the whole sample was 126 cm with a mean weight of 26 kg. The children had higher mean Z-scores of weight & height-for-age compared to the WHO reference population. A total of 136 (2%) children were found to be LHFA and 105 (2 %) to be LWFA. Boys tended to be slightly taller than girls and a larger proportion of boys were found to be LWFA.

Table 28. Offspring anthropometry at birth and at age 7.5 years in the ALSPAC study

	N	Total sample	Boys	Girls	*P **
Birth weight (g), mean (SD)	6,679	3496.2 (466.1)	3554.7 (487.7)	3436.7 (438.6)	<0.0001
Birth length (cm), mean (SD)	4,307	50.8 (2.0)	51.2 (2.0)	50.4 (1.9)	<0.0001
Weight-for-length Z-score, mean (SD)	4,245	-0.18 (0.93)	-0.25 (0.96)	-0.11 (0.90)	<0.0001
Low birth weight (<2,500 g), n (%)	6,679	95 (1.4)	42 (1.3)	53 (1.6)	0.2
High birth weight (>4,500 g), n (%)	6,679	136 (2.0)	101 (3.0)	35 (1.1)	<0.001
Child height measures					
Height (cm), mean (SD)	6,756	125.7 (5.4)	126.2 (5.3)	125.2 (5.4)	<0.0001
Height-for-age Z-score, mean (SD)	6,756	0.3 (0.9)	0.29 (0.9)	0.32 (1.0)	0.2
Low height-for-age, n (%)	6,756	136 (2.0)	76 (2.2)	60 (1.8)	0.2
Child weight measures					
Weight (kg), mean (SD)	6,745	25.8 (4.5)	25.8 (4.3)	25.8 (4.6)	0.8
Weight-for-age Z-score, mean (SD)	6,745	0.4 (1.0)	0.35 (1.07)	0.40 (0.99)	0.03
Low weight-for-age, n (%)	6,745	105 (1.6)	64 (1.9)	41 (1.2)	0.03

*P value using the two-sample t-test for normally distributed continuous variables, and the X^2 test for categorical variables. Significant difference at *P*<0.05.

7.4.4 Relationship between maternal dietary patterns and offspring size at birth

Table 29 and Table 30 show the crude and adjusted associations between offspring size at birth and maternal dietary patterns in pregnancy. Model 1 displays associations with adjustments for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), gestation and infant's sex and model 2 represents adjusted associations with the addition of gestational weight gain (GWG) as a mediator. When looking at the continuous outcomes (Table 29), the ‘modern health conscious’ dietary pattern was found to have a significant positive relationship with both birth weight (g) and birth length (cm) but not WFL Z-score in adjusted analyses. Compared to mothers in the lowest quintile, mothers in the highest quintile had babies born weighing 45 g more (95% CI: 8.6, 81.3, P_{trend}=0.03). This association was strengthened further once adjustments for GWG as a mediator was made (53 g, 95% CI: 16.3, 89.7, P_{trend}=0.008). Similarly, mothers in the highest quintiles also had babies which were longer compared to those in the lowest quintile (0.20 cm, 95% CI: 0.01, 0.40, P_{trend}=0.002) and adjustment for GWG had no influence on this relationship. The second component, ‘traditional meat & vegetables’ had no significant relationship with neither birth weight (g) nor birth length (cm) in unadjusted or adjusted analyses. There was however an association with offspring birth WFL Z-scores. Mothers in the highest quintile score had infants born with a 0.15 higher WFL Z-score (95% CI: 0.06, 0.24, P_{trend}=0.04) compared to mothers in the lowest quintile score. Adjustment for GWG strengthened this association (0.16, 95% CI: 0.06, 0.25, P_{trend}=0.02).

As for the dichotomous outcomes LBW and HBW (Table 30), there were no significant relationships observed with either dietary pattern scores regardless of adjustments for confounders. Mothers in the third and fourth quintile categories of the ‘modern health conscious’ dietary pattern appeared to have over twice the odds of having HBW infants compared to mothers in the lowest quintile, the P for trend however was not significant (P_{trend}=0.2).

Excluding mothers with gestational diabetes in the above analyses did not alter the results (data not shown).

Table 29. The association between maternal dietary patterns in pregnancy and offspring weight (g), length (cm) and WFL (Z-score) at birth in the ALSPAC study

				Modern health conscious					
		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	N			*β* (95 % CI)			*P-trend*[d]	*β* (95 % CI)	*P*
Birth weight (g)									
Crude model[a]	6,679	Ref	30.32 (-5.08,65.72)	13.79 (-21.52,49.10)	49.68 (14.32, 85.03)	46.41 (11.04, 81.78)	0.03	7.35 (1.96, 12.73)	0.008
Model 1[b]	5,990	Ref	8.75 (-25.26,42.76)	6.01 (-28.54,40.56)	42.61 (7.55, 77.66)	44.92 (8.58, 81.26)	0.03	7.25 (1.61, 12.90)	0.012
Model 2[c]	5,535	Ref	12.54 (-21.9, 47.01)	10.27 (-24.68, 45.22)	50.30 (14.76, 85.84)	53.00 (16.26, 89.73)	0.008	8.81 (3.09, 14.53)	0.003
Birth length (cm)									
Crude model[a]	4,307	Ref	0.09 (-0.09, 0.28)	0.10 (-0.09, 0.29)	0.32 (0.13, 0.51)	0.35 (0.16, 0.53)	0.0004	0.06 (0.04, 0.09)	<0.0001
Model 1[b]	3,873	Ref	-0.03 (-0.20, 0.15)	0 (-0.18, 0.18)	0.27 (0.09, 0.45)	0.20 (0.01, 0.39)	0.002	0.04 (0.01, 0.07)	0.003
Model 2[c]	3,619	Ref	-0.02 (-0.20, 0.16)	0 (-0.18, 0.19)	0.28 (0.10, 0.47)	0.20 (0.01, 0.40)	0.002	0.04 (0.01, 0.07)	0.005
WFL Z-score									
Crude model[a]	4,245	Ref	0.03 (-0.06, 0.12)	-0.03 (-0.12, 0.06)	-0.02 (-0.11, 0.07)	-0.04 (-0.13, 0.05)	0.6	-0.01 (-0.02, 0.01)	0.2
Model 1[b]	3,824	Ref	0.03 (-0.06, 0.12)	0.01 (-0.08, 0.11)	0.01 (-0.09, 0.11)	0.05 (-0.05, 0.15)	0.9	0.01 (-0.01, 0.02)	0.5
Model 2[c]	3,573	Ref	0.03 (-0.07, 0.13)	0.02 (-0.08, 0.12)	0.01 (-0.09, 0.11)	0.06 (-0.05, 0.16)	0.8	0.01 (-0.01, 0.02)	0.4
				Traditional meat & vegetables					
		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	N			*β* (95 % CI)			*P-trend*[d]	*β* (95 % CI)	*P*
Birth weight (g)									
Crude model[a]	6,679	Ref	14.32 (-21.03, 49.67)	28.41 (-6.93, 63.76)	25.43 (-9.93, 60.80)	44.05 (8.67, 79.43)	0.16	9.20 (2.21, 16.18)	0.01
Model 1[b]	5,990	Ref	-16.97 (-50.67,16.73)	2.14 (-31.49,35.77)	-9.37 (-43.05,24.30)	-4.33 (-38.16,29.49)	0.8	-0.62 (-7.29, 6.05)	0.9
Model 2[c]	5,535	Ref	-20.35 (-54.40, 13.70)	5.87 (-28.21, 39.95)	-6.34 (-40.32, 27.64)	2.66 (-31.63, 36.95)	0.6	0.70 (-6.03, 7.42)	0.8
Birth length (cm)									
Crude model[a]	4,307	Ref	0.10 (-0.8, 0.29)	0.17 (-0.02, 0.35)	0.23 (0.04, 0.42)	0.16 (-0.02, 0.35)	0.16	0.04 (0.00, 0.80)	0.04
Model 1[b]	3,873	Ref	-0.04 (-0.21, 0.14)	0.05 (-0.12, 0.22)	0.09 (-0.08, 0.27)	-0.09 (-0.27, 0.08)	0.25	-0.01 (-0.04, 0.03)	0.6
Model 2[c]	3,619	Ref	-0.07 (-0.25, 0.11)	0.06 (-0.12, 0.23)	0.06 (-0.11, 0.24)	-0.09 (-0.27, 0.09)	0.3	-0.01 (-0.04, 0.03)	0.66
WFL Z-score									
Crude model[a]	4,245	Ref	0.07 (-0.02, 0.16)	0.09 (0.01, 0.18)	0.07 (0.02, 0.16)	0.15 (0.06, 0.24)	0.02	0.03 (0.01, 0.05)	0.002
Model 1[b]	3,824	Ref	0.06 (-0.03, 0.46)	0.08 (-0.02, 0.17)	0.07 (-0.02, 0.16)	0.15 (0.06, 0.24)	0.04	0.03 (0.01, 0.04)	0.008
Model 2[c]	3,573	Ref	0.04 (-0.05, 0.14)	0.07 (-0.03, 0.16)	0.07 (-0.02, 0.18)	0.16 (0.06, 0.25)	0.02	0.03 (0.01, 0.05)	0.002

[a]Unadjusted model [b]Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), gestation and infant's sex (except the sex-specific WFL). [c]With additional adjustment for gestational weight gain as a mediator. [d]*P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; Ref, reference category; Q, quintile.

Table 30. The association between maternal dietary patterns in pregnancy and low birth weight and high birth weight in the ALSPAC study

				Modern health conscious					
		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	cases/N			OR (95% CI)			*P-trend*[d]	OR (95% CI)	***P***[a]
LBW (<2,500 g)									
Crude model[a]	95/6,679	Ref	0.73 (0.38, 1.39)	0.99 (0.55, 1.80)	0.94 (0.52, 1.73)	0.63 (0.32, 1.24)	0.6	0.95 (0.86, 1.05)	0.3
Model 1[b]	82/5,990	Ref	0.72 (0.35, 1.45)	0.99 (0.51, 1.92)	0.86 (0.42, 1.77)	0.55 (0.25, 1.25)	0.6	0.93 (0.83, 1.06)	0.3
Model 2[c]	79/5,535	Ref	0.64 (0.30, 1.34)	0.98 (0.49, 1.93)	0.95 (0.46, 1.97)	0.58 (0.25, 1.31)	0.5	0.95 (0.84, 1.07)	0.4
HBW (>4,500 g)									
Crude model[a]	136/6,679	Ref	1.89 (1.00, 3.55)	2.21 (1.19, 4.09)	2.15 (1.16, 3.99)	1.88 (1.00, 3.54)	0.1	1.04 (0.96, 1.13)	0.4
Model 1[b]	124/5,990	Ref	1.59 (0.81, 3.12)	2.01 (1.04, 3.88)	2.21 (1.19, 4.09)	1.89 (0.92, 3.89)	0.2	1.06 (0.96, 1.16)	0.3
Model 2[c]	117/5,535	Ref	1.63 (0.82, 3.23)	1.57 (0.79, 3.11)	2.36 (1.22, 4.59)	1.91 (0.92, 3.96)	0.14	1.06 (0.96, 1.18)	0.2
				Traditional meat & vegetables					
		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	cases/N			OR (95% CI)			*P-trend*[d]	OR (95% CI)	***P***[a]
LBW (<2,500 g)									
Crude model[a]	95/6,679	Ref	1.41 (0.76, 2.65)	1.12 (0.58, 2.15)	1.24 (0.65, 2.36)	0.82 (0.40, 1.67)	0.6	0.97 (0.85, 1.10)	0.7
Model 1[b]	82/5,990	Ref	1.69 (0.85, 3.36)	1.25 (0.60, 2.60)	1.38 (0.67, 2.83)	1.16 (0.54, 2.51)	0.6	1.04 (0.91, 1.19)	0.6
Model 2[c]	79/5,535	Ref	1.93 (0.95, 3.93)	1.25 (0.58, 2.66)	1.46 (0.69, 3.06)	1.10 (0.49, 2.47)	0.4	1.03 (0.84, 1.18)	0.7
HBW (>4,500 g)									
Crude model[a]	136/6,679	Ref	1.46 (0.84, 2.53)	1.27 (0.72, 2.24)	1.05 (0.58, 1.89)	1.42 (0.82, 2.47)	0.5	1.03 (0.93, 1.15)	0.5
Model 1[b]	124/5,990	Ref	1.33 (0.74, 2.37)	1.03 (0.56, 1.91)	0.85 (0.45, 1.60)	1.08 (0.60, 1.96)	0.6	0.97 (0.86, 1.08)	0.6
Model 2[c]	117/5,535	Ref	1.43 (0.79, 2.61)	1.11 (0.59, 2.10)	0.87 (0.45, 1.68)	1.13 (0.61, 2.10)	0.7	0.97 (0.87, 1.10)	0.7

[a]Unadjusted model [b]Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), gestation and infant's sex. [c]With additional adjustment for gestational weight gain as a mediator. [d]*P* for trend across dietary pattern quintiles in linear regression models.

CI, confidence interval; LBW, low birth weight; HBW, high birth weight; N, number; OR, odds ratios; Ref, reference category; Q, quintile.

7.4.4.1 Effect modification by maternal pre-pregnancy BMI

As shown by the interaction P values presented in Table 31 below, there was no evidence of effect modification by maternal pre-pregnancy BMI status on any of the relationships.

Table 31. Multivariate* regression estimates from stratified analyses for associations between maternal dietary patterns in pregnancy with offspring size at birth with testing for effect modification by pre-pregnancy maternal BMI (kg/m^2)

	Modern health conscious (Per 1 unit increase)		**Traditional meat & vegetables** (Per 1 unit increase)	
	***β* (95 % CI)**	***P*****	***β* (95 % CI)**	***P*****
Birth weight (g) (n=5,990)		0.2		0.4
BMI <25 (kg/m^2)	5.98 (-0.10, 12.06)		1.33 (-6.19, 8.84)	
BMI ≥25 (kg/m^2)	14.64 (1.36, 27.93)		-5.03 (-19.41, 9.34)	
Birth length (cm) (n=3,873)		0.8		0.9
BMI <25 (kg/m^2)	0.04 (0.01, 0.08)		-0.01 (-0.05, 0.03)	
BMI ≥25 (kg/m^2)	0.05 (-0.01, 0.12)		0.00 (-0.07, 0.07)	
WFL Z-score (n=3,824)		0.9		
BMI <25 (kg/m^2)	0.01 (-0.01, 0.02)		0.03 (0.01, 0.05)	
BMI ≥25 (kg/m^2)	0.01 (-0.03, 0.04)		0.03 (-0.01, 0.07)	
	OR (95 % CI)	***P*****	**OR (95 % CI)**	***P*****
LBW (cases/N= 82/5,990)		0.8		0.9
BMI <25 (kg/m^2)	0.93 (0.81, 1.06)		1.04 (0.89, 1.21)	
BMI ≥25 (kg/m^2)	0.96 (0.74, 1.25)		1.03 (0.77, 1.37)	
HBW (cases/N= 124/5,990)		0.37		0.3
BMI <25 (kg/m^2)	1.02 (0.91, 1.15)		0.92 (0.79, 1.08)	
BMI ≥25 (kg/m^2)	1.11 (0.95, 1.31)		1.04 (0.88, 1.24)	

*Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification as a proxy for socioeconomic status), infant's sex and gestation. **Interaction P value, testing the null hypotheses that associations do not differ by maternal pre-pregnancy BMI status.
CI, confidence interval; LBW, low birth weight; HBW, high birth weight; OR, odds ratio.

7.4.5 Relationship between maternal dietary patterns and offspring anthropometry at age 7.5 years

Table 32 and Table 33 show the crude and adjusted associations between offspring height and weight-for-age Z-scores at 7.5 years and maternal dietary patterns in pregnancy. Model 1 displays associations with adjustments for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), and child height in the WFA models and paternal height in the HFA models. Model 2 represents adjusted associations with the addition of birth weight as a mediator and model 3 with additional adjustment of both offspring birth weight and gestational weight gain as mediators. The 'modern health conscious' dietary pattern was significantly associated with offspring HFA Z-scores at 7.5 years in crude analyses. Compared to mothers in the lowest quintile score, mothers in the highest quintile had offspring with 0.20 higher HWFA Z-scores (95% CI: 0.13, 0.27, P_{trend}<0.0001). However once adjustments for confounders were made this relationship was much attenuated and rendered borderline significant (0.08, 85% CI: -0.01, 0.17, P_{trend}=0.07). Adjustments for birth weight and gestational weight gain as mediators further weakened associations. There were no significant associations observed for this dietary pattern and offspring WFA Z-scores at 7.5 years nor did the ‘traditional meat & vegetables’ dietary pattern have any association with child HFA or WFA Z-scores at 7.5 years.

In terms of the dichotomous outcomes LHFA and LWFA (Table 33), the ‘modern health conscious’ dietary pattern appeared to be significantly associated with offspring LHFA in crude analyses. For every 1 unit increase in that dietary pattern score, mothers had 9% lower odds of having a LHFA child at 7.5 years (95% CI: 0.83, 0.99, *P*=0.03). However there was no linear trend across dietary pattern quintiles and once adjustment for confounders were made the association was rendered insignificant (OR: 0.98, 95% CI: 0.88, 1.11, *P*=0.85; H-L goodness-of-fit test *P*=0.97). The ‘traditional meat & vegetables’ dietary pattern was positively associated with offspring LHFA in adjusted models. Mothers with higher ‘traditional meat & vegetables’ dietary patterns scores had 15% lower odds of having LHFA offspring at age 7.5 years (95% CI: 0.74, 0.99, P=0.04; H-L goodness-of-fit test *P*=0.18). Adjustments for birth weight and GWG further strengthened this relationship (OR: 0.83, 95% CI: 0.71, 0.98, *P*=0.02).

There were no associations observed for either dietary pattern with offspring WFA or LWFA. Excluding mothers with gestational diabetes (n=28) did not alter the results (data not shown).

Table 32. Association between maternal dietary patterns in pregnancy and offspring height-for-age (HFA) and weight-for-age (WFA) Z-scores at age 7.5 years in the ALSPAC study

Modern health conscious

		Q1	Q2	Q3	Q4	Q5		Per 1 unit increase	
	N			*β* (95 % CI)			*P-trend*^{e}	*β* (95 % CI)	*P*
HFA Z-score									
Crude model^a	6,756	Ref	0.08 (0.01, 0.15)	0.10 (0.03, 0.17)	0.20 (0.12, 0.27)	0.20 (0.13, 0.27)	<0.0001	0.03 (0.02, 0.04)	<0.0001
Model 1^b	4,497	Ref	0.01 (-0.08, 0.09)	-0.03 (-0.12, 0.05)	0.04 (-0.04, 0.13)	0.08 (-0.01, 0.17)	0.07	0.01 (0.00, 0.03)	0.06
Model 2^c	4,443	Ref	0.00 (-0.08, 0.08)	-0.03(-0.11, 0.05)	0.04 (-0.05, 0.12)	0.06 (-0.02, 0.15)	0.18	0.01 (0.00,0.02)	0.1
Model 3^d	4,413	Ref	0.00 (-0.08, 0.09)	-0.02(-0.11, 0.07)	0.06 (-0.03, 0.14)	0.07 (-0.02, 0.16)	0.19	0.01 (0.00, 0.03)	0.07
WFA Z-score									
Crude model^a	6,745	Ref	0.08 (0.00, 0.15)	0.06 (-0.02, 0.14)	0.11 (0.03, 0.18)	0.07 (-0.01, 0.15)	0.1	0.01 (-0.01, 0.02)	0.2
Model 1^b	6,047	Ref	0.01 (-0.05, 0.07)	0.02 (-0.04, 0.07)	0.00 (-0.06, 0.06)	0.03 (-0.03, 0.09)	0.9	0.00 (-0.01, 0.01)	0.8
Model 2^c	5,981	Ref	0.01 (-0.05, 0.07)	0.01 (-0.04, 0.07)	-0.01 (-0.07, 0.05)	0.01 (-0.05, 0.08)	0.9	0.00 (-0.01, 0.01)	0.9
Model 3^d	5,526	Ref	0.01 (-0.05, 0.07)	0.02 (-0.04, 0.08)	-0.01 (-0.07, 0.05)	0.01 (-0.05, 0.07)	0.9	0.00 (-0.01, 0.01)	09

Traditional meat & vegetables

		Q1	Q2	Q3	Q4	Q5		Per 1 unit increase	
	N			*β* (95 % CI)			*P-trend*^{e}	*β* (95 % CI)	*P*
HFA Z-score									
Crude model^a	6,756	Ref	-0.00 (-0.07,0.07)	0.04 (-0.03, 0.11)	0.06 (-0.01, 0.13)	0.03 (-0.04, 0.10)	0.4	0.01 (0.00, 0.02)	0.1
Model 1^b	4,497	Ref	0.00 (-0.08, 0.09)	0.05 (-0.03, 0.13)	0.03 (-0.05, 0.11)	0.02 (-0.06, 0.10)	0.8	0.01 (-0.01, 0.03)	0.3
Model 2^c	4,443	Ref	0.01 (-0.07, 0.09)	0.04 (-0.04, 0.12)	0.03 (-0.05, 0.11)	0.01 (-0.07, 0.10)	0.86	0.01 (-0.01, 0.02)	0.3
Model 3^d	4,413	Ref	0.00 (-0.08, 0.09)	0.02 (-0.06, 0.11)	0.03 (-0.05, 0.1)	0.02 (-0.07, 0.10)	0.94	0.01 (-0.01, 0.02)	0.4
WFA Z-score									
Crude model^a	6,745	Ref	0.01 (-0.07, 0.08)	-0.01 (-0.09, 0.07)	0.00 (-0.08, 0.08)	0.0 (-0.08, 0.08)	0.9	0.00 (-0.01, 0.02)	0.6
Model 1^b	6,047	Ref	0.02 (-0.04, 0.08)	-0.01 (-0.07, 0.04)	-0.03 (-0.08, 0.03)	0.02 (-0.04, 0.08)	0.35	0.00 (-0.01, 0.01)	0.9
Model 2^c	5,981	Ref	0.03 (-0.03, 0.08)	-0.01 (-0.07, 0.04)	-0.02 (-0.08, 0.03)	0.02 (-0.04, 0.07)	0.35	0.00 (-0.01, 0.01)	0.9
Model 3^d	5,526	Ref	0.03 (-0.02, 0.09)	-0.02 (-0.08, 0.04)	-0.01 (-0.07, 0.05)	0.01 (-0.05, 0.07)	0.34	0.00 (-0.01, 0.01)	0.9

[a] Unadjusted crude model

[b] Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), and child height in the WFA models and paternal height in the HFA models.

[c] With additional adjustment for offspring birth weight as a mediator.

[d] With additional adjustment for offspring birth weight and gestational weight gain as mediators

[e] *P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; Ref, reference category; Q, quintile.

Table 33. Association between maternal dietary patterns in pregnancy and offspring low height-for-age (LHFA) and low weight-for-age (LWFA) Z-scores at age 7.5 years in the ALSPAC study

Modern health conscious

		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	cases/N			OR (95 % CI)			*P-trend*[e]	OR (95 % CI)	*P*
LHFA (≤2 SD)									
Crude model[a]	136/6,756	Ref	0.85 (0.52, 1.40)	0.80 (0.48, 1.32)	0.68 (0.40, 1.15)	0.54 (0.31, 0.94)	0.2	0.91 (0.83, 0.99)	0.03
Model 1[b]	82/4,497	Ref	0.84 (0.42, 1.65)	0.88 (0.44, 1.76)	0.98 (0.49, 1.98)	0.71 (0.33, 1.55)	0.9	0.98 (0.88, 1.11)	0.85
Model 2[c]	81/4,443	Ref	0.82 (0.42, 1.63)	0.86 (0.42, 1.73)	0.97 (0.48, 2.00)	0.66 (0.30, 1.50)	0.85	0.97 (0.86, 1.10)	0.65
Model 3[d]	75/4,130	Ref	0.80 (0.41, 1.58)	0.77 (0.37, 1.48)	0.68 (0.32, 1.48)	0.54 (0.23, 1.25)	0.7	0.93 (0.81, 1.06)	0.3
LWFA (≤2 SD)									
Crude model[a]	105/6,745	Ref	0.74 (0.41, 1.32)	1.00 (0.58, 1.72)	0.66 (0.36, 1.21)	0.48 (0.24, 0.92)	0.1	0.91 (0.83, 1.00)	0.06
Model 1[b]	87/6,047	Ref	0.62 (0.29, 1.30)	1.15 (0.56, 2.34)	0.61 (0.27, 1.39)	0.55 (0.24, 1.30)	0.3	0.94 (0.82, 1.07)	0.3
Model 2[c]	87/5,981	Ref	0.65 (0.31, 1.38)	1.17 (0.56, 2.43)	0.67 (0.29, 1.55)	0.62 (0.26, 1.49)	0.4	0.96 (0.84, 1.10)	0.6
Model 3[d]	81/5,526	Ref	0.67 (0.32, 1.44)	1.17 (0.55, 2.49)	0.77 (0.33, 1.84)	0.57 (0.23, 1.45)	0.5	0.96 (0.83, 1.11)	0.6

Traditional meat & vegetables

		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	cases/N			OR (95 % CI)			*P-trend*[e]	OR (95 % CI)	*P*
LHFA (≤2 SD)									
Crude model[a]	136/6,756	Ref	1.06 (0.65, 1.74)	0.68 (0.39, 1.18)	0.62 (0.35, 1.09)	0.87 (0.52, 1.46)	0.2	0.94 (0.85, 1.05)	0.3
Model 1[b]	82/4,497	Ref	1.51 (0.82, 2.79)	0.90 (0.45, 1.78)	0.40 (0.17, 0.97)	0.76 (0.37, 1.56)	0.03	0.85 (0.74, 0.99)	0.04
Model 2[c]	81/4,443	Ref	1.56 (0.84, 2.91)	0.94 (0.47, 1.87)	0.42 (0.17, 1.03)	0.78 (0.38, 1.61)	0.03	0.86 (0.74, 0.99)	0.05
Model 3[d]	75/4,130	Ref	1.43 (0.76, 2.70)	0.94 (0.47, 1.89)	0.36 (0.14, 0.92)	0.61 (0.28, 1.34)	0.02	0.83 (0.71, 0.98)	0.02
LWFA (≤2 SD)									
Crude model[a]	105/6,745	Ref	1.22 (0.65,2.29)	1.17 (062, 2.20)	1.05 (0.55, 2.02)	1.39 (0.76, 2.57)	0.8	1.05 (0.93, 1.18)	0.45
Model 1[b]	87/6,047	Ref	1.20 (0.55, 2.65)	1.34 (0.61, 2.98)	1.53 (0.70, 3.37)	1.37 (0.62, 3.03)	0.87	1.08 (0.93, 1.25)	0.34
Model 2[c]	87/5,981	Ref	1.16 (0.53, 2.55)	1.26 (0.57, 2.80)	1.41 (0.64, 3.12)	1.36 (0.61, 3.00)	0.9	1.06 (0.91, 1.24)	0.4
Model 3[d]	81/5,526	Ref	1.19 (0.54, 2.64)	1.24 (0.55, 2.78)	1.44 (0.64, 3.25)	1.30 (0.57, 2.99)	0.9	1.06 (0.90, 1.24)	0.5

[a] Unadjusted crude model

[b] Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), and child height in the WFA models and paternal height in the HFA models.

[c] With additional adjustment for offspring birth weight as a mediator.

[d] With additional adjustment for offspring birth weight and gestational weight gain as mediators

[e] *P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; OR, odds ratio; Ref, reference category; Q, quintile.

7.4.6 Multiple imputed data regression analyses

Adjusted regression results using the multiple imputation dataset are presented in Table 34 & Table 35. Relationships with WFA and LWFA outcomes in the imputed dataset remained largely the same compared to those conducted with complete data for child growth outcomes (Table 32 & Table 33). However, due to the reduction in numbers in the complete dataset from missing data on paternal height, which was adjusted for in the offspring HFA models, the significant positive association between the 'modern health conscious' dietary pattern and HFA Z-scores in the imputed dataset had less impact in the complete dataset (Table 34). The effect sizes were similar, albeit slightly larger and only significant for the imputed dataset, with a difference of 0.08 in HFA Z-scores of offspring of mothers in the highest compared to mothers in the lowest 'modern health conscious' dietary pattern quintile (95 % CI: 0.01, 0.15, P_{trend}=0.01). In addition, the significant protective association between the 'traditional meat & vegetables' and LHFA was completely lost in the imputed dataset (Table 34).

7.4.7 Effect modification

As can be seen from Table 36 below there appeared to be a significant interaction between the 'traditional meat & vegetables' dietary pattern score and breastfeeding status on offspring risk of being LHFA. Mothers who breastfed for more than six months had 35% lower odds (95% CI: 0.48, 0.89, *P*=0.006*, interaction P*=0.047) of having LHFA children at age 7.5 years, after adjusting for maternal age, parity, ethnicity, smoking in pregnancy, educational qualification and paternal height in multivariate logistic regression models.

Table 34. Association between maternal dietary patterns in pregnancy and offspring height-for-age (HFA) and weight-for-age (WFA) Z-scores at 7.5 years in the ALSPAC study using dataset with multiple imputed values for covariates with missing data

Modern health conscious

		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	N			*β* (95 % CI)			*Ptrend*[e]	*β* (95 % CI)	*P*
HFA Z-score									
Model 1[a]	6,756	Ref	0.04 (-0.03, 0.11)	0.02 (-0.05, 0.08)	0.09 (0.02, 0.16)	0.10 (0.03, 0.17)	0.003	0.01 (0.00, 0.03)	0.01
Model 2[b]	6,756	Ref	0.03 (-0.04, 0.10)	0.01 (-0.05,0.08)	0.08 (0.01, 0.15)	0.08 (0.01, 0.15)	0.01	0.01 (0.00, 0.02)	0.038
Model 3[c]	6,756	Ref	0.03 (-0.04, 0.10)	0.01 (-0.05,0.08)	0.08 (0.01, 0.15)	0.08 (0.01, 0.15)	0.01	0.01 (0.00, 0.02)	0.037
WFA Z-score									
Model 1[a]	6,745	Ref	0.03 (-0.03, 0.08)	0.01(-0.05, 0.06)	0.02 (-0.04, 0.07)	0.00 (-0.06, 0.06)	0.9	-0.003 (-0.01, 0.01)	0.6
Model 2[b]	6,745	Ref	0.03 (-0.03, 0.08)	0.01(-0.05, 0.06)	0.02 (-0.04, 0.07)	0.00 (-0.06, 0.06)	0.9	-0.003 (-0.01, 0.01)	0.5
Model 3[c]	6,745	Ref	0.03 (-0.03, 0.08)	0.01(-0.05, 0.06)	0.02 (-0.04, 0.07)	0.00 (-0.06, 0.06)	0.9	-0.003 (-0.01, 0.01)	0.5

Traditional meat & vegetables

		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	N			*β* (95 % CI)			*Ptrend*[e]	*β* (95 % CI)	*P*
HFA Z-score									
Model 1[a]	6,756	Ref	-0.03 (-0.10, 0.04)	0.00 (-0.06, 0.07)	0.00 (-0.07, 0.07)	-0.01 (-0.08, 0.05)	0.9	0.002 (-0.01, 0.02)	0.7
Model 2[b]	6,756	Ref	-0.03 (-0.09, 0.04)	0.00 (-0.07, 0.07)	0.00 (-0.06, 0.07)	-0.02 (-0.08, 0.05)	0.9	0.002 (-0.01, 0.01)	0.8
Model 3[c]	6,756	Ref	-0.03 (-0.09, 0.04)	0.00 (-0.06, 0.07)	0.00 (-0.06, 0.07)	-0.01 (-0.08, 0.05)	0.9	0.002 (-0.01, 0.02)	0.7
WFA Z-score									
Model 1[a]	6,745	Ref	0.02 (-0.04, 0.07)	-0.01 (-0.07, 0.04)	-0.03 (-0.08,0.03)	0.01 (-0.05, 0.06)	0.6	0.00 (-0.01, 0.01)	0.9
Model 2[b]	6,745	Ref	0.02 (-0.04, 0.07)	-0.01 (-0.07, 0.04)	-0.02 (-0.08, 0.03)	0.00 (-0.05, 006)	0.6	0.00 (-0.01, 0.01)	0.9
Model 3[c]	6,745	Ref	0.02 (-0.04, 0.07)	-0.01 (-0.07, 0.04)	-0.02 (-0.08, 0.03)	0.00 (-0.05, 006)	0.7	0.00 (-0.01, 0.02)	0.7

[a] Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), and child height in the WFA models and paternal height in the HFA models.

[b] With additional adjustment for offspring birth weight as a mediator.

[c] With additional adjustment offspring birth weight and gestational weight gain as mediators

[e] *P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; Ref, reference category; Q, quintile.

Table 35. Association between maternal dietary patterns in pregnancy and offspring low height-for-age (LHFA) and low weight-for-age (LWFA) Z-scores at age 7.5 years in the ALSPAC study using dataset with multiple imputed values for covariates with missing data

				Modern health conscious					
		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	cases/N			OR (95 % CI)			*Ptrend*[e]	OR (95 % CI)	*P*
LHFA (≤2 SD)									
Model 1[a]	136/6,756	Ref	0.98 (0.59, 1.69)	0.99(0.59, 1.69)	0.92 (0.52, 1.62)	0.74 (0.40, 1.38)	0.4	0.96 (0.88, 1.06)	0.5
Model 2[b]	136/6,756	Ref	1.01 (0.61, 1.68)	0.99 (0.58, 1.69)	0.94 (0.53, 1.65)	0.77 (0.42, 1.44)	0.4	0.97 (0.88, 1.07)	0.5
Model 3[c]	136/6,756	Ref	1.00 (0.60, 1.67)	0.99 (0.58, 1.69)	0.94 (0.53, 1.65)	0.77 (0.42, 1.43)	0.4	0.97 (0.88, 1.07)	0.5
LWFA (≤2 SD)									
Model 1[a]	105/6,745	Ref	0.72 (0.37, 1.43)	1.16 (0.61, 2.22)	0.74 (0.35, 1.56)	0.58 (0.26, 1.28)	0.3	0.94 (0.83, 1.06)	0.3
Model 2[b]	105/6,745	Ref	0.76 (0.38, 1.49)	1.15 (0.60, 2.22)	0.77 (0.37, 1.62)	0.61 (0.27, 1.37)	0.3	0.95 (0.84, 1.08)	0.4
Model 3[c]	105/6,745	Ref	0.76 (0.38, 1.51)	1.17 (0.61, 2.25)	0.77 (0.37, 1.63)	0.62 (0.28, 1.37)	0.3	0.95 (0.84, 1.08)	0.45
				Traditional meat & vegetables					
		Q1	**Q2**	**Q3**	**Q4**	**Q5**		**Per 1 unit increase**	
	cases/N			OR (95 % CI)			*Ptrend*[e]	OR (95 % CI)	*P*
LHFA (≤2 SD)									
Model 1[a]	136/6,756	Ref	1.23 (0.74, 2.02)	0.77 (0.44, 1.36)	0.74 (0.42, 1.32)	1.01 (0.59,1.71)	0.4	0.97 (0.87, 1.08)	0.6
Model 2[b]	136/6,756	Ref	1.18 (0.71, 1.95)	0.77 (0.44, 1.35)	0.75 (0.42, 1.33)	0.99 (0.58, 1.68)	0.4	0.96 (0.86, 1.08)	0.5
Model 3[c]	136/6,756	Ref	1.18 (0.72, 1.96)	0.77 (0.44, 1.35)	0.74 (0.42, 1.33)	0.99 (0.58, 1.69)	0.4	0.96 (0.86, 1.08)	0.5
LWFA (≤2 SD)									
Model 1[a]	105/6,745	Ref	1.25 (0.61, 2.55)	1.36 (0.66, 2.83)	1.42 (0.69, 2.96)	1.39 (0.68, 2.84)	0.3	1.07 (0.93, 1.22)	0.37
Model 2[b]	105/6,745	Ref	1.26 (0.62, 2.58)	1.34 (0.65, 2.78)	1.36 (0.65, 2.83)	1.37 (0.67, 2.80)	0.4	1.05 (0.92, 1.21)	0.46
Model 3[c]	105/6,745	Ref	1.27 (0.62, 2.60)	1.36 (0.66,2.81)	1.37 (0.66, 2.86)	1.36 (0.66, 2.80)	0.4	1.05 (0.92, 1.21)	0.47

[a] Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), and child height in the WFA models and paternal height in the HFA models.

[b] With additional adjustment for offspring birth weight as a mediator.

[c] With additional adjustment offspring birth weight and gestational weight gain as mediators

[d] *P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; OR, odds ratio; Ref, reference category; Q, quintile.

Table 36. Multivariate* regression estimates from stratified analyses for associations between maternal dietary patterns in pregnancy with offspring height-for-age and weight-for-age at 7.5 years with testing for effect modification by breastfeeding status

	HFA Z-score		**WFA Z-score**		**LHFA (≤2 SD)**		**LWFA (≤2 SD)**	
	(n=4,281)		(n=5,702)		(cases/N= 77/4,281)		(cases/N= 79/5,702)	
	β (95 % CI)	*P***	*β* (95 % CI)	*P***	OR (95 % CI)	*P***	OR (95 % CI)	*P***
Modern health conscious (Per 1 unit increase)		0.9		0.6		0.5		0.7
Never breastfed	0.01 (-0.03, 0.04)		-0.01 (-0.03, 0.02)		1.06 (0.84, 1.35)		0.92 (0.67, 1.26)	
<3 months	0.01 (-0.01, 0.04)		0.01 (-0.01, 0.03)		1.01 (0.78, 1.30)		0.86 (0.65, 1.13)	
3-6 months	0.01 (-0.03, 0.04)		0.00 (-0.03, 0.02)		1.26 (0.92, 1.71)		1.08 (0.70, 1.66)	
>6 months	0.01 (-001, 0.03)		0.01 (-0.01, 0.02)		0.95 (0.77, 1.18)		1.00 (0.81, 1.24)	
Traditional meat & vegetables (Per 1 unit increase)		0.7		0.8		0.047		0.4
Never breastfed	0.00 (-0.04, 0.04)		0.00 (-0.03, 0.03)		0.83 (0.63, 1.07)		1.03 (0.75, 1.43)	
<3 months	-0.01 (-0.04, 0.02)		0.01 (-0.01, 0.03)		1.11 (0.85, 1.45)		0.90 (0.72, 1.29)	
3-6 months	0.00 (-0.04, 0.05)		-0.01 (-0.03, 0.02)		1.09 (0.74, 1.62)		1.01 (0.63, 1.64)	
>6 months	0.02 (-0.01, 0.04)		0.00 (-0.02, 0.02)		0.65 (0.48, 0.89)		1.31 (1.01, 1.71)	

*Adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, educational qualification (as a proxy for socioeconomic status), and child height in the WFA models and paternal height in the HFA models.

**Interaction P value, testing the null hypotheses that associations do not differ by breastfeeding status. CI, confidence interval; N, number; OR, odds ratio.

7.5 Discussion

In this analysis of a large prospective UK cohort of pregnant women, associations between maternal dietary patterns during pregnancy and offspring size at birth as well as child height and weight status at 7.5 years were examined. A dietary pattern, 'modern health conscious', characterised by high intakes of nuts, soya & pulses, fresh fruit, rice, pasta, dark bread and juice was found to be positively associated with both birth length and birth weight, whereas a dietary pattern, 'traditional meat & vegetables', characterised by high intakes of cabbage, root vegetables, other green vegetables, beans and peas, poultry and red meat was found to be associated with higher WFL Z-scores at birth. Neither of the dietary patterns were found to be associated with offspring HFA nor WFA Z-scores at 7.5 years in the complete-case adjusted analyses (N=4,497), however in analysis of the multiple imputed dataset (N=6,756) there appeared to be a positive significant association between the 'modern health conscious' and offspring HFA Z-scores. Mothers who scored highly on the 'traditional meat & vegetables' dietary pattern were shown to have significantly lower odds of having LHFA offspring although this result should be treated with caution as a potential chance finding arising from multiple testing (P_{trend}=0.02) and in the analysis of the multiple imputed dataset this relationship was lost (P_{trend}=0.4).

7.5.1 Dietary patterns in pregnancy

Only two distinct dietary patterns were identified for this analysis and as opposed to other studies assessing offspring size at birth there was no clear 'unhealthy' dietary pattern derived in this cohort. This could be explained by the fact that those participating in follow-up are likely to be more health conscious and might therefore be a more homogenous sample in terms of dietary habit, hence the two relatively healthy dietary patterns observed in this analysis. This is in agreement with Cole et al. (2009) and van den Broek (2015), both studies with longer follow-up of child growth, that similarly derived dietary patterns that had high factor loadings with healthy foods such as fish, fruit, vegetable, nuts, soy and fibre.

7.5.2 Maternal dietary patterns and size at birth

7.5.2.1 Comparison with previous ALSPAC findings

Associations between maternal dietary patterns and birth weight (g) have previously been explored in this cohort. In agreement with results from this analysis, Northstone et al. (2008) found in their analysis of the full cohort of ALSPAC mothers with dietary information and birth data available (N=12,053) that mothers with a higher ‘Health conscious’ dietary pattern scores had babies born 35 g heavier (95% CI: 25.5, 44.5, $P<0.05$). Apart from using energy adjusted dietary data, no adjustments were made for confounders, yet the size of the effect is still much higher than the crude change in birth weight of 7 g for the continuous ‘modern health conscious’ dietary pattern exposure observed in our study. They did not exclude preterm births however and it could be that the size of the association was influenced by this as mothers who give birth to preterm births may have a poorer nutritional status.

7.5.2.2 Comparison with CARE study findings (Chapter 6)

Attempts were made to facilitate between study comparison by the use of a common food grouping for the PCA and statistical treatment of data. However, despite being of the same prospective cohort design, they were both different in terms of setting and dietary assessment methods. PCA is a data driven approach and therefore any dietary pattern derived will be sample specific and may therefore not be transferable across populations.

Only two distinct components were derived from the PCA in comparison to the four in the CARE study analysis which, as highlighted in the section above, may be a result of a more homogenous sample in terms of dietary behaviours rather than the smaller number of food groups entered into the PCA. The two dietary patterns derived for the ALSPAC study sample shared some commonalities with those derived for the CARE cohort. In particular, the ‘fruit & wholegrains’ and the ‘modern health conscious’ patterns both had high positive correlations with fruits and unrefined grains and negative correlations with refined grains, chips, roast potatoes and all meats. They also both had weak correlations with all vegetables apart from salad which showed a moderate positive correlation. The ‘modern health conscious’ dietary pattern additionally had high correlations with nuts, soya, pulses, pasta and rice. As opposed to findings from the CARE study, there was a consistent positive association between both the ‘modern health conscious’ component and offspring birth length and weight as well as the ‘traditional health conscious’ pattern and offspring WFL Z-scores at birth, even after adjustment for important confounders and mediators. In this analysis there was no evidence of effect modification by maternal pre-pregnancy BMI status, whereas in CARE only a significantly lowered risk of having offspring born SGA was found in mothers with higher ‘fruit & wholegrains’ scores who entered pregnancy with a healthy BMI (<25 kg/m^2) (OR: 0.8, 95% CI: 0.66, 0.96, interaction $P=0.03$). Neither of the dietary patterns in the ALSPAC analyses were associated with LBW nor HBW, but as with the CARE data (SGA and LGA) this could be due to a lack of power caused by the low prevalence of these outcomes in the study samples.

7.5.3 Maternal dietary patterns and offspring child growth outcomes

As highlighted earlier, only four studies were identified which investigated associations between maternal dietary patterns in pregnancy in relation to infant and/or child growth. One of these took place in the UK at around the same time period as the ALSPAC using data on 198 pregnant women. From their PCA on 49 food groups Cole et al. (2009) derived one ‘prudent’ dietary pattern in the second trimester similar to the ‘modern health conscious’ component in this study, characterised by high intakes of fruit, vegetables, wholemeal bread, rice, and pasta and low intakes of processed foods, which was found to be significantly associated with offspring lean mass at 9 years (656.0 g increase per 1 SD increase in the ‘prudent’ score; 95% CI: 304.3, 1007.7) but not fat mass. Discrepancies between this study’s findings and theirs is most likely due to improper adjustment for confounders by Cole et al. (2009). In their investigation they only adjusted for maternal age and child gender and considering the longer follow up of 9 years it is likely a multitude of factors will have influenced the association increasing the risk of residual confounding. van den Broek et al. (2015) on the other hand found in their study of 2,520 mother-child pairs, that following adjustment for a range of confounders, the significant association between a more health conscious dietary pattern in the first half of pregnancy, with high intakes of nuts, soy, high-fibre cereals, fruits and fish, and offspring FFM at 6 years was lost. Fernandez-Barres et al. (2016) found no significant associations between mothers with higher MD scores and offspring BMI Z-scores nor overweight or obesity at 4 years in a sample of 1,827 pregnant women. They did however observe a modest significant association between increasing rMED scores and offspring waist circumference where compared to mothers in the lowest tertile category, mothers in the highest rMED tertile category had children with a 0.62 cm lower waist circumference (95% CI: -1.10, -0.14, P_{trend}=0.009). Similarly to this study, the inclusion of mediators such as birth weight did not alter results and neither did analyses stratified by breastfeeding status. Fernandez-Barres et al. (2016) additionally adjusted for child diet at 4 years with no significant confounding effect, whereas van den Broek et al. (2015) included offspring TV watching at 2 years as well as sports participation at 6 years with no change in results (van den Broek et al., 2015).

There was no strong evidence of mediation by birth weight. This could be due to the fact that pregnancies delivered preterm were excluded. The majority of preterm babies are also born with a lower birth weight and could therefore be exposed to catch-up growth which has been suggested to be a risk factor of child overweight status (Ong et al., 2000).

7.5.4 Strengths & limitations

7.5.4.1 Study sample

This analysis used data from a large prospective birth cohort representing 47% of the original study population. The sample size allowed for a better assessment of effect modification based on existing evidence to explain the mechanisms underlying any observed associations. However, the sample used to analyse associations with child height outcomes was considerably smaller due to missing data on paternal height. Therefore, when examining the association between the ‘modern health conscious’ dietary pattern and offspring HFA Z-scores, lack of statistical power may explain the difference in the results between the complete data and multiple imputation models (Table 32 & Table 34). In addition, as outlined in section 7.5.1 above and evidenced from Table 24, differences between the mothers included in this analysis and those excluded were apparent which could affect the generalizability of results. Furthermore, as with the CARE study, the prevalence of LBW babies (<2,500 g) in this sample (1.4%) was low, most likely a result of including term births only. But even for the original cohort, the percentage of LBW was small (4.9%) raising the possibility that women who are more likely to have LBW babies were less likely to participate in this study.

7.5.4.2 Dietary assessment

Diet in this cohort was assessed using a 44 item self-administered FFQ. Issues concerning the use of FFQs as a dietary exposure measure has been highlighted in Chapter 2, section 2.4.2.6. An FFQ is only as good as its foods listed and with quite a low number of food items present in this FFQ, it could be argued that it may not be a very accurate measure of total diet compared to more detailed methods of dietary assessment such as weighed food diaries. In addition, no guidance on food portions was provided, e.g. by the use of photos or examples, but rather assumptions were made by researchers which again might not reflect true intakes. Furthermore, the FFQ was only partly validated (maternal fish consumption was assessed against concentrations of n-3 LC-PUFA26 and mercury concentrations in maternal blood) (Daniels et al., 2004), albeit in a sub-sample of the original pregnancy cohort, and therefore it is unclear how valid a tool it is for measuring total dietary intake in pregnancy. Finally, as with the CARE study, dietary intake was only assessed at one time point (trimester 3) and does therefore not reflect dietary intake throughout pregnancy however previous studies which have assessed dietary change in pregnancy have found little variation in pregnant women's eating habits across trimesters (Rifas-Shiman et al., 2006; Cole, Z. et al., 2013)

7.5.4.3 Dietary pattern analysis

The strengths and limitations of using PCA to derive dietary patterns as well as the use of energy adjusted dietary data have been discussed both in Chapter 2 as well as section 6.5.3.3 of Chapter 6.

7.5.4.4 Outcome measures

A strength of this study was the use of objective measures of child height and weight at 7.5 years which were done by trained skilled staff using standardised methods. In addition, the use of sex and age specific Z-scores allowed for the assessment of the growth of the offspring in comparison to the WHO reference population. The WHO growth reference for school aged children is intended to serve as growth standards, describing how children should grow. In contrast, many national charts are descriptive, describing how children in the reference population did grow. The use of a national reference might have been more suitable allowing for comparison of UK children to a reference group of UK children. However to enable between country comparison the WHO reference, which is based on samples from multiple countries, was deemed more appropriate. All child weight outcome regression models were additionally adjusted for child height to ensure that any association with weight was independent of height. Although a customised birth weight centile was not used, as was the case for the CARE analysis, LBW and HBW outcomes were defined both of which serve as important indicators of future health.

7.5.4.5 Residual confounding

As with the CARE study, because this is not a RCT, there is a possibility that residual confounding may be contributing to the apparent positive associations between mothers who scored highly on the 'modern health conscious' dietary pattern and offspring size at birth as well as HFA Z-scores at 7.5 years. In addition, it stands to reason that for outcomes such as child growth any relationship will be more difficult to ascertain due to participant selection bias as well as the higher potential for confounding along the causal pathway. The influence of breastfeeding as well as maternal pre-pregnancy BMI was assessed and no clear evidence of effect modification was apparent. Similarly offspring birth weight and maternal GWG were assessed as mediators by adding them to the models which did not appear to have a great influence on findings. That birth weight was not found to be a mediator of child height and weight could be due to the fact that pregnancies delivered preterm were excluded. The majority of preterm babies are also born with a lower birth weight and could therefore be exposed to catch-up growth which has been suggested to be a risk factor of child overweight status (Ong et al., 2000). Although adjustments were made for many relevant confounders; no adjustments were made for child factors which could influence child growth such as diet and physical activity.

Both dietary patterns exhibited healthy traits yet the ‘modern health conscious’ component appeared to have the strongest association with offspring growth outcomes. This could indicate that other characteristics of women with high ‘modern health conscious’ dietary pattern scores, rather than the dietary components, drive the associations observed. Although attempts were made to minimise such residual confounding by controlling for known confounders in the analyses.

7.6 Implications for research and practice

Even though dietary patterns from PCA are subject to consumption patterns in the population under study and may therefore not be transferable across populations they represent real dietary habits and patterns of food choice and are therefore of direct relevance to the formulation of future public health messages. Health promotion messages focusing on healthy dietary patterns rather than individual nutrients are more realistic to implement, and when communicated to women before, as well as during their pregnancy are vital for improving the health of the next generation. In this analysis a ‘modern health conscious’ dietary pattern characterised by high intakes of nuts, soya & pulses, fresh fruit, rice, pasta, dark bread and juice was found to be positively associated with both birth weight and birth length with some evidence for longer term positive associations with child height-for-age. These results add to the evidence that early life nutritional factors might have an influence on growth in early childhood. The foods prevalent in this dietary pattern are also prevalent in dietary guidelines for healthy eating and therefore, findings of this analysis support the current dietary guidelines for pregnant women, which aim to ensure optimal health for both the mother and the baby. As the evidence in this area is still very limited in particular with reference to child growth outcomes, further work to replicate these results is needed in order to ensure mothers are given the proper dietary guidance for optimal child growth. Intervention studies rather than observational studies would be of particular interest in order to establish possible causal links.

A randomized controlled trial of high dietary iron intake combined with vitamin C at mealtimes during early pregnancy could provide some important insights.

7.7 Conclusion

The findings in this chapter suggest that mothers who adopted a more health conscious diet in pregnancy, characterised by high intakes of nuts, soya & pulses, fresh fruit, rice, pasta, dark bread and juice had had babies born with higher birth weight and birth length whereas mothers following a more traditional dietary pattern had babies born with higher WFL Z-scores. Some trend was shown for positive links with later child height however more research is needed to explore the longer term effects of diet in pregnancy on offspring growth.

In the next chapter, the association is further explored using data from a large nationally representative birth cohort.

8 Maternal dietary patterns in pregnancy and offspring growth outcomes: the DNBC

Work from this chapter has been presented at a Rank Prize symposium on maternal nutrition and is currently in submission process.

8.1 Chapter overview

Using data from the Danish National Birth Cohort, this study aimed to assess the effect of maternal dietary patterns during pregnancy on offspring size at birth and child height and weight at 7 years.

Dietary data were collected in the second trimester of pregnancy using a 360 item self-reported food frequency questionnaire. The food items were aggregated into 65 food groups and principal component analysis was used to derive dietary patterns. Only mothers with data available on child height and weight at 7 year follow-up were included (n=31,150). Information on delivery details was obtained from hospital maternity records. Offspring growth was expressed as age specific weight (WFA) and height (HFA) Z-scores using the World Health Organisation growth reference. Z-score cut-off points of <2 SD were used to classify low weight-for-age (LWFA) and low height-for-age (LHFA). These were related to dietary patterns expressed as quintile scores in multivariable regression models, taking into account known confounders and assessing possible mediation by birth weight and gestational weight gain as well as effect modification by breastfeeding.

Seven dietary patterns were derived and identified as: Vegetables/Prudent, Alcohol, Western, Nordic, Seafood, Sweets and Rice/Pasta/Poultry. The strongest associations with offspring growth were found for women with a high Nordic dietary pattern score, characterised by high intakes of wholegrain, hard cheese and Nordic berries and lower intakes of white bread, cakes, snacks and soft drinks. In adjusted analyses, compared to those in the lowest quintile score, those in the highest Nordic dietary pattern quintile had offspring with a 42 g higher birth weight (95% CI: 25.6, 58.9; $P_{trend}<0.0001$). This association was strengthened further once adjustments for GWG as a mediator was made (44 g, 95% CI: 25.6, 63.1; $P_{trend}<0.0001$). Positive modest associations were also observed for birth length but not offspring WFL Z-scores. It was the only dietary pattern found to be significantly associated with offspring risk of HBW. Compared to women in the lowest quintile score, women in the highest quintile score had significantly higher odds of having a HBW baby (OR: 1.20, 95% CI: 0.99, 1.46, $P_{trend}=0.03$).

In adjusted analyses, compared to those in the lowest quintile score, those in the highest Nordic dietary pattern quintile had children with higher HFA and WFA z-scores at 7 years (0.12, 95% CI: 0.08, 0.15; P_{trend}<0.0001 and 0.05, 95%CI: 0.03, 0.08; P_{trend}<0.0001 respectively). It was the only dietary pattern found to have a significant association with LWFA and LHFA. Compared to women in the lowest quintile score, women in the highest quintile score had significantly lower odds of having a LHFA child (OR: 0.72, 95% CI: 0.53, 0.96, P_{trend}=0.009) and LWFA child (OR: 0.74, 95% CI: 0.55, 0.99, P_{trend}=0.02).

8.2 Introduction

Chapter 7 explored dietary patterns in pregnancy in relation to both offspring size at birth as well as child height and weight growth outcomes at 7.5 years in the ALSPAC cohort. The strongest association was found for mothers who scored highly on a ‘modern health conscious’ dietary pattern and offspring size at birth with a suggestive trend for longer lasting positive effects on child HFA. To further establish evidence for an association between maternal diet in pregnancy and its possible effect on offspring growth it is necessary to replicate this research in a different setting. As evidenced from the literature reviewed associations with offspring size at birth have been explored in a range of settings, including analyses of large datasets from Scandinavian cohorts. Hillesund et al. (2014) explored the association between a New Nordic Diet (NND), characterised by high intakes of fruits and vegetables, whole grains, potatoes, fish, game, milk and water, and fetal growth in 66,597 mothers from the Norwegian Mother and Child Cohort Study (MoBa). They found in adjusted analyses that mothers who scored highly on the NND had 8% reduced odds of having an infant born SGA (95% CI: 0.86, 0.99, P=0.025) and 7% higher odds of the baby being born LGA (95% CI: 1.00, 1.15; P=0.048) compared to mothers with low scores. They also found the NND facilitated optimal GWG in normal-weight women thus indicating that a Nordic diet may be beneficial to maternal and fetal health. A similar but stronger relationship has been found in a study of 44,612 pregnant women from the DNBC, where a ‘health conscious’ dietary pattern characterised by high intakes of vegetables, tomatoes, green leafy vegetables, fruits, fish and poultry was associated with 26% lower odds of having infants born SGA (95% CI:0.64, 0.86, P=0.0001). Several important confounders however were missing from the latter investigation including energy intake.

8.2.1 Current pregnancy dietary guidelines in Denmark

The current advice for pregnant women in Denmark is to follow the official dietary guidelines for the general population which consist of the 10 recommendations outlined below (Ministry of Environment and Food, 2015):

1) Eat a variety of foods, but not too much, and be physically active
2) Eat fruits and many vegetables
3) Eat more fish
4) Choose whole grains
5) Choose lean meats and lean cold meats
6) Choose low fat dairy products
7) Eat less saturated fat
8) Eat foods with less salt
9) Eat less sugar
10) Drink water

In addition to the 10 dietary recommendations, advice has been put in place regarding consumption of certain food groups during pregnancy (Sundhedsstyrelsen, 2015) which can be found in Table 37 below. As with the UK dietary guidelines for pregnant women (see Chapter 1, Table 1), pregnant women are being advised to limit their intake of predatory fish, tuna (1 can vs. 4 cans in the UK) and cod liver oil. As opposed to the UK guidelines which advise a maximum intake of 140 g fatty fish, there is no limit to the amount of fatty fish consumption. Advice on meat and protein consumption is similar although the Danish guidelines appear less strict, with the allowance of liver pate in small doses. In terms of dairy products, the recommendation is to opt for pasteurised products with no restrictions set in place for mould-ripened and blue-veined cheeses which in the UK are prohibited during pregnancy as they contain listeria bacteria that can cause listeriosis with potential consequences to both maternal and fetal health. Recommendations are also set in place for caffeine and alcohol, with pregnant women being advised to consume no more than 300 mg caffeine; 100 mg more than the current advice in the UK; and to avoid alcohol completely.

Table 37. Food based dietary guidelines in Denmark: additional recommendations for pregnant women

Foods	Recommendation for general population	Additional recommendations for pregnant women
Fruit and vegetables	6 pieces/portions per day (half of which should be veg; 1 portion=100 g)	Same
Fish	2 portions of fish per week (350 g/wk if which 200g should be fatty)	Limit intake of predatory fish (max 100g - most common include tuna and swordfish)

		1 can of tuna per week Only 125 g of Baltic sea salmon Avoid smoked fish and sushi- cook all fish Avoid cod liver oil (contains large quantities of Vitamin A)
Starchy foods	Eat 75 g wholegrain per day (e.g. 1 slice of rye bread or 2 dl porridge oats)	Same
Meat and Protein	Max 500 g of meat per week (beef, veal, lamb or pork) - equivalent of 2-3 dinners and some toppings. Choose poultry, fish, eggs, veg or beans as alternative for the remaining days. Choose lean meat (max 10% fat)	Avoid liver Liver pates and other pates are fine in small doses
Dairy and alternatives	Choose low fat options - 1/4-1/2 litre dairy products per day	Choose pasteurised products
Oils and spreads	Eat less saturated fat Choose rapeseed oil and olive oil Choose soft vs. hard fat	Same
Salt	Eat food with less salt	Same
Foods high in sugar	Eat less sugar, particularly from soft drinks, sweets and cakes. Don't drink more than 0.5 litre soft drink/energy drink per week.	Same
Drinks	Replace soft drinks, alcohol, juice and cordial with water. 1-1.5 litres per day if weather is not too hot. Coffee and tea count toward intake.	Don't drink more than 3 cups of coffee/day (300 mg caffeine) and restrict intakes of other beverages which contain caffeine such as cola and tea Avoid alcohol

8.2.2 Aim & objectives

The main aim of this chapter was to explore the relationship between maternal dietary patterns in pregnancy and offspring size at birth and later child height and weight growth outcomes using data from a large nationally representative sample of pregnant women in Denmark. The following objectives were addressed:

1. Characterise dietary patterns in a Danish cohort of pregnant women
2. Investigate associations between maternal dietary patterns in pregnancy and size at birth
3. Explore the role of maternal pre-pregnancy BMI status as an effect modifier on the association investigated in objective 2
4. Explore the role of GWG as a mediator of the association investigated in objective 2
5. Investigate associations between maternal dietary patterns in pregnancy and child height and weight
6. Explore the role of breastfeeding status as an effect modifier on the association investigated in objective 5
7. Explore the role(s) of GWG and birth weight as mediators of the association investigated in objective 5

8.3 Methods

The DNBC is a prospective national birth cohort study which was set up to investigate pregnancy complications and diseases in offspring as a function of factors operating in pregnancy and early life. Details of the DNBC, including design, setting, dietary assessment, outcome measures and assessment of participant characteristics can be found in Chapter 3. Below are details of the study sample available for analysis, power calculation and statistical methods including details of the dietary pattern analysis.

8.3.1 Mother-offspring pairs available for analysis

Only singleton live births (n=92,668) with maternal dietary data (n=65,482) were included. Mothers who did not participate in the 7 year follow-up were excluded (n=22,633). In addition, mothers whose babies had a gestational age at delivery of <259 days and >294 days, (i.e. three weeks before and two weeks after expected date of delivery), were excluded in order to avoid strata with few observations and to exclude infants with pathologies that may be irrelevant to the purpose of this analysis. A further 67 records were excluded due to extremely low energy intakes (<5000 kJ/day). Finally children with implausible values or missing data on their height and/or weight measurements at the 7 year follow-up and those with no data on age at the time of measurement (age is needed to create the weight-for-age and height-for age Z-scores) were excluded, leaving a final sample size of 31,150 mother-child pairs for analysis. Figure 16 shows a flowchart of the DNBC participants included in this analysis.

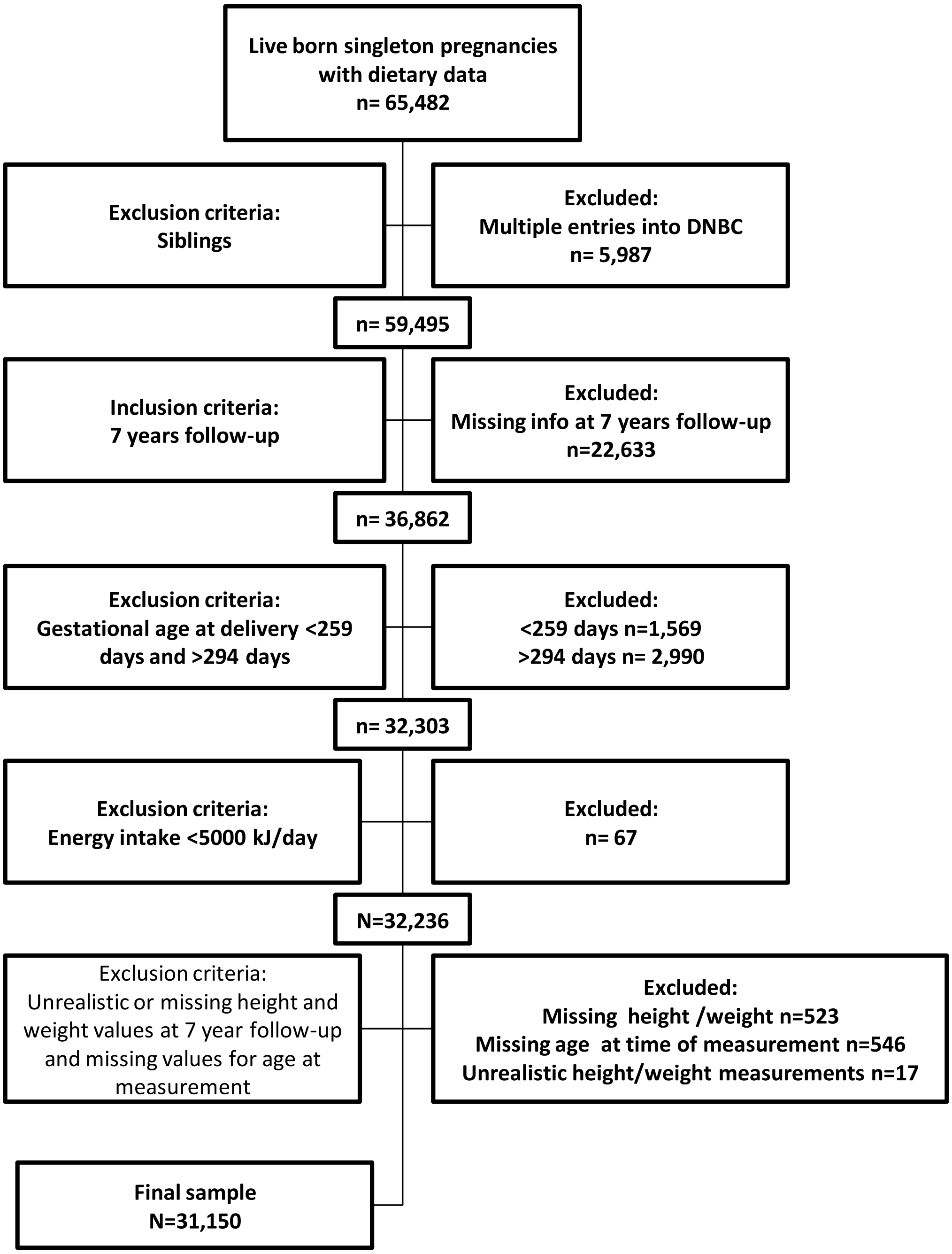

Figure 16. DNBC participant flow chart

8.3.2 The healthy Nordic food index (HNFI)

As this is a Nordic population the derived components were assessed against a Nordic food index. Traditionally, a healthy Nordic diet is characterised by high intakes of foods such as berries, cabbages, apples, pears, root vegetables, oats and rye which have all been ascribed certain health benefits (Olsen, A. et al., 2011). Olsen et al. (2011) have constructed a healthy Nordic food index (HNFI) based on intakes of the following health promoting foods: fish/shellfish, cabbages, whole grain rye (eaten as rye bread), whole grain oats (eaten as oatmeal), apples and pears, and root vegetables (Olsen et al., 2011). This index was derived in a similar style to the Mediterranean diet score developed by Trichopoulou et al. (Trichopoulou et al., 1995). There was no information on oatmeal intake and could therefore not include this in the index. In order to adapt the HNFI to the food data, the whole grain rye category included consumption of a range of whole grain bread products not just rye, as there was no separate information on the latter. This approach has also been used in a recent study investigating the association between the HNFI and mortality (Roswall et al., 2015). The following 5 food groups were each assigned values of 0 or 1 using their respective medians as cut-offs, giving 0 for below median intakes and 1 for above: dark bread (including rye); cabbages; Nordic fruit (including plums, pears, apples and rhubarb); root vegetables and fish/shellfish. This gave a range of 0 (low adherence) to 5 (high adherence).

8.3.3 Statistical power calculation

Comparing the birth weight (g) of babies born to mothers in the lowest dietary pattern quintile category with those in the highest quintile category, and using the SD of 489 g of birth weight for the total sample, this study had 85% power to detect a difference of just over 25 g (representing quite a small size difference) in birth weight for a two sample t-test at $P<0.05$.

8.3.4 Statistical analysis

All analyses were carried out using the Statistical Analyses System software (release 9.4; SAS Institute, Cary, NC).

8.3.4.1 PCA

The PCA method used here has been described in detail elsewhere (Rasmussen et al., 2014). Briefly, PCA with varimax rotation was performed on the 65 energy adjusted food items. The number of factors to retain was decided on the basis of i) scree plot of eigenvalues, ii) eigenvalues above 1 and iii) interpretability of the (rotated) factors. Scores were created for each participant for each of the components identified; these were split into fifths to allow for non-linear associations.

8.3.4.2 Univariable analysis

Characteristics of mothers according the seven dietary dietary pattern quintiles were compared in univariable analyses using the one-way analysis of variance (ANOVA) for normally distributed continuous variables and the Kruskal-Wallis test for non-normally distributed continuous and ordinal variables and the χ2 for nominal categorical variables.

The Spearman's rank correlation coefficients were used to assess any association between the dietary patterns identified from the PCA and the HNFI.

8.3.4.3 Multivariable analysis

Regression analyses were undertaken using the categories defined by the quintiles of dietary pattern score with the lowest quintile score as the referent. Any association with continuous and dichotomous offspring growth outcomes were assessed in multivariable linear and logistic regression models respectively. All offspring size at birth models were adjusted for the following potential confounders identified a priori: maternal pre-pregnancy BMI (18.5, 18.6–24.9, 25–29.9, 30–35, >35 in kg/m2; 5.1% missing), age (<20, 20-39, ≥40; 0 % missing), parity (nulli/multiparous; 3.7 % missing), smoking in pregnancy (smoker/non-smoker; 0.5 % missing), parental SES (high, medium, skilled, unskilled, student, unemployed; 10.8 % missing), gestational age (weeks; 0 % missing) and infant's sex (0 % missing; with the exception of WFL Z-scores which takes into account infant's sex). Models for the sex-and-age specific HFA and WFA offspring growth outcomes at 7 years were similarly adjusted for maternal pre-pregnancy BMI, age, parity, ethnicity, smoking in pregnancy, parental SES and child height (cm) in the WFA models and paternal height (cm; 13 % missing) in the HFA models.Tests for a linear trend (P_{trend}) across the dietary pattern quintiles were done by entering the median factor score from each quintile into the models.

8.3.4.4 Mediation & effect modification

Covariates thought to be on the causal pathway (birth weight and gestational weight gain) were initially excluded from the models and were entered in additional models to assess mediation. Breastfeeding status has been recognised as a possible "programmer" of childhood growth (Singhal and Lanigan, 2007a) and it was therefore assessed as an effect modifier by including an interaction term in the confounder adjusted models. As with the CARE and ALSPAC analyses, maternal BMI was assessed as an effect modifier of the effect of maternal diet on offspring size at birth and stratified analyses have been presented for women who reported a healthy pre-pregnancy BMI at enrolment (<25 kg/m2) and those who were classed as overweight or obese (≥25 kg/m2).

8.3.4.5 Sensitivity analyses

In order to explore whether missing data could have led to biased estimates (e.g. paternal height had 4,155 missing values), multiple imputation was performed using SAS PROC MI to impute missing values for variables included in the main analysis models for the final sample of mother-child pairs (for details on MI see Chapter 3 section 3.10.5.1).

8.4 Results

A total of 31,150 mother-child pairs were included in the final analysis representing 48% of the DNBC cohort of mothers with live born singleton pregnancies and dietary data recorded. The study sample was predominantly of Caucasian origin (~99%) with a mean maternal age of 30.5 years (SD 4.2) and a mean pre-pregnancy BMI (kg/m2) of 23.3 (SD 3.9).

8.4.1 Maternal dietary patterns

Seven components were derived from the PCA; explaining 30.5% of the variance in the dietary data (Rasmussen et al., 2014). These components have been named based on the food items with the highest factor correlations (see **Table 38**). The components have been described in detail by Rasmussen et al. (2014), but briefly, component one was labelled ‘Alcohol’ because of the high correlations with beer, liquor and wine. The second component, labelled ‘Vegetables/prudent’, had high correlations with all vegetables (except Asian vegetables). The third component was labelled ‘Western’ as the predominant foods with high loadings were processed, including French fries, meat products, white bread, butter, dressings and margarine. The fourth component was characterised by high correlations with all fish products and it was therefore labelled ‘Seafood’. The fifth component was labelled ‘Nordic’ because of the high correlations with dark bread (including rye bread), hard cheese and Nordic berries. The sixth component was characterised by high correlations with foods with high sugar content and was labelled ‘Sweets’. Finally, the seventh component ‘Rice/pasta/poultry’ (RPP) correlated highly with rice, pasta and poultry.

Table 38. Factor correlations of the 65 food items in the 7 dietary components obtained using PCA on energy adjusted data

Food item	**Alcohol**	**Vegetables/ prudent**	**Western**	**Seafood**	**Nordic**	**Sweets**	**RPP**
% Variance explained	6.4%	5.4%	4.9%	4.6%	3.2%	3.2%	3.0%
Vegetables							

Asian	0.020	0.058	0.070	**0.345**	-0.057	0.018	0.095
Cabbage	0.064	**0.620**	0.145	**0.246**	**0.204**	-0.137	0.148
Corn	0.014	**0.584**	0.008	0.130	0.032	0.158	0.095
Mushroom	0.056	**0.594**	0.017	0.229	0.051	0.033	**0.216**
Onion	0.061	**0.611**	0.145	**0.383**	0.165	0.021	0.199
Root	**0.705**	**0.440**	0.051	0.162	0.169	0.052	0.076
Salad	0.008	**0.584**	-0.120	**0.252**	0.061	0.128	0.114
Tomato	0.032	**0.582**	0.035	**0.391**	0.110	0.067	**0.225**
Other	0.057	**0.746**	-0.139	**0.366**	**0.206**	0.066	0.185
Potatoes							
Chips	0.079	-0.037	**0.366**	0.021	**-0.263**	**0.324**	0.194
Potatoes	0.026	**0.203**	**0.527**	**0.212**	0.139	0.068	-0.167
Nuts							
Nuts	0.074	0.115	-0.065	**0.208**	0.116	0.127	0.029
Pulses/legumes							
Legumes	0.062	**0.662**	0.108	0.136	0.138	-0.064	0.136
Soya	**0.783**	0.071	0.053	0.108	0.020	0.125	0.009
Fruit & Berries							
Banana	-0.005	0.106	-0.132	0.054	**0.366**	0.025	0.199
Berries	**0.389**	0.121	0.047	**0.218**	0.184	0.163	-0.079
Citrus	0.032	0.012	-0.064	0.079	**0.256**	-0.118	0.140
Dried	0.123	0.150	-0.178	**0.223**	**0.356**	-0.026	0.107
Nordic fruit	0.028	0.175	-0.149	0.068	**0.430**	-0.036	0.169
Other	0.013	**0.313**	-0.131	0.171	0.082	0.185	0.089
Meat							
Beef/veal	0.050	0.173	**0.479**	**0.315**	0.011	0.152	**0.273**
Lamb	0.025	0.162	0.023	**0.501**	0.065	0.033	0.034
Meat toppings	0.013	-0.057	**0.495**	-0.017	**0.313**	0.119	0.030
Processed	0.016	-0.007	**0.586**	0.099	-0.046	0.149	0.046
Offal	0.041	0.044	**0.238**	**0.245**	0.046	-0.062	-0.014
Pork	0.024	0.008	**0.661**	0.046	0.066	0.097	0.001
Poultry	0.003	**0.205**	0.028	0.297	0.021	0.067	**0.496**
Ice cream/sweets/cakes							
Sweets	0.070	-0.002	0.054	-0.009	-0.085	**0.514**	0.172
Chocolate	0.001	-0.048	0.024	0.026	0.069	**0.491**	0.036
Ice cream	**0.242**	0.062	0.019	0.074	-0.009	**0.387**	0.021
Sugar/cakes/ biscuits	0.179	**0.230**	0.047	**0.229**	0.275	**0.451**	-0.087
Sweet spread	0.012	0.074	0.154	0.072	**0.316**	**0.342**	-0.034
Cereal products							
Unrefined grains	0.008	0.089	**0.200**	0.100	**0.640**	0.089	-0.009
Refined grains	0.008	-0.029	**0.446**	0.009	**0.272**	**0.465**	-0.085
Breakfast cereal	0.030	0.079	-0.071	**0.245**	**0.219**	-0.185	0.166
Pasta	-0.030	0.170	0.038	0.136	0.048	0.062	**0.635**
Rice	-0.009	0.190	0.060	0.178	0.086	0.011	**0.587**
Fats							

Butter	0.022	0.043	**0.327**	0.193	0.051	0.195	-0.159
Dressing/sauce	0.025	0.092	**0.482**	**0.267**	0.035	**0.237**	0.097
Margarine	0.031	-0.035	**0.417**	0.021	**0.250**	**0.433**	**-0.204**
Oil	0.029	**0.299**	-0.061	**0.490**	0.046	0.136	0.038
Fish							
Cold fish	0.038	0.131	**0.386**	**0.431**	**0.243**	-0.057	**0.227**
Lean fish	0.046	0.182	**0.234**	**0.535**	0.148	-0.033	0.154
Oily/fatty fish	0.023	**0.225**	-0.026	**0.549**	0.038	-0.021	0.194
Smoked fish	0.031	0.118	0.222	**0.433**	0.111	-0.058	0.179
Shellfish	0.020	0.121	0.185	**0.443**	-0.026	0.051	**0.245**
Beverages							
Beer	**0.928**	0.046	0.070	0.054	0.012	0.166	-0.039
Coffee	0.127	0.024	0.191	-0.039	0.113	0.029	**-0.243**
Juice	**0.231**	0.098	0.060	0.100	0.041	0.114	0.153
Spirits	**0.943**	0.035	0.040	0.018	0.006	0.168	-0.037
Soft drink-diet	**0.238**	0.005	0.090	-0.115	-0.097	0.111	0.158
Soft drink-sugar	**0.296**	0.056	0.105	0.046	-0.168	**0.294**	0.032
Tea	0.086	0.045	-0.074	0.145	**0.228**	0.043	-0.019
Water	0.059	**0.207**	-0.089	0.075	**0.286**	0.015	**0.283**
Wine	**0.878**	0.061	0.030	0.097	0.023	0.172	-0.040
Dairy products							
Cheese	0.029	0.073	-0.002	**0.280**	**0.220**	0.046	-0.065
Fresh cheese	0.008	0.133	0.053	**0.239**	**0.226**	0.045	0.057
Hard cheese	0.028	0.114	0.123	0.133	**0.402**	0.167	-0.022
Chocolate milk	0.271	-0.034	0.113	-0.041	-0.118	**0.216**	0.096
Fermented milk	-0.002	0.086	0.012	**0.310**	0.105	0.082	-0.082
Full fat milk	0.209	0.024	**0.220**	0.098	0.023	0.133	**-0.288**
Low fat milk	0.031	-0.016	0.092	-0.058	0.129	-0.127	**0.267**
Yoghurt	0.031	0.121	0.000	**0.325**	0.152	0.007	0.033
Snacks							
Snack	0.089	-0.022	**0.263**	-0.071	**-0.200**	**0.409**	0.078
Eggs							
Egg	0.138	**0.207**	**0.440**	**0.475**	0.140	0.194	0.059

*For a description of each food group please see Table 8, Chapter 3. Factor correlations above 0.2 are shown in bold.

As has been previously described, the food items entered into the PCA were aggregated into 14 main food groups: vegetables, potatoes, nuts, fruit, meat, ice cream/sweets/cakes, cereals, fats, fish, beverages, dairy, snacks, eggs and pulses/legumes. Table 39 presents the average daily intake of the food groups across dietary pattern quintiles. For clarity, the highest and lowest intakes across all dietary patterns have been highlighted in bold in the table below. For the ‘Alcohol’ component higher scores implied higher intakes of all food groups but cereal and fats where there was no clear trend in intakes. Apart from the beverages food group, where mothers in the highest quintile score had 1/3 higher intakes than mothers in the lowest quintile score, possibly explained by the high correlation with alcoholic beverages for this dietary pattern, increases in consumption of food groups across quintiles appeared modest compared to the other dietary patterns. As for the second component, ‘Vegetables/prudent’, higher scores resulted in higher intakes of all food groups but fat, where as with the first component, there was no clear trend in intakes. This component had not surprisingly the highest intakes of vegetables across all dietary patterns, with a median of 215 g in the highest quintile score, nearly 5 times higher than then median of 44 g in the lowest quintile category. Mothers in the highest quintile category also had the highest intake of legumes & pulses and the second highest intake of fruit, with a median of 229 g. Only modest increments were observed for other food groups such as meat and dairy. The third component, ‘Western’, was characterised by higher intakes of potatoes, legumes, meat, ice cream, cereal products, fats, fish, dairy and eggs and lower intakes of vegetables, nuts and fruit in the higher quintile categories. Mothers in the highest quintile category had the highest meat intake across all dietary patterns (120g) as well as the highest intakes of potatoes and eggs. For the ‘Seafood’ component higher scores implied higher intakes of all food groups. Mothers in the highest quintile had the highest fish intakes across all dietary patterns with a median of 43 g compared to a median of 9.9 g in the lowest quintile category. Similarly to the other dietary patterns, increments across dietary pattern quintile scores for food groups such as meat and dairy as well as fats and ice cream/sweets were modest. Similarly to the ‘Seafood’ dietary pattern, for the fifth component, ‘Nordic’, higher scores implied higher intakes of all food groups, particularly fruit and cereal products, where for fruit, mothers in the highest quintile category had nearly a four times higher intake compared to mothers in the lowest quintile category (244 g vs. 65 g). Similarly for cereal products, mothers in the highest quintile category had double the intake compared to mothers with the lowest quintile scores. For the sixth component, ‘Sweets’, higher scores resulted in higher intakes of vegetables, potatoes, nuts, meat, ice cream/sweets, cereal products, beverages and eggs and lower intakes of legumes and fish. There was no clear trend for the remaining food groups. Mothers in the highest quintile category of this component had the highest intakes of ice cream/sweets/cakes (75 g) compared to any of the other dietary patterns. Higher scores for the final component, ‘Rice/pasta/poultry’, implied higher intakes of all food groups apart from fats, potatoes and eggs, the latter of which there was no clear trend in intakes. Mothers with higher scores had lower intakes of potatoes and fats compared to mothers with lower scores.

As was the case for the ‘Seafood’ and the ‘Nordic’ dietary pattern, increments across quintile scores were modest for the majority of food groups.

Spearman’s correlation coefficient showed a correlation of 0.55 (*P*<0.0001) between the Nordic dietary pattern and the HNFI. The 6 other components were also assessed against the HNFI. The Sweets and Western dietary patterns showed the weakest correlations (r=-0.07 and 0.07 respectively, *P*<0.0001) and the Vegetable/prudent and Seafood dietary patterns the strongest (r=0.53 and 0.42 respectively, *P*<0.0001) (data not shown).

Table 39. Average intake of main food groups* (g/day) across dietary pattern quintile scores based on a FFQ administered at 25 weeks of pregnancy in the DNBC (N=31,150)

			Alcohol		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	78.7 (51.4, 120.6)	86.1 (57.6, 125.4)	94.8 (63.4, 138.6)	106.4 (70.6, 152.9)	129.5 (82.1, 206.5)
Potatoes	109.2 (69.7, 170.4)	110.3 (74.5, 166.0)	113.2 (76.9, 171.6)	116.2 (79.5, 176.3)	124.4 (85.7, 188.4)
Nuts	0 (0, 1.8)	0.6 (0, 1.8)	1.0 (0, 2.2)	1.3 (0, 2.6)	1.5 (0, 3.5)
Legumes/ pulses	4.8 (1.6, 10.1)	5.9 (2.4, 11.8)	6.8 (2.9, 13.4)	7.8 (3.4, 15.2)	9.9 (4.3, 20.0)
Fruit	97.2 (52.2, 224.6)	104.9 (66.2, 231.8)	121.1 (75.9, 240.8)	153.0 (82.0, 249.2)	189.6 (89.4, 260.6)
Meat	74.7 (54.1, 100.2)	76.1 (56.3, 100.3)	77.2 (56.2, 101.9)	79.2 (57.8, 105.2)	81.9 (59.3, 110.5)
Ice cream/ sweets/cakes	39.0 (23.8, 59.0)	37.7 (23.8, 55.7)	39.8 (25.0, 58.1)	41.7 (26.7, 59.8)	44.2 (28.3, 65.2)
Cereal products	294.8 (224.6, 374.3)	278.8 (216.8, 354.0)	276.5 (211.8, 348.7)	283.6 (221.3, 356.0)	287.2 (222.2, 363.0)
Fats	30.6 (18.9, 48.1)	27.8 (17.9, 42.3)	27.3 (17.9, 42.3)	28.3 (18.5, 42.4)	30.0 (19.3, 45.6)
Fish	18.4 (10.1, 30.1)	21.1 (12.1, 33.0)	22.9 (13.6, 35.3)	24.6 (14.6, 38.1)	27.8 (16.1, 42.2)
Beverages	**1471.1** **(1075.6, 1856.5)**	1607.6 (1214.5, 2016.7)	1753.2 (135.9, 2154.1)	1885.1 (1468.6, 2317.5)	**2129.1** **(1691.1, 2660.1)**
Dairy products	583.6 (295.3, 746.8)	611.8 (348.4, 808.2)	624.8 (384.8, 872.1)	654.7 (424.6, 946.7)	671.4 (430.1, 996.8)
Eggs	10.7 (6.8, 16.8)	12.3 (7.8, 18.6)	13.5 (8.5, 19.7)	14.0 (8.9, 20.5)	15.9 (9.9, 23.3)

			Vegetables/prudent		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	**43.6** **(33.2, 54.6)**	70.3 (59.2, 82.7)	97.6 (83.7, 113.6)	132.0 (113.4, 152.1)	**214.8** **(172.6, 297.1)**
Potatoes	100.1	110.5	114.9	119.3	128.9

	(66.0, 145.4)	(73.8, 164.9)	(77.4, 172.6)	(83.1, 182.7)	(89.7, 199.1)
Nuts	0 (0, 1.8)	0.6 (0, 1.8)	1.0 (0, 2.2)	1.3 (0, 2.6)	1.5 (0, 3.2)
Legumes/ pulses	**2.3 (0.8, 4.7)**	4.9 (2.2, 8.1)	7.2 (3.6, 12.1)	10.5 (5.4, 17.1)	**18.5 (9.9, 30.5)**
Fruit	86.6 (48.0, 177.1)	100.8 (59.8, 59.8)	118.7 (76.2, 239.3)	171.3 (85.8, 249.3)	229.2 (103.1, 270.5)
Meat	74.8 (54.4, 99.0)	78.4 (58.9, 104.1)	78.4 (57.9, 102.9)	78.6 (56.8, 104.5)	79.0 (55.3, 108.3)
Ice cream/ sweets/cakes	38.4 (23.1, 57.5)	39.5 (24.7, 57.4)	40.1 (24.7, 57.4)	41.2 (26.4, 60.7)	43.7 (27.7, 64.0)
Cereal products	275.3 (210.5, 352.6)	276.2 (212.6, 351.9)	283.0 (218.6, 356.5)	290.4 (223.4, 263.4)	297.8 (231.5, 376.7)
Fats	28.6 (17.6, 45.1)	28.5 (18.2, 43.2)	28.0 (18.2, 43.7)	28.7 (18.6, 43.7)	29.9 (19.2, 45.0)
Fish	17.4 (9.7, 28.0)	20.6 (11.8, 32.4)	22.8 (13.5, 35.0)	25.3 (15.1, 38.5)	30.0 (17.4, 45.2)
Beverages	1496.4 (1095.9, 1949.2)	1672.5 (1259.6, 2104.1)	1760.3 (1359.3, 2169.8)	1846.7 (1449.8, 2257.4)	2001.7 (1589.0, 2427.4)
Dairy products	623.0 (380.6, 963.7)	621.7 (373.3, 870.9)	624.0 (366.1, 856.9)	624.4 (365.8, 833.4)	633.8 (360.3, 885.1)
Eggs	10.7 (6.7, 16.8)	12.3 (8.4, 19.8)	13.0 (8.4, 19.8)	14.3 (9.0, 20.9)	15.7 (9.8, 23.1)

			Western		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	116.0 (75.1, 172.2)	98.1 (64.1, 147.3)	91.4 (59.0, 137.3)	87.7 (58.6, 131.8)	95.9 (62.7, 142.3)
Potatoes	**77.1 (52.9, 108.3)**	95.9 (67.4, 127.9)	113.4 (81.0, 159.3)	132.2 (99.2, 190.3)	**183.7 (127.0, 243.1)**
Nuts	1.3 (0, 3.0)	1.0 (0, 2.2)	0.9 (0, 2.0)	0.8 (0, 2.2)	0.8 (0, 2.2)
Legumes/ pulses	6.8 (2.7, 13.3)	6.4 (2.7, 13.1)	6.8 (2.7, 13.1)	6.7 (2.8, 13.5)	7.6 (3.1, 16.0)
Fruit	226.5 (104.9, 272.0)	149.2 (79.6, 244.9)	109.7 (69.3, 237.8)	101.1 (58.8, 228.6)	97.5 (54.2, 217.8)
Meat	**47.2 (33.7, 62.8)**	65.1 (51.3, 80.6)	77.0 (62.8, 94.2)	91.5 (75.1, 110.6)	**120.0 (97.5, 146.0)**
Ice cream/ sweets/cakes	38.1 (24.0, 56.7)	38.8 (24.5, 57.2)	39.1 (24.6, 57.6)	41.1 (26.0, 60.0)	45.5 (28.7, 66.2)
Cereal products	244.4 (186.4, 313.2)	263.1 (204.8, 331.1)	278.2 (215.3, 349.5)	299.4 (236.3, 369.7)	344.4 (273.8, 417.7)
Fats	18.1 (12.0, 26.5)	23.1 (15.7, 32.9)	27.7 (19.3, 39.3)	34.6 (24.2, 48.1)	**48.8 (33.7, 70.6)**
Fish	20.1 (11.4, 32.2)	20.6 (12.0, 32.5)	22.2 (12.7, 34.6)	23.1 (13.9, 36.4)	28.9 (16.6, 46.5)
Beverages	1837.0 (1423.3, 2239.1)	1758.4 (1320.9, 2163.6)	1712.7 (1295.8, 2133.5)	1699.9 (1267.7, 2173.0)	1801.7 (1337.1, 2287.2)
Dairy products	**578.2 (308.0, 743.6)**	606.7 (347.2. 801.4)	625.2 (376.2, 883.6)	641.0 (398.5, 955.4)	687.0 (498.2, 1034.4)
Eggs	9.6 (5.8, 15.3)	11.2 (7.2, 17.1)	12.9 (8.4, 19.1)	14.6 (9.6, 21.0)	**18.6 (12.2, 26.2)**

	Seafood				
	Q1	Q2	Q3	Q4	Q5
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Vegetables	64.1 (42.5, 96.4)	79.8 (54.7, 114.0)	96.4 (65.7, 135.9)	114.4 (79.7, 160.1)	149.5 (105.3, 218.3)
Potatoes	108.5 (68.5, 167.7)	109.6 (72.9, 168.3)	113.2 (76.7, 170.7)	116.8 (80.2, 177.1)	125.6 (88.6, 191.5)
Nuts	**0 (0, 1.3)**	0 (0, 1.8)	1.0 (0, 2.2)	1.3 (0, 2.8)	**1.8 (0.5, 3.9)**
Legumes/ pulses	5.0 (1.6, 11.3)	5.6 (2.1, 11.7)	6.7 (2.9, 12.9)	7.7 (3.5, 14.7)	10.0 (4.8, 18.5)
Fruit	93.1 (49.6, 213.8)	101.7 (58.5, 230.5)	118.6 (76.0. 241.8)	162.1 (86.5, 249.5)	211.5 (96.7, 265.9)
Meat	73.7 (54.0, 98.7)	76.0 (56.1, 100.6)	78.2 (58.2, 104.3)	78.6 (56.9, 104.2)	82.8 (58.5, 110.5)
Ice cream/ sweets/cakes	37.0 (22.7, 54.8)	39.0 (24.1, 57.6)	40.7 (25.8, 59.1)	41.6 (26.7, 60.5)	44.7 (28.5, 65.5)
Cereal products	272.1 (205.1, 350.0)	272.0 (207.4, 345.6)	278.6 (216.3, 354.2)	290.0 (225.8, 360.9)	311.6 (243.3, 385.1)
Fats	25.8 (15.7, 41,2)	26.6 (16.9, 41.1)	28.5 (18.4, 42.1)	29.3 (19.1, 43.8)	33.8 (22.7, 50.1)
Fish	**9.9 (5.0, 15.9)**	17.2 (11.0, 24.2)	23.6 (16.1, 32.0)	31.0 (21.4, 41.3)	**43.1 (30.7, 57.3)**
Beverages	1649.0 (1209.0, 2114.8)	1691.5 (1250.5, 2127.4)	1724.6 (1302.6, 2154.7)	1788.8 (1377.1, 2211.3)	1926.6 (1519.0, 2352.9)
Dairy products	603.2 (337.0, 961.0)	613.6 (351.6, 913.8)	626.6 (378.9, 878.3)	640.9 (383.0, 834.6)	645.5 (376.6, 854.8)
Eggs	**8.9 (5.5, 13.5)**	11.6 (7.6, 17.3)	13.3 (8.6, 19.6)	15.3 (10.0, 21.8)	18.6 (12.1, 26.0)

	Nordic				
	Q1	Q2	Q3	Q4	Q5
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Vegetables	78.2 (51.5, 117.4)	87.7 (57.4, 131.4)	95.3 (63.1, 142.7)	107.2 (71.4, 157.2)	122.7 (81.4, 181.6)
Potatoes	110.2 (72.8, 158.8)	108.6 (72.8, 159.7)	113.3 (76.2, 171.9)	116.5 (80.7, 179.5)	125.7 (86.7, 195.3)
Nuts	0 (0, 1.8)	0.7 (0, 1.9)	0.9 (0, 2.2)	1.1 (0, 2.5)	1.4 (0, 3.1)
Legumes/ pulses	5.3 (1.9, 11.1)	6.2 (2.4, 12.4)	6.8 (2.8, 13.8)	7.5 (3.3, 14.8)	9.1 (4.2, 17.7)
Fruit	**64.8 (32.6, 99.7)**	95.2 (58.4, 183.4)	122.7 (81.0, 237.4)	213.5 (100.9, 251.7)	**244.2 (171.8, 289.1)**
Meat	73.5 (514.1, 97.2)	75.0 (54.7, 99.5)	77.0 (56.0, 102.1)	79.2 (58.6, 104.7)	85.7 (61.9, 114.6)
Ice cream/ sweets/cakes	37.9 (23.13, 55.3)	37.5 (23.8, 54.9)	40.0 (25.2, 57.6)	41.4 (26.4, 60.6)	47.1 (30.5, 68.3)
Cereal products	**193.9 (141.0, 242.8)**	249.2 (205.0, 299.1)	284.5 (235.6, 340.1)	323.1 (270.0, 379.6)	**392.4 (331.6, 460.6)**
Fats	24.9 (17.0, 36.1)	27.0 (17.6, 39.5)	28.7 (18.3, 43.1)	30.6 (19.1, 46.4)	34.8 (21.1, 55.3)
Fish	17.4 (9.3, 28.6)	20.4 (11.7, 32.3)	22.8 (13.4, 35.3)	25.1 (15.1, 38.6)	29.2 (17.5, 44.1)
Beverages	1491.7	1640.5	1754.8	1843.0	2015.6

	(1081.4, 1971.2)	(1239.0, 2065.7)	(1337.4, 2183.1)	(1456.6, 2239.1)	(1626.3, 2425.2)
Dairy products	574.3 (284.0, 767.4)	601.4 (339.0, 804.7)	624.0 (380.2, 868.9)	645.4 (408.4, 939.7)	694.8 (502.6, 997.3)
Eggs	11.4 (7.1, 17.7)	12.3 (7.7, 18.8)	13.1 (7.7, 18.8)	13.6 (8.8, 20.3)	15.6 (9.7, 22.7)

			Sweets		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	98.3 (63.1, 149.8)	93.3 (61.7, 140.8)	94.7 (62.2, 140.7)	96.3 (61.4, 143.8)	105.5 (66.5, 156.6)
Potatoes	110.3 (71.2, 173.1)	110.5 (74.3, 167.2)	112.1 (75.7, 170.9)	114.0 (79.6, 174.1)	126.6 (86.2, 190.8)
Nuts	0.6 (0, 1.8)	0.9 (0, 1.8)	1.0 (0, 2.2)	1.0 (0, 2.5)	1.4 (0, 3.2)
Legumes/ pulses	8.1 (3.3, 16.8)	6.9 (2.9, 13.8)	6.7 (2.8, 13.2)	6.3 (2.6, 12.4)	6.5 (2.6, 13.4)
Fruit	134.8 (75.1, 247.4)	114.4 (72.0, 241.3)	114.6 (72.0, 239.3)	116.6 (74.6, 239.5)	136.9 (76.2, 245.5)
Meat	69.5 (48.7, 92.7)	73.9 (53.6, 97.8)	76.8 (57.3, 102.9)	81.7 (61.0, 107.2)	88.1 (64.8, 116.1)
Ice cream/ sweets/cakes	**21.3** **(15.6, 28.4)**	30.9 (22.9, 40.8)	40.5 (29.4, 51.4)	51.9 (40.2, 64.9)	**74.5** **(58.1, 92.5)**
Cereal products	252.1 (196.5, 326.0)	266.8 (206.8, 337.8)	279.7 (216.7, 352.6)	296.3 (232.2, 368.7)	326.7 (258.9, 405.3)
Fats	28.7 (18.4, 43.9)	**18.1** **(12.2, 26.4)**	24.2 (16.6, 34.2)	34.4 (23.3, 49.0)	47.4 (31.3, 69.5)
Fish	25.5 (15.0, 40.3)	22.8 (13.2, 35.3)	22.0 (12.9, 34.6)	21.9 (12.6, 34.6)	22.0 (12.0, 35.4)
Beverages	1660.5 (1221.5, 2060.6)	1711.3 (1288.5, 2129.6)	1743.0 (1316.2, 2180.2)	1797.3 (1370.0, 2241.9)	1908.3 (1460.1, 2408.1)
Dairy products	653.3 (515.4, 990.2)	622.3 (375.3, 886.7)	618.3 (360.1, 817.0)	615.7 (338.0, 823.1)	620.2 (339.3, 851.8)
Eggs	10.7 (6.6, 17.5)	12.2 (7.6, 18.4)	12.8 (8.3, 19.5)	13.9 (9.0, 20.4)	16.1 (10.5, 23.4)

			Rice/pasta/poultry		
	Q1	**Q2**	**Q3**	**Q4**	**Q5**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Vegetables	79.8 (50.7, 121.7)	87.1 (57.4, 130.2)	96.0 (63.7, 140.9)	105.3 (70.1, 153.7)	124.1 (81.4, 181.6)
Potatoes	148.4 (101.3, 205.9)	120.1 (83.0, 181.2)	110.8 (76.0, 162.5)	104.5 (72.0, 145.9)	98.6 (65.0, 142.4)
Nuts	0.6 (0, 1.8)	0.9 (0, 2.2)	1.0 (0, 2.2)	1.1 (0, 2.4)	1.1 (0, 2.6)
Legumes/ pulses	5.8 (2.1, 12.1)	6.2 (2.6, 12.2)	6.6 (2.9, 13.2)	7.4 (3.2, 14.8)	8.6 (3.4, 17.6)
Fruit	91.7 (50.4, 174.7)	103.1 (62.1, 227.1)	127.7 (77.7, 241.4)	184.6 (85.6, 250.9)	222.6 (94.7, 262.2)
Meat	74.4 (53.9, 99.5)	75.1 (55.0, 99.1)	77.2 (57.1, 101.1)	79.4 (58.2, 105.0)	84.0 (59.4, 114.3)
Ice cream/ sweets/cakes	37.9 (23.7, 57.6)	39.2 (24.7, 57.1)	40.1 (25.0, 58.0)	41.7 (26.3, 61.0)	43.6 (26.5, 64.3)

Cereal products	282.8 (214.1, 363.1)	276.2 (210.3, 350.1)	276.6 (215.4, 347.9)	281.8 (218.3, 357.8)	303.4 (238.1, 378.4)
Fats	39.6 (24.9, 60.6)	30.0 (19.8, 45.2)	27.1 (18.0, 40.6)	25.6 (16.8, 37.5)	24.3 (15.8, 36.4)
Fish	18.1 (10.1, 29.0)	20.7 (12.2, 31.9)	23.3 (13.9, 35.8)	25.1 (14.7, 38.4)	28.8 (16.0, 45.7)
Beverages	1589.9 (1171.0, 2058.0)	1642.8 (1229.2, 2066.6)	1744.2 (1335.4, 2143.7)	1827.9 (1427.3, 2240.6)	1996.0 (1579.0, 2435.3)
Dairy products	579.8 (301.3, 754.7)	599.0 (329.6, 762.4)	623.3 (375.5, 841.9)	653.2 (448.6, 960.2)	**696.5 (523.7, 1048.5)**
Eggs	13.8 (8.5, 20.6)	12.9 (8.2, 19.5)	12.9 (8.2, 19.7)	12.9 (8.3, 19.3)	13.1 (7.9, 20.0)

*For a description of each food group please see Table 8. The highest and lowest average value for each food group and nutrient across all dietary patterns are shown in bold. CI, confidence interval; IQR, interquartile range; Q, quintile.

8.4.2 Characteristics of mothers across quintile categories of dietary patterns scores

Characteristics of participants in the DNBC across quintile categories of the seven dietary pattern scores can be found in Table 40. Mothers who scored highly on the ‘Alcohol’ component were significantly more likely to be older, have a lower pre-pregnancy BMI, to smoke, to be in a higher level proficiency occupation, have a higher energy intake (kcal/day) and alcohol intake (40% in the highest quintile score consumed ≥2 units/week) than those in the lower quintile scores. They were less likely to be nulliparous and breastfeed for less than three months. Those in the higher quintile categories of the ‘Vegetables/prudent’ component were significantly older than mothers in the lower categories, they also had a lower pre-pregnancy BMI, were more likely to be in higher and medium level skilled occupations, to take dietary supplements, have a higher energy intake (kcal) and consume ≥2 units of alcohol/week. They were less likely to smoke. As for the third component, ‘Western’, mothers in the highest quintile category were more likely to be younger, have a higher pre-pregnancy BMI, to smoke in pregnancy, have a lower gestational weight gain, a higher energy intake (kcal/day), have offspring with lower birth weight compared to mothers in lower categories. They were less likely to be in a high level or medium skilled occupation, be nulliparous, take dietary supplements, consume ≥2 units of alcohol/week and to breastfeed for more than 6 months. Mothers who scored highly on the fourth component, ‘Seafood’, were significantly more likely to be older, have a lower pre-pregnancy BMI, to be in a higher level proficiency occupation, take dietary supplements, have a greater gestational weight gain, have a higher energy intake (kcal/day) and alcohol intake and breastfeed for more than six months than those in the lower quintile scores. They were less likely to smoke. Those in the higher quintile categories of the ‘Nordic’ component were similarly more likely to be older, have a lower pre-pregnancy BMI, to be in a higher level proficiency occupation, take dietary supplements, have a greater gestational weight gain, have a higher energy intake (kcal/day), breastfeed for more than six months) and have offspring with higher birth weight compared to mothers in lower categories. They were less likely to smoke, drink ≥ 2 units of alcohol/week and to be nulliparous. As for the sixth component, ‘Sweets’ mothers in the highest quintile category were more likely to be younger, have a slightly lower pre-pregnancy BMI, smoke in pregnancy and have a higher energy intake (kcal/day) compared to mothers in lower categories. They were less likely to be nulliparous and to breastfeed for more than 6 months. Mothers who scored highly on the final component, ‘Rice/pasta/poultry’, were more likely to be in a high to mid-level skilled occupation, be nulliparous, take dietary supplements, have a greater gestational weight gain and a higher energy intake (kcal/day) compared to mothers in the lowest quintile category. They were less likely to smoke and consume ≥2 units of alcohol/week.

Table 40. DNBC study sample characteristics according to quintile categories of dietary pattern scores (n=31,150)*

	Alcohol						**Vegetables/prudent**					
	Q1 (n=6,230)	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-value*ǂ**	**Q1 (n=6,230)**	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-value*ǂ**
Age of mother (years), n (%)						0.003						0.0004
≤20	58 (0.9)	45 (0.7)	32 (0.5)	20 (0.3)	33 (0.5)		75 (1.2)	30 (0.5)	25 (0.4)	32 (0.5)	26 (0.4)	
>21-39	6128 (98.4)	6145 (98.6)	6151 (98.7)	6132 (98.4)	6100 (97.9)		6117 (98.2)	6156 (98.8)	6148 (98.7)	6134 (98.5)	6101 (97.9)	
≥40	44 (0.7)	40 (0.6)	47 (0.8)	78 (1.3)	97 (1.6)		38 (0.6)	44 (0.7)	57 (0.9)	64 (1.0)	103 (1.7)	
Pre-pregnancy BMI (kg/m^2), n (%)						0.0001						0.0001
≤18.5	261 (4.1)	249 (4.2)	245 (4.1)	247 (4.2)	240 (4.1)		255 (4.0)	217 (3.7)	230 (3.9)	263 (4.4)	278 (5.0)	
18.6-24.9	4032 (68.1)	4175 (70.4)	4252 (71.8)	4245 (71.9)	4265 (72.3)		3939 (66.8)	4101 (69.0)	4274 (72.0)	4274 (72.5)	4381 (74.2)	
25-29.9	1134 (19.2)	1080 (18.2)	1050 (17.7)	1072 (18.0)	1105 (18.7)		1233 (20.9)	1175 (19.8)	1072 (18.1)	1032 (17.5)	929 (15.7)	
30.0-34.9	358 (6.1)	326 (5.5)	268 (4.5)	271 (4.6)	230 (3.9)		352 (6.0)	334 (5.6)	284 (4.8)	245 (4.2)	238 (4.0)	
≥35	136 (2.3)	98 (1.7)	108 (1.8)	68 (1.2)	59 (1.0)		119 (2.0)	113 (1.9)	74 (1.3)	85 (1.4)	78 (1.3)	
Smoking in pregnancy, n (%)	603 (9.7)	602 (9.7)	678 (10.9)	666 (10.7)	780 (12.6)	0.0001	945 (15.2)	673 (10.8)	659 (10.6)	560 (9.0)	492 (8.0)	0.0001
Parental SES, n (%)						0.0001						0.0001
High level proficiencies	1113 (19.4)	1236 (21.9)	1403 (25.3)	1400 (25.7)	1550 (28.7)		870 (16.5)	1160 (21.0)	1337 (24.0)	1577 (27.9)	1758 (30.7)	
Medium level proficiencies	1800 (31.4)	1856 (32.9)	1817 (32.8)	1730 (31.7)	1667 (30.9)		1433 (27.1)	1725 (31.2)	1862 (33.5)	1925 (34.0)	1925 (33.6)	
Skilled	1631 (28.4)	1531 (27.2)	1391 (25.1)	1402 (25.7)	1215 (22.5)		1761 (33.3)	1568 (28.3)	1388 (24.9)	1279 (22.6)	1174 (20.5)	
Unskilled	803 (14.0)	643 (11.4)	574 (10.4)	549 (10.1)	544 (10.1)		801 (15.2)	701 (12.7)	611 (11.0)	505 (8.9)	495 (8.6)	
Student	264 (4.6)	252 (4.5)	231 (4.2)	232 (4.3)	249 (4.6)		231 (4.4)	243 (4.4)	231 (4.2)	256 (4.5)	267 (4.7)	
Unemployed	130 (2.3)	120 (2.1)	131 (2.4)	140 (2.6)	168 (3.1)		190 (3.6)	129 (2.5)	136 (2,4)	113 (2.0)	111 (1.9)	
Nulliparous, n (%)	3278 (54.5)	3153 (52.4)	3075 (51.2)	2916 (48.7)	2701 (45.1)	<0.0001	3072 (51.2)	2985 (49.6)	2985 (49.7)	3008 (50.3)	3073 (51.3)	0.2
Dietary supplements during pregnancy (% yes), n (%)	5796 (95.0)	5815 (94.8)	5822 (95.1)	5848 (95.0)	5745 (94.0)	0.3	5724 (93.7)	5784 (94.5)	5857 (95.3)	5829 (95.0)	5832 (95.7)	<0.0001
Gestational weight gain (g/week), mean (SD)	467.6 (218.1)	465.9 (204.0)	468.0 (207.8)	464.0 (205.1)	459.5 (204.6)	0.3	468.2 (220.2)	461.1 (207.4)	466.8 (203.6)	463.0 (205.2)	466.0 (203.0)	<0.0001
Total energy intake	2234	2239	2300	2430	2613	0.0001	2226	2267 (1923,	2327	2413	2569	0.0001

(kJ/day), mean (SD)	(1863, 2644)	(1894, 2613)	(1969, 2698)	(2082, 2830)	(2208, 3090)		(1862, 2634)	2675)	(1984, 2722)	(2052, 2814)	(2183, 3021)	
Energy adjusted alcohol intake (≥2 units/wk, n (%)	150 (2.4)	617 (9.9)	1264 (20.3)	2117 (34.0)	3090 (40.0)	<0.0001	1242 (20.0)	1483 (23.8)	1469 (23.7)	1591 (25.6)	1443 (23.4)	<0.0001
Neonatal characteristics												
Breast feeding duration, n (%)						<0.0001						<0.0001
<3 months	1051 (22.1)	925 (19.8)	837 (18.0)	799 (17.0)	759 (16.5)		1185 (25.5)	958 (20.5)	806 (17.2)	737 (15.6)	685 (14.7)	
3-6 months	850 (17.9)	895 (19.1)	814 (17.5)	822 (17.5)	799 (17.3)		945 (20.3)	886 (19.0)	830 (17.7)	839 (14.6)	680 (18.0)	
>6 months	2855 (60.0)	2864 (61.1)	3011 (64.6)	3086 (65.6)	3056 (66.2)		2515 (54.1)	2831 (60.6)	3065 (65.2)	3159 (66.7)	3302 (70.8)	
Birth weight (g), mean (SD)	3613.1 (492.6)	3618.0 (485.2)	3624.1 (493.2)	3629.1 (484.1)	3624.0 (487.6)	0.4	3604.2 (489.2)	3635.8 (481.1)	3625.3 (489.3)	3616.6 (493.1)	3626.2 (489.6)	0.005
Child sex (% male), n (%)	3100 (49.8)	3170 (50.9)	3240 (52.0)	3210 (51.5)	3161 (50.7)	0.1	3117 (50.0)	3248 (52.1)	3152 (50.6)	3121 (50.1)	3243 (52.1)	0.03

Table 38 cont. DNBC study sample characteristics according to quintile categories of dietary pattern scores (n=31,150)*

	Western						**Seafood**					
	Q1 (n=6,230)	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-valueǂ***	**Q1 (n=6,230)**	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-valueǂ***
Age of mother (years), n (%)						0.0008						0.0001
≤20	10 (0.2)	30 (0.5)	38 (0.6)	37 (0.6)	73 (1.2)		66 (1.1)	40 (0.6)	34 (0.6)	29 (0.5)	19 (0.3)	
>21-39	6142 (98.6)	6147 (98.7)	6136 (98.5)	6137 (98.5)	6094 (97.8)		6142 (98.6)	6150 (98.7)	6141 (98.6)	6145 (98.6)	6078 (97.6)	
≥40	78 (1.3)	53 (0.9)	56 (0.9)	56 (0.9)	63 (1.0)		22 (0.4)	40 (0.6)	55 (0.9)	56 (0.9)	133 (2.1)	
Pre-pregnancy BMI (kg/m^2), n (%)						0.0008						0.0001
≤18.5	268 (4.6)	206 (3.5)	217 (3.7)	231 (3.9)	320 (5.4)		208 (3.5)	202 (3.4)	245 (4.1)	263 (4.5)	324 (5.5)	
18.6-24.9	4584 (78.4)	4315 (72.7)	4188 (70.7)	4009 (67.7)	3873 (65.2)		3696 (62.5)	3982 (67.4)	4245 (71.6)	4448 (75.2)	4598 (78.0)	
25-29.9	806 (13.8)	1069 (18.0)	1124 (19.0)	1218 (20.6)	1224 (20.6)		1394 (23.6)	1255 (21.1)	1088 (18.4)	938 (15.9)	766 (13.0)	
30.0-34.9	163 (2.8)	276 (4.7)	293 (4.9)	347 (5.9)	374 (6.3)		455 (7.7)	338 (5.7)	277 (4.7)	208 (3.5)	175 (3.0)	
≥35	30 (0.5)	73 (1.2)	106 (1.8)	114 (1.9)	146 (2.5)		165 (2.8)	135 (2.3)	74 (1.3)	59 (1.0)	36 (0.6)	
Smoking in pregnancy, n (%)	226 (3.7)	433 (7.0)	617 (10.0)	796 (12.8)	1257 (20.3)	0.0001	1031 (16.6)	741 (12.0)	622 (10.0)	529 (8.5)	406 (6.6)	0.0001

Parental SES, n (%)						0.0001						0.0001
High level proficiencies	1881 (34.5)	1544 (27.6)	1372 (24.8)	1120 (20.1)	815 (14.2)		677 (12.5)	1029 (18.7)	1357 (24.3)	1624 (28.9)	2015 (33.5)	
Medium level proficiencies	1871 (34.4)	1941 (35.4)	1820 (32.9)	1691 (30.4)	1547 (26.9)		1461 (27.1)	1696 (30.8)	1899 (34.0)	1956 (34.8)	1858 (32.9)	
Skilled	870 (16.0)	1204 (21.9)	1407 (25.4)	1699 (30.6)	1990 (34.7)		1952 (36.1)	1720 (31.2)	1433 (25.7)	1138 (20.2)	927 (16.4)	
Unskilled	354 (6.5)	457 (8.3)	553 (10.0)	720 (13.0)	1029 (17.9)		916 (17.0)	705 (12.8)	567 (10.2)	500 (8.9)	425 (7.5)	
Student	384 (7.1)	275 (5.0)	225 (4.1)	176 (3.2)	168 (2.9)		212 (3.9)	227 (4.1)	213 (3.8)	285 (5.1)	291 (5.2)	
Unemployed	87 (1.6)	100 (1.8)	153 (2.8)	155 (2.8)	194 (3.4)		183 (3.4)	133 (2.4)	118 (2.1)	123 (2.2)	132 (2.3)	
Nulliparous, n (%)	3891 (65.4)	3303 (54.9)	2951 (49.0)	2678 (44.6)	2300 (38.2)	<0.0001	3065 (51.0)	3074 (51.3)	2990 (49.7)	3023 (50.4)	2971 (49.7)	0.3
Dietary supplements during pregnancy (% yes), n (%)	5935 (96.5)	5887 (95.9)	5822 (95.1)	5781 (94.2)	5601 (92.5)	<0.0001	5690 (93.3)	5777 (94.5)	5842 (94.4)	5867 (95.5)	5850 (95.6)	<0.0001
Gestational weight gain (g/week), mean (SD)	465.6 (181.0)	467.3 (201.8)	467.3 (210.7)	465.5 (210.4)	459.4 (232.1)	<0.0001	455.7 (231.0)	464.7 (214.0)	469.1 (203.4)	468.2 (190.8)	467.6 (197.9)	0.01
Total energy intake (kJ/day), median (IQR)	2011 (1717, 2348)	2147 (1853, 2488)	2289 (1983, 2625)	2949 (2573, 3384)	2495 (2190, 2832)	0.0001	2146 (1806, 2539)	2228 (1884, 2606)	2329 (1993, 2716)	2441 (2090, 2835)	2671 (2283, 3119)	0.0001
Energy adjusted alcohol intake (≥2 units/wk, n (%)	1639 (26.3)	1509 (24.2)	144.3 (23.2)	1389 (22.3)	1258 (20.4)	<0.0001	941 (15.1)	12.8 (20.6)	1468 (23.6)	1627 (26.1)	1918 (31.0)	<0.0001
Neonatal characteristics												
Breast feeding duration, n (%)						0.0001						0.0001
<3 months	555 (12.2)	779 (16.6)	857 (18.3)	956 (20.4)	1224 (25.5)		1342 (28.6)	1036 (22.2)	810 (17.3)	656 (14.0)	527 (11.3)	
3-6 months	701 (15.4)	808 (17.2)	843 (18.0)	895 (19.1)	933 (19.5)		1030 (21.9)	955 (20.5)	824 (17.6)	784 (16.7)	587 (12.6)	
>6 months	3312 (72.5)	3102 (66.2)	2973 (63.6)	2844 (60.6)	2641 (55.0)		2324 (49.5)	2677 (57.4)	3055 (65.2)	3257 (69.3)	3559 (76.2)	
Birth weight (g), mean (SD)	3604.8 (475.5)	3626.0 (482.0)	3641.3 (487.3)	3628.6 (494.4)	3607.5 (502.3)	0.0001	3601.1 (494.8)	3631.0 (488.5)	3633.9 (490.5)	3628.2 (479.9)	3613.9 (488.2)	0.0005
Child sex (% male), n (%)	3211 (51.5)	3152 (50.6)	3166 (50.8)	3221 (51.7)	3131 (50.3)	0.4	3210 (51.5)	3165 (50.8)	3216 (51.6)	3181 (51.1)	3109 (49.9)	0.3

Table 38 cont. DNBC study sample characteristics according to quintile categories of dietary pattern scores (n=31,150)*

	Nordic						**Sweets**					
	Q1 (n=6,230)	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-valueǂ***	**Q1 (n=6,230)**	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-valueǂ***
Age of mother (years), n (%)						0.002						0.03
≤20	95 (1.5)	39 (0.6)	19 (0.3)	16 (0.3)	19 (0.3)		28 (0.5)	34 (0.6)	28 (0.5)	38 (0.6)	60 (1.0)	
>21-39	6112 (98.1)	6157 (98.8)	6148 (98.7)	6119 (98.2)	6120 (98.2)		6120 (98.2)	6135 (98.5)	6139 (98.5)	6151 (98.7)	6111 (98.1)	
≥40	23 (0.4)	34 (0.6)	63 (1.0)	95 (1.5)	91 (1.5)		82 (1.3)	61 (1.0)	63 (1.0)	41 (0.7)	59 (1.0)	
Pre-pregnancy BMI (kg/m^2), n (%)						0.0001						0.05
≤18.5	236 (4.0)	222 (3.8)	229 (3.9)	267 (4.5)	288 (4.9)		195 (3.3)	198 (3.3)	213 (3.6)	244 (4.1)	392 (6.6)	
18.6-24.9	3740 (63.3)	4102 (69.3)	4195 (70.9)	4392 (74.0)	4540 (77.0)		4092 (69.7)	4146 (70.0)	4253 (71.8)	4256 (71.9)	4222 (71.1)	
25-29.9	1331 (22.5)	1183 (20.0)	1123 (19.0)	976 (16.4)	828 (14.1)		1165 (19.9)	1162 (19.6)	1073 (18.1)	1048 (17.7)	993 (16.7)	
30.0-34.9	441 (7.7)	317 (5.4)	294 (5.0)	221 (3.7)	180 (3.1)		314 (5.4)	320 (5.4)	295 (5.0)	279 (4.7)	245 (4.1)	
≥35	157 (2.7)	92 (1.6)	80 (1.4)	82 (1.4)	58 (1.0)		104 (1.8)	100 (1.7)	86 (1.5)	96 (1.6)	83 (1.4)	
Smoking in pregnancy, n (%)	1001 (16.2)	722 (11.6)	619 (10.0)	541 (8.7)	446 (7.2)	0.0001	573 (9.2)	642 (10.4)	641 (10.3)	666 (10.8)	807 (13.0)	0.0001
Parental SES, n (%)						0.0001						0.006
High level proficiencies	1133 (20.2)	1238 (22.3)	1330 (24.0)	1455 (26.3)	1546 (28.1)		1224 (23.3)	1340 (24.2)	1386 (24.8)	1386 (24.5)	1366 (23.8)	
Medium level proficiencies	1567 (27.9)	1739 (31.3)	1840 (33.2)	1841 (33.3)	1883 (34.2)		1642 (31.2)	1799 (32.5)	1824 (32.7)	1828 (32.7)	1777 (31.0)	
Skilled	1707 (30.4)	1569 (31.3)	1840 (33.2)	1841 (33.3)	1883 (34.2)		1401 (26.6)	1400 (25.3)	1409 (25.2)	1428 (25.3)	1532 (26.7)	
Unskilled	827 (14.7)	646 (11.6)	578 (10.4)	558 (10.1)	504 (9.2)		567 (10.8)	616 (11.1)	606 (10.9)	636 (11.3)	688 (12.0)	
Student	227 (4.0)	222 (4.0)	219 (4.0)	271 (4.9)	289 (5.3)		286 (5.4)	237 (4.3)	224 (4.0)	252 (4.5)	229 (4.0)	
Unemployed	163 (2.9)	143 (2.6)	146 (2.6)	120 (2.2)	117 (2.1)		141 (2.7)	145 (2.6)	135 (2.4)	120 (2.1)	148 (2.6)	
Nulliparous, n (%)	3421 (56.9)	3094 (51.7)	3039 (50.6)	2852 (47.5)	2717 (45.4)	<0.0001	3092 (51.8)	3106 (51.6)	3065 (51.1)	2930 (48.8)	2930 (48.8)	<0.0001
Dietary supplements during pregnancy (% yes), n (%)	5654 (93.0)	5784 (94.5)	5863 (95.4)	5844 (95.3)	5881 (96.1)	<0.0001	5761 (94.4)	5839 (95.1)	5825 (94.8)	5850 (95.5)	5751 (94.5)	0.03
Gestational weight gain (g/week), mean	461.0 (229.1)	459.4 (214.3)	463.7 (206.3)	467.8 (192.0)	473.4 (196.0)	0.01	440.5 (212.9)	454.7 (204.9)	468.5 (203.7)	470.1 (203.6)	490.5 (211.6)	<0.0001

(SD)												
Total energy intake (kJ/day), median (IQR)	1947 (1658, 2297)	2139 (1857, 2470)	2316 (2032, 2653)	2512 (2215, 2854)	2890 (2543, 3304)	0.0001	2034 (1735, 2369)	2158 (1862, 2500)	2312 (1988, 2646)	2489 (2167, 2835)	2894 (2512, 3338)	0.0001
Energy adjusted alcohol intake (≥2 units/wk, n (%)	1545 (24.8)	1561 (25.1)	1477 (23.7)	1454 (23.4)	1201 (19.4)	<0.0001	1303 (20.9)	1464 (23.5)	1533 (24.6)	1487 (23.9)	1451 (23.5)	<0.0001
Neonatal characteristics												
Breast feeding duration, n (%)						0.0001						0.003
<3 months	1262 (27.5)	962 (20.8)	829 (17.6)	726 (15.5)	592 (12.3)		841 (18.0)	853 (18.2)	840 (17.8)	895 (19.0)	942 (20.3)	
3-6 months	997 (21.7)	923 (20.0)	890 (18.9)	724 (15.5)	646 (13.4)		832 (17.8)	830 (17.7)	826 (17.5)	845 (18.0)	847 (18.3)	
>6 months	2332 (50.8)	2742 (59.3)	3002 (63.6)	3222 (69.0)	3574 (74.3)		3004 (64.2)	3006 (64.1)	3051 (64.7)	2960 (63.0)	2851 (61.4)	
Birth weight (g), mean (SD)	3581.5 (490.3)	3618.4 (486.4)	3617.0 (485.7)	3640.0 (486.0)	3651.3 (491.7)	<0.0001	3630.2 (494.5)	3626.1 (486.6)	3621.6 (488.9)	3620.6 (486.2)	3609.6 (486.6)	0.2
Child sex (% male), n (%)	3172 (50.9)	3188 (51.2)	3182 (51.1)	3152 (50.6)	3187 (51.2)	0.9	3160 (50.7)	3155 (50.6)	3263 (52.4)	3146 (50.5)	3157 (50.7)	0.2

Table 38 cont. DNBC study sample characteristics according to quintile categories of dietary pattern scores (n=31,150)*

	Rice/pasta/poultry					
	Q1 (n=6,230)	**Q2 (n=6,230)**	**Q3 (n=6,230)**	**Q4 (n=6,230)**	**Q5 (n=6,230)**	***P-value*ǂ**
Age of mother (years), n (%)						0.0001
≤20	41 (0.7)	43 (0.7)	35 (0.6)	27 (0.4)	42 (0.7)	
>21-39	6070 (97.4)	6121 (98.3)	6134 (98.5)	6173 (99.1)	6158 (98.8)	
≥40	119 (1.9)	66 (1.1)	61 (1.0)	30 (0.5)	30 (0.5)	
Pre-pregnancy BMI (kg/m^2), n (%)						0.3
≤18.5	338 (5.7)	259 (4.4)	214 (3.6)	225 (3.8)	206 (3.5)	
18.6-24.9	4177 (70.7)	4183 (70.3)	4232 (71.8)	4198 (70.9)	4179 (70.8)	
25-29.9	1011 (17.1)	1101 (18.5)	1078 (18.3)	1132 (19.1)	1119 (19.0)	
30.0-34.9	288 (4.9)	302 (5.1)	286 (4.9)	281 (4.8)	296 (5.0)	
≥35	97 (1.6)	105 (1.8)	81 (1.4)	86 (1.5)	100 (1.7)	
Smoking in pregnancy, n (%)	1144 (18.4)	711 (11.5)	575 (9.3)	449 (7.2)	450 (7.3)	0.0001

Parental SES, n (%)						0.0001
High level proficiencies	1032 (19.3)	1362 (24.9)	1443 (26.0)	1484 (26.1)	1381 (24.2)	
Medium level proficiencies	1519 (28.4)	1680 (30.7)	1787 (32.2)	1907 (33.6)	1977 (34.6)	
Skilled	1586 (29.7)	1435 (26.2)	1385 (25.0)	1415 (24.9)	1349 (23.6)	
Unskilled	758 (14.2)	648 (11.8)	573 (10.3)	530 (9.3)	604 (10.6)	
Student	210 (3.9)	225 (4.1)	255 (4.6)	244 (4.3)	294 (5.2)	
Unemployed	238 (4.5)	130 (2.4)	108 (2.0)	104 (1.8)	109 (1.9)	
Nulliparous, n (%)	2214 (37.0)	2764 (45.8)	2980 (49.9)	3401 (56.5)	3764 (62.9)	<0.0001
Dietary supplements during pregnancy (% yes), n (%)	5606 (92.3)	5758 (94.1)	5879 (95.5)	5890 (96.0)	5893 (96.3)	<0.0001
Gestational weight gain (g/week), mean (SD)	451.1 (219.7)	461.0 (211.0)	466.3 (199.0)	470.1 (201.0)	476.8 (208.8)	<0.0001
Total energy intake (kJ/day), median (IQR)	2362 (1941, 2821)	2246 (1891, 2655)	2288 (1949, 2675)	2362 (2018, 2754)	2533 (2171, 2972)	0.0001
Energy adjusted alcohol intake (≥2 units/wk, n (%)	1587 (25.6)	1662 (26.7)	1479 (23.8)	1391 (22.3)	1119 (18.1)	<0.0001
Neonatal characteristics						
Breast feeding duration, n (%)						0.0001
<3 months	1018 (21.4)	873 (18.6)	850 (18.1)	778 (16.7)	852 (18.4)	
3-6 months	803 (16.9)	833 (17.8)	815 (17.4)	825 (17.7)	904 (19.5)	
>6 months	2927 (61.7)	2979 (63.6)	3025 (64.5)	3053 (65.6)	2888 (62.2)	
Birth weight (g), mean (SD)	3600.7 (503.2)	3626.2 (484.0)	3630.6 (486.9)	3624.1 (483.9)	3626.5 (484.2)	0.005
Child sex (% male), n (%)	3170 (50.9)	3142 (50.4)	3199 (51.4)	3157 (50.7)	3213 (51.6)	0.7

*Where numbers do not add up this is due to a small proportion of missing data. **P value using two sample t-test for normally distributed and Mann-Whitney U-test for non-normally distributed continuous variables and the χ2 test for categorical variables. Significant difference at P<0.05. BMI, body mass index; g, gram; n, number; IQR, interquartile range; Q, quintile; SD, standard deviation; SES, socio economic status.

8.4.3 Offspring anthropometry

Table 39 shows offspring size at birth as well as child height and weight measures at the 7 years follow-up. Mean birth weight for the whole sample was just over 3.6 kg with 1 % (n=328) of infants born with LBW and 4 % (n=1,306) born with HBW. The mean birth length was around 50 cm and the infants had an overall lower mean WFL Z-score at birth compared to the WHO reference population. Boys tended to be significant longer and heavier than girls at birth. At the 7 years follow-up, the average height for the whole sample was 126 cm with a mean weight of 25 kg. The children had higher mean Z-scores of weight & height-for-age compared to the WHO reference population. A total of 655 (2%) children were found to be LHFA and 629 (2 %) to be LWFA. Boys tended to be slightly taller and heavier than girls and a larger proportion of boys were found to be LWFA and LHFA.

Table 41. Offspring anthropometry at birth and at age 7 years in the DNBC

	N	**Total sample**	**Boys (n=15,881)**	**Girls (n=15,269)**	*P* *
Birth weight (g), mean (SD)	31,012	3621.6 (488.6)	3685.5 (494,4)	3555.1 (473.3)	<0.0001
Birth length (cm), mean (SD)	30,891	52.4 (2.2)	52.8 (2.2)	52.0 (2.1)	<0.0001
Weight-for-length Z-score, mean (SD)	30,864	-0.93 (1.14)	-1.00 (1.18)	-0.86 (1.09)	<0.0001
Low birth weight (<2,500 g), n (%)	31,012	328 (1.1)	133 (0.4)	195 (0.6)	0.0001
High birth weight (>4,500 g), n (%)	31,012	1,306 (4.2)	873 (2.8)	433 (1.4)	<0.0001
Child height measures					
Height (cm), mean (SD)	31,150	125.8 (5.5)	126.4 (5.5)	125.2 (5.5)	<0.0001
Exact age at height measurement (years), mean (SD)	31,150	7.05 (0.3)	7.05 (0.3)	7.04 (0.3)	0.32
Height-for-age Z-score, mean (SD)	31,150	0.79 (1.0)	0.82 (1.0)	0.76 (1.0)	<0.0001
Low height-for-age, n (%)	31,150	655 (2.1)	364 (2.3)	291 (1.9)	0.02
Child weight measures	31,150				
Weight (kg), mean (SD)	31,150	24.89 (3.9)	25.15 (3.8)	24.61 (4.0)	<0.0001
Exact age at weight measurement (years), mean (SD)	31,150	7.05 (0.3)	7.05 (0.3)	7.04 (0.3)	0.16
Weight-for-age Z-score, mean (SD)	31,150	0.49 (1.0)	0.53 (1.0)	0.46 (0.9)	<0.0001
Low weight-for-age, n (%)	31,150	629 (2.0)	345 (2.2)	284 (1.9)	0.05

*P value using the two-sample t-test for normally distributed continuous variables, and the X^2 test for categorical variables. Significant difference at *P*<0.05.

8.4.4 Relationship between maternal dietary patterns and size at birth

Table 40 and Table 41 show the crude and adjusted associations between offspring size at birth and maternal dietary patterns in pregnancy. Model 1 displays associations with adjustments for maternal pre-pregnancy BMI, age, parity, smoking in pregnancy, parental SES, gestation and infant's sex and model 2 represents adjusted associations with the addition of gestational weight gain (GWG) as a mediator.

8.4.4.1 Birth weight

Of the seven dietary patterns, five were found to have a significant association with birth weight in adjusted analyses (Table 42). The strongest association was found for mothers who scored highly on the Nordic dietary pattern, where, compared to mothers in the lowest quintile score, those in the highest quintile had children with a 42 g higher birth weight (95% CI: 25.6, 58.9; P_{trend}<0.0001). This association was strengthened further once adjustments for GWG as a mediator was made (44 g, 95% CI: 25.6, 63.1; P_{trend}<0.0001). A similar associations was seen for mothers who scored highly on the RPP dietary pattern; where compared to women in the lowest quintile, mothers in the highest quintile had babies born weighing 34 g more (95% CI: 16.8, 50.4, P_{trend}=0.0001). Testing for possible mediation by GWG slightly attenuated this relationship and lead to wider CIs due to a reduction in numbers from missing data (27 g, 95% CI: 7.55, 45.52; P_{trend}=0.01). The 'Seafood' dietary pattern was also seen to have a positive association with birth weight where mothers in the highest quintile score had babies weighing 30 g more (95% CI: 11.3, 49.7, P_{trend}=0.005) compared to babies born to mothers in the lowest quintile This relationship however only appeared once GWG were added to the model. The 'Alcohol' dietary pattern was also seen to have a positive, albeit smaller, association with birth weight, which was further strengthened once adjustments for GWG as a mediator was made where mothers in the highest dietary pattern quintile had babies weighing 27 g more (95% CI: 6.5, 46.8; P_{trend}=0.002) compared to babies born to mothers in the lowest quintile. Mothers who scored highly on the 'Sweets' dietary pattern had babies born weighing 20 g less (95% CI:-39.0, -1.8; P_{trend}=0.03) than babies born to mothers in the lowest quintile score. But as with the 'Seafood' dietary patterns, this association only appeared once adjustment for GWG as a mediator was made. Neither the vegetables/prudent nor the Western dietary patterns showed any significant association with birth weight.

8.4.4.2 Birth length

All but the 'Sweets' dietary pattern showed significant associations with length at birth and with the exception of the Western dietary pattern, relationships were all positive. Similar modest positive effect sizes in offspring birth length ranging between 0.11 and 0.15 cm were observed when comparing mothers in the highest quintile category to those in the lowest quintile across the different dietary patterns. As with birth weight, significant associations were only observed for ‘Seafood’ once adjustment for GWG as a mediator was made; as was the case for the Vegetables/prudent dietary pattern.

8.4.4.3 Weight-for-length Z-score

Only the Vegetables/prudent dietary pattern was found to have a significant association with offspring WFL Z-scores. Mothers who scored highly on the Vegetables/prudent dietary pattern had babies born with a -0.04 lower WFL Z-score (95% CI: -0.08, 0.00, P_{trend}=0.05) compared to babies born to mothers in the lowest quintile. However, once adjustment for GWG as a mediator was made the association was rendered insignificant (-0.03, 95% CI: -0.08, 0.02, P_{trend}=0.2).

8.4.4.4 Low birth weight

Neither of the dietary patterns were shown to be significantly associated with offspring LBW in adjusted analyses (Table 43).

8.4.4.5 High birth weight

After adjustments for confounders, only the Nordic dietary pattern was found to be significantly associated with offspring HBW. Compared to women in the lowest quintile score, women in the highest quintile score had significantly higher odds of having a HBW baby (OR: 1.20, 95% CI: 0.99, 1.46, P_{trend}=0.03, H-L goodness-of-fit test P=0.99). Adjustment of GWG as a mediator did not alter this relationship noticeably; although it did lead to wider CIs due to a reduction in numbers from missing data (OR: 1.21, 95% CI: 0.96, 1.52, P_{trend}=0.03) (Table 43).

Table 42. Association between maternal dietary patterns in pregnancy and offspring weight (g), length (cm) and WFL (Z-score) at birth in the DNBC

				Alcohol			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	4.94 (-12.26, 22.13)	11.01 (-6.19, 28.21)	16.01 (-1.19, 33.21)	10.89 (-6.31, 28.09)	0.09
Model 1[b]	27,197	Ref	-3.72 (-18.78,15.93)	10.86 (-5.46, 27.18)	17.55 (0.91, 34.19)	23.05 (5.21, 40.88)	0.0009
Model 2[c]	20,612	Ref	-2.11 (-20.21,15.98)	10.85 (-7.46, 29.16)	21.38 (2.64, 40.11)	26.63 (6.48, 46.77)	0.002
Birth length (cm)							
Crude model[a]	30,891	Ref	0.03 (-0.05, 0.11)	0.07 (-0.01, 0.14)	0.08 (0.01, 0.16)	0.06 (-0.01, 0.14)	0.07
Model 1[b]	26,821	Ref	0.00 (-0.07, 0.07)	0.07 (-0.00, 0.14)	0.08 (0.01, 0.16)	0.11 (0.03, 0.20)	0.0009
Model 2[c]	20,329	Ref	-0.01 (-0.09, 0.08)	0.07 (-0.01, 0.15)	0.09 (0.00, 0.17)	0.14 (0.05, 0.23)	0.0005
WFL Z-score							
Crude model[a]	30,864	Ref	-0.01 (-0.05, 0.03)	-0.01 (-0.05, 0.03)	0.00 (-0.04, 0.04)	-0.02 (-0.06, 0.02)	0.5
Model 1[b]	27,066	Ref	-0.01 (-0.05, 0.03)	-0.01 (-0.05, 0.03)	0.01 (-0.04, 0.05)	-0.01 (-0.05, 0.04)	0.9
Model 2[c]	20,517	Ref	-0.00 (-0.05, 0.05)	-0.00 (-0.05, 0.04)	0.01 (-0.04, 0.06)	-0.01 (-0.06, 0.04)	0.9
				Vegetables/prudent			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	31.66 (14.48, 48.85)	21.19 (4.00, 38.38)	12.28 (-4.71, 29.67)	22.04 (4.48, 39.24)	0.2
Model 1[b]	27,197	Ref	13.88 (-2.66, 30.42)	11.86 (-4.71, 28.42)	7.51 (-9.08, 24.09)	8.92 (-7.70, 25.54)	0.5
Model 2[c]	20,612	Ref	12.43 (-6.18, 31.04)	10.17 (-8.45, 28.00)	11.43 (-3.32, 30.02)	15.40 (-3.32, 34.12)	0.17
Birth length (cm)							
Crude model[a]	30,891	Ref	0.12 (0.04, 0.19)	0.11 (0.03, 0.19)	0.06 (-0.01, 0.14)	0.16 (0.08, 0.24)	0.003
Model 1[b]	27,091	Ref	0.06 (-0.02, 0.13)	0.07 (-0.01, 0.14)	0.04 (-0.04, 0.11)	0.09 (0.01, 0.16)	0.08
Model 2[c]	20,534	Ref	0.04 (-0.04, 0.13)	0.05 (-0.03, 0.14)	0.03 (-0.05, 0.12)	0.12 (0.03, 0.20)	0.02
WFL Z-score							
Crude model[a]	30,864	Ref	0.02 (-0.02, 0.06)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.02)	-0.05 (-0.09, -0.01)	0.004
Model 1[b]	27,066	Ref	0.002 (-0.04, 0.04)	-0.01 (-0.05, 0.03)	-0.01 (-0.06, 0.03)	-0.04 (-0.08, 0.00)	0.05
Model 2[c]	20,517	Ref	0.01 (-0.04, 0.05)	-0.01 (-0.06, 0.04)	-0.00 (-0.05, 0.05)	-0.03 (-0.08, 0.02)	0.2
				Western			

		Q1	Q2	Q3	Q4	Q5	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	21.94 (4.00, 38.39)	36.51 (19.32,53.70)	23.84 (6.65, 41.03)	2.72 (-14.47, 19.91)	0.7
Model 1[b]	27,197	Ref	2.06 (-14.43, 18.55)	12.85 (-3.76, 29.46)	8.93 (-7.88, 25.75)	-5.98 (-23.16, 11.20)	0.8
Model 2[c]	20,612	Ref	-3.03 (-21.66,15.60)	7.49 (-11.28, 26.26)	-1.78 (-20.79, 17.23)	-4.11 (-23.46, 15.25)	0.8
Birth length (cm)							
Crude model[a]	30,891	Ref	0.06 (-0.02, 0.14)	0.05 (-0.03, 0.13)	-0.02 (-0.09, 0.06)	-0.09, -0.17, 0.02)	0.002
Model 1[b]	26,821	Ref	0.05 (-0.02, 0.13)	0.02 (-0.06, 0.19)	-0.03 (-0.06, 0.09)	-0.01 (-0.08, 0.07)	0.6
Model 2[c]	20,329	Ref	0.02 (-0.06, 0.11)	-0.05 (-0.13, 0.04)	-0.06 (-0.14, 0.03)	-0.03 (-0.12, 0.06)	0.2
WFL Z-score							
Crude model[a]	30,864	Ref	0.04 (-0.00, 0.08)	0.09 (0.05, 0.13)	0.10 (0.06, 0.14)	0.09 (0.05, 0.13)	<0.0001
Model 1[b]	27,066	Ref	-0.01 (-0.05, 0.08)	0.03 (-0.01, 0.08)	0.03 (-0.02, 0.07)	-0.00 (-0.05, 0.04)	0.5
Model 2[c]	20,517	Ref	0.00 (-0.05, 0.05)	0.06 (0.01, 0.11)	0.04 (-0.01, 0.09)	0.02 (-0.03, 0.07)	0.2

Seafood

		Q1	Q2	Q3	Q4	Q5	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	29.93 (12.47, 47.12)	32.81 (15.63, 50.00)	27.07 (9.88, 44.27)	12.80 (-4.39, 30.00)	0.25
Model 1[b]	27,197	Ref	27.40 (10.91, 43.90)	31.44 (14.86, 48.03)	27.40 (10.91, 43.90)	16.93 (-0.08, 33.95)	0.1
Model 2[c]	20,612	Ref	28.96 (10.41, 47.50)	33.61 (14.98, 52.25)	29.79 (10.97, 48.60)	30.50 (11.30,49.70)	0.005
Birth length (cm)							
Crude model[a]	30,891	Ref	0.15 (0.07, 0.23)	0.16 (0.08, 0.24)	0.17 (0.09, 0.25)	0.12 (0.05, 0.20)	0.02
Model 1[b]	26,821	Ref	0.12 (0.04, 0.20)	0.14 (0.06, 0.21)	0.11 (0.04, 0.20)	0.08 (0.00, 0.16)	0.08
Model 2[c]	20,329	Ref	0.14 (0.06, 0.23)	0.15 (0.07, 0.24)	0.16 (0.07, 0.24)	0.15 (0.06, 0.23)	0.003
WFL Z-score							
Crude model[a]	30,864	Ref	-0.01 (-0.05, 0.03)	-0.02 (-0.06, 0.02)	-0.05 (-0.09, -0.01)	-0.06 (-0.10, -0.02)	0.0007
Model 1[b]	27,066	Ref	0.00 (-0.04, 0.04)	-0.01 (-0.05, 0.03)	-0.03 (-0.07, 0.02)	-0.02 (-0.06, 0.03)	0.25
Model 2[c]	20,517	Ref	-0.02 (-0.06, 0.03)	-0.01 (-0.06, 0.04)	-0.04 (-0.09, 0.01)	-0.02 (-0.07, 0.03)	0.35

Nordic

		Q1	Q2	Q3	Q4	Q5	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	36.89 (19.71, 54.07)	35.45 (18.28, 52.62)	58.51 (41.33,75.68)	69.79 (52.62,86.98)	<0.0001

Model 1[b]	27,197	Ref	20.19 (3.90, 36.50)	17.84 (1.49, 34.19)	32.84 (16.39,49.28)	42.23 (25.62,58.85)	<0.0001
Model 2[c]	20,612	Ref	17.81 (-0.57, 36.18)	20.42 (2.02, 38.81)	32.14 (13.60,50.69)	44.34 (25.63,63.06)	<0.0001
Birth length (cm)							
Crude model[a]	30,891	Ref	0.13 (0.05, 0.20)	0.11 (0.03, 0.18)	0.25 (0.17, 0.32)	0.24 (0.16, 0.32)	<0.0001
Model 1[b]	26,821	Ref	0.06 (-0.02, 0.13)	0.04 (-0.06, 0.09)	0.14 (0.07, 0.22)	0.12 (0.04, 0.19)	0.0002
Model 2[c]	20,329	Ref	0.08 (-0.00, 0.17)	0.03 (-0.05, 0.11)	0.16 (0.08, 0.25)	0.12 (0.04, 0.21)	0.0008
WFL Z-score							
Crude model[a]	30,864	Ref	0.03 (-0.01, 0.07)	0.03 (-0.01, 0.07)	0.01 (-0.03, 0.05)	0.05 (0.01, 0.09)	0.1
Model 1[b]	27,066	Ref	0.03 (-0.02, 0.07)	0.04 (-0.00, 0.08)	-0.00 (-0.04, 0.04)	0.05 (0.01, 0.09)	0.1
Model 2[c]	20,517	Ref	0.01 (-0.04, 0.05)	0.03 (-0.02, 0.07)	-0.02 (-0.07, 0.03)	0.05 (-0.00, 0.10)	0.2

Sweets

		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	-4.07 (-21.26,13.13)	-8.65 (-25.84, 8.55)	-9.57 (-26.76, 7.63)	-20.65 (-37.85, -3.45)	0.02
Model 1[b]	27,197	Ref	-1.35 (-17.89,15.19)	-3.87 (-20.86, 12.63)	-0.17 (-16.64,16.29)	-4.10 (-20.56,12.36)	0.7
Model 2[c]	20,612	Ref	-5.43 (-24.25,13.38)	-12.83 (-31.46, 5.81)	-10.62 (-29.24,8.00)	-20.38 (-39.01, -1.75)	0.03
Birth length (cm)							
Crude model[a]	30,891	Ref	-0.05 (-0.13, 0.03)	-0.04 (-0.12, 0.04)	-0.05 (-0.13, 0.03)	-0.11 (-0.19, -0.04)	0.01
Model 1[b]	26,821	Ref	-0.05 (-0.12, 0.03)	-0.04 (-0.12, 0.04)	-0.03 (-0.10, 0.05)	-0.05 (-0.13, 0.02)	0.3
Model 2[c]	20,329	Ref	-0.00 (-0.09, 0.09)	-0.04 (-0.13, 0.05)	-0.04 (0.13, 0.05)	-0.07 (-0.16, 0.03)	0.08
WFL Z-score							
Crude model[a]	30,864	Ref	0.02 (-0.02, 0.06)	0.00 (-0.04, 0.04)	-0.01 (-0.05, 0.03)	0.00 (-0.04, 0.04)	0.6
Model 1[b]	27,066	Ref	0.03 (-0.01, 0.07)	0.01 (-0.03, 0.05)	0.00 (-0.04, 0.05)	0.01 (-0.04, 0.05)	0.7
Model 2[c]	20,517	Ref	0.00 (-0.05, 0.05)	-0.02 (-0.07, 0.03)	-0.02 (-0.07, 0.03)	-0.03 (-0.08, 0.02)	0.2

Rice/pasta/poultry

		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
Birth weight (g)							
Crude model[a]	31,012	Ref	25.51 (8.31, 42.70)	29.97 (12.77, 47.16)	23.40 (6.20, 40.60)	25.85 (8.65, 43.05)	0.005
Model 1[b]	27,197	Ref	14.35 (-2.25, 30.94)	17.63 (1.00, 34.26)	23.61 (6.94, 40.29)	33.58 (16.80,50.36)	0.0001
Model 2[c]	20,612	Ref	12.17 (-6.57, 30.92)	12.73 (-6.03, 31.48)	15.26 (-3.55, 34.07)	26.54 (7.55, 45.52)	0.01
Birth length (cm)							
Crude model[a]	30,891	Ref	0.16 (0.08, 0.23)	0.19 (0.11, 0.26)	0.16 (0.08, 0.24)	0.15 (0.07, 0.22)	0.001

Model 1[b]	26,821	Ref	0.08 (-0.01, 0.16)	0.09 (0.01, 0.16)	0.10 (0.03, 0.18)	0.11 (0.04, 0.14)	0.005
Model 2[c]	20,329	Ref	0.06 (-0.03, 0.14)	0.05 (-0.04, 0.13)	0.07 (-0.02, 0.15)	0.09 (0.01, 0.18)	0.05
WFL Z-score							
Crude model[a]	30,864	Ref	-0.03 (-0.07, 0.01)	-0.04 (-0.08, 0.00)	-0.03 (-0.07, 0.01)	-0.03 (-0.07, 0.01)	0.2
Model 1[b]	27,066	Ref	-0.00 (-0.05, 0.04)	-0.00 (-0.05, 0.04)	0.01 (-0.03, 0.06)	0.02 (-0.02, 0.06)	0.3
Model 2[c]	20,517	Ref	0.01 (-0.04, 0.06)	0.02 (-0.03, 0.07)	0.01 (-0.04, 0.06)	0.02 (-0.03, 0.07)	0.5

[a] Unadjusted model [b] Adjusted for maternal pre-pregnancy BMI, age, parity, smoking in pregnancy, alcohol intake, parental SES, gestation and infant's sex (except the sex-specific WFL). [c] With additional adjustment for gestational weight gain as a mediator. [d] *P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; Q, quintile; Ref, reference category; WFL, weight-for-length.

Table 43. Association between maternal dietary patterns in pregnancy and offspring low birth weight (LBW) and high birth weight (HBW) in the DNBC

				Alcohol			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95% CI)			*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	0.80 (0.56, 1.13)	0.94 (0.67, 1.32)	1.04 (0.75, 1.45)	0.90 (0.64, 1.27)	0.5
Model 1[b]	293/27,197	Ref	0.76 (0.52, 1.11)	0.93 (0.65, 1.34)	0.96 (0.67, 1.38)	0.77 (0.51, 1.14)	0.5
Model 2[c]	217/20,612	Ref	0.73 (0.47, 1.14)	0.91 (0.59, 1.39)	0.94 (0.62, 1.44)	0.78 (0.49, 1.24)	0.6
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	0.92 (0.77, 1.10)	1.07 (0.90, 1.27)	1.04 (0.87, 1.24)	0.91 (0.76, 1.09)	0.55
Model 1[b]	1,140/27,197	Ref	0.91 (0.75, 1.10)	1.10 (0.91, 1.34)	1.15 (0.94, 1.39)	1.07 (0.86, 1.33)	0.1
Model 2[c]	849/20,612	Ref	0.96 (0.77, 1.21)	1.05 (0.84, 1.32)	1.21 (0.96, 1.51)	1.05 (0.82, 1.36)	0.3

				Vegetables/prudent			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95% CI)			*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	0.75 (0.53, 1.06)	0.96 (0.70, 1.33)	0.82 (0.59, 1.14)	0.73 (0.51, 1.03)	0.5
Model 1[b]	293/27,197	Ref	0.76 (0.52, 1.10)	0.92 (0.64, 1.31)	0.83 (0.57, 1.19)	0.80 (0.55, 1.16)	0.4
Model 2[c]	217/20,612	Ref	0.75 (0.49, 1.15)	0.89 (0.59, 1.34)	0.75 (0.49, 1.16)	0.69 (0.44, 1.09)	0.16
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	1.05 (0.88, 1.26)	1.09 (0.91, 1.31)	1.18 (0.99, 1.41)	1.29 (1.08, 1.54)	0.002
Model 1[b]	1,140/27,197	Ref	1.05 (0.86, 1.28)	1.07 (0.87, 1.30)	1.08 (0.89, 1.32)	1.13 (0.93, 1.38)	0.2
Model 2[c]	849/20,612	Ref	1.09 (0.87, 1.37)	1.04 (0.83, 1.33)	1.09 (0.86, 1.33)	1.11 (0.88, 1.34)	0.6

				Western			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95% CI)			*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	1.10 (0.75, 1.59)	1.11 (0.77, 1.62)	1.88 (1.35, 1.62)	1.88 (1.35, 2.63)	0.0008
Model 1[b]	293/27,197	Ref	1.19 (0.79, 1.78)	1.12 (0.74, 1.70)	0.96 (0.63, 1.47)	1.42 (0.95, 2.12)	0.3
Model 2[c]	217/20,612	Ref	1.06 (0.65, 1.72)	1.16 (0.72, 1.86)	1.11 (0.69, 1.80)	1.33 (0.84, 2.13)	0.1
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	1.09 (0.91, 1.31)	1.18 (0.99, 1.41)	1.19 (1.00, 1.43)	1.17 (0.98, 1.40)	0.7
Model 1[b]	1,140/27,197	Ref	0.97 (0.79, 1.18)	0.99 (0.81, 1.21)	1.01 (0.83, 1.24)	1.00 (0.82, 1.23)	0.8
Model 2[c]	849/20,612	Ref	0.91 (0.72, 1.15)	0.93 (0.74, 1.18)	0.98 (0.77, 1.24)	0.99 (0.78, 1.25)	0.8

				Seafood			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95% CI)			*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	0.92 (0.66, 1.28)	0.80 (0.56, 1.12)	0.73 (0.51, 1.04)	0.99 (0.71, 1.37)	0.9
Model 1[b]	293/27,197	Ref	1.08 (0.75, 1.56)	0.98 (0.67, 1.43)	0.90 (0.60, 1.34)	1.37 (0.94, 1.99)	0.3
Model 2[c]	217/20,612	Ref	1.30 (0.86, 1.97)	1.04 (0.67, 1.61)	0.69 (0.42, 1.14)	1.23 (0.79, 1.92)	0.7
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	1.04 (0.87, 1.24)	1.11 (0.93, 1.31)	0.90 (0.75, 1.08)	1.02 (0.86, 1.22)	0.7
Model 1[b]	1,140/27,197	Ref	1.16 (0.95, 1.41)	1.27 (1.05, 1.55)	1.04 (0.85, 1.28)	1.27 (1.04, 1.56)	0.1
Model 2[c]	849/20,612	Ref	1.13 (0.90, 1.43)	1.31 (1.05, 1.65)	1.02 (0.80, 1.30)	1.20 (0.95, 1.53)	0.3
				Nordic			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95% CI)			*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	0.63 (0.45, 0.84)	0.75 (0.54, 1.03)	0.61 (0.43, 0.86)	0.73 (0.53, 1.00)	0.06
Model 1[b]	293/27,197	Ref	0.71 (0.49, 1.02)	0.78 (0.55, 1.12)	0.71 (0.49, 1.03)	0.91 (0.63, 1.29)	0.6
Model 2[c]	217/20,612	Ref	0.77 (0.50, 1.18)	0.87 (0.58, 1.33)	0.82 (0.53, 1.27)	0.99 (0.65, 1.51)	0.9
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	1.08 (0.91, 1.29)	1.07 (0.90, 1.28)	1.03 (0.86, 1.23)	1.10 (0.92, 1.31)	0.5
Model 1[b]	1,140/27,197	Ref	1.02 (0.84, 1.25)	1.07 (0.88, 1.30)	1.14 (0.94, 1.39)	1.20 (0.99, 1.46)	0.03
Model 2[c]	849/20,612	Ref	0.93 (0.73, 1.18)	1.10 (0.87, 1.38)	1.11 (0.89, 1.40)	1.21 (0.96, 1.52)	0.03
				Sweets			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95% CI)			*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	1.11 (0.79, 1.57)	1.05 (0.74, 1.48)	0.86 (0.59, 1.23)	1.19 (0.85, 1.67)	0.9
Model 1[b]	293/27,197	Ref	1.10 (0.76, 1.59)	1.02 (0.70, 1.49)	0.76 (0.51, 1.12)	1.09 (0.76, 1.58)	0.6
Model 2[c]	217/20,612	Ref	0.97 (0.63, 1.50)	0.92 (0.60, 1.42)	0.63 (0.39, 1.01)	1.12 (0.74, 1.70)	0.7
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	0.86 (0.73, 1.03)	0.88 (0.74, 1.04)	0.89 (0.75, 1.06)	0.87 (0.73, 1.03)	0.2
Model 1[b]	1,140/27,197	Ref	0.92 (0.76, 1.11)	0.92 (0.76, 1.11)	0.98 (0.81, 1.19)	1.03 (0.85, 1.25)	0.6
Model 2[c]	849/20,612	Ref	0.86 (0.69, 1.09)	0.88 (0.70, 1.11)	0.93 (0.74, 1.16)	0.94 (0.75, 1.17)	0.8
				Rice/pasta/poultry			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	

	cases/N	OR (95% CI)					*P-trend*[d]
LBW (<2,500 g)							
Crude model[a]	328/31,012	Ref	0.62 (0.45, 0.86)	0.60 (0.44, 0.84)	0.53 (0.38, 0.75)	0.60 (0.44, 0.84)	0.001
Model 1[b]	293/27,197	Ref	0.66 (0.46, 0.94)	0.72 (0.50, 1.03)	0.64 (0.43, 0.93)	0.71 (0.49, 1.03)	0.1
Model 2[c]	217/20,612	Ref	0.64 (0.42, 0.98)	0.76 (0.50, 1.17)	0.77 (0.50, 1.19)	0.76 (0.49, 1.17)	0.5
HBW (>4,500 g)							
Crude model[a]	1,306/31,012	Ref	1.01 (0.85, 1.21)	1.07 (0.90, 1.28)	0.96 (0.80, 1.15)	1.03 (0.87, 1.23)	0.9
Model 1[b]	1,140/27,197	Ref	0.95 (0.78, 1.15)	1.00 (0.82, 1.21)	0.99 (0.81, 1.20)	1.12 (0.92, 1.36)	0.2
Model 2[c]	849/20,612	Ref	0.97 (0.77, 1.22)	1.01 (0.80, 1.27)	1.04 (0.82, 1.30)	1.13 (0.90, 1.42)	0.2

[a] Unadjusted model [b] Adjusted for maternal pre-pregnancy BMI, age, parity, smoking in pregnancy, alcohol intake, parental SES, gestation and infant's sex.
[c] With additional adjustment for gestational weight gain as a mediator. [d] *P* for trend across dietary pattern quintiles in linear regression models.
CI, confidence interval; LBW, low birth weight; HBW, high birth weight; N, number; OR, odds ratios; Q, quintile; Ref, reference category.

8.4.4.6 Effect modification by maternal pre-pregnancy BMI

There was a significant interaction observed between the ‘RPP’ dietary pattern and maternal pre-pregnancy BMI on offspring birth length and risk of being HBW (Table 23). For every 1 unit increase in the ‘RPP’ dietary pattern score, mothers with a pre-pregnancy BMI ≥25 (kg/m2) had babies born with a 0.06 cm longer birth length (95% CI: 0.02, 0.09, interaction *P*=0.04) and they were also 10% more likely to have and infant born HBW (95% CI: 1.03, 1.18, interaction *P*=0.005). A significant interaction was also observed between the ‘Seafood’ dietary pattern and maternal pre-pregnancy BMI status, however the association was not significant (Table 44).

Table 44. Multivariate[a] regression estimates from stratified analyses for associations between maternal dietary patterns in pregnancy with offspring size at birth with testing for effect modification by maternal pre-pregnancy BMI (kg/m^2)

	Birth weight (g) (N=27,197)		Birth length (cm) (N=27,066)		WFL Z-score (N=27,066)		LBW (<2,500 g) (cases/N=293/27,197)		HBW (>4,500 g) (cases/N=1,140/27,197)	
	β (95 % CI)	*P*[b]	*β* (95 % CI)	*P*[b]	*β* (95 % CI)	*P*[b]	OR (95 % CI)	*P*[b]	OR (95 % CI)	*P*[b]
Alcohol (Per 1 unit increase)		0.6		0.6		0.8		0.2		0.8
BMI <25 (kg/m^2)	10.50 (-0.95, 21.96)		0.08 (0.02, 0.13)		-0.03 (-0.06, 0.004)		1.01 (0.79, 1.28)		1.13 (1.00, 1.28)	
BMI ≥25 (kg/m^2)	17.02 (-2.61, 36.65)		0.10 (0.01, 0.19)		-0.02 (-0.07, 0.03)		0.70 (0.41, 1.21)		1.10 (0.93, 1.30)	
Vegetables/prudent (Per 1 unit increase)		0.8		0.6		0.2		0.7		0.2
BMI <25 (kg/m^2)	-1.07 (-4.28, 2.14)		0.01 (-0.00, 0.03)		-0.01 (-0.02, -0.00)		0.98 (0.91, 1.06)		1.03 (0.99, 1.07)	
BMI ≥25 (kg/m^2)	-0.24 (-5.96, 5.48)		0.00 (-0.02, 0.03)		-0.002 (-0.02, 0.01)		1.01 (0.89, 1.14)		0.98 (0.93, 1.04)	
Western (Per 1 unit increase)		0.9		0.7		0.9		0.9		0.9
BMI <25 (kg/m^2)	-2.47 (-6.36, 1.43)		-0.02 (-0.03, 0.00)		0.003 (-0.01, 0.01)		1.09 (1.01, 1.18)		0.99 (0.94, 1.05)	
BMI ≥25 (kg/m^2)	-2.45 (-9.16, 4.26)		-0.01 (-0.04, 0.02)		0.002 (-0.02, 0.02)		1.08 (0.93, 1.25)		1.00 (0.94, 1.07)	
Seafood (Per 1 unit increase)		0.05		0.08		0.5		0.8		0.8
BMI <25 (kg/m^2)	-3.13 (-7.25, 0.98)	0.1	-0.01 (-0.02, 0.01)		-0.01 (-0.02, 0.00)		1.08 (0.99, 1.17)		1.04 (0.98, 1.09)	
BMI ≥25 (kg/m^2)	5.56 (-1.97, 13.08)	0.1	0.03 (-0.01, 0.06)		-0.003 (-0.02, 0.02)		1.05 (0.89, 1.23)		1.01 (0.94, 1.08)	
Nordic (Per 1 unit increase)		0.1		0.8		0.5		0.9		0.6
BMI <25 (kg/m^2)	7.16 (2.90, 11.42)		0.03 (0.01, 0.05)		0.01 (-0.01, 0.02)		0.97 (0.88, 1.06)		1.03 (0.98, 1.09)	
BMI ≥25 (kg/m^2)	13.81 (9.24, 21.38)		0.03 (0.00, 0.07)		0.01 (-0.01, 0.03)		0.96 (0.81, 1.15)		1.06 (0.99, 1.13)	
Sweets (Per 1 unit increase)		0.9		0.6		0.2		0.5		0.9
BMI <25 (kg/m^2)	-1.55 (-5.82, 2.72)		-0.02 (-0.03, 0.00)		0.002 (-0.01, 0.01)		1.03 (0.94, 1.13)		1.01 (0.96, 1.07)	
BMI ≥25 (kg/m^2)	-2.18 (-9.88, 5.52)		-0.002 (-0.04, 0.03)		-0.01 (-0.03, 0.01)		0.97 (0.80, 1.16)		1.01 (0.94, 1.09)	
Rice/pasta/poultry (Per 1 unit increase)		0.1		0.04		0.2		0.7		0.005
BMI <25 (kg/m^2)	6.65 (2.04, 11.26)		0.01 (-0.01, 0.04)	(0.2)	0.01 (-0.003, 0.02)		0.88 (0.79, 0.97)		0.96 (0.91, 1.03)	0.3
BMI ≥25 (kg/m^2)	13.35 (5.72, 20.98)		0.06 (0.02, 0.09)	(0.002)	-0.01 (-0.03, 0.01)		0.91 (0.76, 1.10)		1.10 (1.03, 1.18)	0.006

[a] Adjusted maternal pre-pregnancy BMI, age, parity, smoking in pregnancy, alcohol intake, parental SES, gestation and infant's sex (except the sex-specific WFL). [b] Interaction P value, testing the null hypotheses that associations do not differ by maternal pre-pregnancy BMI status. BMI, body mass index; CI, confidence interval; LBW, low birth weight; HBW, high birth weight; OR, odds ratio; WFL, weight-for-length.

8.4.5 Relationship between maternal dietary patterns and offspring anthropometry at age 7 years

Table 45 shows the crude and adjusted associations between child WFA and HFA Z-scores at the 7 year follow-up and maternal dietary patterns in pregnancy. Of the 7 dietary patterns, 4 were found to have a significant association with HFA Z-scores after adjusting for important confounders. The strongest association was found for women in the Nordic dietary pattern, where, compared to those in the lowest quintile score, those in the highest quintile had children with a 0.12 higher HFA Z-score (95% CI: 0.08, 0.15; $P_{\mathrm{trend}}<0.0001$). Both the Rice/pasta/poultry and the Alcohol dietary patterns were also seen to have a positive, albeit smaller, association with child HFA Z-scores. The Sweet dietary pattern was found to have a negative association with HFA Z-scores; compared to women in the lowest quintile, children born of mothers in the highest quintile had a lower HFA Z-score (-0.06; 95% CI: -0.09, -0.02; $\mathrm{P}_{\mathrm{trend}} <0.001$). Only the Nordic and the Seafood dietary patterns were found to have significant associations with child WFA Z-scores. After adjusting for confounders, the Nordic dietary pattern was seen to have a small positive association with WFA Z-scores. Compared to women in the lowest quintile children born to mothers in the highest quintile had a slightly higher WFA Z-score (0.05; 95% CI: 0.03, 0.08; $\mathrm{P}_{\mathrm{trend}}<0.0001$) whereas the Seafood dietary pattern was seen to have a small negative association (-0.03; 95%CI: -0.05, 0.00; $\mathrm{P}_{\mathrm{trend}}=0.03$).

Table 46 presents crude and adjusted odd ratios (OR) of having a LWFA or LHFA child at the 7 year follow-up across the 7 dietary patterns. After adjusting for confounders, only the Nordic dietary pattern was found to have a significant association. Compared to women in the lowest quintile score, women in the highest quintile score had significantly lower odds of having a LHFA child (OR: 0.72, 95% CI: 0.53, 0.96, $\mathrm{P}_{\mathrm{trend}}=0.009$, H-L goodness-of-fit test $P=0.99$) and LWFA child (OR: 0.74, 95% CI: 0.55, 0.99, $\mathrm{P}_{\mathrm{trend}}=0.02$, H-L goodness-of-fit test $P=0.99$).

Including gestational weight gain in the models did lead to wider CIs due to a reduction in numbers from missing data (Model 2 in Table 45) and for LHFA the association with the Nordic dietary pattern was rendered insignificant (Model 2 in

Table 46). Testing for possible mediation by birth weight slightly attenuated any association with LWFA. It did not alter the results for any of the other associations (Model 3 in Table 45 & Table 46).

Table 45. Association between maternal dietary patterns in pregnancy and offspring height-for-age (HFA) and weight-for-age (WFA) Z-scores at age 7 years in the DNBC

				Alcohol			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	0.02 (-0.02, 0.05)	0.01 (-0.02, 0.05)	0.05 (0.02, 0.09)	0.04 (0.00, 0.07)	0.008
Model 1[b]	24,364	Ref	0.02 (-0.02, 0.06)	0.02 (-0.02, 0.06)	0.06 (0.02, 0.09)	0.05 (0.01, 0.09)	0.002
Model 2[c]	18,485	Ref	0.03 (-0.02, 0.07)	0.02 (-0.03, 0.06)	0.07 (0.03, 0.11)	0.07 (0.02, 0.11)	0.003
Model 3[d]	24,263	Ref	0.02 (-0.01, 0.06)	0.02 (-0.02, 0.05)	0.05 (0.02, 0.09)	0.05 (0.01, 0.08)	0.003
WFA Z-score							
Crude model[a]	31,150	Ref	0 (0.02, 0.04)	0 (-0.04, 0.03)	0.01 (-0.02, 0.05)	0.03 (0.00, 0.07)	0.02
Model 1[b]	27,085	Ref	-0.01 (-0.04, 0.01)	-0.01 (-0.03, 0.02)	-0.02 (-0.04, 0.01)	0.01 (-0.02, 0.03)	0.5
Model 2[c]	20,520	Ref	-0.03 (-0.06, 0.00)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.01)	0.01 (-0.02, 0.04)	0.2
Model 3[d]	26,970	Ref	-0.01 (-0.04, 0.01)	-0.01 (-0.03, 0.02)	-0.02 (-0.04, 0.01)	0.01 (-0.02, 0.03)	0.5
				Vegetables/prudent			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	0.03 (-0.01, 0.06)	0.03 (-0.00, 0.07)	0.03 (-0.01, 0.06)	0.05 (0.02, 0.08)	0.01
Model 1[b]	24,364	Ref	0.01 (-0.03, 0.04)	0.02 (-0.02, 0.06)	0.01 (-0.03, 0.05)	0.03 (-0.012, 0.07)	0.2
Model 2[c]	18,485	Ref	0.01 (-0.04, 0.05)	0.03 (-0.01, 0.07)	0.02 (-0.02, 0.06)	0.04 (-0.01, 0.08)	0.1
Model 3[d]	24,263	Ref	0.00 (-0.04, 0.04)	0.02 (-0.02, 0.05)	0.01 (-0.03, 0.04)	0.02 (-0.01, 0.06)	0.2
WFA Z-score							
Crude model[a]	31,150	Ref	0.00 (-0.03, 0.03)	-0.02 (-0.06, 0.01)	0.00 (-0.04, 0.03)	-0.01 (-0.04, 0.02)	0.5
Model 1[b]	27,085	Ref	-0.01 (-0.03, 0.02)	-0.02 (-0.04, 0.01)	0.01 (-0.02, 0.04)	0.00 (-0.03, 0.02)	0.8
Model 2[c]	20,520	Ref	-0.01 (-0.04, 0.02)	-0.02 (-0.05, 0.01)	0.01 (-0.02, 0.04)	0.00 (-0.03, 0.03)	0.4
Model 3[d]	26,970	Ref	-0.01 (-0.03, 0.02)	-0.02 (-0.04, 0.01)	0.01 (-0.01, 0.04)	0.00 (-0.03, 0.02)	0.8
				Western			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	-0.02 (-0.06, 0.01)	-0.02 (-0.06, 0.01)	-0.04 (-0.07, -0.00)	-0.05 (-0.09, -0.02)	0.002
Model 1[b]	24,364	Ref	0.00 (-0.04, 0.03)	0.01 (-0.03, 0.05)	0.00 (-0.04, 0.04)	0.01 (-0.03, 0.04)	0.6

Model 2[c]	18,485	Ref	-0.02 (-0.07, 0.02)	-0.02 (-0.07, 0.02)	-0.04 (-0.08, -0.01)	-0.01 (-0.06, 0.03)	0.5
Model 3[d]	24,263	Ref	-0.01 (-0.04, 0.03)	0.00 (-0.04, 0.03)	-0.01 (-0.04, 0.03)	0.01 (-0.03, 0.05)	0.9
WFA Z-score							
Crude model[a]	31,150	Ref	0.01 (-0.02, 0.04)	0.02 (-0.01, 0.06)	0.03 (-0.01, 0.06)	0.04 (0.01, 0.08)	0.01
Model 1[b]	27,085	Ref	0.00 (-0.02, 0.03)	0.00 (-0.02, 0.03)	-0.01 (-0.03, 0.02)	0.00 (-0.03, 0.03)	0.8
Model 2[c]	20,520	Ref	0.01 (-0.02, 0.04)	0.00 (-0.03, 0.03)	-0.01 (-0.04, 0.02)	0.00 (-0.03, 0.03)	0.6
Model 3[d]	26,970	Ref	0.00 (-0.03, 0.03)	0.00 (-0.03, 0.02)	-0.01 (-0.03, 0.02)	0.00 (-0.03, 0.03)	0.8
				Seafood			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	0.00 (-0.03, 0.04)	0.02 (-0.01, 0.06)	0.03 (-0.00, 0.07)	0.01 (-0.03, 0.04)	0.5
Model 1[b]	24,364	Ref	-0.01 (-0.04, 0.03)	0.01 (-0.01, 0.04)	0.02 (-0.02, 0.06)	-0.01 (-0.04, 0.03)	0.9
Model 2[c]	18,485	Ref	-0.01 (-0.05, 0.04)	0.03 (-0.01, 0.08)	0.03 (-0.01, 0.07)	0.01 (-0.03, 0.05)	0.4
Model 3[d]	24,263	Ref	-0.02 (-0.05, 0.02)	0.02 (-0.02, 0.05)	0.01 (-0.02, 0.05)	-0.01 (-0.04, 0.03)	0.9
WFA Z-score							
Crude model[a]	31,150	Ref	-0.03 (-0.06, 0.01)	-0.05 (-0.08, -0.01)	-0.06 (-0.10, -0.03)	-0.01 (-0.13, -0.07)	<0.0001
Model 1[b]	27,085	Ref	0.00 (-0.03, 0.02)	-0.02 (-0.04, 0.01)	-0.02 (-0.05, 0.00)	-0.03 (-0.05, 0.00)	0.03
Model 2[c]	20,520	Ref	0.00 (-0.03, 0.03)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.02)	-0.03 (-0.06, 0.00)	0.08
Model 3[d]	26,970	Ref	-0.01 (-0.03, 0.02)	-0.02 (-0.05, 0.00)	-0.03 (-0.05, 0.00)	-0.03 (-0.05, 0.00)	0.03
				Nordic			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	0.03 (-0.06, 0.07)	0.05 (0.02, 0.09)	0.08 (0.04, 0.11)	0.09 (0.05, 0.12)	<0.0001
Model 1[b]	24,364	Ref	0.04 (0.01, 0.08)	0.06 (0.02, 0.10)	0.10 (0.06, 0.13)	0.12 (0.08, 0.15)	<0.0001
Model 2[c]	18,485	Ref	0.06 (0.01, 0.10)	0.07 (0.03, 0.12)	0.09 (0.05, 0.14)	0.12 (0.07, 0.16)	<0.0001
Model 3[d]	24,263	Ref	0.04 (0.00, 0.07)	0.05 (0.02, 0.09)	0.08 (0.04, 0.11)	0.10 (0.06, 0.13)	<0.0001
WFA Z-score							
Crude model[a]	31,150	Ref	0.03 (0.00, 0.07)	0.04 (0.01, 0.07)	0.05 (0.02, 0.09)	0.04 (0.01, 0.07)	0.01
Model 1[b]	27,085	Ref	0.03 (0.01, 0.06)	0.05 (0.02, 0.07)	0.05 (0.03, 0.08)	0.05 (0.03, 0.08)	<0.0001
Model 2[c]	20,520	Ref	0.04 (0.01, 0.07)	0.06 (0.03, 0.09)	0.06 (0.03, 0.09)	0.05 (0.02, 0.08)	0.001
Model 3[d]	26,970	Ref	0.03 (0.00, 0.05)	0.04 (0.03, 0.07)	0.05 (0.02, 0.07)	0.04 (0.02, 0.07)	0.0005
				Sweets			

		Q1	Q2	Q3	Q4	Q5	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	-0.02 (-0.06,0.01)	-0.03 (-0.06, 0.01)	-0.05 (-0.09, -0.02)	-0.09 (-0.13, -0.06)	<0.0001
Model 1[b]	24,364	Ref	-0.03 (-0.06, 0.01)	-0.03 (-0.07, 0.01)	-0.05 (-0.08, -0.01)	-0.06 (-0.09, -0.02)	0.0001
Model 2[c]	18,485	Ref	-0.02 (-0.06, 0.02)	-0.02 (-0.09, 0.00)	-0.06 (-0.11, -0.02)	-0.06 (-0.11, -0.02)	0.002
Model 3[d]	24,263	Ref	-0.03 (-0.07, 0.01)	-0.03 (-0.06, 0.01)	-0.05 (-0.08, -0.01)	-0.06 (-0.10, -0.02)	0.001
WFA Z-score							
Crude model[a]	31,150	Ref	-0.02 (-0.05, 0.02)	-0.04 (-0.07, 0.00)	-0.05 (-0.08, -0.02)	-0.08 (-0.11, -0.05)	<0.0001
Model 1[b]	27,085	Ref	0.00 (-0.02, 0.03)	-0.01 (-0.04, 0.01)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.01)	0.2
Model 2[c]	20,520	Ref	0.00 (-0.03, 0.03)	-0.02 (-0.05, 0.01)	-0.01 (-0.04, 0.02)	-0.02 (-0.05, 0.01)	0.2
Model 3[d]	26,970	Ref	0.00 (-0.03, 0.03)	-0.01 (-0.04, 0.01)	-0.01 (-0.04, 0.01)	-0.01 (-0.04, 0.01)	0.2

Rice/pasta/poultry

		Q1	Q2	Q3	Q4	Q5	
	N			*β* (95 % CI)			*P-trend*[d]
HFA Z-score							
Crude model[a]	31,150	Ref	0.09 (0.05, 0.12)	0.10 (0.07, 0.14)	0.11 (0.08, 0.15)	0.11 (0.08, 0.15)	<0.0001
Model 1[b]	24,364	Ref	0.06 (0.03, 0.10)	0.07 (0.03, 0.11)	0.06 (0.03, 0.10)	0.07 (0.03, 0.11)	0.002
Model 2[c]	18,485	Ref	0.06 (0.02, 0.10)	0.06 (0.02, 0.11)	0.07 (0.02, 0.11)	0.06 (0.02, 0.11)	0.01
Model 3[d]	24,263	Ref	0.06 (0.02, 0.10)	0.06 (0.02, 0.10)	0.06 (0.02, 0.10)	0.06 (0.02, 0.09)	0.01
WFA Z-score							
Crude model[a]	31,150	Ref	0.03 (0.00, 0.10)	0.05 (0.01, 0.08)	0.05 (0.02, 0.08)	0.03 (0.00, 0.07)	0.05
Model 1[b]	27,085	Ref	-0.01 (-0.04, 0.02)	0.01 (-0.02, 0.04)	0.01 (-0.01, 0.04)	-0.01 (-0.04, 0.02)	0.9
Model 2[c]	20,520	Ref	0.01 (-0.02, 0.04)	0.01 (-0.01, 0.04)	0.02 (-0.02, 0.05)	-0.00 (-0.03, 0.03)	0.9
Model 3[d]	26,970	Ref	-0.01 (-0.03, 0.02)	0.01 (-0.02, 0.03)	0.01 (-0.02, 0.04)	-0.01 (-0.04, 0.01)	0.6

[a] Unadjusted crude model. [b] Adjusted maternal pre-pregnancy BMI, age, parity, smoking, SES, and child height in the WFA models and paternal height in the HFA models. [c] With additional adjustment for gestational weight gain as a mediator. [d] With additional adjustment for offspring birth weight as mediators. [e] *P* for trend across dietary pattern quintiles in linear regression models. CI, confidence interval; HFA, height-for-age; OR, odds ratio; Q, quintile; Ref, reference category; WFA, weight-for-age;

Table 46. Association between maternal dietary patterns in pregnancy and offspring low height-for-age (LHFA) and low weight-for-age (LWFA) Z-scores at age 7 years in the DNBC

				Alcohol			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95 % CI)			*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	0.91 (0.71, 1.16)	1.08 (0.85, 1.36)	0.92 (0.72, 1.17)	0.87 (0.68, 1.12)	0.3
Model 1[b]	500/24,364	Ref	0.85 (0.64, 1.14)	1.08 (0.82, 1.41)	0.97 (0.73, 1.28)	0.94 (0.70, 1.24)	0.9
Model 2[c]	375/18,485	Ref	0.91 (0.66, 0.13)	1.04 (0.76, 1.42)	0.87 (0.62, 1.20)	0.83 (0.59, 1.16)	0.4
Model 3[d]	499/24,263	Ref	0.86 (0.64, 1.14)	1.10 (0.84, 1.44)	1.00 (0.75, 1.32)	0.95 (0.71, 1.26)	0.9
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	0.98 (0.77, 1.27)	1.16 (0.91, 1.48)	1.04 (0.81, 1.33)	0.85 (0.65, 1.10)	0.2
Model 1[b]	541/27,085	Ref	1.07 (0.81, 1.43)	1.17 (0.88, 1.54)	1.07 (0.80, 1.43)	0.77 (0.57, 1.05)	0.08
Model 2[c]	433/20,520	Ref	1.16 (0.84, 1.59)	1.11 (0.81, 1.52)	1.07 (0.77, 1.48)	0.82 (0.57, 1.16)	0.2
Model 3[d]	538/26,970	Ref	1.04 (0.78, 1.39)	1.13 (0.85, 1.50)	1.05 (0.78, 1.41)	0.76 (0.56, 1.03)	0.1
				Vegetables/prudent			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95 % CI)			*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	0.80 (0.69, 1.02)	1.00 (0.79, 1.27)	0.94 (0.74, 1.20)	0.93 (0.73, 1.19)	0.7
Model 1[b]	500/24,364	Ref	0.81 (0.61, 1.09)	0.99 (0.75, 1.31)	0.97 (0.73, 1.29)	0.98 (0.74, 1.30)	0.9
Model 2[c]	375/18,485	Ref	0.76 (0.54, 1.07)	0.88 (0.63, 1.23)	0.99 (0.72, 1.37)	0.98 (0.71, 1.35)	0.5
Model 3[d]	499/24,263	Ref	0.84 (0.62, 1.12)	1.01 (0.76, 1.34)	0.96 (0.72, 1.28)	0.98 (0.74, 1.30)	0.8
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	1.00 (0.77, 1.30)	1.14 (0.89, 1.47)	1.08 (0.84, 1.39)	1.17 (0.91, 1.50)	0.2
Model 1[b]	541/27,085	Ref	1.02 (0.76, 1.38)	0.99 (0.73, 1.33)	1.02 (0.76, 1.38)	1.13 (0.84, 1.52)	0.6
Model 2[c]	433/20,520	Ref	1.15 (0.83, 1.60)	0.97 (0.69, 1.36)	0.94 (0.67, 1.31)	1.07 (0.77, 1.49)	0.9
Model 3[d]	538/26,970	Ref	1.03 (0.76, 1.39)	0.95 (0.71, 1.29)	0.98 (0.74, 1.32)	1.02 (0.76, 1.37)	0.9
				Western			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95 % CI)			*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	1.09 (0.84, 1.41)	1.01 (0.78, 1.31)	1.38 (1.08, 1.77)	1.34 (1.04, 1.71)	0.004
Model 1[b]	500/24,364	Ref	1.02 (0.75, 1.38)	0.92 (0.68, 1.26)	1.28 (0.96, 1.72)	1.11 (0.82, 1.51)	0.2

Model 2[c]	375/18,485	Ref	1.03 (0.73, 1.46)	0.92 (0.64, 1.32)	1.33 (0.94, 1.88)	1.09 (0.74, 1.62)	0.4
Model 3[d]	499/24,263	Ref	1.02 (0.75, 1.38)	0.94 (0.69, 1.28)	1.27 (0.95, 1.71)	1.09 (0.81, 1.48)	0.3
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	1.13 (0.87, 1.45)	1.12 (0.87, 1.44)	1.19 (0.92, 1.53)	1.10 (0.85, 1.42)	0.5
Model 1[b]	541/27,085	Ref	1.18 (0.87, 1.59)	1.12 (0.83, 1.52)	1.18 (0.87, 1.59)	1.01 (0.73, 1.38)	0.9
Model 2[c]	433/20,520	Ref	1.03 (0.73, 1.45)	1.03 (0.73, 1.46)	1.18 (0.84, 1.65)	0.97 (0.68, 1.38)	0.9
Model 3[d]	538/26,970	Ref	1.19 (0.88, 1.61)	1.18 (0.86, 1.60)	1.21 (0.89, 1.64)	1.02 (0.74, 1.40)	0.9
				Seafood			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95 % CI)			*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	0.88 (0.69, 1.11)	0.76 (0.59, 0.97)	0.91 (0.72, 1.15)	0.81 (0.64, 1.03)	0.2
Model 1[b]	500/24,364	Ref	0.98 (0.74, 1.30)	0.81 (0.60, 1.09)	1.12 (0.84, 1.47)	0.95 (0.71, 1.28)	0.9
Model 2[c]	375/18,485	Ref	0.92 (0.67, 1.28)	0.80 (0.57, 1.12)	1.13 (0.83, 1.56)	0.86 (0.62, 1.20)	0.7
Model 3[d]	499/24,263	Ref	1.02 (0.77, 1.35)	0.83 (0.62, 1.12)	1.13 (0.86, 1.50)	0.94 (0.70, 1.26)	0.9
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	0.78 (0.60, 1.01)	0.83 (0.64, 1.06)	1.04 (0.82, 1.32)	1.05 (0.82, 1.33)	0.1
Model 1[b]	541/27,085	Ref	0.70 (0.52, 0.95)	0.77 (0.57, 1.04)	0.95 (0.72, 1.27)	0.92 (0.69, 1.23)	0.6
Model 2[c]	433/20,520	Ref	0.70 (0.50, 0.98)	0.74 (0.53, 1.04)	0.89 (0.65, 1.23)	0.86 (0.62, 1.20)	0.9
Model 3[d]	538/26,970	Ref	0.70 (0.51, 0.95)	0.74 (0.55, 1.01)	0.93 (0.70, 1.25)	0.88 (0.65, 1.18)	0.9
				Nordic			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N			OR (95 % CI)			*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	0.91 (0.72, 1.14)	0.93 (0.73, 1.17)	0.75 (0.59, 0.96)	0.74 (0.58, 0.95)	0.01
Model 1[b]	500/24,364	Ref	0.92 (0.70, 1.21)	1.06 (0.81, 1.40)	0.73 (0.55, 0.98)	0.72 (0.53, 0.96)	0.009
Model 2[c]	375/18,485	Ref	0.95 (0.69, 1.31)	1.14 (0.84, 1.56)	0.77 (0.55, 1.09)	0.81 (0.57, 1.13)	0.1
Model 3[d]	499/24,263	Ref	0.95 (0.72, 1.23)	1.07 (0.82, 1.40)	0.76 (0.57, 0.02)	0.74 (0.55, 0.99)	0.02
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	0.85 (0.67, 1.08)	0.79 (0.62, 1.01)	0.71 (0.55, 0.91)	0.83 (0.62, 1.06)	0.06
Model 1[b]	541/27,085	Ref	0.85 (0.64, 1.13)	0.84 (0.63, 1.11)	0.71 (0.53, 0.96)	0.74 (0.55, 0.99)	0.02
Model 2[c]	433/20,520	Ref	0.94 (0.69, 1.30)	0.81 (0.59, 1.12)	0.74 (0.53, 1.03)	0.72 (0.51, 1.00)	0.02
Model 3[d]	538/26,970	Ref	0.86 (0.67, 1.17)	0.85 (0.64, 1.13)	0.75 (0.55, 1.01)	0.88 (0.59, 1.05)	0.06
				Sweets			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	

	cases/N		OR (95 % CI)				*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	0.81 (0.63, 1.04)	0.99 (0.78, 1.25)	0.87 (0.68, 1.11)	1.04 (0.83, 1.32)	0.5
Model 1[b]	500/24,364	Ref	0.90 (0.67, 1.20)	1.11 (0.84, 1.50)	0.90 (0.67, 1.20)	1.05 (0.79, 1.39)	0.7
Model 2[c]	375/18,485	Ref	0.84 (0.59, 1.18)	1.11 (0.80, 1.53)	0.89 (0.63, 1.24)	1.04 (0.75, 1.44)	0.7
Model 3[d]	499/24,263	Ref	0.90 (0.67, 1.22)	1.11 (0.84, 1.48)	0.89 (0.66, 1.19)	1.06 (0.80, 1.40)	0.7
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	0.94 (0.73, 1.22)	1.04 (0.81, 1.34)	1.05 (0.82, 1.35)	1.13 (0.88, 1.44)	0.2
Model 1[b]	541/27,085	Ref	0.95 (0.70, 1.29)	1.05 (0.78, 1.41)	1.07 (0.79, 1.44)	0.99 (0.73, 1.33)	0.9
Model 2[c]	433/20,520	Ref	1.02 (0.72, 1.45)	1.08 (0.76, 1.52)	1.18 (0.84, 1.47)	1.05 (0.75, 1.47)	0.6
Model 3[d]	538/26,970	Ref	0.95 (0.70, 1.30)	1.06 (0.78, 1.43)	1.09 (0.81, 1.47)	0.99 (0.74, 1.34)	0.8

				Rice/pasta/poultry			
		Q1	**Q2**	**Q3**	**Q4**	**Q5**	
	cases/N		OR (95 % CI)				*P-trend*[e]
LHFA (≤2 SD)							
Crude model[a]	655/31,150	Ref	0.78 (0.62, 0.99)	0.89 (0.71, 1.12)	0.63 (0.49, 0.81)	0.77 (0.61, 0.98)	0.01
Model 1[b]	500/24,364	Ref	0.84 (0.63, 1.11)	0.99 (0.75, 1.30)	0.78 (0.58, 1.05)	0.89 (0.67, 1.19)	0.4
Model 2[c]	375/18,485	Ref	0.88 (0.64, 1.23)	1.00 (0.73, 1.39)	0.92 (0.66, 1.28)	0.99 (0.71, 1.38)	0.9
Model 3[d]	499/24,263	Ref	0.85 (0.64, 1.13)	1.01 (0.77, 1.33)	0.79 (0.59, 1.07)	0.93 (0.70, 1.23)	0.5
LWFA (≤2 SD)							
Crude model[a]	629/31,150	Ref	0.82 (0.64, 1.05)	0.88 (0.70, 1.12)	0.85 (0.67, 1.08)	0.72 (0.56, 0.92)	0.02
Model 1[b]	541/27,085	Ref	0.90 (0.68, 1.21)	0.91 (0.68, 1.21)	0.99 (0.74, 1.31)	0.76 (0.56, 1.02)	0.1
Model 2[c]	433/20,520	Ref	0.89 (0.64, 1.23)	0.92 (0.66, 1.27)	1.02 (0.74, 1.41)	0.73 (0.52, 1.03)	0.2
Model 3[d]	538/26,970	Ref	0.88 (0.66, 1.19)	0.91 (0.68, 1.22)	0.99 (0.74, 1.32)	0.78 (0.59, 1.06)	0.2

[a] Unadjusted crude model. [b] Adjusted maternal pre-pregnancy BMI, age, parity, smoking, SES, and child height in the WFA models and paternal height in the HFA models. [c] With additional adjustment for gestational weight gain as a mediator. [d] With additional adjustment for offspring birth weight as mediator. [e] *P* for trend across dietary pattern quintiles in logistic regression models. CI, confidence; HFA, height-for-age; WFA, weight-for-age; LHFA, low height-for-age; LWFA, low weight-for-age. interval; OR, odds ratio; Ref, reference category; Q, quintile.

8.4.6 Multiple imputed data regression analyses

The results were largely similar when using the multiple imputed dataset (Table 47) compared to using the complete data for child HFA and WFA growth outcomes at 7 years (Table 45), although the effect estimates were slightly attenuated for the relationship between the Nordic dietary pattern and LWFA & LHFA (Table 47) compared to findings from the complete case analysis (Table 46).

Table 47. Multivariate[a] regression estimates for associations between maternal dietary patterns in pregnancy and offspring height-for-age and weight-for-age Z-score outcomes at age 7 years in the DNBC using multiple imputation dataset (N=31,150)

	HFA Z-score (n= 31,150)		**WFA Z-score (n= 31,150)**		**LHFA (≤2 SD) (cases/N= 655/31,150)**		**LWFA (≤2 SD) (cases/N= 629/31,150)**	
	β (95 % CI)	P*trend*[b]	β (95 % CI)	P*trend*[b]	OR (95% CI)	P*trend*[b]	OR (95% CI)	P*trend*[b]
Alcohol								
Q1	Ref	0.03	Ref	0.8	Ref	0.4	Ref	0.3
Q2	0.01 (-0.02, 0.05)		-0.01 (-0.03, 0.02)		0.95 (0.81, 1.12)		1.03 (0.87, 1.23)	
Q3	0.01 (-0.03, 0.04)		-0.01 (-0.03, 0.01)		1.13 (0.98, 1.32)		1.14 (0.97, 1.34)	
Q4	0.05 (0.01, 0.08)		-0.02 (-0.05, 0.00)		0.97 (0.82, 1.14)		1.10 (0.93, 1.31)	
Q5	0.03 (0.00, 0.06)		0.01 (-0.02, 0.03)		0.92 (0.78, 1.08)		0.82 (0.68, 0.98)	
Vegetables/prudent								
Q1	Ref	0.2	Ref	0.3	Ref	0.6	Ref	0.2
Q2	0.01 (-0.02, 0.04)		0.00 (-0.03, 0.02)		0.86 (0.73, 1.01)		0.97 (0.81, 1.15)	
Q3	0.01 (-0.02, -0.05)		-0.01 (-0.04, 0.01)		1.07 (0.92, 1.25)		1.02 (0.86, 1.21)	
Q4	0.01 (-0.03, 0.04)		0.02 (-0.01, 0.04)		1.05 (0.89, 1.22)		1.02 (0.86, 1.21)	
Q5	0.03 (-0.01, 0.06)		0.01 (-0.02, 0.03)		1.02 (0.87, 1.20)		1.08 (0.92, 1.30)	
Western								
Q1	Ref	0.7	Ref	0.9	Ref	0.09	Ref	0.9
Q2	-0.01 (-0.04, 0.03)		0.00 (-0.03, 0.02)		0.96 (0.82, 1.13)		1.05 (0.88, 1.25)	
Q3	0.00 (-0.03, 0.03)		0.00 (-0.03, 0.02)		0.89 (0.75, 1.05)		1.05 (0.88, 1.25)	
Q4	-0.01 (-0.04, 0.02)		0.00 (-0.03, 0.02)		1.19 (1.02, 1.38)		1.07 (0.91, 1.27)	
Q5	-0.02 (-0.04, 0.03)		0.01 (-0.02, 0.04)		1.08 (0.92, 1.26)		0.94 (0.78, 1.12)	
Seafood								
Q1	Ref	0.8	Ref	0.04	Ref	0.5	Ref	0.3
Q2	-0.01 (-0.04, 0.02)		-0.00 (-0.03, 0.02)		1.01 (0.86, 1.18)		0.85 (0.71, 1.02)	

Q3	0.01 (-0.03, 0.04)		-0.01 (-0.04, 0.01)		0.87 (0.74, 1.03)		0.92 (0.77, 1.10)	
Q4	0.01 (-0.02, 0.05)		-0.02 (-0.04, 0.01)		1.07 (0.91, 1.25)		1.07 (0.90, 1.26)	
Q5	-0.01 (-0.05, 0.02)		-0.02 (-0.05, 0.00)		0.96 (0.82, 1.14)		1.08 (0.93, 1.28)	
Nordic								
Q1	Ref	<0.0001	Ref	<0.0001	Ref	0.008	Ref	0.04
Q2	0.03 (0.00, 0.06)		0.04 (0.02, 0.06)		1.07 (0.92, 1.25)		1.04 (0.88, 1.24)	
Q3	0.06 (0.03, 0.09)		0.04 (0.02, 0.07)		1.08 (0.93, 1.26)		0.94 (0.79, 1.12)	
Q4	0.09 (0.05, 0.12)		0.05 (0.03, 0.08)		0.88 (0.74, 1.04)		0.88 (0.73, 1.05)	
Q5	0.10 (0.07, 0.13)		0.05 (0.03, 0.08)		0.86 (0.72, 1.01)		0.95 (0.80, 1.13)	
Sweets								
Q1	Ref	<0.0001	Ref	0.3	Ref	0.9	Ref	0.9
Q2	-0.01 (-0.05, 0.02)		0.00 (-0.02, 0.02)		0.87 (0.74, 1.03)		0.96 (0.81, 1.15)	
Q3	-0.02 (-0.05, 0.01)		-0.02 (-0.04, 0.01)		1.07 (0.91, 1.25)		1.03 (0.87, 1.22	
Q4	-0.05 (-0.08, -0.01)		-0.01 (-0.03, 0.02)		0.94 (0.80, 1.11)		1.00 (0.84, 1.19)	
Q5	-0.06 (-0.10, -0.03)		-0.01 (-0.04, 0.01)		1.05 (0.90, 1.22)		0.99 (0.83, 1.17)	
Rice/pasta/poultry								
Q1	Ref	0.002	Ref	0.6	Ref	0.1	Ref	0.2
Q2	0.06 (0.03, 0.10)		0.00 (-0.03, 0.02)		0.95 (0.81, 1.12)		1.00 (0.84, 1.19)	
Q3	0.06 (0.03, 0.10)		0.02 (-0.01, 0.04)		1.13 (0.97, 1.32)		1.01 (0.85, 1.20)	
Q4	0.06 (0.03, 0.10)		0.02 (0.00, 0.05)		0.83 (0.70, 0.98)		1.04 (0.88, 1.24)	
Q5	0.06 (0.03, 0.10)		0.00 (-0.02, 0.02)		0.97 (0.83, 1.15)		0.88 (0.73, 1.06)	

[a]Adjusted maternal pre-pregnancy BMI, age, parity, smoking, SES, and child height in the WFA models and paternal height in the HFA models. [b]P for trend across the dietary pattern quintiles in linear and logistic regression models. CI, confidence; HFA, height-for-age; WFA, weight-for-age; LHFA, low height-for-age; LWFA, low weight-for-age. interval; OR, odds ratio; Ref, reference category; Q, quintile.

8.4.7 Effect modification

There was no evidence of any effect modification by breastfeeding status, expressed as <3 months, 3-6 months and >6 months, on any of the adjusted relationships (Table 48).

Table 48. P-values[a] for interaction between breastfeeding status[b] and maternal dietary patterns in relation to child height-and-weight for age measures

	HFA Z-score† (N= 18,585)	WFA Z-scoreǂ (N=20,669)	LHFA† (cases/N=377/18,585)	LWFAǂ (cases/N=404/20,669)

Alcohol	0.7	0.3	0.06	0.4
Vegetables/prudent	0.9	0.9	0.5	0.4
Western	0.9	0.4	0.4	0.4
Seafood	0.9	0.9	0.5	0.4
Nordic	0.4	0.4	0.9	0.06
Sweets	0.8	0.5	0.07	0.9
Rice/pasta/poultry	0.4	0.2	0.7	0.2

[a]Adjusted maternal pre-pregnancy BMI, age, parity, smoking, SES, and child height in the WFA models and paternal height in the HFA models. HFA, height-for-age; WFA, weight-for-age; LHFA, low height-for-age; LWFA, low weight-for-age. [b]Categorised into <3 months; 3-6 months and >6 months.

8.5 Discussion

The Nordic dietary pattern was the only dietary pattern which was found to be consistently associated with both offspring size at birth and child height as well as weight outcomes. Mothers who scored highest on the Nordic dietary pattern were found to be 26% less likely to have a LWFA child, compared to those with the lowest scores. They were also more likely to have taller and heavier children. Of the remaining 6 dietary patterns, the Rice/pasta/poultry and the Alcohol dietary patterns had smaller positive associations with child height, whereas the Sweet dietary pattern was found to have a small negative association. The only other dietary pattern which had an association with child weight was the Seafood dietary pattern where compared to those in the lowest score, children born to mothers with a high Seafood score tended to weigh slightly less.

Children in this study had higher weight and height z-scores compared to the WHO reference. This is in agreement with Nielsen et al. (2010) who found in their Danish cohort study of 4,105 healthy children aged 0-5 that they were taller, heavier and had a higher BMI than the WHO reference (Nielsen et al., 2010).

8.5.1 Maternal dietary patterns and size at birth

8.5.1.1 Comparison with previous DNBC findings

Knudsen et al. (2008) explored the association between maternal dietary patterns in pregnancy and SGA in the offspring. In their analysis of 44,612 mother-offspring pairs they found that the odds ratio of having a SGA infant (with a birth weight below the 2.5th percentile for gestational age and gender) was 0.74 (95% CI: 0.64, 0.86) for mothers following a ‘health conscious’ pattern compared to mothers following a ‘Western’ pattern, whereas in the current analysis, no association with LBW was observed. The difference in results between this study and that by Knudsen et al. (2008) can have multiple causes. First, this study consisted of a smaller study population. The analyses were performed on this smaller sample and therefore the findings might be explained by this selection. Secondly, 64 food groups were defined, whereas Knudsen et al. (2008) defined 36 food groups and likely lost diet variety resulting in a smaller set of components. Thirdly, they adjusted for parity, maternal smoking, age, height, pre-pregnancy weight and father's height but failed to adjust for energy intake as well as maternal alcohol consumption which could increase chances of residual confounding.

8.5.1.2 Comparison with CARE and ALSPAC study findings (Chapter 6 & 7)

As opposed to findings from the ALSPAC and CARE cohorts 7 dietary patterns were derived from the PCA in this analysis illustrating a higher amount of heterogeneity in the dietary data, possibly due to the much larger sample size, despite the long follow-up and the increased chance of having a sample that is more homogenous in terms of healthy lifestyle habits. However, the dietary patterns identified in ALSPAC and CARE did show some commonalities with the ones derived from the DNBC data. In particular, the 'Nordic' dietary pattern identified in the DNBC, the 'fruit & wholegrains' component derived from the CARE analysis and the 'modern health conscious' from the ALSPAC data all had high correlations with fruits and unrefined grains and negative correlations with refined grains and chips. The CARE and DNBC component further shared high correlations with water and breakfast cereal and both had positive correlations with all fish but shellfish and the majority of dairy products except full-fat milk (CARE) and chocolate milk (DNBC). These were also the components that showed the most convincing associations with offspring growth outcomes. In terms of size at birth, when comparing results between ALSPAC and DNBC, associations with birth weight (g) were very similar with an adjusted change of 45 g and 42 g respectively comparing mothers in the highest quintile score with mothers in the lowest quintile score. Adjusted associations with birth length were stronger in ALSPAC (0.2 cm vs. 0.12 cm in DNBC) and neither of the components were associated with WFL Z-scores. Whereas the 'modern health conscious' dietary pattern in ALSPAC was not associated with HBW, the 'Nordic' component showed a significant linear trend across quintile scores with HBW in adjusted analysis. With a P-value of 0.03 however there is a possibility this could be due to a type I error and thus results should be treated with caution. Pre-pregnancy BMI (kg/m^2) did not appear to modify the effect of either dietary pattern on the associations observed.

8.5.2 Maternal dietary patterns and offspring child growth outcomes

8.5.2.1 Comparison with ALSPAC findings (Chapter 7)

There are a range of theories of how exposures during fetal life can influence future health outcomes including developmental plasticity, fetal programming and epigenetics. The underlying mechanisms mediating these effects however, still remain unclear (Adamo et al., 2012; Macaulay et al., 2014). There was no strong evidence of mediation by birth weight nor was there any evidence of breastfeeding as a potential effect modifier in the relationship between maternal dietary patterns and child height and weight. Similar findings have been found in other studies which have explored maternal lifestyle exposures such as smoking (Gravel et al., 2011) and caffeine intake during pregnancy (Li et al., 2015) and child body composition. None of the studies which have investigated maternal diet during pregnancy and child growth outcomes found any evidence of birth weight acting as a mediator on later child growth and neither did the findings from the ALSPAC analysis. As stated previously, this could be due to the fact that pregnancies delivered preterm were excluded. The majority of preterm babies are also born with a lower birth weight and could therefore be exposed to catch-up growth which has been suggested to be a risk factor of child overweight status (Ong et al., 2000).

Whereas there were no significant associations observed with LWFA nor LHFA in the ALSPAC analysis (although a protective effect of the ‘traditional meat & vegetables’ component appeared for LHFA this association was completely lost in the sample using imputed values for missing data), there were significant associations observed in the DNBC data. This could be explained in part by the much larger sample size and therefore increased power to detect relationships. The ‘modern health conscious’ component did show a suggestive positive association with HFA Z-scores in the ALSPAC dataset however, possibly due to a large proportion of missing data on paternal height, once adjustments were made this significance was lost. In analysis using multiple imputed data however the association remained significant once adjustments for important confounders were made. Comparing the effect sizes the associations between the ‘Nordic’ dietary pattern and offspring HFA Z-scores were largely similar (0.12, 95% CI: 0.08, 0.15, P_{trend}<0.0001) to that observed for the ‘modern health conscious’ component (0.10, 95%: 0.03, 0.17, P_{trend}=0.003) comparing mothers in the highest quintile score to mothers in the lowest quintile.

8.5.3 Strengths & limitations

8.5.3.1 Study sample

The major strengths of this study is its prospective study design as well as the huge sample size of over 30,000 mother-child pairs resulting in relatively stable effect estimates and allowing for investigation of relationships within strata of breastfeeding status and maternal pre-pregnancy BMI. It could be argued that having such a large sample size often leads to findings that are statistically significant but in reality are weak in terms of effects and therefore of little public health relevance. However, the finding in this analysis of differences in birth weight adjusted for confounders of 44 g comparing mothers in the highest versus mothers in the lowest quintile scores of the Nordic dietary pattern should not be regarded as of insignificant importance to health.

8.5.3.2 Dietary assessment

Although the dietary data was collected using a validated FFQ, it may still be subject to measurement error. In addition, diet was only assessed at one time point and does therefore not reflect dietary intake throughout pregnancy however as stated before, previous studies which have assessed dietary change in pregnancy have found little variation in pregnant women's eating habits across trimesters (Rifas-Shiman et al., 2006; Crozier et al., 2009).

8.5.3.3 Residual confounding

Using the HNFI we found the Nordic dietary pattern to be correlated with a traditional Nordic diet characterised by high intakes of dark bread (including rye); cabbages; Nordic fruit (including plums, pears, apples and rhubarb); root vegetables and fish/shellfish. These food groups are also foods which are promoted in dietary guidelines for pregnant women and for the population in general, both in Denmark as well as in the UK (co-operation, 2014; NHS, 2015; Education, 2015). Conversely, the HNFI was also positively correlated with the Vegetable & Seafood dietary patterns of which only the latter showed small negative associations with child weight. This could indicate that other characteristics of women with high Nordic dietary pattern scores, rather than the Nordic dietary components, drive the associations observed. Attempts however were made to minimise such residual confounding by controlling for known confounders in analyses.

Although adjustments were made for many relevant confounders; child factors which could influence child growth such as diet and physical activity were not available. In addition, child growth outcomes at 7 years were parent reported despite being measured by the GP.

8.5.4 Implications for research and practice

Even though dietary patterns from PCA are subject to consumption patterns in the population under study and may therefore not be transferable across populations they represent real dietary habits and patterns of food choice and are therefore of direct relevance to the formulation of future public health messages. Health promotion messages focusing on healthy dietary patterns rather than individual nutrients are more realistic to implement, and when communicated to women before, as well as during their pregnancy are vital for improving the health of the next generation. The foods promoted in the Nordic diet are well known and commonly consumed in many European countries and it may therefore be easier to increase consumption of foods prevalent in this dietary pattern as opposed to foods found in other dietary patterns. In addition, it has been argued that not only is the Nordic diet more suitable to a Northern European climate but it is also environmentally more sustainable (Bere and Brug, 2009; Kyro et al., 2013; Mithril et al., 2013).

8.6 Conclusion

In conclusion it was found that mothers who adopted a more Nordic diet in pregnancy, characterised by high intakes of Nordic berries, wholegrain and hard cheese, were less likely to have LWFA and LHFA children and had babies born with higher birth weight and birth length. These results support the current dietary guidelines for pregnant women, which aim to ensure optimal health for both the mother and the baby. They also add evidence that this type of dietary pattern can have longer term benefits to child growth.

9 Discussion & conclusion

9.1 Chapter overview

The aim of this thesis was to explore the association between maternal dietary habits during pregnancy and offspring growth outcomes using data from two large prospective British birth cohorts and one large nationally representative Danish birth cohort.

All of the individual analysis chapters contain discussions which include strengths, weaknesses and implications of findings for each study and suggestions for future directions. This chapter will provide a brief summary of main findings and their possible implications. This is followed by reviewing the main strengths and limitations of this thesis as a whole. This leads to the general conclusion of this thesis.

9.2 Summary of research findings

To meet the main aim (reiterated above), the work of this thesis was divided into meeting several objectives. A summary of the findings that meet each objective are summarised in turn below.

1. *Review the evidence linking dietary patterns to offspring growth outcomes*

Chapter 2 presented the results of a narrative systematic review of the literature to meet this objective. The key findings included:

- One existing literature review from July 2016 was identified which assessed the evidence base relating maternal dietary patterns in pregnancy to infant size at birth and concluded that diets with higher intakes of fruits, vegetables, legumes and fish have positive pregnancy outcomes in general and that this evidence should be communicated to women
- A total of 21 studies were deemed relevant of which 18 explored associations with offspring size at birth and 4 with infant/child growth
- All but two studies were of a prospective cohort design but varied greatly in terms of sample size, setting, exposure and outcome measures, dietary pattern analysis as well as statistical treatment of data making between study comparison difficult
- A clear need for a more uniform approach when it comes to *a posteriori* driven methods was identified and particular attention should be given to food grouping prior to dietary pattern analysis as well as energy adjustment of dietary data as both appear to affect resulting patterns

- Findings relating to infant size at birth were largely in keeping with the hypothesis that optimal perinatal nutrition, gained from a healthy maternal dietary pattern, leads to favourable pregnancy outcomes in terms of size at birth
- The evidence was not clear for child growth outcomes, partly due to heterogeneity and lack of studies

The overall conclusion of Chapter 2 was that the evidence – for offspring size at birth but not child growth outcomes – is generally supportive of the nutritional programming theory

2. *Characterise dietary patterns in pregnancy using data from English and Danish birth cohorts*

Chapters 3 (methods), 6, 7 & 8 addressed this objective

- A common food grouping was applied to all three dataset and PCA was done on energy adjusted food data
- Choice of components to retain were based on 1) the scree plot, 2) % variance explained and 3) interpretability
- For the CARE cohort, the PCA on 73 food groups resulted in 4 distinct components which were named after the food items with the highest factor correlations: ‘fruit & wholegrains’, ‘traditional meat & vegetables’, ‘vegetables & oils’ and ‘cheese, pasta & sauce’
- For the ALSPAC cohort, the PCA on 44 food groups resulted in 2 distinct components which were given names representative of the food groups with the highest correlations: ‘modern health conscious’ and ‘traditional health conscious’
- For the DNBC, the PCA on 65 food groups resulted in 7 distinct components which have been given names representative of the food groups with the highest correlations: ‘Alcohol’, ‘Vegetables/prudent’, ‘Western’, ‘Nordic’, ‘Seafood’, ‘Sweets’ and ‘Rice/Pasta/Poultry’

3. *Examine the relationship of maternal alcohol consumption in pregnancy with offspring size at birth in the CARE study*

Chapter 4 addressed this objective. The results indicated that:

- A large proportion of women drink more than the recommended intake of no more than 2 units/week prior to and in the first part of pregnancy

- Adjusted associations with offspring size at birth were strongest for intakes above 2 units/week compared to non-drinkers in the periods prior to pregnancy and trimester 1 & 2.
- Even women who adhered to the recommendations in the first trimester were at a significantly higher risk of having babies born with lower birth weight and birth centile compared to non-drinkers, after adjusting for confounders ($P<0.05$).

The overall conclusion of Chapter 4 was that women should be advised to abstain from alcohol when planning to conceive and throughout pregnancy.

4. *Examine the relationship of maternal fatty fish intake in pregnancy with offspring size at birth in the CARE study*

Chapter 5 addressed this objective. Results indicated that:

- Maternal fatty fish intake was assessed prior to pregnancy and trimester specifically.
- Additional dietary data from multiple 24 hour recalls during pregnancy were used to estimate an average fatty fish portion size of ~100 g, much lower than the DoH assumed portion size of 140 g.
- Intake was classified as ≤2 portions/week and >2 portions/week with a no fatty fish category as referent
- Over 40% of women reported no fatty fish consumption prior to and throughout pregnancy and mean intakes were considerably lower than the recommended two portions/week
- No association was observed between intake of fatty fish before pregnancy or during other pregnancy trimesters with size at birth

The overall conclusion of this chapter was that consumption of fatty fish prior to and/or during pregnancy did not influence birth weight, when taking into account known confounders

5. *Examine the relationship between maternal dietary patterns in pregnancy and offspring size at birth*

Chapters 6, 7 & 8 addressed this objective. Results indicated that:

- A dietary pattern characterised by high intakes of fruit, in particular Nordic fruits, wholegrains and water and lower intakes of white bread, cakes, snacks and soft drinks had the strongest positive association with offspring size at birth.

- No significant association was apparent in the CARE data after adjustment for important confounders; possibly due to the smaller sample size and low numbers in the quintile categories.
- There was no convincing evidence for effect modification by pre-pregnancy BMI status across the three cohorts.
- GWG did not appear to mediate any relationships with size at birth

The overall conclusion is that findings are supportive of the hypothesis that optimal perinatal nutrition, gained from a healthy maternal dietary pattern, leads to favourable pregnancy outcomes in terms of size at birth

6. *Examine the relationship between maternal dietary patterns in pregnancy and offspring growth outcomes at age 7 years*

Chapters 7 & 8 addressed this objective. Results indicated that:

- Similarly to offspring size at birth; a dietary pattern characterised by high intakes of fruit, in particular Nordic fruits, wholegrains and water and lower intakes of white bread, cakes, snacks and soft drinks had the strongest positive association with offspring growth outcomes.
- Evidence appeared most convincing for child HFA outcomes.
- Only the Nordic dietary pattern in the DNBC appeared to have protective effects against offspring risk of being LWFA and LHFA at 7 years.

The overall conclusion is that findings add some evidence that this type of dietary pattern can have longer term benefits to child growth; however more research is needed before more solid inferences can be drawn.

7. *Compare and contrast dietary patterns of pregnant women living in England and Denmark*

Chapters 8 & 9 addressed this objective. Results indicated that:

- The CARE ‘fruit & wholegrains’ component, the ALSPAC ‘modern health conscious’ and the DNBC ‘Nordic’ dietary pattern all shared commonalities however PCA is a data driven approach therefore complicating between study comparisons.

9.3 Strengths & limitations of this research

Many of the limitations of this research have been detailed throughout the preceding chapters. The summary below is intended to reiterate the main strengths and limitations, which are important to take into account when interpreting the results.

9.3.1 Study design

As highlighted in the individual chapters, none of the studies were randomized controlled trials (RCTs), which according to the CRD (2009) present the highest form of evidence (CRD, 2009). It is important to note that because of the absence of trial evidence, causal relationships cannot be established and conclusions drawn from the analysis of observational data will be limited. Nevertheless, all were of a prospective design with the exposure being measured before the outcome allowing for temporality to be established and minimising error arising from measuring exposure after the outcome.

9.3.2 Study samples

All three cohorts consisted of large samples of pregnant women and in total 39,015 mother-offspring pairs were studied for the maternal dietary pattern and offspring growth associations in this thesis (CARE= 1,109; ALSPAC= 6,756; DNBC= 31,150).

All mothers participated on a voluntarily basis and no incentives were given. It is therefore likely that the study samples differed from the general pregnant population in certain aspects and selection bias may have been introduced as volunteers are often more likely to have a healthier lifestyle than non-participants. This would likely reduce the variation in nutrient intake, and thereby the variation in exposure, but it is assumed to not affect the direction of the association between dietary habits and offspring growth. The mothers recruited for the CARE study consisted of low risk pregnancies and that could help explain the lack of association observed for this dataset, although with the much smaller sample size it is underpowered to detect small associations.

9.3.3 Exposure measures

As stated in Chapter 2, measuring diet in an accurate way is one of the greatest challenges faced by research in nutritional epidemiology. The dietary assessment tools have been discussed in individual analysis chapters. The three studies all assessed diet at different time points using different tools making it difficult to compare actual intakes. In addition, all cohorts used country specific food composition tables and portion size estimates further complicating between country comparisons.

9.4 Implications for practice & further research

This thesis falls in the realm of observational epidemiology research. Therefore, no direct recommendations for practice can be drawn from it without taking the findings further and using them to inform the design of intervention studies.

Recommendations for further research include:

1. A meta-analysis of observational studies to investigate the association of maternal dietary patterns in pregnancy with offspring size at birth taking into account findings from this thesis
2. A systematic review and meta-analysis of trials of dietary interventions (excluding trials of supplements alone) during pregnancy and size at birth
3. A RCT to assess the impact of a maternal Nordic diet versus usual diet on birth outcomes where women will be randomized to receive either a Nordic diet or no dietary intervention from early pregnancy to term measuring birth outcomes with follow up to assess health outcomes in the offspring.

9.5 Concluding remarks

Despite the limitations outlined above, this research has added to the evidence relating to infant size at birth and findings were largely in keeping with the hypothesis that optimal perinatal nutrition, gained from a healthy maternal dietary pattern, leads to favourable pregnancy outcomes in terms of size at birth. The findings support the current dietary guidelines for pregnant women, which aim to ensure optimal health for both the mother and the baby. They also add evidence that this type of dietary pattern can have longer term benefits to child growth and should therefore be promoted to both pregnant women and women trying to conceive. Pregnancy can be viewed as an opportunity for behaviour change plus there is a high contact with health services which is not comparable to other stages in life. The motivation for having a healthy baby is high and expecting mothers or women trying to conceive may therefore be more susceptible to making sustainable dietary changes that can have positive effects on not only their own health but that of their unborn baby's immediate and longer term health.

Appendix A: Literature review data extraction form

Study reference no:	**Data of data extraction:**

General information	
Author(s):	
Journal title:	
Article title:	
Year, month, volume & issue no:	
Source:	

Study characteristics	
Aims and objectives:	
Dates of recruitment:	
Dietary exposure:	
Inclusion criteria:	
Exclusion criteria:	
Selection method:	

Sample characteristics	
Age:	
Number of participants:	
Response rate:	
Number of dropouts:	

Methodological quality of the study	
Setting and country:	
Study design:	
Study name:	
Length of follow up & intervals:	

Exposure measures and quality assessment	
Dietary assessment method:	
Dietary pattern identification method:	
Energy adjustment of dietary data?	
Standardisation of dietary data?	
Number of participants at each follow up:	
Who carried out measurements:	
Were the same method of measurement used at each follow up:	
Self reporting- how is the validity ensured?	

Outcome measures and quality assessment	
Outcomes	
Outcome measures:	
Number of participants at each follow up:	
Other risk factors included and adjusted for:	
Who carried out measurements:	
Were the same method of measurement used at each follow up:	

Self reporting- how is the validity ensured?	

Analysis	
Statistical technique(s) used:	
Does the technique adjust for confounding factors?	

Main findings/outcomes of interest	
What are the main findings?	
Do they answer the research question?	
What are the main limitations stated?	
Recommendations for future research:	

Appendix B: CARE study 24 hour recall form

24-hour diet recall: *14-18 weeks gestation*

ID No: ϶϶϶϶϶

Name:________________________________

Date of recall:_____/___/___________

Day of recall:_____/___/___________

Please use this sheet to record all intake of foods and drinks for 24 hours from midnight the previous night to midnight last night (i.e. everything that was eaten or drunk yesterday)

Example

Before breakfast

Food/drink consumed	Description and preparation	Amount
Milk	*Whole milk*	*1 average glass*

Breakfast

Food/drink consumed	Description and preparation	Amount
Toast	*White bread sliced*	*2 thick slices*
Spread	*St. Ivel Gold*	*Thick spread on both slices*
Orange juice	*Pure, unsweetened*	*1 average glass*
Tea	*Made with whole milk*	*1 average mug*

Between breakfast and lunchtime

Food/drink consumed	Description and preparation	Amount
Rolos		*5*
Water	*Tap*	*1 pint*

Lunchtime

Food/drink consumed	Description and preparation	Amount
Chicken salad sandwich	*White bread*	*2 medium slices*
	Butter	*Thinly spread on both slices*
	Chicken slices (processed)	*2*
	Lettuce	*2 small leaves*
	Tomato	*4 slices*
Diet coke		*1 average can*

Between lunchtime and evening meal

Food/drink consumed	Description and preparation	Amount
Crisps	*Salt and vinegar*	*1 average bag*

Evening meal

Food/drink consumed	Description and preparation	Amount
Chicken	*Breast, no skin*	*1 average breast*
Potatoes	*New, boiled*	*4*
Broccoli	*Green, boiled*	*4 spears*
Gravy	*Bisto granules, made with water*	*half a cup*

During the evening

Food/drink consumed	Description and preparation	Amount
Chocolate mousse	*Low fat*	*1 small pot*

24-hour diet recall

Before breakfast

Food/drink consumed	Description and preparation	Amount

Breakfast

Food/drink consumed	Description and preparation	Amount

Between breakfast and lunchtime

Food/drink consumed	Description and preparation	Amount

Lunchtime

Food/drink consumed	Description and preparation	Amount

Between lunchtime and evening meal

Food/drink consumed	Description and preparation	Amount

Evening meal

Food/drink consumed	Description and preparation	Amount

During the evening

Food/drink consumed	Description and preparation	Amount

Check for:

Bread type – brown or wholemeal; white or high fibre white, multigrain/granary etc

Sugar – in drinks or on cereal

Low fat or ordinary products (also diet vs low fat)

Fats and oils – state brand, whether full fat or reduced fat, margarine or butter, low fat butter or low fat spread

Vegetables/potatoes – skin on or off; with or without butter/spread added

Remember extras – spread on sandwiches, sweets, chewing gum, sauces, salad dressings, salt, pepper, vinegar

Get recipes for composite dishes or brand names if ready meals

Pizza bases, bread etc – thick or thin base/slices

Cooking methods – fried, grilled, steamed, baked, roasted etc.

Skin on chicken, lean meat/fatty

Did you take any dietary supplements e.g. Vitamin C today? YES / NO

- **if yes**, please state which supplement you took: ____________________

____

Was this day typical of your usual intake? YES / NO

- **if no**, did you…

eat more ϶1 eat less ϶ 2 eat different foods ϶3

Please comment:

____

____

____

____

Did you suffer from nausea during this time? YES / NO

Thank you for your help

Appendix C: Stata code for multiple imputation analysis in ALSPAC

```
/* MI ALSPAC*/

use "M:\Camilla\ALSPAC analysis\Multiple imputation\data for
MI2.dta"

misstable summarize

mi set mlong

/*sets the style of the format in which the data are stored.

Marginal long style "mlong" is suitable for when you want to
modify existing variables and is memory efficient*/

mi register imputed  parity gesthyp preeclampsia smoking
vegetarian supplements ///

ethnicity lwfa breastfeeding diabetes BMI gwg_grams kz030 ///

paw010 c373 maternal_edu

mi register regular bestgest maternal_age Comp1 Comp2 sex height
_zhfa energy_kcal

set seed 29390 /*sets random seed number for reproducibility*/

mi impute chained (regress) BMI gwg_grams paw010 kz030 ///

(logit, augment) parity gesthyp preeclampsia smoking ethnicity
maternal_edu ///

(ologit, augment) breastfeeding ///

(mlogit, augment) diabetes= ///

bestgest maternal_age Comp1 Comp2 sex height energy_kcal _zhfa,
add(5)

/*MI MV regression 7.5 yrs WFA and HFA*/

/*WFA*/

mi estimate: regress _zwfa Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity height

mi estimate: regress _zwfa Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity height

/*quintiles of comp*/

mi estimate: regress _zwfa i.q_Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity height

mi estimate: regress _zwfa i.q_Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity height

/*HFA*/
```

```
mi estimate: regress _zhfa Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity paw010

mi estimate: regress _zhfa Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity paw010

/*quintiles of comp*/

mi estimate: regress _zhfa i.q_Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity paw010

mi estimate: regress _zhfa i.q_Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity paw010

/*with birth weight (kz030) as a mediator*/

/*HFA*/

mi estimate: regress _zhfa Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

mi estimate: regress _zhfa Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

/*quintiles of comp1*/

mi estimate: regress _zhfa i.q_Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

mi estimate: regress _zhfa i.q_Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

/*WFA*/

mi estimate: regress _zwfa Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

mi estimate: regress _zwfa Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

/*quintiles of comp1*/

mi estimate: regress _zwfa i.q_Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

mi estimate: regress _zwfa i.q_Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

/*with birth weight and gestational weight gain as mediators*/

/*HFA*/

mi estimate: regress _zhfa Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
paw010

mi estimate: regress _zhfa Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
paw010
```

```
/*quintiles of comp*/

mi estimate: regress _zhfa i.q_Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
paw010

mi estimate: regress _zhfa i.q_Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
paw010

/*WFA*/

mi estimate: regress _zwfa Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
height

mi estimate: regress _zwfa Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
height

/*quintiles of comp1*/

mi estimate: regress _zwfa i.q_Comp1 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
height

mi estimate: regress _zwfa i.q_Comp2 i.maternal_age i.BMI_cat
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
height

/*testing for effect modification by breastfeeding*/

//Logistic regression

/*LHFA*/

mi estimate, or mcerror: logistic lhfa Comp1 i.maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity paw010

mi estimate, or mcerror: logistic lhfa Comp2 i.maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity paw010

/*quintiles of components*/

mi estimate, or mcerror: logistic lhfa i.q_Comp1 i.maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity paw010

mi estimate, or mcerror: logistic lhfa i.q_Comp2 i.maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity paw010

/*LWFA*/

mi estimate, or mcerror: logistic lwfa Comp1 i.maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity height

mi estimate, or mcerror: logistic lwfa Comp2 i.maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity height

/*quintiles of components*/
```

```
mi estimate, or mcerror: logistic lwfa i.q_Comp1 i.maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity height

mi estimate, or mcerror: logistic lwfa i.q_Comp2 i.maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity height

/*with birth weight (kz030) as a mediator*/

/*LHFA*/

mi estimate, or mcerror: logistic lhfa Comp1  maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

mi estimate, or mcerror: logistic lhfa Comp2  maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

/*quintiles of components*/

mi estimate, or mcerror: logistic lhfa i.q_Comp1  maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

mi estimate, or mcerror: logistic lhfa i.q_Comp2  maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030 paw010

/*LWFA*/

mi estimate, or mcerror: logistic lwfa Comp1 maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

mi estimate, or mcerror: logistic lwfa Comp2 maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

/*quintiles of components*/

mi estimate, or mcerror: logistic lwfa i.q_Comp1 maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

mi estimate, or mcerror: logistic lwfa i.q_Comp2 maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030 height

/*with birth weight and gestational weight gain as mediators*/

/*LHFA*/

mi estimate, or mcerror: logistic lhfa Comp1  maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
paw010

mi estimate, or mcerror: logistic lhfa Comp2  maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
paw010

/*quintiles of components*/

mi estimate, or mcerror: logistic lhfa i.q_Comp1  maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030
gwg_grams paw010
```

```
mi estimate, or mcerror: logistic lhfa i.q_Comp2  maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030
gwg_grams paw010

/*LWFA*/

mi estimate, or mcerror: logistic lwfa Comp1 maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
height

mi estimate, or mcerror: logistic lwfa Comp2 maternal_age BMI
i.smoking i.maternal_edu i.parity i.ethnicity kz030 gwg_grams
height

/*quintiles of components*/

mi estimate, or mcerror: logistic lwfa i.q_Comp1 maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030
gwg_grams height

mi estimate, or mcerror: logistic lwfa i.q_Comp2 maternal_age
BMI i.smoking i.maternal_edu i.parity i.ethnicity kz030
gwg_grams height
```

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