THE ASSOCIATION OF MATERNAL NUTRIENT AND DIETARY PATTERN INTAKE AND MATERNAL HEALTH CHARACTERISTICS DURING PREGNANCY

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Abstract

Background: Nutritional status of the pregnant mother is pivotal in the health and development of the foetus, although less is known about the effects on maternal health. Nutritional status may be related to the development of gestational diabetes mellitus (GDM) and adverse gestational weight gain (GWG), both of which are thought to play an important role in the health outcomes of both the mother and the offspring.

Aim: The study aimed to determine associations between nutrient and dietary intake and maternal health characteristics such as glycaemic status during pregnancy and GWG.

Methods: Using guidelines from Cochrane Systematic Reviews, a systematic review of literature and narrative synthesis was conducted in 4 databases to assess whether intake of free sugar during pregnancy is associated with GWG. In the second part of the study, multinomial logistic regression analysis was carried out using data from a prospective cohort of pregnant women (ALSPAC) to analyse the cross-sectional associations of energy, macronutrient and free sugar intake and adherence to data-driven dietary patterns at 32 weeks gestation with glycaemic status (n= 8507) and GWG (n= 7989).

Findings: Of the 320 eligible studies identified, 4 were included in the narrative synthesis. Current literature suggests an association of free sugar intake during pregnancy and GWG, however the pool of available studies was small and of low quality. In the ALSPAC cohort, intake of energy from fat was positively associated with glycosuria, adherence to the ‘health

conscious' and the 'traditional' dietary pattern groups were negatively associated with glycosuria. Intake of energy from protein was positively associated with both existing DM and GDM. Intake of energy from free sugar and adherence to the 'confectionary' dietary pattern was negatively associated with both existing DM and GDM. There was no evidence of any associations between energy or macronutrient intake and GWG, however, adherence to the 'health conscious' and the 'confectionary' dietary pattern were associated with insufficient and excessive weight gain.

Conclusions: The evidence suggests associations of macronutrient and specific dietary patterns with glycaemic status and GWG during pregnancy. This may be important in defining interventions to prevent the negative outcomes associated with adverse glycaemic status and adverse GWG in pregnant women.

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Chapter 1 Background and literature review

1.1 Introduction

Maternal diet during pregnancy plays a vital role in the growth and development of offspring and is suggested to play a role in predisposing offspring to the development of chronic disease in adulthood (Hyde et al., 2016). However, the implications of diet on the health of the pregnant woman are less well recognised (Diemert et al., 2016a)

Maternal health characteristics such as hyperglycaemia and adverse gestational weight gain (GWG) are associated with a number of short and long-term health outcomes, for both the mother and the offspring; including macrosomia, preterm birth, transgenerational obesity and type 2 diabetes (T2DM) (Viswanathan et al., 2008; Schoenaker et al., 2016; Tielemans et al., 2016). These health characteristics are also associated with increased need for assisted delivery, additional neonatal and maternal care after birth and the additional use of health care services tracking through the lifespan (Oteng-Ntim et al., 2013), presenting an increased cost to health care services.

There is a paucity of evidence examining the influence of diet on GWG, and the existing evidence is contradictory (Soltani, 2012). Often, the evidence is limited by the variability and confounding factors of pregnancy weight gain, such as the contribution of foetal weight, pre-pregnancy BMI and the self-reporting of maternal weight measurements; and alongside heterogeneity in study design and the collection of dietary data. Similarly, studies examining

diet and glycaemic status of pregnant women are conflicting due to confounding and often mediated by pre-pregnancy Body Mass Index (BMI) and pregnancy weight gain.

Considering the implication of adverse pregnancy health characteristics on maternal and offspring outcomes and the cost implications to health services, particularly as the NHS is facing severe financial pressure and increasing demand for services (NHS Confederation, 2017), there is a clear need for further research into whether diet affects association of diet with glycaemic status and weight gain in pregnant women.

It has been suggested that pregnancy offers a 'teachable moment', a naturally occurring event which may promote healthy behaviour change (Phelan, 2010). The use of this 'teachable moment' to reduce unhealthy behaviours such as poor diet and lack of physical activity may help to reduce some of the maternal characteristics complicating pregnancy. This will contribute to reducing negative outcomes impacting short and long-term health of the mother and offspring and the wider impact associated with the cost of healthcare services.

This thesis is a two-part study, firstly looking to examine if there is an association between intake of free sugars during pregnancy and gestational weight gain and secondly, examining the associations between dietary intake at 32 weeks' gestation and glycaemic status and GWG in pregnant women from the Avon Longitudinal Study of Parents and Children (ALPAC) study.

In the UK, free sugar intake has been a public health concern for a number of years (Public Health England, 2015). In 2015, the Scientific Advisory

Committee for Nutrition (SACN) published a report of Carbohydrates and Health, reviewing the latest evidence on links between carbohydrate consumption, including sugar, and health outcomes. This review reported on free sugar intake and the associated health outcomes, including a higher risk of tooth decay and risk of higher energy intake and increases in BMI and type 2 diabetes in those consuming higher amounts of free sugar (SACN, 2015). Alongside the SACN report, Public Health England (PHE) published 'Sugar reduction: responding to the challenge' to identify possible actions needed to reduce the population's free sugar intake (PHE, 2015). The report identifies the need for a multi-faceted approach to sugar reduction, tackling availability of free sugar in food supply, restricting food marketing for both adults and children and focussing on promoting healthy behaviours. The opening statement of this report 'We are eating too much sugar and it is bad for our health' (Public Health England, 2015) demonstrates the attitude and urgency of PHE's approach to free sugar reduction.

An industry levy on sugar sweetened beverages (SSB) was announced as part of the UK government's 'plan for action' to reduce childhood obesity. The levy became effective in April 2018 and is partnered with plans to reduce overall sugar content of a range of products contributing to sugar intakes by at least 20% by 2020 (HM Government, 2016), highlighting the importance of sugar reduce for health outcomes of the UK population.

Current research suggests there are a number of detrimental effects of increased sugar intake including dental caries, increased risks of cardiovascular disease, obesity and diabetes (Macdonald, 2016). Dietary intake has been heavily implicated in the adverse glycaemic status and

weight gain in general populations (Macdonald, 2016). A number of systematic reviews have found evidence that free sugar intake is a determinant of body weight in general populations (Malik et al., 2006; Te Moranga et al., 2012; Hu, 2013). Similarly, evidence supports the suggestion that consumption of SSB is associated with higher incidence of type 2 diabetes, independent of body weight (Greenwood et al., 2014; Imaura, et al., 2015). However, there is a lack of evidence for the association of free sugar intake during pregnancy and GWG and there is a possibility this could be an important determinant in adverse weight gain in pregnant women, thus an important determinant in the construction of effective prevention strategies. Therefore, systematic review titled ‘The association of free sugar intake and gestational weight gain: a systematic review’ was carried out to address this research question.

The second study of this thesis addressed the influence of overall nutritional intake and dietary patterns of pregnant women on glycaemic status and GWG, such as hyperglycaemia identified as glycosuria and gestation diabetes mellitus (GDM). In the current literature, the majority of studies examining glycaemic status and health outcomes consider only the impact of overt diabetes (type 1 or type 2 and gestational diabetes). However, hyperglycaemia without an overt diabetes diagnosis has been implicated in future adverse health outcomes (Jacklin et al., 2017). Thus, hyperglycaemia during pregnancy, without overt diabetes, is also an important area of research when attempting to reduce negative health outcomes for both mother and offspring.

The dietary data analysed in this thesis was collected from participants of ALSPAC, as unadjusted absolute macronutrient intakes of energy (in kJ) and fat (g), carbohydrate (g), protein (g) and non-milk extrinsic sugars (g) (as a marker of free sugar intake) using a food frequency questionnaire. As macronutrient intakes are correlated with total energy intake (Rhee et al., 2014), the absolute intakes were adjusted for total energy intake in order to control for confounding. Both adjusted percentage intakes and absolute intakes are presented in the Chapter 6 of this thesis.

Alongside percentage of energy intakes, data-driven dietary patterns (Northstone et al., 2008) of pregnant women at 32 weeks gestation were also analysed. Dietary pattern analysis examines the overall diet rather than nutrients in isolation and can provide some insight into eating behaviours and the interaction with health (Agnoli et al., 2019).

Combining dietary patterns and percentage of energy intake allows a closer look at the overall diet of pregnant women at 32 weeks gestation, rather than isolating single nutrients; as nutrients are eaten together in the diet rather than separately (Agnoli et al., 2019). This will provide an insight into not only macronutrient intake during pregnancy, but also actual foods consumed within the diet.

This thesis seeks to determine if there is an association between dietary and nutrient intake and maternal characteristics during pregnancy, including hyperglycaemia in the forms of glycosuria, gestational diabetes and existing diabetes (type 1 and type 2) during pregnancy and GWG, which may impact on the long-term health of the mother and offspring.

Aim:

To identify cross-sectional associations of maternal dietary intake with maternal health characteristics such as gestational weight gain and varying levels of hyperglycaemia during pregnancy, in two separate analyses.

Objectives:

1. To conduct a systematic review of the literature to evaluate the associations between free sugar intake during pregnancy and gestational weight gain.
2. To determine the association of maternal energy and macronutrient protein, fat and carbohydrate) and free sugar intake and dietary patterns at 32 weeks' gestation and hyperglycaemia (glycosuria, gestational diabetes and overt diabetes during pregnancy) and GWG, using data from a prospective population cohort, the Avon Longitudinal Study of Parents and Children (ALSPAC).

This thesis is split into two parts, reflecting the two separate objectives.

Chapter one gives an introduction and in-depth literature review of human pregnancy, nutrition during pregnancy and the risk factors and implications of maternal obesity, GWG and hyperglycaemia on maternal and offspring health. It considers the impact of dietary intake, diet patterns and sociodemographic characteristics that may impact on the incidence of these health characteristics.

Chapter two details the methodological approach used to undertake a systematic review of literature titled ‘The association of free sugar intake and gestational weight gain: a systematic review’.

Chapter three presents the findings from the systematic review, first presenting the study inclusion and then the results from the included studies.

Chapter four presents a discussion and interpretation of the findings from the systematic review, combined with current evidence collated in the literature review.

Chapter five describes the methodological approach undertaken when analysing associations of dietary and nutrient intake and maternal health characteristics in ALSPAC women.

Chapter six presents the results from the analysis of ALSPAC data, presenting the results from analyses of dietary intake and maternal weight and diabetes status.

Chapter seven presents the discussion and interpretation of results from the ALSPAC data analysis, drawing on existing evidence presented in the literature review.

Chapter eight presents a conclusion summarising the findings from both parts of the thesis and presents recommendations for future research and practice.

1.2 Human pregnancy

The human gestation period lasts for 40 weeks, counted from the last menstrual period of the mother up to birth occurring at around 38 weeks. Pregnancy is separated into three ‘trimesters’ corresponding to the phases of development (Langley-Evans, 2009). The first trimester of pregnancy (0-12 weeks) involves the establishment of the foetal organ systems including the placenta, through which the foetus is dependent on for oxygen and nutrients passed through maternal stores. The second trimester (13-27 weeks) sees the largest period of foetal growth, from 25g to 875g. Rapid foetal growth still occurs throughout the third trimester (28-40 weeks) and this is also the period of maturation of all foetal organ systems, deposition of fat and other nutrient stores also occurs (Talbot and Maclennan, 2016).

During pregnancy many changes in the maternal physiology, metabolism and endocrine system occur (Talbot and Maclennan, 2016). Maternal cardiac output increases by up to 30-50% due to increased heart rate and stroke volume, resulting in a 60% increase in CO_2 production and oxygen consumption by term (Talbot and Maclennan, 2016). Blood and plasma volume increase by 30-45%, renal blood flow and glomerular filtration rate increase by 50%, meaning urinary protein and glucose levels also increase (Langley-Evans, 2009). The uterus displaces the stomach and gastrointestinal absorption increases, increasing the time in which nutrients are absorbed in (Langley-Evans, 2009).

During healthy pregnancy, glucose uptake is inhibited by increasing progesterone concentration and insulin sensitivity is reduced by increasing levels of oestrogen. Maternal insulin resistance results in use of fats for maternal energy, rather than carbohydrates, allowing the foetus an adequate supply of carbohydrate for energy (Sonagra et al., 2014). Human placental growth hormone (hPGH) is suggested to decrease glucose uptake, induce hyperinsulinaemia and disturb the suppression of hepatic gluconeogenesis. Insulin resistance is a normal physiological process during pregnancy and is compensated by increased insulin secretion, both of which increase with advancing gestation (Sonagra et al., 2014). However, women who do not have the physiological capacity to increase insulin secretion may develop GDM (Kuhl, 1991). Insulin sensitivity can be improved by diet modification and increased physical activity, if introduced at an early stage of pregnancy, to reduce progression into GDM (Sonagra et al., 2014).

1.2.1 The intrauterine environment

The long-term effect of maternal nutritional status on offspring is well recognised in human and animal studies (Lawlor, 2013). This suggests that there are ‘critical periods’ in the life course, where an exposure acting during a specific period has the potential of lifelong effects on the structure or functions of the organs and body systems, known as nutritional programming (Lawlor, 2013). The early life environment is considered one of the first critical periods in the human lifespan, with exposures within the intrauterine environment influencing biological development in utero and in later life (Lawlor, 2013).

The developmental origins of health and disease (DOHaD) hypothesis evolved from studies by Barker (1995), who initially identified the possible effect of foetal undernutrition on death rates in adult men; leading to the hypothesis that poor foetal growth caused by environmental factors increases risk of disease in adult life (Wadhwa et al., 2009).

This has led to further the foetal overnutrition hypothesis, suggesting that as well as environmental factors such as diet and physical activity, maternal health markers such as body mass index (BMI), weight status, plasma glucose and free fatty acid levels can also influence offspring health (Lawlor, 2006). This hypothesis proposes that the current obesity epidemic could be transgenerational (see figure 1.1), resulting from changes in the offspring epigenome *in utero* (Dabelea and Crume, 2011; Lawlor et al., 2006). In vitro animal and human studies have shown that development of the pancreas and foetal fat accretion is influenced by availability of foetal fuels (glucose, lipid and amino acids), these fuels are determined by maternal weight status and fuel store (positively associated with maternal BMI) (Lawlor, 2013).

Animal studies suggest that nutrient supply can be responsible for epigenetic changes through altered DNA methylation; this can contribute to later life development of metabolic disease, cardiovascular disease, cancer and neurological disease (Williams et al., 2014). However, the mechanisms for this are yet to be fully understood (Ho-sun, 2015).

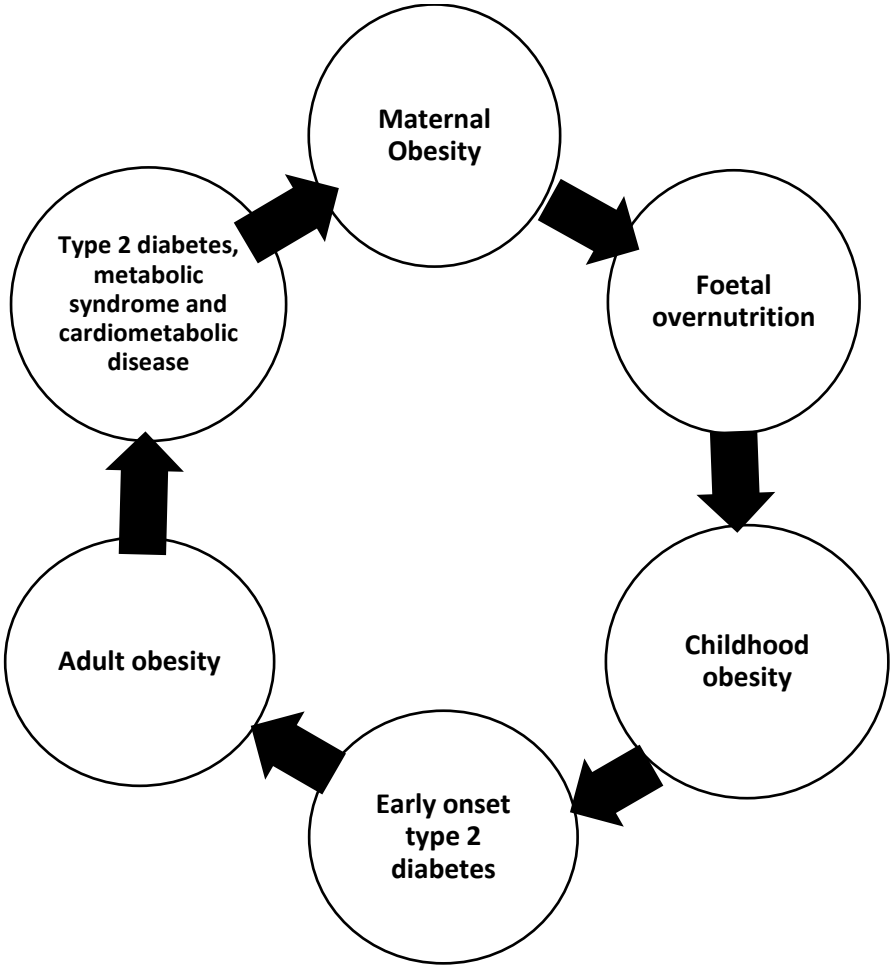

Figure 1.1 Potential cycle of transgenerational obesity adapted from Dabelea and Crume (2011)

1.3 Nutrition during pregnancy

In considering the role of under and overnutrition during pregnancy, it is well recognised that diet plays an important role in outcomes for both mother and offspring (Diemert et al., 2016), as well as foetal growth and development (Ramakrishnan et al., 2012).

1.3.1 Undernutrition during pregnancy

Undernutrition during pregnancy is linked with poor foetal growth and may impact on the long term health of offspring, through possible programming *in utero* (Ramakrishnan et al., 2012). Findings from the Dutch famine birth cohort study infer that undernutrition can programme chronic disease in later life, such as cardiovascular disease, diabetes and hypertension, through adaptations in the uterine environment (Roseboom et al., 2006). A case-control of 385 participants exposed to the Dutch famine during the gestation period and 590 unexposed controls found an earlier onset of coronary artery disease in those conceived during the famine; suggesting that maternal undernutrition during pregnancy could affect onset of heart disease (Painter et al., 2006). Offspring exposed to the Dutch famine *in utero* had reduced glucose tolerance and higher insulin concentrations, higher risk of breast cancer and increased prevalence of metabolic and heart diseases in adulthood (Roseboom et al., 2006).

1.3.2 Overnutrition during pregnancy

Similarly, overnutrition prior to and during pregnancy has been implicated in adverse health outcomes in the mother and offspring. Maternal overweight increases risks for macrosomia (babies born >4500 g) and large for gestational age (LGA), thereby increasing risk of metabolic syndrome and possible obesity in later life of the offspring (Grieger and Clifton, 2015).

Maternal overnutrition is associated with GDM, excessive GWG and weight retention in the mother, contributing to the transgenerational cycle of obesity and its comorbidities (Tanentsapf et al., 2011; Diemert et al., 2016b).

1.3.3 Dietary recommendations for pregnancy in UK

The Committee on Medical Aspects of Food Policy (COMA) (a now disbanded UK advisory committee) released recommended energy reference values for the UK population in 1991. COMA recommended that pregnant women only consume an extra 191 kcal (kilocalories) per day in the last trimester of pregnancy (1991). This advice was based on the calculation that the energy cost of pregnancy is roughly 40,000 kcal in women with a pre-pregnancy weight of around 60kg. It is estimated that the BMR increases throughout the pregnancy by about 30,000 kcal due to body weight changes; so, the overall cost of pregnancy was estimated at around 70,000 kcal (The Committee on Medical Aspects of Food Policy, 1991). However, this theoretical need is rarely met according to UK dietary surveys and studies, it is possible that pregnant women reduce their physical activity to compensate for this energy cost (Streuling et al., 2011). Therefore, the recommended extra 191 kcal per day in the final trimester amounts to an average 17,300 kcal increase over the whole pregnancy.

The Scientific Advisory Committee for Nutrition (SACN) is an independent scientific institution who have replaced COMA in advising the government and Public Health England on nutrition issues in the UK. The SACN subgroup on Maternal and Child Nutrition (SMCN) advise pregnant women to

achieve an adequate nutritional status pre-conceptually to help achieve optimal outcomes during pregnancy. The SACN released updated energy reference values in 2011, based on new evidence and the use of more accurate methods of assessing energy expenditure (Scientific Advisory Committee on Nutrition, 2011). The SACN and SMCN support the 1991 COMA recommendation of 191 kcal increment per day in the last trimester of pregnancy but recognise that this figure is based on a 60kg pre-pregnancy weight; so women who are entering pregnancy as overweight or underweight may have different requirements. However, there is not enough evidence to make a recommendation for these women (SACN, 2011).

The National Institute of Health and Care Excellence (NICE) provide medical guidance to NHS and other health professionals. The NICE pregnancy guidelines emphasise the importance of folic acid supplementation of 400 microgram (µg) daily, for women who may become pregnant and women in early pregnancy to reduce risk of neural tube defects (National Institute for Health and Care Excellence, 2008). Low folate status is associated with neural tube defects, preterm delivery and low birth weight (Scientific Advisory Committee of Nutrition, 2011). Vitamin D is required in response to calcium needs of the foetus and there is some evidence that inadequate vitamin D status is associated with low birthweight, therefore daily supplementation of 10 µg of vitamin D is advised. (SACN, 2011).

Within the NHS, pregnant women are recommended ‘a healthy diet’ and advise women to base their intake on the Eatwell Guide (NHS, 2017). Advice focuses on general information on about a healthy diet during pregnancy including 5 portions of fruit and vegetables a day, one portion of oily fish per

week, foods to avoid during pregnancy and how to prepare food safely (NHS, 2017). The advice for pregnant women is general and there is a lack of specific recommendations for calorie intake or weight gain during pregnancy.

1.3.3.1 Dietary recommendations outside of UK

The USA energy dietary reference intakes (DRI) for pregnancy recommends increased intake of 340 kcal/day in the second trimester and 452 kcal/day in the third trimester, with no increase in the first trimester (Institute of Medicine and Council, 2009). Similar to the US recommendation, the Food and Agriculture Organization of the United Nations (FAO) recommend increased energy intake of 85 kcal/day, 285 kcal/day and 475 kcal/day in first, second and third trimesters respectively (World Health Organization et al., 2004). This requirement was calculated on the need for appropriate gestational weight gain (mean gain of 12kg) and a total energy cost of pregnancy as 77,000 kcal. The FAO recommendation was based on several worldwide studies, including those from low income countries.

A possible criticism of the FAO recommendation is its appropriateness of use for those living in high income countries and increasingly developing countries; where the populations are at a lower risk of malnutrition and higher risk of overnutrition, therefore this could result in excessive GWG.

Dietary and energy intake recommendations for pregnancy differ around the world as does perinatal care and maternal mortality rates (WHO, 2004). This reflects the differences in education status, food security and availability and rates of obesity and malnutrition between high, middle and low-income

countries, this suggests that pregnancy outcomes are highly variable within populations. This implies that more personalised requirements may be needed as a broad, inclusive approach to nutrition may not be conducive for good maternal and child outcomes, even within national populations.

1.3.4 Dietary intakes in pregnant populations

As in the UK dietary intakes of pregnant women are not routinely recorded, there is a lack of diet data for pregnant women (Bath et al., 2014). However, the National Diet and Nutrition Survey (NDNS) routinely records nutritional intake of general populations, although not a direct measurement of pregnant women's intake, this survey provides insight into the diets of UK women aged 19-64 years old.

The NDNS reported that just 28% of women (in the general UK population) aged 19-64 years met the 5-A-Day recommendation in 2014/15. Mean daily intakes of most vitamins and minerals (with the exception of vitamin A, riboflavin, iron, magnesium, potassium and selenium) met the Lower Reference Nutrient Intake (LRNI) in girls and women. Saturated fat intake exceeded recommendations of no more than 11% of total energy, however total fat intake was not reported to be over 35% total energy as recommended. Women exceeded the recommendation of no more than 11% of non-milk extrinsic sugars (free sugars) and intakes of fibre were well below the DRV of 18g at the time (13/14g per day intake) (Public Health England, 2016).

This provides some evidence for nutritional intake of women at reproductive and postmenopausal age and can be assumed that pregnant women have a

similar intake. Adequate preconceptual nutritional status of the mother is considered essential for optimum foetal development and child health outcomes (SACN, 2011), so interventions to improve dietary quality and address health inequalities for women of a reproductive age are a priority.

Many factors such as education level, income and age affect dietary intake during pregnancy along with maternal health characteristics such as GDM and GWG (Heslehurst et al., 2010). Although there are limited survey data on maternal dietary intakes during pregnancy, a number of studies do collect such data however, variability in methods used to collect or measure dietary data can result in a high variability in results (Ribas-Barba et al., 2009).

To assess the associations between dietary intake and maternal health, such as the consequences of inadequate or excessive GWG and the interactions between diet and glycaemic status, there is a need for regular collection of dietary intake data in pregnant populations to be established.

1.4 Maternal health characteristics

A number of health characteristics during pregnancy can impact the pregnancy, birth and health outcomes for both the mother and the child. Pregnancy is a complex period of the female lifespan, with the occurrence of endocrine and physiological adaptations which can be interrupted by characteristics such as GDM and adverse GWG. These characteristics can be further complicated by maternal obesity and health outcomes are significantly better for women of a healthy weight when entering pregnancy (Oteng-Ntim et al., 2013). This section aims to discuss the incidence and

consequences of maternal health characteristics such as maternal obesity, GWG and GDM.

1.5 Maternal obesity

Obesity prevalence has increased by more than 50% worldwide from 1980 to 2014 (World Health Organisation, 2016). Obesity is defined by the World Health Organisation (WHO) as a BMI of greater than or equal to 30 kg/m^2 in adults over 20 years (World Health Organisation, 2017). In 2014, 13% of the world's population over 18 years old were obese, of this 15% of women and 11% of men were obese. An estimated 41 million children under the age of 5 were overweight or obese (World Health Organisation, 2016).

As well as increased prevalence in developed countries, many low and middle-income countries are experiencing rapidly rising rates in noncommunicable diseases associated with obesity. These countries are often experiencing under nutrition and obesity concurrently (World Health Organisation, 2016).

The Health Survey for England (HSE) found that in 2015, 62.9% of UK adults were overweight or obese and only 39.5% of women have a healthy BMI (18.5-24.9 kg/m^2) (Public Health England, 2017b). The proportion of obese women in the UK has increased from 8% to 16% over 19 years (1989-2007) and thus there has been a 12% decrease in the healthy BMI group in that time (Heslehurst et al., 2007).

1.5.1 Overweight and obesity during pregnancy

It is estimated that around 1/6 women in England enter pregnancy as obese (Oteng-Ntim et al., 2013). The Centre for Maternal and Child Enquiries (CMACE) found that in 2009, 5% of pregnant women had a BMI of over 35kg/m^2 and 2% of those were morbidly obese (≥40kg/m^2) (Public Health England, 2017a).

A study using data from the ALSPAC cohort measuring BMI and waist circumference in women 16 years after pregnancy, reported that women who gained more weight than recommended by the Institute of Medicine (IOM), had higher mean BMI (OR 2.90 [95% CI 2.27, 3.52]) and waist circumference (OR 5.84 [95% CI 4.15, 7.57]) than women who gained within the recommended range (Fraser et al., 2011). This is problematic as it implies that GWG may result in post-partum weight retention and therefore increase the prevalence of women entering subsequent pregnancies as overweight or obese. This could also put subsequent offspring at risk of obesity-related outcomes such as macrosomia, increasing risk of future obesity and perpetuating the transgenerational cycle of obesity and its co-morbidities. In the ALSPAC cohort, women who were overweight or obese gained more weight than is recommended by IOM during pregnancy, whereas healthy and underweight women gained within the recommended range (Fraser et al., 2011). This suggests that women who are already overweight or obese are more likely to gain more weight during pregnancy, resulting in higher risk of obesity after the pregnancy.

1.5.2 Maternal obesity and public health

Obesity is thought to be highly correlated with health inequalities and is a major public health concern (Mullins et al., 2016). Obesity prevention is considered a more viable option when compared with intervention, which is costlier and more difficult (Heslehurst et al., 2011). Although current government initiatives are targeting childhood obesity; it may be considered more prudent to use pregnancy, a 'teachable moment', as the starting point for obesity prevention (Phelan, 2010). Understanding the modifiable factors contributing to obesity is a crucial step in developing obesity interventions and preventions.

1.5.3 Factors associated with maternal obesity

Women from the most deprived areas in the UK are almost two and a half times more likely to be obese at the start of pregnancy (OR 2.42 [95% CI 1.69, 2.98]) compared to those living in the least deprived area (Heslehurst et al., 2011). This is an important consideration, as the social gradient of health determines that inequalities in socioeconomic status relate to inequalities in health status (Kosteniuk and Dickinson, 2003). There is a positive relationship between family socioeconomic status and maternal health, with strong evidence that this tracks through a child's life from birth (Dowd, 2007).

Education level has also been implicated as a predictor of obesity. In a prospective population cohort of 6959 women, maternal obesity was associated with low education level (Gaillard et al., 2013). These findings

were echoed in a Norwegian cross-sectional study of 6711 pregnant women, in which women of a lower educational level were more likely to obese when entering pregnancy (Brantsæter et al., 2014); suggesting a similar pattern in other high-income countries.

In the USA, ethnicity was found to be associated with maternal obesity in a pregnant cohort of 329,988; nearly 12% of black women had a pre-pregnancy weight of ≥90kg compared with 5.2% of Hispanic, 4.8% White and less than 1% of Asian women (Rosenberg et al., 2005). Similarly, a UK sample of 17,910 pregnant women reported that 14% of the overall sample were obese. Of these; 24% of black women were obese compared with 9% white, 9% Asian and 3% oriental women. Black women in this cohort showed higher population attributable risk fractions in all pregnancy outcomes than the other groups, driven by the high prevalence of maternal obesity (Oteng-Ntim et al., 2013). However, ethnicity was not associated with maternal obesity in a study of 36,821 pregnant women in Middlesbrough, UK. The majority (91.9%) of this sample were Caucasian, therefore this study could be underpowered to find an association between maternal obesity and other ethnic groups (Heslehurst et al., 2007).

Findings such as these may suggest a need to identify the different risk factors involved for each ethnicity and model interventions based on these, to reduce the adverse pregnancy outcomes for those at a higher risk.

This was attempted in a study of 8478 South Asian and White British pregnant women from the Born in Bradford cohort. The study examined whether a lower South Asian specific BMI cut off could identify women at risk

of adverse pregnancy and birth outcomes. However, no increased risk of adverse birth outcomes at the lower BMI threshold of 27.5kg/m^2 was reported; suggesting that a South Asian specific BMI would not result in more effective identification of at risk pregnant women (Bryant et al., 2014).

1.5.4 Short term consequences of maternal obesity

1.5.4.1 Maternal outcomes

In a cross-sectional analysis of 17,910 women, increasing BMI was related to increasing risk of adverse pregnancy outcomes for the mother (Oteng-Ntim et al., 2013). The odds ratio for women requiring an emergency caesarean section increased from 1.49 (95% CI 1.31, 1.69) for obese women and 2.05 (95% CI 1.75, 2.24) for morbidly obese women. Similarly, when compared with healthy weight women, the odds ratio for women experiencing a post-partum haemorrhage was 1.47 (95% CI 1.18, 1.67) for obese and 2.20 (95% CI 1.88, 2.58) for morbidly obese when compared with women with a healthy BMI (Oteng-Ntim et al., 2013).

A meta-analysis of 4,143,700 births from 39 studies, examining the impact of obesity on pregnancy outcomes, reported that length of hospital stay increased with increasing BMI; as did the rate for post-partum infection (Heslehurst et al., 2008).

Maternal obesity is a known risk factor for GDM (Lashen et al., 2004). Obese women are at a significantly higher risk of GDM compared with normal weight women ($p< 0.001$), GDM is considered high risk for delivery and maternal and foetal outcomes (Lashen et al., 2004).

Evidence from a systematic review of 12 studies suggests a positive association between increasing maternal pre-pregnancy obesity and lower rates of initiation and duration of breastfeeding (Wojcicki, 2011). However, the authors of this review suggested that a number of factors such as ethnicity, GDM and social factor also have an impact on breastfeeding rates and reported that not all studies adjusted appropriately for such confounding factors (Wojcicki, 2011).

A large study using data from the Danish National Birth Cohort of 37,459 women, reported that 14.4% of obesity class III women had ceased exclusive breastfeeding by the end of the first week of delivery, compared with 3.5% of healthy weight women. Interestingly, by 16 weeks postpartum, the proportion of women who continued any breastfeeding decreased with increasing BMI. (Baker et al., 2007). Similarly, in a study of 431 first time mothers, the odds ratio for delayed onset of breastfeeding was 1.84 times higher in overweight and 2.21 higher in obese women compared with healthy weight women (Nommsen-Rivers et al., 2010).

The benefits of breastfeeding are numerous, including cognitive development, lower rates of obesity and reduction of chronic disease such as hypertension, CVD, hyperlipidaemia and some types of cancer in the offspring (Binns et al., 2016) and reduced risk of breast cancer, ovarian cancer and postpartum weight retention in the mother (Ross-Cowdery et al., 2017).

1.5.4.2 Offspring outcomes

Maternal obesity is associated with increased risk of macrosomia; the odds ratio for macrosomia in offspring of overweight women was 1.5 (95% CI 1.33, 1.70) and 2.37 (95% CI 1.92, 2.92) for obese women in an analysis of 17,910 women (Oteng-Ntim et al., 2013). In the short term, macrosomia increases the need for assisted and induced delivery, caesarean section and risk of birth injury such as shoulder dystocia (Hehir et al., 2015). Offspring born to obese mothers are at a higher risk of admission to neonatal intensive care units (NICU), one study found the odds ratio for admission to NICU was 1.42 (95% CI 1.17, 1.72) for obese women when compared with healthy weight women (Oteng-Ntim et al., 2013).

A meta-analysis of 96 studies reported that pre-pregnancy overweight and obesity was the top ranking modifiable risk factor for stillbirth in high income countries, with an increased odds of 23% in overweight women and 60% in obese women (Flenady et al., 2011).

In agreement with this, a study of 4932 pregnant women found obese women had a significantly higher incidence of early miscarriage when compared to normal weight controls (p= 0.04) (Lashen et al., 2004).

The short-term risks associated with maternal obesity put pressure on health services, through increased need for assisted delivery and neonatal care after birth. Many of the short-term consequences also carry a potential to affect mother and child in the long term; including the physical after effects of birth injuries, psychological effects of birth trauma and psychosocial effects

of weight stigma. This potentially reduces quality of life and cycles the transgenerational effects of obesity.

1.5.5 Long term consequences of maternal obesity

1.5.5.1 Maternal health outcomes

Maternal obesity can increase the risk for maternal diabetes later in life, Oteng-Ntim et al. (2013) reported an OR of 2.38 (95% CI 1.84, 3.04) for overweight and 9.29 (95% CI 6.64, 12.98) for obese compared to women in the healthy weight group, in 17,910 women.

Pregnancy can contribute to long term overweight and obesity; women with subsequent pregnancies may have a higher pre-pregnancy BMI with each pregnancy due to post-partum weight retention (Nagl et al., 2016) .

Obesity is associated with mental health disorders in non-pregnant populations (Avila et al., 2015) and so may also be associated with pregnant populations. Women who were obese when pregnant were more likely to have antenatal depression when compared to healthy weight women (OR 1.43 [95% CI 1.27,1.61]) (Molyneaux et al., 2014). This is supported by a study using data from the ALSPAC cohort, which found obese pregnant women had significantly higher odds of antenatal depression than those of a healthy weight (OR 1.39 [95% CI 1.05, 1.84]) (Molyneaux et al., 2016).

1.5.5.2 Offspring health outcomes

A meta-analysis of 45 studies reported that pre-pregnancy obesity increased the risk of offspring LGA (OR 2.08 [95% CI 1.95, 2.23]), high birth weight (OR 2.00 [95% CI 1.84, 2.18]) and macrosomia (OR 3.23 [95% CI 2.39, 4.37]) when compared with healthy BMI mothers (Yu et al., 2013). An increase in offspring overweight/obesity was reported in those born to obese mothers (OR 3.06 [95% CI 2.68, 3.49]), suggesting the transgenerational effects of obesity. However, although this systematic review contained high and medium quality studies; the results of the meta-analysis were limited due to high variability in methods used to assess pre-pregnancy BMI, infant birth weight and obesity (Yu et al., 2013).

1.5.6 Weight management during pregnancy

The SACN highlight the need to increase the public understanding of the risks involved with maternal obesity (SACN, 2011). There is little evidence to make weight-management recommendations for obese and overweight pregnant women and during pregnancy weight loss is not advised (SACN, 2011). It is thought that those who are overweight or obese may not require the increment of 191kcal per day in the final trimester as suggested by SACN, but there is a paucity of evidence to support this (SACN, 2011). The consensus is that a healthy weight upon entering pregnancy is desirable for optimum outcomes (SACN, 2011; Diemert et al., 2016). The absence of evidence-based guidelines for energy requirements for overweight and obese women in the UK may result in a lack of emphasis in the importance

of a healthy pre-conception weight and the implications of entering pregnancy as overweight or obese.

1.6 Gestational Weight Gain

GWG is highly variable among women and is related to several changes including increased blood volume, water retention, weight of the uterus and fat stores (Langley-Evans, 2009). The placenta, foetus and amniotic fluid accounts for around 35% of total GWG. As a complex phenomenon which compromises of foetal weight as well as maternal weight, it is difficult to define modifiable factors affecting GWG.

1.6.1 IOM Gestation Weight Gain Recommendations

The Institute of Medicine is a division of The National Academies, a non-profit institution providing independent advice to the government and private sector in the USA (Institute of Medicine and Council, 2009). In 2009, the IOM updated their 1990 guidelines for gestational weight gain limits in pregnancy (see Table 1.1), these guidelines have since been adopted by some health professionals as the standard optimal outcomes for pregnant women. The IOM categorises GWG as either insufficient, adequate or excessive (IOM, 2009). It has been reported that almost 1/3 of women gain above or below the IOM recommended weight gain during pregnancy (Mamun et al., 2010) and this can potentially have implications for the future health of the mother and child.

The IOM puts focus on the importance of pre-pregnancy BMI and weight gain recommendations relating to BMI categories, in order to reduce adverse outcomes (Hutcheon and Oken, 2016).

Table 1.1.1 Recommendations for total and rate of weight gain during pregnancy, adapted from IOM 2009 (IOM, 2009)

Pre-pregnancy BMI (kg/m^2)	Total Weight Gain (kg)	Rates of Weight Gain 2nd and 3rd Trimester (Mean in kg/week) *	Total Weight Gain (lbs)	Rates of Weight Gain 2nd and 3rd Trimester (Mean in lbs/week) *
Underweight (<18.5)	12.5 - 18	0.51 (range 0.44-0.58)	28 - 40	1 (range 1-1.3)
Normal weight (18.5-24.9)	11.5 - 16	0.42 (range 0.35-0.50)	25 - 35	1 (range 0.8-1)
Overweight (25.0-29.9)	7 - 11.5	0.28 (range 0.23-0.33)	15 - 25	0.6 (range 0.5-0.7)
Obese (≥30.0)	5 - 9	0.22 (range 0.17-0.27)	11 - 20	0.5 (range 0.4-0.6)
***Calculations assume 0.5-2 kg weight gain in the first trimester**				

The current IOM guidelines are lacking recommendations for the different classes of obesity; obese class I (30-34.9 kg/m^2), class II (35-39.9 kg/m^2) and class III (≥40kg/m^2) (World Health Organisation, 2017). Appropriate weight gain recommendations for these BMI groups may be necessary, as the evidence suggests that obese class III women (≥40kg/m^2) have significantly higher risk of adverse pregnancy outcomes when compared with

non-obese and obese class I and II women (Kumari, 2001; Marshall et al., 2010)

As the IOM recommendations are made based on research including mainly white, US populations, there may be a lack of external validity when setting weight gain goals in other ethnic groups. Similarly, there are no comprehensive weight gain recommendations for multiple foetus pregnancies. It has been suggested that during lactation, fat is mobilised from the mother's thighs and mid-section and there is some evidence to suggest that breastfeeding promotes weight loss due to excess calorie cost (McClure et al., 2012). As such, it may be helpful to consider a mother's intention to breastfeed before recommending weight gain goals.

1.6.2 UK Recommendations for gestational weight gain

NICE recommends a general healthy diet and physical activity programmes; for before, during and after pregnancy. The recommendations are based on 'effective strategies and weight-loss programmes', yet state that weight loss programmes are not recommended during pregnancy. They advise for women with a BMI of >30kg/m^2 to try to lose 5-10% of their body weight before becoming pregnant, to improve health outcomes (National Institute for Health and Care Excellence, 2010). Calorie restriction during pregnancy is not advised as this may harm the foetus. The NICE guidelines for weight management during pregnancy are lacking guidance for women who are underweight (BMI<18.5 kg/m^2) and the clinical management of obese pregnant women.

The UK is lacking specific ranges for GWG adequacy. NICE and the Public Health Intervention Advisory Committee (PHIAC) have observed a lack of evidence and large-scale controlled trials in the impact of GWG on UK women, including those under 18 years old and from different ethnic groups. NICE do not support the IOM guidelines as they are based on observational data, from US populations, and may not represent the UK population (National Institute for Health and Care Excellence, 2010). Therefore, the IOM recommendations are not used in practice by UK health professionals.

Interestingly, in a cohort of 292 US women, those who had a concordant goal with IOM guidelines were 65% less likely to have excessive GWG than those with no weight gain goal (OR= 0.35 [95% CI 0.1, 1.1], these results were marginally non-significant, however the sample size may have limited this study in finding significant associations (Tovar et al., 2011). Similarly, a systematic review of 5 studies and 971 pregnant women concluded that studies basing interventions on goal setting were effective at the prevention of excessive GWG. However, between-study comparisons of the specific aspect of the goal setting were difficult due to study heterogeneity (Brown et al., 2012).

This suggests that goal setting could be an important factor in limiting excessive or inadequate GWG, therefore implementation of guidelines relating to specific weight gain limits may be important for preventing maternal obesity and adverse GWG in the UK.

1.6.3 Risk factors associated with adverse gestational weight gain

Understanding the risk factors associated with inadequate or excessive weight gain is important to prepare interventions preventing adverse outcomes. The most commonly identified determinants of health behaviours are a genetic predisposition, environmental factors, social interactions and socioeconomic climate (Azevedo and Vartanian, 2015).

There is some evidence of an association of dietary intake and GWG (Streuling et al., 2011), however the results are not consistent (Jebeile et al., 2016). There are many components of dietary intake such as macronutrient and micronutrient intake, total energy intake, individual nutrient or food components and overall dietary quality and dietary patterns; this enhances the complexity of understanding the interactions between diet and GWG.

Energy and free sugar intake were found to be significantly positively associated with higher GWG in 200 pregnant women in Germany (Diemert et al., 2016). This is supported by a recent systematic review of 12 studies, which found that increased energy intake is associated with higher GWG, although this review contained a high proportion of low-quality observational studies, so the results must be interpreted with caution (Tielemans et al., 2016). Conversely, Jebeile et al. (2016) found that energy intake in pregnant women increased by only 140 kJ (around 33 kcal) per day and although GWG was significant (+12 kg); this meta-analysis of 18 studies did not find any association between energy intake and GWG. As previously mentioned GWG involves not only maternal fat accretion but also foetal components, so

it has been suggested that the effects of energy intake on body composition and mass may differ in pregnant and non-pregnant populations (Tielemans et al., 2016).

There is paucity of evidence on the effects of different dietary composition on GWG (Tobias and Bao., 2014). It may be prudent to assume that examining dietary pattern rather than single nutrients or foods, may be more beneficial in designing interventions to prevent GWG and reducing adverse birth outcomes as single nutrients are rarely consumed (Hu, 2002).

In a US study of 490 pregnant women, diet quality was not associated with adequate GWG, however the sample was mainly White and had a higher education level when compared to the general population (Shin et al., 2014). Results from the Generation R Study concluded that when using both *a priori* and *a posteriori* dietary patterns, the composition of the diet may play a small role in early pregnancy weight gain but has no association with total GWG (Tielemans et al., 2015). Current studies are limited due to differences in measures of diet and GWG, which results in difficulty interpreting and comparing results and as previously discussed, weight gain during pregnancy is variable and has several confounding factors (Tobias and Bao, 2014).

Pre-pregnancy BMI is thought to be one of the main mediators of GWG. One theory in the relationship of pre-pregnancy BMI and GWG is that fat storage in pregnancy is in response to foetal requirements and obese women may not need to gain any extra weight (Thornton et al., 2009).

This is supported by a study of 793 mothers in Italy; those who were underweight when entering pregnancy gained more weight than those who were of a normal+ BMI (this gain was still within IOM recommendations) and that this did not have adverse effects for the mother or the infant (Zanardo et al., 2016). Similar to this, a study of 1884 mother-offspring pairs found lower risk of the excessive GWG (measured from IOM categories) when pre pregnancy BMI was higher (OR 0.46 [95% CI 0.23, 0.91]) (Heude et al., 2012).

In contrast to this, 55% of obese pregnant women and 33% of morbidly obese were found to have gained above the IOM recommendations, in a retrospective cohort of 499 women, and the combination of pre-pregnancy BMI and GWG resulted in higher infant birth weight (Heerman et al., 2014). A UK study of 13,617 women found that overweight and obese women gained above the IOM recommendations and those with a lower BMI gain lower GWG than recommended (Fraser et al., 2011).

It is clear that pre-pregnancy BMI is associated with GWG, but it is not fully understood how or exactly why (Diemert et al., 2016). It is important to better understand the influences on GWG to design public health interventions to reduce adverse gain.

1.6.4 Short term implications of adverse gestational weight gain

1.6.4.1 Maternal health outcomes

A large meta-analysis of 150 studies examining birth and maternal outcomes associated with GWG, found weak evidence for the link between GWG and pregnancy-induced hypertension and reported that the potential relationship can be explained by oedema experienced during hypertension rather than actual weight gain (Viswananthan et al., 2008). The same meta-analysis reported inconsistent evidence for the association between GWG and GDM (Viswananthan et al., 2008) however, it is well recognised that maternal pre-pregnancy obesity is a risk factor for GDM (Torloni et al., 2009; Gaillard et al., 2013). A randomised controlled trial of 7,985 women found inconsistent evidence for the relationship between GWG and GDM, due to differing criteria in diagnosis of GDM and glucose intolerance (Carreno et al., 2012).

1.6.4.2 Offspring health outcomes

There is evidence for an association between preterm birth (before 37 weeks gestation) and both excessive and insufficient GWG (Viswananthan et al., 2008; Faucher et al., 2016). Supporting this, a meta-analysis of 10,171 pregnant women reported that excessive GWG in obese women was associated with increased risk for medically induced preterm delivery but the evidence for spontaneous preterm delivery and GWG was inconclusive (Faucher et al., 2016). Preterm birth is the leading cause of infant mortality in the world (WHO, 2015), in order to improve outcomes pregnant women

should be fully counselled prior to and during pregnancy on lifestyle modifications for adequate GWG.

There is strong evidence to suggest that GWG is associated with infant birth weight. Diemert et al. (2016) found that birth weight was significantly positively correlated with total GWG ($p=0.020$) as well as pre-pregnancy BMI ($p<0.001$). A meta-analysis of 35 studies found strong evidence of an association between GWG over the IOM recommended limits and macrosomia and similarly, GWG below recommendations and low foetal birthweight (Siega-Riz et al., 2009). This is echoed by a separate meta-analysis which found strong evidence for a relationship between increasing GWG and increasing birthweight (Viswananthan et al., 2008).

1.6.5 Long term implications of adverse gestational weight gain

1.6.5.1 Maternal health outcomes

Weight gain during pregnancy and failure to lose weight post pregnancy is an important risk factor for obesity in the mother (Fraser et al., 2011). A meta-analysis of 11 studies found moderate evidence of a relationship between excessive GWG and weight retention from 3 months up to 3 years post-pregnancy (Viswananthan et al., 2008). Evidence from a Dutch pregnancy cohort that suggested that mothers who gained excessive weight during pregnancy gained 4.6kg (95% CI 1.4, 8.8) six years post childbirth, when compared with adequate GWG who gained 2.6kg (95% CI 0.2, 5.2) (Tielemans et al., 2015). This can put women at higher risk of entering

subsequent pregnancies as overweight or obese and therefore, increase risks of adverse outcomes for both the mother and subsequent child.

1.6.5.2 Offspring health outcomes

A systematic review found that offspring of women who gained excessive weight during pregnancy had a 40% increased risk of later life obesity when compared with offspring born to mothers who gained within the IOM recommendations (Mamun et al., 2013). This is consistent with the relationship between GWG and infant birthweight, both macrosomia and low infant birthweight have been associated with later life obesity and metabolic syndrome (Boney et al., 2005).

1.7 Hyperglycaemia during pregnancy

Hyperglycaemia is defined as elevated blood glucose levels (WHO, 2006). According to WHO (2006), a fasting blood glucose level of 4-7mmol/l and postprandial level of 8.5-9mmol/l is considered normal and blood glucose levels above these ranges are considered hyperglycaemic.

As discussed in section 1.2, normal pregnancy is a state of increased insulin resistance which facilitates the transport of glucose across the placenta, stimulating foetal pancreatic insulin secretion, which acts an essential foetal growth hormone (Farrar, 2016). If resistance to maternal insulin activity becomes too great, maternal hyperglycaemia occurs and GDM may be diagnosed (Farrar, 2016).

Although all pregnant women in the UK are not routinely tested for GDM, unless presenting with risk factors (see below), urine testing for glycosuria takes place at each antenatal visit. The National Institute for Health and Care Excellence (NICE) advise that glycosuria of 2+ or above on one occasion, or 1+ on two or more occasions may indicate GDM and if this is observed, testing for GDM should be carried out (NICE, 2015).

Alongside glycosuria testing, any woman with one or more of the following risk factors will be tested for GDM, using a 2-hour 75g oral glucose tolerance test (OGTT) at approximately 28 weeks gestation:

- BMI above 30 kg/m^2
- Previous GDM
- Previous macrosomic baby
- Family history of diabetes

- Ethnic minority family origin with high prevalence of diabetes (NICE, 2015)

1.7.1 Glycosuria in pregnancy

Glycosuria occurs when the renal threshold for plasma glucose concentration is exceeded and glucose is excreted in the urine (Cowart and Stachura, 1990). Small amounts of glucose are present in the urine in normal individuals, glycosuria is defined as a level of more than 25mg/dl in random sample of urine. In a healthy individual, the renal tubules reabsorb most of the glucose present in the normal glomerular filtrate. When this balance is interrupted, due to elevated blood glucose or impaired absorptive capacity of the tubule, glucose exceeds the capacity of the renal tubes and results in glucose excretion in the urine. Pregnancy is known to decrease the renal threshold for glucose and diabetes during pregnancy is responsible for elevated blood glucose levels (Cowart and Stachura, 1990).

Routine urine testing for glycosuria, an indicator of hyperglycaemia, is undertaken throughout the pregnancy despite general agreement that glycosuria is not a valid screening test for GDM (Coolen and Verhaeghe, 2010). A narrative review of 4 studies concluded that glycosuria testing was a poor tool in the diagnosis of GDM in 3 studies, but the fourth study suggested glycosuria testing may be beneficial in the first two trimesters only (Alto, 2005). Alto (2005) argues that glycosuria is common during pregnancy due to increased glomerular filtration rate and routine glycosuria screening is no longer required. However, the inclusion of only four studies in this review highlights the paucity of evidence surrounding glycosuria testing and

identifies that the results of the review should be interpreted with caution. Although there is debate on the efficacy of glycosuria testing for GDM diagnosis, a positive glycosuria test does suggest the presence of hyperglycaemia during pregnancy without an overt GDM diagnosis and this may be important in the health of the mother and offspring.

Interestingly, glycosuria has been linked with weight gain (Carlson and Campbell, 1993; Coolen and Verhaeghe, 2010). A controlled trial of 6 non-pregnant, insulin-dependent diabetic adults and 6 non-diabetic volunteers found an association between glycosuria and weight gain. Intensive insulin therapy in the participants improved glycaemic control, but body weight increased by 2.6 kg (+ or – 0.8kg), and of the weight gain 70% could be accounted for by the elimination of glycosuria and 30% by reduction in daily energy expenditure (Carlson and Campbell, 1993). Glycosuria equates energy loss (Coolen and Verhaeghe, 2010) so it has been speculated that glycosuria may be a determinant of GWG, but this is an understudied area and needs further studies before any causality can be implied.

The Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) study identified a linear association between increasing levels of maternal hyperglycaemia and adverse perinatal outcomes, including induction of labour, caesarean section, LGA, macrosomia and shoulder dystocia, even present in those within normal blood glucose ranges and without a diabetes diagnosis (Jacklin et al., 2017). This provides some evidence that women with hyperglycaemia such as glycosuria may be at risk of negative health outcomes if not treated.

Although it is generally agreed that glycosuria testing is a poor tool in the diagnosis of GDM (Alto, 2005; Coolen and Verhaeghe, 2010) it is possible that it provides a marker of glycaemic control and possible body weight determinants in pregnancy. Thus, it is important to recognise that hyperglycaemia during pregnancy may affect birth outcomes and hyperglycaemia is a potential modifiable risk factor that could improve outcomes for both mothers and offspring. Although there is debate as to whether glycosuria testing provides a marker for GDM in current pregnancy, it may provide a 'teachable moment' for women to be aware of blood glucose levels and weight gain in subsequent pregnancies.

1.7.2. Factors associated with hyperglycaemia

The risk factors associated with hyperglycaemia, without a GDM diagnosis, during pregnancy are not well studied, unlike risk factors for overt pregnancy diabetes (see section 1.7.5.1). It can be assumed that there may be some shared risk factors for both hyperglycaemia and GDM, as GDM is considered a severe form of hyperglycaemia in pregnancy (Farrar, 2016).

1.7.2.1 Dietary intakes and hyperglycaemia

There is paucity of evidence linking dietary intake with altered glycaemic status such as glycosuria, however, there may be evidence for the association of dietary intake and GDM (see section 1.7.5.2)

1.7.3 Short term health implications of hyperglycaemia during pregnancy

There is limited evidence for perinatal outcomes of women with hyperglycaemia as indicated by the presence of glycosuria during

pregnancy; rather than as indicated by an oral glucose tolerance test (OGTT). However, as mentioned in section 1.7.1, the HAPO study reported an association between increasing levels of maternal hyperglycaemia (without overt diabetes diagnosis) and adverse outcomes for both mother and offspring (Jacklin et al., 2017).

Similarly, in a historical cohort of 2904 non-diabetic pregnant women, it was reported that increasing glucose levels, as diagnosed by an OGTT, were associated with induced labour (OR 1.11 [95% CI 1.02, 1.22]), caesarean delivery (OR 1.16 [95% CI 1.05, 1.28]), macrosomia (OR 1.16 [95% CI 1.01, 1.34]) and shoulder dystocia (OR 1.78 [95% CI 1.32, 2.40]), these results were not changed when adjusted for GWG (Jensen et al., 2001). This demonstrates that outcomes similar to those with GDM can be seen in women with milder degrees of hyperglycaemia, the authors of this study hypothesise that this is due to foetal hyperinsulinaemia caused by maternal hyperglycaemia which leads to accelerated growth and macrosomia (Jensen et al., 2001).

This is supported by a systematic review of 25 studies, including 4466 women, which reported that women one abnormal glucose value (defined as borderline GDM), as diagnosed by a 3-hour, 100-g OGTT, had significantly worse health outcomes compared to women with no abnormal value. Increasing glucose intolerance was associated with macrosomia (OR 1.38 [95% CI 1.09, 1.76]), neonatal hypoglycaemia (OR 1.88 [95% CI 1.05, 3.38]), caesarean delivery (OR 1.69 [95% CI 1.40, 2.05]) and maternal hypertension (OR 1.55 [95% CI 1.31, 1.83]); concluding that these women experienced outcomes comparable to those diagnosed with GDM (Roeckner et al., 2016).

1.7.4 Long term health implications of hyperglycaemia during pregnancy

A study of 10,591 women-offspring pairs from the ALSPAC cohort, examined glycaemic status and birthweight and found that maternal glycosuria was associated with offspring macrosomia (OR 1.70 [95% CI 1.28-2.25]) when compared to women with no diabetes. This was attenuated when adjusted for maternal pregnancy BMI, but the positive association remained (OR 1.58 [95% CI 1.18 2.12]). Similarly, higher odds ratio of higher offspring BMI (OR 0.62 [0.32, 1.23]), central adiposity (OR 0.12 [95% CI 0.01, 0.23]) and fat mass z scores (OR 1.31 [95% CI 1.00, 1.72]) at age 9-11 years were seen in those with mothers with glycosuria. Interestingly, women in this study who had glycosuria had similar offspring outcomes as those with GDM and existing diabetes, when compared to those with no diabetes; suggesting that hyperglycaemia is related to adverse offspring outcomes (Lawlor et al., 2010).

In agreement with this, a longitudinal study of 421 ethnically diverse, mother-daughter pairs, found that girls who were exposed to maternal hyperglycaemia in utero were at a higher risk of childhood adiposity, defined as BMI ≥85th percentile (OR 2.28 [95% CI 1.08-4.84]) when compared to those born to mothers with normal blood glucose, independently of maternal age, BMI, ethnicity and daughter's age and age at onset of puberty. The risk of childhood obesity was highest amongst those born to mothers withGDM (OR 5.56 [95% CI 1.70, 18.2]) and a pre-pregnancy BMI of 30 kg/m^2 or more (OR 3.73 [95% CI 1.89, 7.37]) (Kubo et al., 2014).

In contrast, a HAPO study of 1,677 pregnant women underwent an OGTT at 28 weeks gestation, the subsequent offspring anthropometry was examined and found that mild untreated hyperglycaemia (with no diagnosis of GDM) was not independently associated with obesity, measured by BMI and skin folds, in offspring aged 5-7 years old. However, it was reported that maternal pregnancy BMI and offspring birth weight were independent predictors of offspring overweight [(regression coefficient 0.06 per kg/m^2 [95% CI 0.05-0.07]) (0.14 [95% CI 0.08-0.20]) respectively]. Interestingly, maternal pregnancy BMI accounted for the relationship between maternal hyperglycaemia and later offspring adiposity, which highlights the importance of a healthy pre-pregnancy BMI (Thaware et al., 2015).

In a study of 8,515 women from the ALSPAC cohort, associations between maternal glycaemic status and cognitive measures at School Entry Assessment results (SEA) (aged 4), IQ (aged 8), and GCSE results (aged 16) were examined. Inverse associations between adverse maternal glycaemic status and all cognitive measures were reported, however, all confidence intervals included the null value. This evidence suggests that educational outcomes were worst in offspring with mothers who had impaired glycaemic status during pregnancy, compared to those with normal glycaemic status. This may have implications for the future of the offspring, as educational attainment at GCSE level is linked with higher education and therefore employment prospects (Crawford et al., 2016) indicating that the transgenerational outcomes of glycaemic status may not be limited to damaging health (Fraser et al., 2012).

In agreement with this, a Mendelian randomisation study used genotype data from 3771 mothers and 5078 children from the ALSPAC cohort to establish whether glucose levels during pregnancy and in the offspring are associated with cognitive ability for the offspring. This study found that offspring whose mothers had diabetes and glycosuria had a lower IQ score than children born to mothers without diabetes and glycosuria (mean difference -3.5 [95% CI -5.6, -1.5]) when adjusted for confounders. However, in contrast, it was also found that the allele that increases risk of developing type 2 diabetes was associated with a higher IQ score (Bonilla et al., 2012). Although for this part of the analysis, the authors were not able to look at glycaemic status separately and so GDM, existing DM and glycosuria were all equated similarly.

A study of 5,038 ALSPAC mother-offspring pairs examined associations between impaired glycaemic status and cardiometabolic risk factors in offspring at 15.5 years old. Maternal glycosuria was found to be associated with offspring fasting insulin levels (mean difference 1.12 [95% OR 1.01, 1.24]), suggesting again that maternal glycosuria may be associated with future glycaemic health of the offspring (Patel et al., 2012).

Another study of the ALSPAC cohort examined associations of maternal pregnancy diabetes and glycosuria and pre-pregnancy BMI with offspring markers of non-alcoholic fatty liver disease (NAFLD). The study used ultrasound scan (USS) to determine fatty liver and shear velocity (a marker of fibrosis) and included 1,215 mother-offspring pairs with USS outcomes. Offspring whose mothers had pregnancy diabetes and glycosuria were more likely to have USS fatty liver (OR 6.72 [95% CI 1.89, 24.00]) and had higher

mean shear velocity (OR 1.08 [95% CI 1.04, 1.13]), adjustment for confounders and mediators (including pre-pregnancy BMI, offspring birthweight and later offspring adiposity) did not provide a marked change in the results. This evidence suggests that maternal diabetes and glycosuria during pregnancy may be associated with NAFLD, rather than maternal and offspring adiposity, in this cohort (Patel et al., 2016).

The evidence suggests that adverse maternal hyperglycaemia, even without an overt diagnosis of GDM, increases the risk for negative perinatal outcomes for both mother and offspring. Therefore, it is important to determine pregnant women who are at risk of or already experiencing hyperglycaemia. Using glycosuria testing as a marker of glycaemic status could help to identify the women at risk, and the 'teachable moment' found in pregnancy can be used as an opportunity for lifestyle counselling to prevent the adverse perinatal outcomes.

1.7.5 Gestational Diabetes Mellitus

The UK guidelines for diagnosing GDM is a fasting plasma glucose level of 5.6 mmol/l or above, or a 2-hour plasma glucose level of 7.8 mmol/l or above (National Institute for Health and Care Excellence, 2015b).

Findings from the Fifth International Workshop-Conference on Gestational Diabetes consider there to be two forms of GDM; a pregnancy-induced insulin resistance driven by hormonal changes and a chronic form of pre-existing insulin resistance (Metzger et al., 2007). Around 35,000 women have either pre-existing or gestational diabetes each year in England and Wales, around 80% of women with diabetes in pregnancy is related to GDM

and around 7.5% to pre-existing T2DM (National Institute for Health and Care Excellence, 2015a).

Prevalence of GDM has increased over the last 20 years and is expected to continue rising as rates of obesity also rise (Schoenaker et al., 2016). It is thought that women with existing increased insulin resistance or reduced insulin secretion prior to pregnancy are at a higher risk of T2DM later in life (Bao et al., 2015). In fact, it is estimated around 40% of women diagnosed with GDM will go on to develop T2DM within 10 years of their GDM pregnancy (Kaaja and Ronnemaa, 2008).

Reasons for the increase in GDM prevalence are difficult to define due to varying diagnostic criteria, various confounders, such as maternal age, pre-pregnancy BMI and ethnicity, and heterogeneity between studies or lack of data from different populations (Metzger et al., 2007)

1.7.5.1 Factors associated with gestational diabetes mellitus

Pregnancy and birth outcomes associated with GDM are well studied and there are several identified risk factors that influence the incidence of GDM. In order to reduce the prevalence, interventions should be based around identification of risk factors, as defined by NICE (section 1.7). However, the risk factors for GDM can be closely correlated with each other and therefore it is important to determine the impact of these separately.

GDM is linked with the socioeconomic status of the mother. A study of 191,097 women in Scotland found a decrease in the prevalence of GDM as maternal deprivation decreased ($p=0.011$) (Collier et al., 2016). In support of

this, GDM risk was two thirds higher for women living in lowest socioeconomic postcode compared with those in the highest area in an Australian, multi-ethnic, population-based study of 950,747 births (Anna et al., 2008). However, this study was limited by the lack of weight-related data collected from the participants and consequent lack of adjustment for maternal obesity.

Obesity and pre-pregnancy BMI >25 kg/m^2 are known risk factors for GDM (Gaillard et al., 2013). A study of 17,910 women found obese women were at a higher risk of GDM when compared to healthy weight women (OR 3.87 [95% CI 2.87, 5.22]) (Oteng-Ntim et al., 2013). This is supported by a meta-analysis of 70 studies, which reported that overweight women were more likely to develop GDM than healthy weight women (OR 1.97 [95% CI 1.77, 2.19]) and obese women had an odds ratio of 3.76 (95% CI 3.31, 4.28) compared to healthy weight women. It was also suggested that for each 1kg/m^2 increment in BMI, GDM prevalence increased by 0.92% (Torloni et al., 2009). However, there was a high level of heterogeneity in this systematic review due to differing assessments of BMI and GDM within the studies (Torloni et al., 2009).

Ethnicity is a strong risk factor for T2DM, UK data shows some ethnic minorities have a higher risk of a diabetes diagnosis than other populations (Office for National Statistics, 2012). A literature review by Yuen and Wong (2015) identified the prevalence of GDM as higher in Aboriginal, Middle Eastern, Pacific Island and South Asian women than other ethnicities and a higher BMI in these women can also play a role. Interestingly, a study of

17,910 women used adjusted population attributable fractions to examine the effects of maternal obesity on obstetric outcomes for different ethnic groups. There was a significant association of obesity and diabetes in all groups (p= 0.03), and the odds ratio were highest for the Oriental group (OR 6.62 [95% CI 2.43, 12.35]) and lowest for the Black group (OR 2.73 [95% CI 2.01, 3.69]) (Oteng-Ntim et al., 2013).

1.7.5.2 Dietary intakes and gestational diabetes

There is some evidence that dietary interventions are successful in managing GDM but there is inconsistent evidence as to whether dietary interventions can prevent gestational diabetes (Schoenaker et al., 2016). This may be due to heterogeneity between study design and the inability to draw cause and effect from observational trials.

A population-based cohort known as the Australian Longitudinal Study on Women's Health (ALSWH) collected dietary data from 3853 women, 292 of which had GDM, measured the effect of diet 12 months' pre-pregnancy on GDM. Exploratory factor analysis was used to determine four dietary patterns ('meats, snacks and sweets', 'Mediterranean style', 'fruit and low-fat dairy' and 'cooked vegetables') (Schoenaker et al., 2015). The Mediterranean style (MS) pattern was associated with higher GDM risk in obese women and those with a lower educational status. However, women eating this pattern were more likely to be obese, which is a risk factor for GDM- this suggests that BMI may be a mediator in the association between intake of MS pattern and GDM. The MS pattern was associated with a lower risk of GDM in all other weight groups of women but the mechanisms for this are unknown

(Schoenaker et al., 2015). It could be speculated that as the Mediterranean diet is thought to play a role in weight management (Buckland et al., 2008) that the low risk for GDM is modulated by a healthy weight.

Similarly, a prospective study of 168 pregnant women reported that a 'prudent' dietary pattern (with high loadings of vegetables, fruit, seafood, oils, nuts and seeds, cereals and pasta) was associated with a lower risk of GDM (OR 0.36 [95% CI 0.13, 0.75]). Importantly, GDM risk was still reduced in overweight and obese women, if they adhered to the 'prudent' dietary pattern. This suggests that a dietary pattern or quality similar to the 'Mediterranean diet' may be important in lowering GDM risk in pregnant women (Tryggvadottir et al., 2016).

Contrary to this, a study investigating the effect of diet during early pregnancy and GDM, collected data from 1733 women and found no evidence that diet quality or diet pattern was associated with increased risk of impaired glucose tolerance or GDM. There was also no evidence that total carbohydrate intake and carbohydrate quality were with increased risk of GDM (Radesky et al., 2007).

When examining macronutrient intake and risk of GDM, a prospective cohort of 205 participants reported that intake of percentage of energy from saturated fat ($p= 0.005$) and added sugar ($p= 0.02$) was found to be associated with increased fasting glucose levels. Diets with lower percentage of energy from carbohydrate and higher percentage energy from fat were associated with increased risk of GDM (Ley et al., 2011).

Similarly, a US prospective cohort of 1698 pregnant women, reported that increasing the carbohydrate intake and decreasing fat intake, as percentage of energy, reduced the risk of glucose intolerance and GDM in the participants (RR 1.1 [95% CI 1.02, 1.12] and RR 1.1 [95% CI 1.02, 1.10] respectively) (Saldana et al., 2004).

These findings were also echoed in a randomised controlled lifestyle intervention of 234 pregnant women reported that a high dietary intake of fat and saturated fat, combined with a low intake of carbohydrate increased the risk of GDM in high risk women (Meinilä et al., 2015).

1.7.6 Short term health implications of gestational diabetes

GDM can increase risks of adverse short and long-term outcomes for both the mother and child and untreated GDM holds greater risks of adverse pregnancy outcomes and T2DM for mother and child in later life (Law and Zhang, 2017).

1.7.6.1 Maternal health outcomes

There is an increased risk of development of T2DM for GDM mothers (Kaaja and Ronnemaa, 2008). A study using the prospective cohort NHS II found that maternal BMI, when measured within 2 years of the GDM diagnosis, was strongly associated with a greater risk of developing later life T2DM (Bao et al., 2015). It was also reported that weight gain after GDM was positively associated with the development of T2DM after pregnancy, suggesting that weight control is an important factor in the development of T2DM in those with a history of GDM. However, this study was based on self-reported body weight of mostly white, US women, so may not be representative of UK populations (Bao et al., 2015).

1.7.6.2 Offspring health outcomes

Macrosomia in the infant is associated with a number of adverse outcomes. A retrospective study of adverse neonatal outcomes in macrosomic and control groups (total 5738 women), reported that macrosomic infants born to diabetic mothers had significantly higher incidence of hypoglycaemia ($p<0.001$), hyperbilirubinemia ($p=0.04$) and cardiomyopathy ($p=0.01$) when compared to non-diabetic mothers (Gyurkovits et al., 2011). Macrosomia puts the infant at higher risk of shoulder dystocia, hypoxia and increases admissions to NICU (Chu et al., 2007). There is also an increased risk of later life metabolic syndrome, T2DM, CVD, obesity and some childhood cancers (Kaaja and Ronnemaa, 2008; Gyurkovits et al., 2011). Macrosomia also increases risk of perineal tears, post-partum haemorrhage and higher

occurrence of caesarean section for the mother (Chu et al., 2007; Gyurkovits et al., 2011)

Factors influencing foetal growth such as GDM increase risk of childhood cancers which are associated with increased birth weight (Contreras et al., 2016). In a study of 11,149 childhood cancer cases, it was identified that pre-pregnancy diabetes increased risk of all leukaemia (OR 1.23 [95% CI 1.01,1.49]) and of Wilm's tumour (OR 1.45 [95% CI 0.97, 2.18]). There was also an increased risk in all leukaemia for infants born to mother who had an overweight pre-pregnancy BMI (OR 1.27 [95% CI 1.01,1.59]), however these results may be underpowered due to the small sample size for GDM and pre-pregnancy BMI group (Contreras et al., 2016).

Neonatal hypoglycaemia is common in infants born to mothers with diabetes, particularly if the diabetes has not been well controlled throughout the pregnancy. Neonatal hypoglycaemia is caused by foetal hyperinsulinaemia as a result of maternal hyperglycaemia and if severe, can result in neurological damage to the offspring (Flore-le Roux et al., 2012).

1.7.7 Long term implications of gestational diabetes

Some evidence suggests that GDM during pregnancy could contribute to the current childhood obesity epidemic (Kim et al., 2012). However, a retrospective longitudinal cohort study of 15710 mother-offspring pairs, measuring children's overweight status, found that GDM was not associated with childhood overweight (OR 0.89 [CI 95% 0.77, 1.03]), although this may not be relevant for the association between GDM and later life obesity due to

measurements taken at only 2 years old (Bider-Canfield et al., 2017). Conversely, a systematic review by Chu et al. (2007) found that offspring of GDM women are more likely to be overweight or obese and develop T2DM in later life, although the mechanism is not fully understood, it was suggested that this could be due to decreased insulin sensitivity and foetal overgrowth *in utero*. This is supported by a review of studies which concluded that a positive association between GDM and offspring adiposity exists, even after adjustment for pre-pregnancy BMI (Kim et al., 2012) .

A meta-analysis of 12 studies and 6,140 infants measuring cognitive impairments in offspring born to mothers with diabetes during pregnancy found a significant reduction in IQ at 3-12 years old (95% CI -1.42, -0.13). Mental and psychomotor development was measured at 1-2 years and offspring of maternal diabetes was found to have an effect of 0.41 lower than the offspring of non-diabetic mothers (95% CI -0.59, -0.24). However, the meta-analysis was conducted from observational studies so cause and effect cannot be established (Robles et al., 2015). A study of the ALSPAC cohort found impaired maternal glycaemic status was associated with lower IQ and educational attainment in offspring. This raises question for the future of the child as could result in impaired later life quality due to future employment, income and socioeconomic status (Fraser et al., 2012).

1.8 Conclusion

Pregnancy is a complex time in which a woman will experience many physiological and hormonal adaptations. There are numerous factors associated with the incidence and prevalence of pregnancy related characteristics such as glycaemic status, GWG and maternal obesity. The consequences of these characteristics can impact the short and long-term health of the mother and the child and increase the need for additional medical intervention. If rates of obesity and comorbid conditions continue to rise there may be implications for the future burden on healthcare systems.

There is a need for more timely and in-depth intervention in early pregnancy, to allow pregnant women to feel empowered to take control of their health and decrease the risks of the adverse pregnancy outcomes.

General ‘healthy diet’ advice may not provide enough information for women in the UK. Defining GWG goals and staging interventions to increase the dietary quality of the general population may lead to better health outcomes in birth and pregnancy.

There is a clear need to better understand the implications of dietary intake in pregnant women in events such as GDM and GWG, using reproducible methods to allow comparison of results between studies. This thesis seeks to determine if there are any associations between macronutrient intake and dietary patterns and glycaemic status and GWG, using a large pregnancy cohort from the 1990’s.

Part I

Chapter 2 Methodology

2.1 Introduction

As presented in the previous chapter, nutritional status during pregnancy plays an important role in the health of the mother and future health of the offspring. This thesis sought to determine any associations between nutrient intake and dietary patterns during pregnancy and health characteristics of the mother, such as GDM and GWG. The research was carried out in two closely related sections; a systematic review and data analysis of pre-collected data from a longitudinal cohort.

2.2 Systematic review research question

A specific research question was framed from the current literature on dietary intake and GWG: 'The association of free sugar intake and gestational weight gain'. Initially a free form question of interest was developed and then searched within PROSPERO protocol library to avoid duplication of reviews (National Institute for Health Research, no date). The free form question was defined into a structured question using a PICOS table (populations, intervention/exposure, comparator/control, outcome, study design) (see table 2.1) (Moher et al., 2015).

Table 2.1 PICOS table supporting research question

PICOS	Selection Criteria
Population	Pregnant women, >18 years old, singleton gestations, term (>37 weeks) pregnancies
Intervention/exposure	Carbohydrate Intake Sugar Intake
Comparison	Low Carbohydrate Low Sugar Not applicable for cohort and case-control studies
Outcome	Gestational Weight Gain (all measurements of)
Study Design	Human studies only including RCT, intervention, observational.

2.3 Protocol

In accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011) and PRISMA guidelines, a protocol was developed and published in the PROSPERO protocol library (National Institute for Health Research, no date). The protocol established the methods to be used prior to beginning the review. Publishing protocols for systematic reviews minimises author's bias, allows for transparent methodology and allows the author to avoid duplication of the review question (Higgins and Green, 2011).

2.4 Search strategy

The search strategy was created prior to the search being carried out. Search terms were compiled from relevant literature and Medline was checked for Medical Subject Headings (MeSH) terms as shown in table 2.2. As the research question could not be considered medically typical there were few MeSH terms, so free text terms were derived from the current literature to use in the search.

The literature searches were carried out using the 'title, abstract and keywords' field in PubMed Central, Scopus, Web of Science and Science Direct; chosen based on likely content as advised by the 'Food and Nutrition' subject guide from Manchester Metropolitan University library (Manchester Metropolitan University, 2017). To avoid bias and to capture all the relevant studies, no language or publication date restrictions were used in the final search strategy.

Using Boolean operators, the final terms were "sugar OR carbohydrate OR sucrose OR "non-milk extrinsic sugars" AND "gestational weight gain" OR "maternal weight gain" OR "pregnancy weight gain" OR "maternal obesity" OR "maternal overweight"; carried out on 9th February 2017. Each search was saved in each database and exported into a Microsoft Excel spreadsheet.

Table 2.1.2 MeSH terms derived from Medline search

Free text term searched	MesH terms given
Pregnant	gravidity, gravid, maternal
Sugar	carbohydrate, dietary sucrose, dietary sugar, high fructose corn syrup
Non-extrinsic milk sugars	no terms found
Gestational weight gain	no terms found
Weight gain	body weight
Maternal	maternal nutrition, maternal health

2.5 Screening process

The initial search provided 480 citations for screening, as shown in figure 2.1.

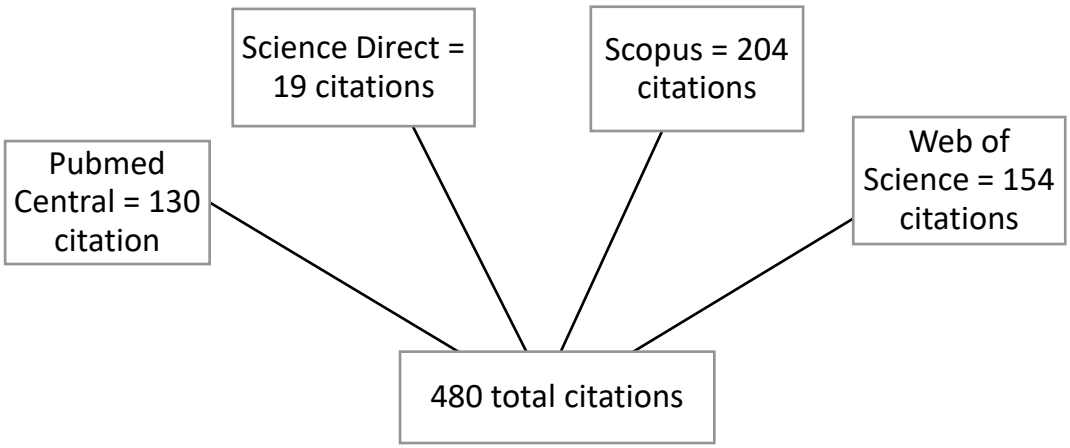

Figure 2.2.1 Breakdown of initial search results in each database

In line with the protocol, citation screening was conducted in four stages; de-duplication, initial screening, full text screening and data extraction (see figure 3.1).

In order to yield an effective and consistent collection of studies, the first stage of the screening process of a systematic review is de-duplication of the citations (Kwon et al., 2015). Therefore, the duplicate citations were removed manually by importing all citations into an Excel spreadsheet and ordering alphabetically. Citations were deemed as duplicates if they shared the same author, title, publication date and study population. The abstracts were consulted if there was any doubt in duplications. Two hundred and twenty duplicate citations were removed and saved in a ‘duplicates’ tab of the Excel database for future reference.

Once de-duplicated the remaining 260 citations were independently screened by title and abstract by two independent reviewers. The titles were screened against the PICOS criteria as defined in the protocol (see table 2.1). Both excluded and included citations were saved separately in the Excel database and the reason for exclusion or inclusion were recorded by each reviewer. As the outcome of interest was GWG in humans, all animal studies were excluded at this stage of screening.

Both independently reviewed databases were then compared to find any disagreements in excluded or included titles. The reviewers met with a third independent reviewer to discuss a disagreement of 11 citations, during this stage the independent reviewer decided to include all 11 citations and a total of 42 citation were agreed and included in the next stage of the systematic review.

Seven relevant systematic reviews, reviewing similar topics to the current review, were identified in the initial search. The reference lists of these systematic reviews were hand-searched for citations which matched the PICOS criteria. Ninety-four citations were identified and after de-duplication, 60 citations remained. These were screened by the same two independent reviewers in the same manner as the initial search, and the reviewers agreed on 31 articles for inclusion (see figure 2.2).

Figure 2.2 Citations included from hand-searched reference lists of relevant systematic reviews

In total, 320 citations were screened and 247 were excluded and the reasons for this were recorded (see figure 3.1). Seventy-three citations were included in the final data extraction process.

2.6 Data extraction

A data extraction form was created (see appendix B) by modifying the data extraction and quality assessment template provided by the Cochrane Public Health Group (Cochrane Public Health, 2016). The extraction form was designed to extract data on the following areas:

- Study characteristics
- Population characteristics

- Participant demographics
- Method of dietary assessment
- Method of GWG assessment and categorisation
- Covariates
- Sensitivity analyses and data analysis
- Association estimates (crude and adjusted)
- Results/findings
- Main conclusions

Of the final 73 papers included in the data extraction, the data were extracted by the principal reviewer and a random sample of 20% were checked for accuracy by the co-reviewer according to the guidelines from the Cochrane Handbook (Higgins and Green, 2011). Forty-seven papers had reported recording dietary intake during pregnancy, but not specified the intake of free sugars. The authors of these papers were written to via email to determine whether they had measured intake of free sugar. A system was developed in which the author was contacted initially and given a two week reply deadline, after this a reminder email was sent with another two-week deadline, and finally a third reminder was sent with a one-week deadline. If there was no response after the third email, it was assumed there was no free sugar measure and the paper was excluded.

Following the data extraction of the 73 full texts, 4 papers were included in the final analysis of the systematic review. Sixty-nine texts were excluded, and the reasons were recorded in an Excel database (see figure 3.1).

2.7 Risk of bias and quality assessment

Risk of bias within the included studies was assessed using assessment tools developed by the Cochrane Bias Methods Group; the RoB 2.0 tool, ROBINS-I assessment Risk of Bias in Non-randomised Studies of Interventions: version 19 and the Cochrane Tool to Assess Risk of Bias in Cohort Studies (Sterne et al., 2016). Rather than using a point scoring system, the tools used a system of scoring the studies as 'low, medium or high' risk in the following areas (Cochrane Methods Bias, 2017):

- Selection bias
- Performance bias
- Detection bias
- Attrition bias
- Reporting bias
- Any other sources of bias

Risk of bias was completed by one reviewer for each study, all completed assessments were doublechecked by the second independent reviewer for accuracy. Any discrepancies were discussed and amended.

Quality of study design was assessed using the NICE Quality appraisal checklist. This checklist was chosen for the quality assessment due to its appropriateness for use for randomised controlled trials, case-control studies, cohort studies, controlled-before -and-after studies and interrupted time series (National Institute for Health and Care Excellence, 2012). The checklist addresses the following characteristics of study design:

- Characteristics of participants

- Definition and allocation to intervention and control groups
- Outcomes assessed over different time periods
- Analytical methods

The checklist assesses both internal and external validity, awarding an overall study quality grade for each (National Institute for Health and Care Excellence, 2012).

2.8 Narrative Synthesis

The study results included data from a range of different study designs and due to the heterogeneity in exposure and outcomes measurement methods, a meta-analysis could not be applied. Therefore, narrative synthesis was used to report the results in the systematic review using Cochrane guidance for data synthesis and analysis (Ryan, 2013).

Chapter 3 Results

3.1 Study inclusion

A meta-analysis could not be performed due to the variability in the methods used to calculate GWG and to measure free sugar intake, so a narrative synthesis was undertaken.

Of the 73 articles screened for full data extraction; 30 were excluded as sugar intake was not recorded or reported; 6 papers included participants who were <18 years; 10 did not meet PICOS requirements for study design (table 2.1); 14 authors did not respond to enquiries for data and further information and 5 authors were uncontactable (see figure 3.1).

Eight studies were identified as having measured free sugar intake but only two of those had directly examined the association between free sugar intake and GWG (Maslova et al., 2015: Renault et al., 2015). Six authors were contacted with a request for further data. Of those authors contacted; 2 responded with further data allowing inclusion in the systematic review (Kinnunen et al., 2007; Wolff et al., 2008), 1 author did not respond (Althuizen et al., 2009), 2 authors did not feel they could send the data out within the 6-week deadline (Latva-Pukkila et al., 2010; Luoto et al., 2011), 2 authors felt their data did not match the PICOS criteria (Petrella et al., 2014; Morisset et al., 2014) and one author could not access the data required to run the further analyses (Chortatos et al., 2013) (see figure 3.2).

Finally, four studies were included in the narrative synthesis (Kinnunen et al., 2007; Wolff et al., 2008; Maslova et al., 2015; Renault et al., 2015).

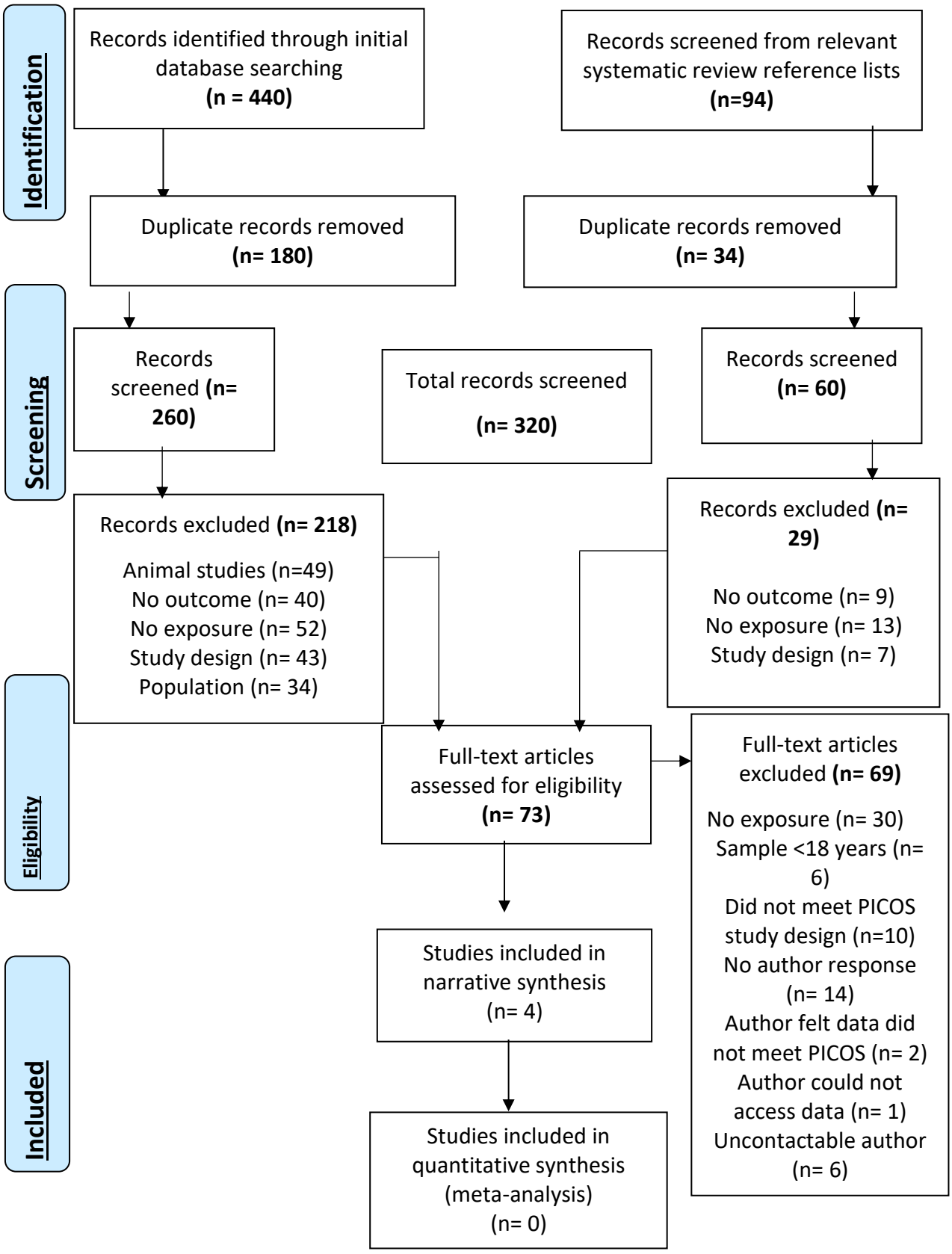

Figure 3.1 Flow diagram of systematic review search results adapted from PRISMA (Moher et al., 2009)

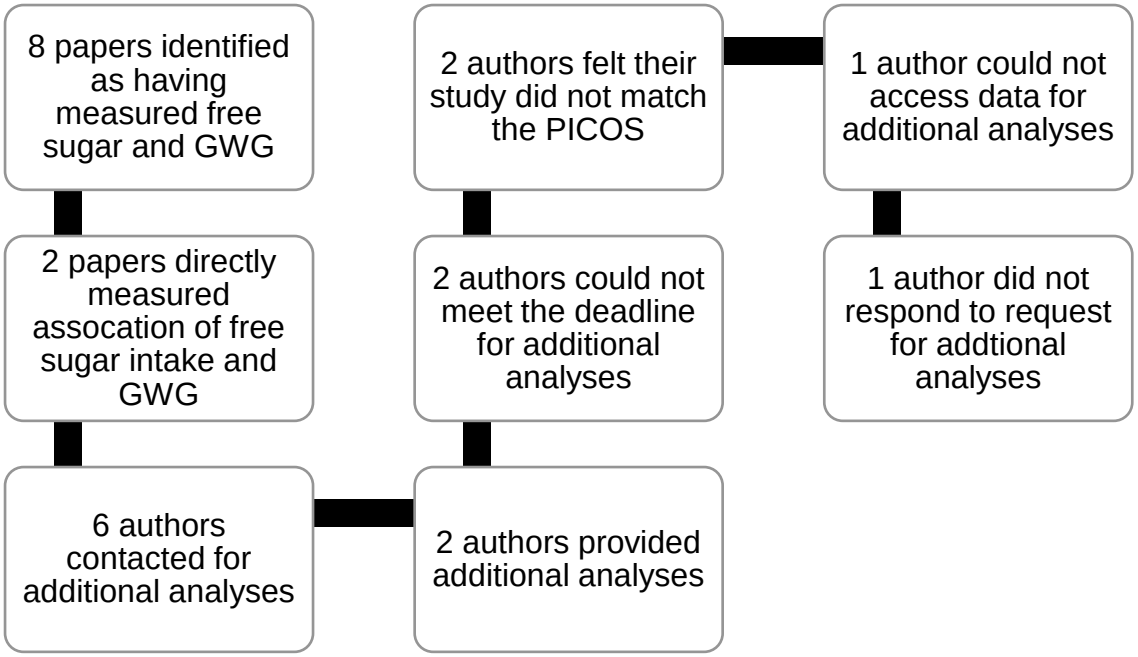

Figure 3.2 Outcome of additional data requests sent to study authors

3.2 Study characteristics

Table 3.1 reports the characteristics of the four included studies. Sample size ranged from 50 to 46,262 participants across the studies. Two studies were randomised controlled trials (Wolff et al., 2008; Renault et al., 2015), one a parallel controlled trial (Kinnunen et al., 2007) and one a prospective cohort study (Maslova et al., 2015). Three studies were based in Denmark (Wolff et al., 2008; Maslova et al., 2015; Renault et al., 2015) and one in Finland (Kinnunen et al., 2007).

The methods used to evaluate of exposure and outcome differed in each study (see table 3.1). Maslova et al. (Maslova et al., 2015) measured added

sugar intake from 300-item food frequency questionnaire (FFQ) sent at 25 weeks gestation and reported mean g/day and percentage of energy intake.

Renault et al.(Renault et al., 2015) measured free sugar intake using a 300-item FFQ at baseline (11-14 weeks) and endpoint (36-37 weeks). Intakes were reported as percentage of energy intake for total added sugar, added sugar from food and added sugar from drinks. Wolff et al. (Wolff et al., 2008) measured free sugar intake at 27 weeks (g/day) from 7 day weighed food records. Free sugar intake was measured as mean intake of saccharose (g/day) at baseline (8.3 weeks gestation) and follow up visit (36.6 weeks gestation) from 3-day food records by Kinnunen et al. (2007).

Maslova et al. (2015) calculated GWG using self-reported measurements of weight, at week 12 and week 30 of the pregnancy to determine the rate of GWG (g/week). Renault et al. (2015) calculated GWG as the difference between the self-reported pre-pregnancy weight and weight measured at endpoint (36-37 weeks gestation) and assessed by the IOM adequacy of weight gain recommendations. Total GWG was calculated as the difference between self-reported pre-pregnancy weight and last measured weight before delivery (36 weeks) by Wolff et al. (2008). Rate of GWG was calculated using the difference between weight at inclusion and at 36 weeks, divided by the number of weeks form inclusion to endpoint. Kinnunen et al. (2007) calculated GWG (g/week) based on measured weight at the first visit (mean 8.3 weeks gestation) and the last visit during pregnancy (mean 38.3 weeks gestation).

Table 3.1 Table of characteristics and results from included studies

<table>
<tr><th>Study Details</th><th>Population and Setting</th><th>Methods and Study Quality</th><th>Study Findings</th></tr>
<tr>
<td>Author: Maslova et al.

Year: 2015

Study duration: 1996-2002

Country: Denmark

Study Design:
Prospective cohort.

Aim of Study: To examine the relationship between protein: carbohydrate ratio (higher protein and lower carbohydrate is postulated as potentially limiting excessive GWG) and added sugar intake in pregnancy and gestational weight gain.</td>
<td>Number of participants: 46,262

Mean age (years):
Quintiles of P/C ratio. Mean (SD):
Q1: 29.8 (4.2)
Q2: 30.2(4.1)
Q3: 30.4 (4.1)
Q4: 30.5 (4.2)
Q5: 30.6 (4.3)

Mean pre-pregnancy BMI (kg/m^2):
<table><tr><td>BMI</td><td>Q1 (%)</td><td>Q2 (%)</td><td>Q3 (%)</td><td>Q4 (%)</td><td>Q5 (%)</td></tr><tr><td>≥18</td><td>5</td><td>5</td><td>4</td><td>4</td><td>4</td></tr><tr><td>18.6 – 24.9</td><td>70</td><td>70</td><td>70</td><td>69</td><td>64</td></tr><tr><td>25 – 29.9</td><td>18</td><td>18</td><td>19</td><td>20</td><td>22</td></tr><tr><td>≥ 30</td><td>7</td><td>7</td><td>7</td><td>8</td><td>10</td></tr></table>
Energy intake:
Energy intake (Kcal/day). Mean (SD)
Q1: 2373 (658)
Q2: 2427 (622)
Q3: 2425 (621)</td>
<td>Data collection methods:
Danish National Birth Cohort database, collected data through 2 self-administered questionnaires, 4 computer assisted telephone interviews, 3 blood samples. Maternal health and birth records extracted through registry linkages.

Primary outcomes:
Intake of protein: carbohydrate ratio, protein intake and added sugar intake during 25th gestational week in relation to GWG.
Secondary outcomes: important of source of protein and GWG.</td>
<td>Main findings: Participants in highest quintile of added sugar intake (89±26 g/day) had higher rate of GWG when compared with lowest quintile (19±5 g/day; 34g/week; CI 95% 28-40). The results suggest pregnant women consuming a higher added sugar intake (89±26 vs 19±5 g/day) would have a higher weight gain of 1.4kg (95% CI 1.1 – 1.6).

Strengths: Large study population, detailed dietary assessment and extensive data on covariates.

Limitations:
Observational study, diet was assessed at 25 weeks only, use of self-reported</td>
</tr>
</table>

<table>
<tr>
<td>Funding: Danish Research Councils</td>
<td>Q4: 2410 (621)
Q5: 2366 (661)

Parity:
Primiparas (percent)
Q1: 56
Q2: 53
Q3: 53
Q4: 52
Q5: 51

Socioeconomic status:
Measured by vocation:
<table>
<tr><th></th><th>Q1 (%)</th><th>Q2 (%)</th><th>Q3 (%)</th><th>Q4 (%)</th><th>Q5 (%)</th></tr>
<tr><td>High Level skills</td><td>23</td><td>24</td><td>24</td><td>24</td><td>22</td></tr>
<tr><td>Medium skills</td><td>31</td><td>33</td><td>33</td><td>32</td><td>30</td></tr>
<tr><td>Skilled</td><td>27</td><td>27</td><td>27</td><td>28</td><td>29</td></tr>
<tr><td>Student</td><td>7</td><td>6</td><td>5</td><td>5</td><td>5</td></tr>
<tr><td>Unskilled</td><td>11</td><td>9</td><td>10</td><td>10</td><td>12</td></tr>
<tr><td>Unemployed</td><td>2</td><td>1</td><td>1</td><td>1</td><td>2</td></tr>
</table>
</td>
<td>Exposure measurement method: Collected at 25 weeks gestation using a 300-item, validated FFQ for intake over the previous 4 weeks.

Outcome measurement method: Rate of GWG in g per week, using self-reported measurements from week 12 to week 30.

Data analysis: Dietary variables divided into quintiles of intake of protein: carbohydrate ratio to account for non-linearity. Univariable a multivariable linear regression used to examine association between dietary intake and GWG.

Adjustment: Adjusted for socioeconomic status, maternal parity, maternal</td>
<td>dietary data and weight measurements.</td>
</tr>
</table>

		pre-pregnancy BMI, maternal height, maternal smoking civil status and total energy intake. **Risk of Bias:** Scored low risk for four areas and high risk for three areas. Weighted as an overall medium risk of bias. **NICE quality appraisal:** Scored low for external validity and low for internal validity. Overall low-quality assessment score.	
Study Details	**Population and Setting**	**Methods and Study Quality**	**Study Findings**
Author: Renault et al. **Year:** 2015 **Study Duration:** 2009-2011 **Country:** Denmark	**Number of participants:** 342 **Mean age (years):** Control: 31.4 (4.2) PA: 31.3(4.7) PA+D: 31.5 (4.0) **Mean pre-pregnancy BMI (kg/m^2):**	**Data collection methods:** Randomisation of participants to 1:1:1 to either diet and physical activity (PA+D), physical activity intervention alone (PA) or control (C).	**Main findings:** The association between baseline intake of total added sugar was not significantly associated with GWG (p for trend 0.82). Intake of added sugar from foods was

Study Design: Randomised controlled trial **Aim of study:** Evaluate improvements and relevance of different lifestyle and dietary factors targeted with respect to gestational weight gain in a 3-arm Randomised Controlled Trial among obese pregnant women with BMI≥30 **Funding:** The Danish Council for Strategic Research	Control: 33.4 (3.3) PA: 33.8 (4.0) PA+D: 34.1 (4.0) **Energy intake (MJ/day):** Control: 8.1 (3.5) PA: 7.9 (2.6) PA+D: 8.0 (2.1) **Parity:** Primiparas (percent) Control: 46% PA: 43% PA+D: 43% **Socioeconomic Status:** Not reported	Dietary intervention of hypocaloric Mediterranean style diet (5000-7000 kJ per day) and physical activity (daily step count of 11,000). Diet assessed at baseline and endpoint. **Primary Outcomes:** Gestational weight gain at the end of pregnancy. Dietary changes during pregnancy due to the intervention compared to the control group. **Exposure measurement method:** Collected at baseline (11-14 weeks) and endpoint (36-37 weeks) using a 300-item FFQ, recording dietary intake over the previous 4 weeks. **Outcome measurement method:** Calculated as	positively associated with GWG (p for trend= 0.02). The observed difference was 2.8kg (95% CI 0.8, 4.8) when comparing women with highest to lowest quartile of intake at baseline. Intake of added sugar from soft drinks showed an inverse non-significant trend (p for trend= 0.13) **Strengths:** Randomisation was retained despite small size compared to full trial. High rate of completion (81%). Use of validated FFQ at two-time points in pregnancy to examine intakes. **Limitations:** Use of self-reported dietary data in an obese population as this group is considered to underreport intakes. Added sugar intake is difficult to quantify as

		difference between self-reported pre-pregnancy weight and weight measured at endpoint (36-37 weeks). **Data analysis:** T-test for differences between groups, Wilcoxon rank sum test for differences between groups of skewed variables. Linear regression was used to examine association between nutrients and GWG. **Adjustment:** Adjusted for total energy intake, maternal age, parity, smoking during pregnancy, pre-pregnancy BMI and intervention group. **Risk of Bias:** Scored as low risk on three of six areas, medium risk on three of six areas.	amount added to comparable foods may differ. Observational setting means role of maternal covariates cannot be excluded.

		Weighted overall as low/medium risk of bias with some concerns. **NICE quality assessment:** Scored medium for external validity and low/medium for internal validity. Overall low/medium quality score.	
Study Details	**Population and Setting**	**Methods and Study Quality**	**Study Findings**
Author: Kinnunen et al. **Year:** 2007 **Study Duration:** 2004-2005 **Country:** Finland **Study Design:** Controlled trial. **Aim of study:** To investigate whether	**Number of participants:** 105 **Mean age (years):** Intervention: 27.6 (4.5) Control: 28.8 (4.1) **Mean pre-pregnancy BMI (kg/m^2):** Intervention: 23.7 (3.9) Control: 22.3 (2.1) **Energy intake:** Not reported **Parity:** All primipara	**Data collection methods:** Three maternity clinics in intervention and three in control. Intervention of dietary counselling, physical activity and a control of standard public health care. **Primary Outcomes:** Gestational weight gain at the end of pregnancy. Meal pattern, overall	**Main findings:** Intake of saccharose was not significantly associated with GWG (p=0.792). **Strengths:** High participation rate (88%). One of few studies providing intervention with the aim of reduction excessive GWG. Controlled trial.

<table>
<tr>
<td>individual counselling on diet and physical activity and information on gestational weight gain recommendations during pregnancy can have positive effects on the diet and total leisure time physical activity and reduce the proportion of primiparas exceeding the IOM recommended level of GWG (pilot study).

Funding: Doctoral Programs in Public Health, National Institutes of Health in the US, Ministry of Education, Ministry of Social Affairs and Health in Finland.</td>
<td>Socioeconomic Status:
Education Level n (%)
<table>
<tr><td>Basic or secondary education</td><td>27 (57)</td><td>20 (36)</td></tr>
<tr><td>Polytechnic education</td><td>9 (19)</td><td>12 (21)</td></tr>
<tr><td>University education</td><td>11 (23)</td><td>24 (43)</td></tr>
</table>
</td>
<td>vegetables intake, use of high-fibre bread, intake of high-sugar snacks and total energy intake. Total METmin/week as outcome for physical activity.

Exposure measurement method: 57-item FFQ for the previous month, at baseline (8-9 weeks) mid-pregnancy (22-24 weeks) and endpoint (37th week)

Outcome measurement method: Weight measured at each maternity clinic visit (8-9 weeks, 16-18, 22-24, 34-34 and 36-37 weeks), total of 5 measurements. Pre-pregnancy weight was self-reported.

Data analysis: ANCOVA for differences in weight by gestational week,</td>
<td>Limitations: Lack of randomisation. Pilot study for larger study, so small sample size. Control clinics recommended 2-3kg less WG than the intervention (IOM) so may have lowered GWG in control group. Self-reported pre-pregnancy weight and dietary intake.</td>
</tr>
</table>

		changes in dietary outcomes, changes in METmin/week from baseline to endpoint. Total GWG compared using 2-sided independent t-test. Differences in proportions of adequacy of WG tested using 2-sided x^2 test. Excessive gestational weight gain analysed with logistic regression. **Adjustment:** Adjusted for total energy intake, socioeconomic status, maternal age, parity and maternal pre-pregnancy BMI. **Risk of Bias:** Scored low risk on five areas, medium risk on one area and high risk on another area. Weighted overall as a medium risk of bias.	

		NICE quality appraisal: Scored high for external validity and low/medium for internal validity. Overall medium quality score.	
Study Details	**Population and Setting**	**Methods and Study Quality**	**Study Findings**
Author: Wolff et al. **Year:** 2008 **Study duration:** Not reported **Country:** Denmark **Study Design:** Randomised controlled trial	**Number of participants:** 50 **Mean age (years):** Intervention: 28±4 Control: 30±5 **Mean pre-pregnancy BMI (kg/m^2):** Intervention: 34.9±4 Control: 34.6±3 **Energy intake (kJ/day):** Intervention: 7319 ±1817 (at 27 weeks) Control: 9867±2057 (at 27 weeks)	**Data collection methods:** Eligible participants recruited in early pregnancy from register of newly diagnosed pregnancies. Randomised into intervention or control. Intervention designed to limit GWG using dietary advice and restricted energy intake.	**Main findings:** Sugar intake at 27 weeks significantly predicted total GWG (β= 0.079, p= 0.002) as did assignment to intervention or control group (β= -6.948, p= 0.003). **Strengths:** Randomised design. Intensive monitored weight development and

Aim of Study: To investigate whether restriction of gestational weight gain in obese women can be achieved by dietary counselling and whether this restriction could reduce the pregnancy-induced increases in insulin, leptin and glucose. **Funding:** Desiree and Niels Yde Foundation and Pharma Vinci, Denmark Vitamins.	**Parity:** Not reported **Socioeconomic status:** Not reported	**Primary outcomes:** Gestational weight gain in relation to energy and macronutrient intake. Levels of s-leptin and s-insulin and fasting glucose concentrations. Effect of intervention on infant and birth outcomes. **Exposure measurement method:** Dietary intake measured at 3-time points (inclusion, 27 weeks and 36 weeks) using 7-day weighed food record for one week. **Outcome measurement method:** Weight measured at 3-time points (inclusion, 27 and 36 weeks). Total GWG calculated using difference between self-reported pre-pregnancy weight and weight at 36 weeks. Rate of weight	measured insulin, leptin and glucose. **Limitations:** extra USS and blood samples may have increased dropout numbers, favouring recruitment of more motivated participants. The control group knew they were participating in a study limiting GWG. Small sample size.

		gain calculated using difference between actual weight at inclusion and 36 weeks, divided by number of weeks from inclusion to 36 weeks. **Data analysis:** Simple student's t test for differences between intervention and control. Linear regression was used to analyse association between free sugar intake and GWG. **Adjustment:** Controlled for energy intake, maternal age and maternal parity. **Risk of Bias:** Scored low risk of bias on five areas and medium risk on one area. Weighted overall as low risk of bias. **NICE quality appraisal:** Scored medium for	

		external validity and low/medium for internal validity. Overall medium quality score.	

3.2.1 Free sugar intake

Maslova et al. (2015) reported quintile 1 of protein: carbohydrate (P:C) ratio had a mean intake of 11% total energy from added sugar and 25% energy from total sugars, compared with quintile 5 in which the mean intake was 6% from added sugar and 19% from total sugars (see table 3.2).

Renault et al. (2015) reported that when compared with control, there was a mean difference in percentage of energy from added sugar of 0.1 (95% CI -1.2, 1.5) in the PA group and -1.3 (95% CI -2.6, -0.0) in the PA+D group. A similar mean difference was seen in the percentage of energy from added sugar in food with 0.6 (95% CI -0.3, 1.5) difference in the PA group and -0.8 (95% CI -1.7, 0.1) in the PA+D group. However, when assessing the percentage energy of added sugar from sugar sweetened beverages (SSB); compared with the control, there was a mean difference of -0.4 (95% CI -1.5, 0.6) and -0.5 (95% CI -1.5, 0.4) in the PA and the PA and diet groups respectively (see table 3.3).

Wolff et al. (2008) reported a significantly decreased mean intake of sugar when comparing the intervention (28.0 g/day) with the control group (64.9 g/day) at 27 weeks gestation (p= 0.000) (see table 3.4).

Kinnunen et al. (2007) reported a mean intake of saccharose of 30.94 g/day, in tertile 1 compared with tertile 3 who had mean intake of 63.57 g/day (see table 3.5).

Table 3.2 Sugar intake across quintiles of protein: carbohydrate ratio in mid-pregnancy (Maslova et al., 2015)

Added sugar intake for n= 46,262 participants					
Quintiles	**1**	**2**	**3**	**4**	**5**
Total sugar [c]	25 (7)	21 (6)	20 (5)	19 (5)	19 (5)
Added sugar [c]	11 (6)	9 (4)	8 (4)	7 (3)	6 (3)

[c] Percentage of total energy intake reported as mean (SD)

Table 3.3 Change between baseline and endpoint total added sugar, added sugar from foods and drinks as percentage of energy intake (Renault et al., 2015)

CHANGES BETWEEN BASELINE AND ENDPOINT % OF ENERGY INTAKE			
	Control	**PA**	**PA+D**
Added sugar [a]:	Reference	0.1 (-1.2, 1.5)	-1.3 (-2.6, -0.0)
From Food [a]:	Reference	0.6 (-0.3, 1.5)	-0.8 (-1.7, 0.1)
From Soft Drinks [a]:	Reference	-0.4 (-1.5, 0.6)	-0.5 (-1.5, 0.4)

[a]% energy intake mean difference (95% CI)

Table 3.4 Mean sugar intake in intervention and control at 27 weeks gestation (Wolff et al., 2008)

	Intervention (n= 30)	**Control (n= 30)**	**P value**
Mean intake of sugar (g/day)	28.0 (17.8)	64.9 (41.2)	0.000

Reported as mean (SD)

Table 3.5 Mean intake of saccharose per tertile (g/day) (Kinnunen et al., 2007)

	Tertile 1 (n= 34)	Tertile 2 (n= 35)	Tertile 3 (n= 34)
Absolute saccharose intake per tertile (g/day)	30.94 (6.61)	46.32 (4.26)	63.57 (6.95)

Reported as mean (SD)

3.2.2 Gestational weight gain

Maslova et al. (2015) reported that the those in quintile 5 (highest P:C ratio) had 458 g per week compared with quintile 1 (lowest P:C ratio) who had a mean of 482 g/week (see table 3.6).

Renault et al. (2015) reported an overall mean GWG for the total population of 10 kg. Twenty one percent of women gained below the recommended, 26% gained within the recommended and 53% gained above the recommended amounts according to IOM (see table 3.7).

Wolff et al. (2008) found the mean GWG for intervention and control group was 6.5 kg and 8.9 kg respectively (p= 0.215). When categorising the participants by their weight gain according to the IOM; 29.6% of the intervention group gain excessive weight, compared with 40.6% of the control group (table 3.8).

Kinnunen et al. (2007) reported total weight gain was 14.6kg in the intervention group and 14.3kg for control group (p=0.77). The odds ratio for excessive weight gain was 1.82 (0.65-5.14) when compared with the control group (p=0.26) (see table 3.9).

Table 3.6 Gestational weight gain in grams per week across quintiles of the protein:carbohydrate ratio in mid-pregnancy (Maslova et al., 2015)

Gestational weight gain (g/week) across quintiles of the protein: carbohydrate ratio in mid-pregnancy, n= 46, 262				
Q1	**Q2**	**Q3**	**Q4**	**Q5**
482 (226)	477 (215)	471 (217)	467 (223)	458 (239)

Table 3.7 Adequacy (IOM) and total gestational weight gain (Renault et al., 2015)

GWG (n= 342)		Physical activity intervention[a]	Physical activity + diet intervention[a]
IOM categories (%)			
Inadequate	21	1.24 (0.73, 2.09)	1.33 (0.80, 2.21)
Adequate	26	Reference	Reference
Excessive	53	0.86 (0.68, 1.08)	0.73 (0.57, 094)
Mean GWG (kg)	10		

[a] Relative risk (95% CI)

Table 3.8 Total gestational weight gain in obese control and intervention groups (Wolff et al., 2008)

	Intervention n= 26	Control n= 30	P value
Total GWG (kg) Mean (SD)	6.5 (6.4)	8.9 (7.7)	0.215
IOM categories, n (%)			
Inadequate	10 (37.0)	8 (25.0)	
Adequate	9 (33.3)	11 (34.4)	
Excessive	8 (29.6)	13 (40.6)	

Table 3.9 Gestational weight gain in control and intervention groups categorised by IOM recommendations (Kinnunen et al., 2007)

	Intervention group (n= 48)	Control group (n= 56)	P value
Total GWG (kg)	14.6 (5.4)	14.3 (4.1)	0.77
IOM categories n (%)			
Inadequate gain	16 (33)	15 (27)	
Adequate gain	10 (21)	24 (43)	
Excessive gain	22 (46)	17 (30)	
OR for excessive gain	1.94 (0.87 – 4.34)	1.00 (reference)	0.11
Adjusted OR for excessive gain[a]	1.82 (0.65 - 5.14)	1.00 (reference)	0.26

[a] Adjusted for total energy intake, socioeconomic status, maternal age, parity, maternal pre-pregnancy BMI.

3.3 Association of free sugar intake and GWG

Maslova et al. (2015) reported that those with an intake in the highest free sugar quartile (89±26 g/day) had a significantly higher rate of GWG (34 g/week) when compared to those in the lowest quintile (19±5 g/day) ($p<0.0001$) (see table 3.10).

In the study by Renault et al. (2015), intake of added sugar from food was positively associated ($p=0.02$) with GWG. When comparing the lowest intake of sugar (3.0% of total energy) with the highest (10.1% of total energy), there was a mean difference of 2.8 (95% CI 0.8, 4.8). However, added sugar from soft drinks was inversely and non-significantly associated with GWG, and the association between total added sugar intake and GWG was not significant (see table 3.11).

The findings from Wolff et al. (2008) reported that predictors explained 53% of the variance (R^2= 0.53, F (6,48)= 9.02, p=0.000). It was reported that sugar intake was associated with GWG (β= 0.079, p= 0.002), as was the assignment to either intervention or control (β= -6.948, p= 0.003) (see table 3.12).

Kinnunen et al. (2007) reported no evidence of an association between the mean intake of added sugar and GWG. Although intake in the lowest tertile compared to the highest tertile differed by a mean of 17.25 g/day, there was no significant difference in the GWG in g/week (p=0.792) (see table 3.13).

Table 3.10 Association of intake of added sugar during mid-pregnancy and GWG (Maslova et al., 2015)

Association between intake of added sugar and (GWG g/week) n= 46,262					
	Added sugar g/day	**CRUDE GWG g/week**	**P for trend**	**ADJUSTED* GWG g/week**	**P for trend**
Q1	19±5	0 reference	<0.0001	0 reference	<0.0001
Q2	31±3	23 (16, 29)		17 (11, 23)	
Q3	41±3	29 (22, 35)		23(16, 29)	
Q4	54±5	35 (29, 41)		27(21, 33)	
Q5	89±26	40 (33, 46)		34 (28, 40)	

*Adjusted for SES, maternal age, parity, PPBMI, maternal height, maternal smoking, civil status and total energy intake

Table 3.11 Association of intake of added sugar at baseline and GWG (Renault et al., 2015)

Association between intake of added sugar at baseline and GWG n=366					
Added sugar (median, e%)	**Total Added Sugar**	**Median, %E**	**From Food**	**Median, %E**	**From soft drinks**
	Mean change in GWG compared to reference in kg (95% CI)				
Q1 (3.0)	Reference	(2.6)	Reference	(0.0)	Reference
Q2 (4.8)	1.6 (-0.3, 3.4)	(4.1)	2.1 (0.2, 3.9)	(0.2)	-0.3 (-2.1, 1.5)
Q3 (6.9)	0.8 (-1.1, 2.6)	(5.5)	1.3 (-0.5, 3.2)	(0.8)	-1.1 (-2.9, 0.8)
Q4 (10.1)	0.4 (-1.7, 2.5)	(8.8)	2.8 (0.8, 4.8)	(2.8)	-1.3 (-3.2, 0.6)
P for trend	0.82		0.02		0.13

Table 3.12 Association of sugar intake at 27 weeks and total GWG in obese mothers (Wolff et al., 2008)

GWG	Coefficient	P value
Sugar intake (g/day)	0.079 (0.02, 0.12)	0.002
Assignment to control or intervention	-6.948 (-11.39, -2.51)	0.003
Age	0.049 (-0.32, 0.42)	0.791
Parity **1 child** **2 children**	 -1.91 (-5.35, 1.52) -1.90 (-6.39, 2.57)	 0.268 0.397

Table 3.13 Association of mean intake of added sugar (8 and 36 weeks) and GWG (Kinnunen et al., 2007)

		GWG g/week			
Tertile	**Added sugar intake (g/day) mean (SD)**	**Crude Mean (95% CI)**	**P value**	**Adjusted * Mean (95% CI)**	**P value**
1 (n=34)	30.94 (6.61)	0.436 (0.389, 0.483)	0.784	0.448 (0.401, 0.496)	0.792
2 (n=35)	46.32 (4.26)	0.442 (0.398, 0.486)		0.428 (0.384, 0.472)	
3 (n=34)	63.57 (6.95)	0.419 (0.371, 0.467)		0.429 (0.382, 0.476)	

*Adjusted for maternal age, pre-pregnancy BMI, maternal education level.

3.4 Risk of bias and quality assessment.

The study by Maslova et al. (2015) was of a medium risk of bias and an overall low study quality score. The study by Renault et al. (2015) was of a low/medium risk of bias, with some concerns, and a low/medium quality score. The study by Wolff et al. (2008) was of a low risk of bias and was found to have a medium quality score. The study by Kinnunen et al. (2007) was of a medium risk of bias, and a medium quality score. Table 3.1 reports the results from the Cochrane risk of bias assessment and NICE quality appraisal checklist.

Chapter 4 Discussion

4.1 Main Findings

Four studies were included in this systematic review, of these three were RCTs and one was an observational study. There was some heterogeneity between the studies which meant a meta-analysis could not be carried out; free sugar intake was quantified differently in each study and methods of GWG measurement also differed. There was also heterogeneity in the methods used to quantify weight gain, including whether GWG was measured as absolute gain, rates of gain or adequacy according to IOM recommendations.

Findings from this systematic review suggest that there is evidence of an association between free sugar intake and GWG however due to the heterogeneity and varying quality of the included studies, caution must be applied when interpreting the results. Each study differed in aim and thus design, which resulted in difficulty in combining the results.

Three studies found an association between intake of free sugar during pregnancy and GWG (Wolff et al., 2008; Maslova et al., 2015; Renault et al., 2015), these studies adjusted for energy intake. However, two studies did not adjust for physical activity during pregnancy (Maslova et al., 2015; Wolff et al., 2008). Body weight change is associated with an imbalance between physical activity and energy intake (Hall et al., 2012) therefore it may be difficult to differentiate between effects from increased physical activity and decreased energy intake in an intervention setting or where physical activity was not controlled for.

One of the studies identified, reported no evidence of an association between free sugar intake and GWG (Kinnunen et al., 2007), although the intervention was successful in limiting both GWG and lowering the free sugar intake.

4.2 The role of diet in gestational weight gain

There have been two recent systematic reviews examining energy intake and GWG. Jebeile et al. (2016) reported no evidence of an association between energy intake and GWG, even though body weight increased by 12 kg. Of the 18 studies included in the meta-analysis, only one reported pregnant woman increasing their energy intake to the recommended amount (1700 kJ/day), the other studies indicated that women do not significantly increase their energy intake during pregnancy. Conversely, a systematic review of 12 studies reported that increasing energy was associated with increasing GWG but found inconsistent evidence for the relationship between macronutrient intake and GWG. A meta-analysis was not carried out in the systematic review as, similarly to this review, there was significant heterogeneity in the studies due to differing methods of dietary and weight assessment during pregnancy (Tielemans et al., 2016).

Although neither of these systematic reviews looked specifically at free sugar intake, the conflicting results are interesting. It is possible that the differing findings could represent an overall reduction in energy intake in response to IOM guideline goal setting, although this seems unlikely as GWG significantly increased by 12kg in one review (Jebeile et al., 2016). The review by Jebeile et al. restricted the search date to 1990-2014, to capture

women who had been influenced by the updated IOM 1990 weight gain guidelines, thereby excluding any studies from before 1990. Whereas Tielemans et al. did not restrict the search dates in their search strategy.

The contrasting results of both systematic reviews highlights the issue of heterogeneity between both included studies and reviews. There is difficulty in generating meaningful results where methodological approaches to measuring exposure and outcome differ (Bisson et al., 2016), this may have an overall impact on setting guidelines for pregnant women in this area of research.

Determining possible dietary causes for adverse GWG is complex and examining effects of dietary patterns and dietary quality, rather than individual nutrients, may be more beneficial (Cespedes and Hu, 2015). A study examining diet and physical activity during pregnancy found no evidence of an association between macronutrient intake and GWG (Stuebe et al., 2009). However, there were positive associations between intake of dairy and fried foods and excessive weight gain and there was an inverse association between vegetarian diets and excessive GWG. Therefore, it may be of importance to consider diets containing high levels energy dense foods, such as free sugar, when examining the effects of diet on GWG.

Intake of free sugar in the UK has been associated with obesity, dental caries and type 2 diabetes (Hashem et al., 2016). The consumption of free sugar has been particularly implicated in rising obesity trends and associated with a number of comorbidities such as diabetes, cardiovascular disease, metabolic syndrome and some cancers (Malik et al., 2013).

Foods containing high levels of free sugar are energy dense and so provide more calories than other foods when eaten in relative amounts and provide little satiation (Drewnowski and Specter, 2004). The average UK adult intake of free sugars was at least 10% in 2014, twice the recommended 5% (Scientific Advisory Committee on Nutrition, 2015). Further to this, a cross sectional survey of 169 different types of sugar sweetened beverages reported that SSB are one of the top contributors to free sugar intake in the UK diet (Hashem et al., 2016). This intake is assumed to be similar in pregnant women. The mean intake of free sugars in the study by Wolff et al. (2008) was 47.8 g/day and women in the highest quintile of added sugar consumption in the study by Maslova et al. (2015) had a mean intake of 89 g/day; both of which exceeds the 30 g/day currently recommended by the SACN (2015).

Evidence suggests that increasing or decreasing the proportion of calories from sugars leads to a corresponding increase or decrease in energy intake, potentially leading to weight gain in the non-pregnant adult population (SACN, 2015). In support of this, a systematic review of 30 studies reported a positive association between consumption of SSB and adult weight gain, in the general non-pregnant population (Malik et al., 2013). This was echoed by the SACN (2015), who reported that evidence of a positive effect between SSB consumption and increasing BMI in the UK general population, however this was based on evidence from observational studies only. With this in mind, it is possible that pregnancy as a time of increased insulin resistance and weight gain, may be an important time to reduce the intake of free sugars in order to prevent adverse pregnancy outcomes.

The 2015 report from the SACN reported no evidence of an association between total sugar intake and T2DM, yet consumption of SSB was found to be associated with increased risk of T2DM (SACN, 2015). A prospective study by Chen et al. (2009) suggested pre-pregnancy intake of sugar-sweetened cola associated with increased risk of GDM, yet no evidence of an association was found for other SSB. Chapter 6 of this thesis presents results from analyses of free sugar intake at 32 weeks gestation and diabetes status in the ALSPAC cohort, providing some insight into associations between free sugar intake and GDM.

The findings of this systematic review indicate that there is currently a limited number of studies that addressed the research question and highlights the need to strengthen studies, by agreeing uniform methods of dietary and weight status in pregnant women, in order to examine dietary influences on GWG. This will provide a good evidence base for advice on the importance of a healthy diet in limiting adverse weight gain and therefore improving pregnancy outcomes for both mother and offspring.

4.3 Strengths and limitations

The strengths of this review are that it is the first to explore the association of free sugar intake and gestational weight gain. The inclusion of only four studies in this systematic review highlights the extremely limited evidence available on this topic. This indicates a need to improve reproducible methodological approach including dietary assessment and measurement and classification of GWG, in order to facilitate further research in this area. It is difficult to provide evidence-based recommendations during pregnancy when the literature is not robust enough to draw meaningful conclusions.

Another strength is the comprehensive and systematic search strategy used in all four databases, with no date or language restrictions which resulted in a full and inclusive search of the available literature. The use of two independent reviewers to review all 320 titles and an impartial third reviewer reduced bias in the screening process is considered a strength. Another strength was in the strategy used to contact authors of identified studies, allowing either inclusion or exclusion to the systematic review. During this contact, two study authors provided further analysis of their original study results to investigate the association of free sugar intake and GWG. The use of tools developed by the Cochrane Bias Methods Group for risk of bias assessment and the NICE quality appraisal assessment provided a strong and comprehensive approach to study appraisal.

One major limitation of this systematic review was the lack of available studies examining the association between free sugar intake during pregnancy and GWG. This highlights the limited research available in this area.

Another limitation was that the included studies were of a low or medium quality score and one was observational in nature, which means that causation cannot be implied by the results. Another limitation is that due to heterogeneity between the exposure and outcome assessment, a meta-analysis could not be applied. The methods used to assess free sugar intake and weight gain during pregnancy differed between studies; one study used a 7-day weighed food record to obtain dietary intake, the remaining studies used a food frequency questionnaire; all at differing points during the pregnancy. The accuracy of using a FFQ in dietary assessment has been

questioned (Vioque et al., 2013) and it has been suggested that use of an FFQ may lead to under reporting of dietary intakes, particularly in obese women (Ledikwe et al., 2006). All studies used a self-reported pre-pregnancy weight and one study used self-reported weight measurements throughout the pregnancy, however self-reported weights have been shown to be correlated with actual weights in pregnant women (Holland et al., 2013). Not all studies controlled for the same confounders in relation to GWG and so some residual confounding may remain.

In conclusion, there is some evidence to suggest a positive association between free sugar intake and GWG, however as not all of the studies controlled for the same confounders and none were of a high quality, this result must be interpreted with caution. The results of the systematic search suggest this area of dietary intake has not been well studied and highlights an important area for further research.

Part II

Chapter 5 Methodology: data analysis

5.1 Introduction to Avon Longitudinal Study of Parents and Children (ALSPAC)

The Avon Longitudinal Study of Children and Parents (http://www.bristol.ac.uk/alspac) is a multi-generational cohort established to examine how genotype and environment affect the health of the mothers and children. Information on environmental habits have been extensively collected from both children and parents since 1991 (Fraser et al., 2013). The aim of the current research was to identify cross-sectional associations between maternal dietary intake and health characteristics during pregnancy.

5.2 Participants

All pregnant women living in the three health districts of Avon (Southmead, Frenchay and Bristol & Weston) in Bristol, UK with an estimated delivery date between 1st April 1991 and 31st December 1992 were eligible to take part in the cohort. 14,893 women enrolled in the initial study and dietary information was collected on 12,104 women at 32 weeks' gestation (Rogers et al., 1998). Ethical approval was obtained from the ALSPAC Law and Ethics Committee and the Local Research Ethics Committees.

5.3 Recruitment process

As described in a previous review of the ALSPAC mother's cohort (Boyd et al., 2013), the ALSPAC recruitment process used antenatal and maternity services to promote the study by distribution of an 'expression of interest' card. If the card was returned, women could obtain further information on the study or decline to participate in the study (Boyd et al., 2013). Participation consent was 'opt out' and this meant that any woman who did not decline participation would be contacted further for data collection (Boyd et al., 2013).

Participants were recruited in three phases; 82.6% of women were recruited during 1990-92 (phase I) and the remaining 17.4% were recruited 7 years after the initial recruitment (phase II and III). Those who were recruited in Phases II and III were not able to provide data collected during pregnancy, infancy and early childhood (Boyd et al., 2013) and so are not included in the current study.

5.4 Data collection

Obstetric data was obtained for 13,706 women, extracted by trained midwives from medical records and recorded in an electronic database (Fraser et al., 2013). This data included repeated antenatal measurements such as weight, blood pressure, glycosuria and proteinuria (Lawlor et al., 2011).

5.4.1 Gestational diabetes and glycosuria

Information on existing diabetes (DM) and previous history of GDM was collected at recruitment using a questionnaire. Urine testing for glycosuria and proteinuria was carried out routinely during antenatal screening. Glycosuria (recorded as none, trace, +, ++, +++ or more) was defined as a record of at least ++ on at least two occasions during the pregnancy (Lawlor et al., 2011).

Based on this information the participants were categorised into four groupings ‘no glycosuria or diabetes’, ‘existing diabetes’, ‘gestational diabetes’ and ‘glycosuria’. Women with type 1 and type 2 were included in the ‘existing diabetes’ group.

A number of assumptions were made in the current study, with regards to GDM status in the participants. It was assumed that GDM was diagnosed around 24-28 weeks gestation and that those who were diagnosed with GDM during pregnancy would have received dietary and lifestyle counselling, to facilitate self-management of the diabetes (Negrato and Gomes, 2013). It was assumed that the women with existing diabetes (either type 1 or type 2) would have had extensive dietary and blood glucose management counselling throughout the entire pregnancy and prenatally. It was also assumed that women without a diagnosis of diabetes/glycosuria and women with glycosuria would have received little to no dietary advice related to glycaemic control during the pregnancy.

5.4.2 Gestational weight

Predicted weight change variables were derived using linear spline models, producing knots which resulted in four variables: 'pre-pregnancy weight (kg)', 'Change in weight between 0 and 18 weeks (kg/week)', 'Change in weight between 18 and 28 weeks (kg/week') and 'Change in weight between 28 weeks and birth (kg/week)' (Lawlor et al., 2011). However, the purpose of the current study was to examine the associations of dietary intake and absolute GWG as categorised by the IOM, rather than weight change at different stages of the pregnancy; therefore, the measured absolute weight gain variable was used in the analyses.

The measured absolute weight gain variable was obtained by subtracting the first obstetric weight measurement and the last obstetric weight measurement. This was combined with the pre-pregnancy BMI to categorise women to the IOM categories of lower than, recommended and higher than recommended weight gain during pregnancy (Lawlor et al., 2011).

Pre-pregnancy weight was self-reported and obtained from a questionnaire sent at 32 weeks gestation and used with self-reported height to calculate pre-pregnancy BMI and classified using the World Health Organisation categories (Macdonald-Wallis et al., 2013).

5.4.3 Dietary assessment

A self-completion food frequency questionnaire (FFQ) was sent to the ALSPAC mothers at 32 weeks' gestation (see appendix A) (Rogers et al., 1998). Although the questionnaire was not validated prior to use, it was

based on a questionnaire used in a neighbouring area and weighed dietary intake data from non-pregnant women in the local area (Emmett et al., 2015).

The FFQ contained questions regarding the weekly frequency of consumption of 43 different food groups, daily consumption of 8 further foods and preparation of food and drinks. The participants were asked to indicate how often the food was consumed within the last three months from completion, using the options 1) never or rarely; 2) once in 2 weeks; 3) 1-3 times a week; 4) 4-7 times a week; and 5) more than once a day (Emmett et al., 2015).

5.5 Nutrient calculation

Approximate daily and weekly nutrient intakes were calculated for each mother based on frequency of food consumption and nutrient content of foods as discussed in a previous study (Emmett et al., 2015). A weekly consumption was calculated by multiplying the weekly frequency of consumption of a food by the nutrient content of a portion of that food and summing this for all the foods consumed, this was divided by 7 to obtain daily intake (Emmett el al., 2015).

There were more detailed questions for foods that were usually consumed daily. This supplied information on which types of bread were eaten, what kinds of fat was used for cooking and eating, what type of milk was consumed and how often and many cups of tea and cola were consumed (Emmett et al., 2015). As this data differed from the weekly consumption, all

data were standardised by subtracting the mean and dividing by the standard deviation for each variable (Northstone et al., 2008).

5.5.1 Dietary patterns

Principal component analysis (PCA) was used in a previous study to derive dietary patterns from the food and beverage items consumed by the ALSPAC cohort (Northstone et al., 2008). The dietary pattern labels were applied by the previous researchers based on which food items were included in the components.

Briefly, PCA forms linear combinations and groups together correlated variables, the coefficients of the combinations are known as ‘factor loadings’ and are defined as the correlations of a food item with a component (Northstone et al., 2008). To calculate a component score, the factor loading was multiplied by the corresponding value for each food and summed across all of the food items. A higher score indicated a closer adherence to that dietary pattern and loadings above 0.3 were consumed to be closest to that dietary pattern (Northstone et al., 2008).

The five dietary components are shown in table 5.1.

Table 5.1 Dietary patterns derived from principal component analysis (PCA) (Northstone et al., 2008)

Assigned Pattern Name	Description of dietary pattern
Health conscious	High loadings of brown/wholemeal bread, whole grain breakfast cereals, fish, cheese, pulses, pasta, rice, salad, fresh fruit, fruit juice.
Traditional	High loadings of leafy green and other green vegetables, carrots, root vegetables, peas, plain potatoes (not chips)
Processed	High loadings of white bread, meat pies, sausages/burgers, fried foods, pizza, eggs, chips, roast potatoes, baked beans
Confectionary	High loadings of biscuits, puddings, cakes/buns, sweets, chocolates, chocolate bars, crisps
Vegetarian	High loadings of meat substitutes, pulses, nuts and herbal tea

5.6 Covariate variables

Covariate variables were collected using the same questionnaire sent at 32 weeks, assessing dietary intake (Northstone et al., 2008). These included: education level; age; housing; ethnic background; parity; marital status; employment status; social class and lifestyle factors such as smoking status and physical activity (Northstone et al., 2008).

Of the 11,670 women with obstetric data, the number of those with completed covariate data varied (from 7989 for the GWG sample and 8507 for the GDM sample). This study used only the participants with all the required data.

5.7 Statistical analysis

Macronutrient intake is correlated with energy intake (Willett et al., 1997). If energy intake is not adjusted for associations between nutrient intakes and disease risk can be obscured and confounding can be introduced to the model (Willett et al., 1997). Therefore, the absolute macronutrient and NMES intakes were energy adjusted into standardized residuals, using the nutrient residual model, and nutrient densities, using the nutrient density method as described by Willett et al. (1997). Briefly, the nutrient density method requires that the nutrient intake is divided by energy intake and expressed as a percentage of energy. The nutrient residual model involves computing residuals of nutrient intakes by regressing the nutrient intakes on their total energy intakes, thereby removing the extraneous variation caused by total energy intake (Willett et al., 1997).

The exposure data was checked for normality using frequency distributions and Q-Q plots. All intakes except non-milk extrinsic sugars (NMES) were normally distributed. NMES was left-skewed and natural log transformation was used to transform into normal distribution.

The residuals and densities were checked and no correlation was found.

For each exposure; energy adjusted residuals, nutrient densities and PCA scores, a one-way ANOVA was conducted for the outcomes (diabetes and weight gain status). Results from the ANOVA were reported as means and standard deviations.

Multinomial logistic regression analysis was used to analyse associations between dietary intake and adherence to dietary patterns at 32 weeks

(exposures) and diabetes/glycosuria status and gestational weight gain categorised by IOM (outcomes). Results from the regression analyses were reported as relative risk ratios and 95% confidence intervals.

For the analysis, only participants who had complete data for all variables, including covariates, were included. Three models were used in the multinomial regression; model 1 (basic): age adjusted, model 2: adjusted for age and confounders and model 3 adjusted for age, confounders and mediators (see table 5.2). Confounders and mediators were decided *a priori*.

The use of pre-pregnancy BMI as a mediator in the third model was not ideal, as pre-pregnancy BMI occurred before the exposure measurement (32 weeks). However, a lack of other weight gain measurements meant the use of pre-pregnancy BMI was the most practical solution, as the literature suggests prevalence of GDM and adverse GWG is associated with pre-pregnancy weight status (Gaillard et al., 2013; Oteng-Ntim et al., 2013; Zanardo et al., 2016).

All data analysed using SPSS (version 24) (Statistical Package for Social Sciences) and Stata (Texas).

Table 5.2 Models used in multinomial logistic regression analyses of dietary intake and patterns at 32 weeks gestation, diabetes and GWG status

Regression model	Covariates adjusted for
Model 1 (basic)	Age
Model 2 (confounder)	Age, maternal parity, maternal smoking, physical activity, maternal social class, maternal education level
Model 3 (mediator)	Age, maternal parity, maternal smoking, physical activity, maternal social class, maternal education level, pre-pregnancy BMI

Chapter 6 Results

6.1 Maternal demographics and glycaemic status

Of the 14,269 women with singleton pregnancies, 8507 had both data on diabetes during pregnancy and all covariates used in the multinomial regression model (shown in figure 6.1). Table 6.1 shows the distributions of maternal characteristics from the sample included in the current study (n= 8507) and the entire eligible ALSPAC sample (n= 11670).

There was little difference between the maternal demographics of the two groups and the distributions of the covariates did not differ greatly, demonstrating that the eligible sample was representative of the whole sample.

Mean maternal age in both samples was 28 years old and mean maternal BMI was shown to be 22.9 kg/m^2. The majority of women in both samples were shown to be of a non-manual social class and educated to at least O Level (GCE or GSCE). More than half of the women were physically active and did not smoke during the pregnancy.

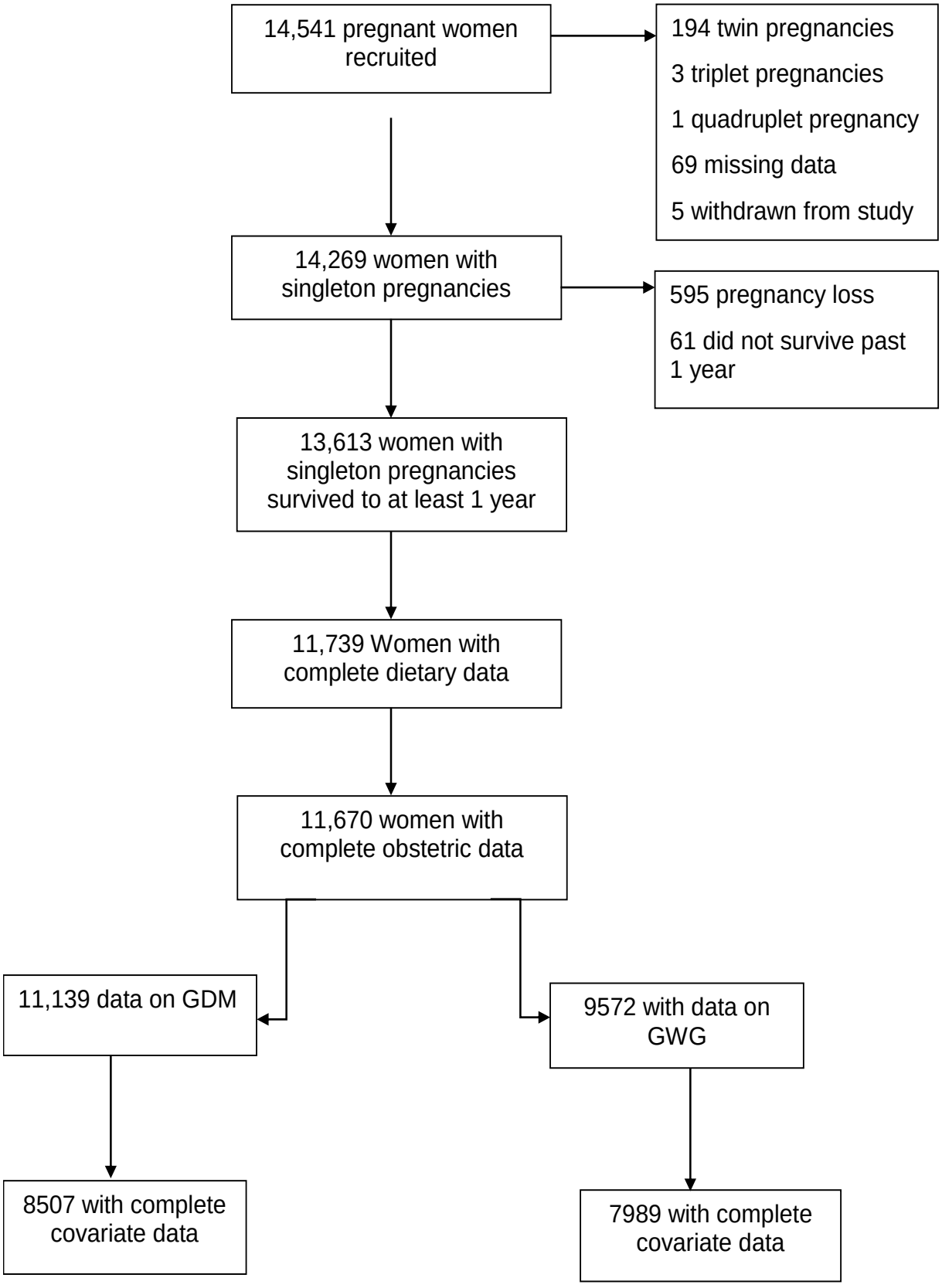

Figure 6.1 Flow diagram of inclusion into final analyses

Table 6.1 Maternal demographics of ALSPAC cohort

Characteristic	Included sample (n= 8507)	ALSPAC sample (n= 11670)
Maternal age y, mean (SD)	28.6 (4.7)	28.3 (4.9)
Maternal parity, n (%)		
0	4190 (49.3)	5074 (43.5)
1	2983 (35.1)	3978 (34.1)
2	1012 (11.9)	1585 (13.6)
≥3	322 (3.8)	617 (5.3)
Maternal pre-pregnancy BMI (kg/m^2), mean (SD)	22.9 (3.7)	22.9 (3.8)
Maternal social class n (%)		
I	515 (6.1)	576 (4.9)
II	2744 (32.3)	3052 (26.2)
III (non-manual)	3656 (43.0)	4144 (35.5)
III manual	626 (7.4)	763 (6.5)
IV	798 (9.4)	945 (8.1)
V	168 (2.0)	210 (1.8)
Maternal education level, n (%)		
Degree	1278 (15.0)	1497 (12.8)
A Level	2188 (25.7)	2630 (22.5)
O Level	3100 (36.4)	4028 (34.5)
Vocational	777 (9.1)	1149 (9.8)
CSE	1164 (13.7)	2297 (19.7)
Physical activity during pregnancy, n (%)		
Yes	5780 (67.9)	7900 (67.7)
No	2727 (32.1)	3674 (31.5)
No smoking during pregnancy, n (%)		
Yes	1719 (20.2)	2681 (23.0)
No	6788 (79.8)	8762 (75.1)

Presented as means (SD) or n (%)

6.2 Unadjusted maternal macronutrient and free sugar intake at 32 weeks gestation and glycaemic status

As shown in table 6.2, women with existing diabetes and those with GDM had lower mean intakes of unadjusted macronutrients when compared with those with no diabetes and those with glycosuria, although women with GDM had a higher protein intake than both existing DM and glycosuria. The mean intakes of energy, in kJ, carbohydrates and non-milk extrinsic sugars (NMES) was significantly different across the four groups, those with existing DM had the lowest mean intakes.

The percentage of energy from fat was similar in all four groups. Those with existing DM and GDM had a slightly lower intake of percentage of energy from carbohydrates when compared with women with no DM and women with glycosuria. Mean intakes of energy from protein were significantly higher in those with existing DM and GDM. Conversely, intakes of energy from NMES were significantly lower in the same groups when compared to those with no diabetes.

Table 6.2 ANOVA of maternal macronutrient and sugar intake at 32 weeks gestation and glycaemic status (n= 8507)

Unadjusted daily intakes	None (n= 8,185)	Existing DM (n= 33)	GDM (n= 35)	Glycosuria (n= 254)	P value
Energy (kJ)	7275.1 (1928.8)	5966.4 (1497.9)	6960.6 (2074.0)	7114.9 (1993.9)	0.0001
Fat (g)	71.9 (22.6)	59.2 (18.6)	68.6 (25.6)	71.7 (24.0)	0.01
Carbohydrate (g)	213.5 (59.8)	166.5 (43.7)	197.5 (58.6)	207.2 (60.4)	<0.001
Protein (g)	70.4 (19.0)	65.2 (15.4)	74.3 (20.7)	67.5 (18.4)	0.02
NMES (g)	59.5 (31.9)	30.9 (17.0)	38.7 (20.9)	58.2 (34.5)	<0.001
Percentage of energy					
% energy from fat	36.3 (4.5)	36.5 (5.0)	35.9 (5.4)	37.0 (4.7)	0.13
% energy from carbohydrate	47.0 (4.8)	44.7 (4.9)	45.8 (4.9)	46.7 (4.8)	0.01
% energy from protein	16.6 (2.7)	18.8 (2.2)	18.4 (2.7)	16.3 (2.5)	<0.001
% energy from NMES	12.8 (5.1)	8.2 (3.9)	9.0 (4.7)	12.7 (5.3)	<0.001

Presented as means (SD)

6.3 Percentage intakes of energy from nutrients in mothers at 32 weeks gestation and hyperglycaemia risk

As shown in table 6.3, there was evidence of a positive association of percentage of energy from fat with glycosuria in the basic and fully adjusted models, but no similar association was seen for existing diabetes or GDM. There was weak evidence of negative association of percentage of energy from carbohydrate with existing diabetes in the basic and fully adjusted models.

Positive associations were seen between percentage energy from protein and those with existing diabetes and GDM, but no similar association was seen for glycosuria.

There was evidence of a negative association of percentage energy from NMES with both existing diabetes and GDM, but no similar association was seen for glycosuria.

The patterns of association reported above were replicated in the results when using energy adjusted macronutrient values, using the residual method, in place of percentage energy intakes (see appendix B).

Table 6.3 Multinomial logistic regression analysis of percentage of energy from macronutrients and free sugar at 32 weeks gestation and glycaemic status

	RRR (95% CI)[a]			
Percentage of energy from nutrients at 32 weeks gestation	**None (n= 8185)** **Reference**	**Existing diabetes (n= 33)**	**GDM (n= 35)**	**Glycosuria (n= 254)**
Fat (%)				
M1[b]	1	1.01 (0.93, 1.08)	0.98 (0.91, 1.05)	1.03 (1.00, 1.06)
M2[c]	1	1.02 (0.94, 1.10)	0.97 (0.91, 1.05)	1.04 (1.01, 1.07)
M3[d]	1	1.01 (0.94, 1.09)	0.96 (0.90, 1.04)	1.03 (1.01, 1.06)
Carbohydrate (%)				
M1	1	0.90 (0.84, 0.97)	0.95 (0.88, 1.02)	0.98 (0.96, 1.01)
M2	1	0.90 (0.84, 0.97)	0.95 (0.88, 1.02)	0.98 (0.96, 1.01)
M3	1	0.91 (0.85, 0.98)	0.97 (0.90, 1.04)	0.98 (0.96, 1.01)
Protein (%)				
M1	1	1.32 (1.18, 1.48)	1.25 (1.11, 1.40)	0.95 (0.91, 1.00)
M2	1	1.32 (1.17, 1.48)	1.25 (1.11, 1.40)	0.96 (0.91, 1.01)
M3	1	1.30 (1.16, 1.47)	1.23 (1.10, 1.38)	0.95 (0.90, 1.00)
NMES (%)				
M1	1	0.74 (0.66, 0.82)	0.80 (0.73, 0.88)	0.99 (0.97, 1.02)
M2	1	0.74 (0.66, 0.82)	0.80 (0.73, 0.88)	0.99 (0.97, 1.02)
M3	1	0.75 (0.66, 0.83)	0.81 (0.74, 0.89)	1.00 (0.97, 1.02)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

6.4 Unadjusted energy, macronutrient and free sugar intakes at 32 weeks and hyperglycaemia risk

As reported in table 6.4, there was evidence of a negative association between intake of both fat (g) and carbohydrate (g) and existing diabetes. This was not found in those with GDM or those with glycosuria.

There was evidence of a negative association between intake of NMES (g) in both those with existing diabetes and those with GDM, but no evidence of an association for NMES and glycosuria.

Table 6.4 Multinomial logistic regression analysis of unadjusted energy, macronutrient and free sugar intake at 32 weeks and glycaemic status

	RRR (95% CI)[a]			
Dietary intakes at 32 weeks gestation	**None (n= 8185)** **Reference**	**Existing diabetes (n= 33)**	**GDM (n= 35)**	**Glycosuria (n= 254)**
Energy (kJ)				
M1[b]	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M2[c]	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M3[d]	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Fat (g)				
M1	1	0.97 (0.95, 0.99)	0.99 (0.98, 1.01)	0.99 (0.98, 1.01)
M2	1	0.91 (0.95, 0.99)	0.99 (0.98, 1.01)	1.00 (0.99, 1.01)
M3	1	0.97 (0.95, 0.99)	0.99 (0.99, 1.01)	1.00 (1.00, 1.01)
Carbohydrate (g)				
M1	1	0.98 (0.98, 0.99)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M2	1	0.98 (0.98, 0.99)	0.99 (0.99,1.00)	1.00 (1.00, 1.00)
M3	1	0.98 (0.98, 0.99)	1.00 (0.99, 1.00)	1.00 (1.00, 1.00)
Protein (g)				
M1	1	0.98 (0.97, 1.00)	1.01 (0.99, 1.03)	0.99 (0.98, 1.00)
M2	1	0.98 (0.96, 1.00)	1.01 (0.99, 1.03)	0.99 (0.99, 1.00)
M3	1	0.99 (0.97, 1.01)	1.01 (0.99, 1.03)	0.99 (0.99, 1.00)
NMES (g)				
M1	1	0.94 (0.92, 0.96)	0.97 (0.95, 0.98)	1.00 (0.99, 1.00)
M2	1	0.94 (0.91, 0.96)	0.96 (0.95, 0.98)	1.00 (0.99, 1.00)
M3	1	0.94 (0.92, 0.96)	0.97 (0.95, 0.98)	1.00 (1.00, 1.00)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

6.5 Maternal dietary pattern intake (PCA score) and glycaemic status

Mothers with no diabetes had a higher adherence to both the 'health conscious' and the 'confectionary' PCA groups. Those with existing DM were more likely to adhere to the 'health conscious' PCA group. Mothers with GDM also had a higher adherence to the 'health conscious' PCA group and the 'traditional' PCA group. Those with glycosuria had a higher adherence to the 'processed' and 'confectionary' PCA groups (see table 6.5).

Table 6.5 ANOVA of maternal PCA scores at 32 weeks and glycaemic status

PCA Scores	None (n= 8185)	Existing DM (n= 33)	GDM (n= 35)	Glycosuria (n= 254)	P value
PCA 1 'Health conscious'	0.11 (0.97)	0.26 (0.90)	0.18 (0.95)	-0.06 (0.95)	0.03
PCA 2 'Traditional'	-0.01 (0.95)	-0.32 (0.91)	0.14 (1.04)	-0.20 (0.86)	0.003
PCA 3 'Processed'	-0.07 (0.89)	-0.06 (0.79)	-0.01 (0.92)	0.01 (0.94)	0.58
PCA 4'Confectionery'	0.02 (0.96)	-0.65 (0.60)	-0.57 (0.64)	0.04 (1.08)	<0.001
PCA 5 'Vegetarian'	-0.02 (1.00)	-0.18 (0.74)	-0.26 (0.84)	0.02 (0.90)	0.36

6.6 Adherence to dietary patterns and hyperglycaemia risk

To test adherence to dietary patterns and diabetes risk, multinomial regression analyses were performed (see table 6.6).

There was evidence of a negative association of the PCA group ‘health conscious’ and those with glycosuria, the association was slightly attenuated when adjusted for confounders and mediators but remained significant. Similar associations were not present for ‘health conscious’ and existing DM and GDM.

There was also a negative association of the PCA group ‘traditional’ and those with glycosuria, this was not seen in those with existing DM and GDM.

There was a negative association for the PCA group ‘confectionary’ and both those with existing DM and GDM, no similar association was seen in those with glycosuria.

There was no evidence of an association with adherence to the PCA group ‘processed’ or the PCA group ‘vegetarian’ and any of the hyperglycaemic status groups.

Table 6.6 Multinomial logistic regression analysis of adherence to dietary patterns at 32 weeks gestation and glycaemic status

	RRR (95% CI)[a]			
Maternal PCA scores	**None (n= 8185)** **Reference**	**Existing DM (n= 33)**	**GDM (n= 35)**	**Glycosuria (n= 254)**
PCA 1 'Health conscious'	1	1.18 (0.82, 1.70)	1.03 (0.72, 1.48)	0.81 (0.70, 0.93)
M1[b]	1	1.13 (0.75, 1.71)	1.04 (0.69, 1.56)	0.81 (0.69, 0.95)
M2[c]	1	1.23 (0.81, 1.86)	1.20 (0.80, 1.79)	0.84 (0.72, 0.99)
M3[d]				
PCA 2 'Traditional'	1	0.66 (0.43, 1.03)	1.15 (0.84, 1.59)	0.79 (0.68, 0.91)
M1	1	0.98 (0.44, 1.05)	1.15 (0.83, 1.59)	0.79 (0.68, 0.91)
M2	1	0.67 (0.44, 1.04)	1.13 (0.82, 1.57)	0.78 (0.67, 0.91)
M3				
PCA 3 'Processed'	1	1.01 (0.98, 1.50)	1.11 (0.77, 1.62)	1.10 (0.96, 1.27)
M1	1	1.10 (0.73, 1.64)	1.09 (0.74, 1.61)	1.11 (0.96, 1.28)
M2	1	1.07 (0.71, 1.62)	1.00 (0.67, 1.50)	1.10 (0.95, 1.27)
M3				
PCA 4 'Confectionary'	1	0.29 (0.16, 0.52)	0.36 (0.21, 0.62)	1.02 (0.90, 1.16)
M1	1	0.28 (0.15, 0.50)	0.34 (0.19, 0.59)	1.02 (0.90, 1.16)
M2	1	0.28 (0.15, 0.51)	0.34 (0.20, 0.60)	1.04 (0.92, 1.18)
M3				
PCA 5 'Vegetarian'	1	0.84 (0.57, 1.23)	0.75 (0.51, 1.11)	1.04 (0.92, 1.17)
M1	1	0.84 (0.58, 1.24)	0.79 (0.53, 1.17)	1.05 (0.92, 1.18)
M2	1	0.85 (0.58, 1.25)	0.81 (0.54, 1.21)	1.06 (0.93, 1.20)
M3				

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

6.7 Maternal demographics and gestational weight gain status.

Of the 9572 participants with data on measured GWG, 7989 also had data on all covariates used in the regression models. For these analyses measured GWG was used rather than predicted GWG (see appendix E), as this study examines the associations of dietary intake and overall GWG as categorised by IOM, rather than at different stages of the pregnancy.

Table 6.7 shows the maternal demographics of the sample included in these analyses (n= 7989) and the wider eligible ALSPAC sample (n= 11670). There was little difference in the maternal demographics of both groups; mean maternal age was 28 years old and mean maternal BMI was 22.9 kg/m^2. The majority of both samples were of a non-manual social class and educated to at least O level standard (equivalent to GSE or GCSE). More than half of both samples did not smoke and were physically active during pregnancy.

Table 6.7 Maternal demographics of ALSPAC and GWG cohort

Characteristic	Included cohort (n= 7989)	ALSPAC sample (n= 11670)
Maternal age y, mean (SD)	28.6 (4.70)	28.3 (4.9)
Maternal parity, n (%)		
0	3925 (49.1)	5074 (43.5)
1	2820 (35.3)	3978 (34.1)
2	941 (11.8)	1585 (13.6)
≥3	303 (3.8)	617 (5.3)
Maternal pre-pregnancy BMI (kg/m^2), mean (SD)	22.9 (3.7)	22.9 (3.8)
Maternal social class, n (%)		
I	488 (6.1)	576 (4.9)
II	2576 (32.2)	3052 (26.2)
III (non-manual)	3425 (42.9)	4144 (35.5)
III manual	589 (7.4)	763 (6.5)
IV	752 (9.4)	945 (8.1)
V	159 (2.0)	210 (1.8)
Maternal education level, n (%)		
Degree	1216 (15.2)	1497 (12.8)
A Level	2031 (25.4)	2630 (22.5)
O Level	2920 (36.6)	4028 (34.5)
Vocational	734 (9.2)	1149 (9.8)
CSE	1088 (13.6)	2297 (19.7)
Physical activity during pregnancy, n (%)		
Yes	5439 (68.1)	7900 (67.7)
No	2550 (31.9)	3674 (31.5)
Smoked during pregnancy, n (%)		
Yes	1608 (20.1)	2681 (23.0)
No	6381 (79.9)	8762 (75.1)

6.8 Maternal macronutrient and free sugar intake and gestational weight gain status

Table 6.8 shows the mean unadjusted daily intakes and percentage of energy intakes of mothers at 32 weeks gestation. Women who gained less weight than recommended consumed less energy than those who gained within the recommended amounts and those who gained more than the IOM recommended weights. Similarly, less fat and carbohydrate were consumed in those who gained less than recommended. Women who gained within the recommended amount of weight gain consumed more protein than the other two groups. However, intake of free sugar was similar in all three groups.

Mean percentage of energy from macronutrients and sugar were similar across all groups and were comparable to the national averages in the UK (Public Health England, 2016).

Table 6.8 ANOVA of maternal macronutrient and sugar intake at 32 weeks gestation and weight status (n= 7475)

Unadjusted daily intakes, mean (SD)	Less than recommended (n= 2442)	Within recommended (n= 2959)	More than recommended (n= 2074)	P value
Energy (kJ)	7170.3 (1963.7)	7328.6 (1880.0)	7305.1 (1934.8)	0.01
Fat (g)	70.8 (23.1)	72.4 (22.1)	72.4 (22.3)	0.02
Carbohydrate (g)	210.4 (60.5)	214.8 (57.8)	214.2 (60.1)	0.02
Protein (g)	69.3 (19.1)	71.1 (18.7)	70.4 (19.0)	<0.001
NMES (g)	59.1 (33.0)	59.1 (30.1)	59.5 (31.3)	0.90
Percentage of energy intake, mean (SD)				
% of energy from fat	36.3 (4.6)	36.4 (4.5)	36.5 (4.5)	0.42
% of energy from CHO	47.0 (4.8)	46.9 (4.8)	46.9 (4.6)	0.87
% of energy from protein	16.6 (2.8)	16.6 (2.5)	16.5 (2.6)	0.34
% of energy from NMES	12.9 (5.4)	12.6 (4.8)	12.7 (4.9)	0.19

6.9 Association of percentage intakes from energy and gestational weight gain.

As shown in table 6.9, there was no evidence of associations for percentage energy from protein, energy from fat, energy from carbohydrate or energy from NMES intakes in those with insufficient and excessive weight gain. This was consistent across all three of the confounder and mediator adjusted models.

Table 6.9 Multinomial regression analysis of percentage of energy intake from macronutrient and free sugar intake at 32 weeks gestation and gestational weight status

	RRR (95% CI)[a]		
Percentage from energy intakes at 32 weeks	**Recommended (n= 2442)** **Reference**	**Less than recommended (n= 2959)**	**More than recommended (n= 2074)**
Fat (%)			
M1[b]	1	1.00 (0.99, 1.01)	1.00 (0.99, 1.02)
M2[c]	1	0.99 (0.98, 1.00)	1.00 (0.99, 1.02)
M3[d]	1	0.99 (0.98, 1.00)	1.00 (0.99, 1.01)
Carbohydrate (%)			
M1	1	1.00 (0.99, 1.01)	0.99 (0.98, 1.01)
M2	1	1.00 (0.99, 1.01)	0.99 (0.98, 1.00)
M3	1	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)
Protein (%)			
M1	1	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)
M2	1	1.01 (0.99, 1.03)	1.01 (0.99, 1.03)
M3	1	1.01 (0.99, 1.04)	0.99 (0.97, 1.02)
NMES (%)			
M1	1	1.01 (1.00, 1.02)	1.00 (0.99, 1.01)
M2	1	1.01 (1.00, 1.02)	0.99 (0.98, 1.00)
M3	1	1.01 (0.99, 1.02)	1.00 (0.99, 1.02)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

6.10 The association of unadjusted macronutrient and NMES intakes at 32 weeks and gestational weight gain

As shown in table 6.10, there was no evidence of associations for energy, protein, fat carbohydrate and NMES intakes in those with insufficient and excessive weight gain. This was consistent across all three of the confounder and mediator adjusted models.

Table 6.10 Multinomial logistic regression analysis of unadjusted energy, macronutrient and free sugar intake at 32 weeks and gestational weight status

	RRR (95% CI)[a]		
Dietary intakes at 32 weeks	**Recommended (n= 2442)** **Reference**	**Less than recommended (n= 2959)**	**More than recommended (n= 2074)**
Energy (kJ)			
M1[b]	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M2[c]	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M3[d]	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Fat (g)			
M1	1	1.00 (0.99, 1.00)	1.00 (1.00, 1.00)
M2	1	1.00 (0.99, 1.00)	1.00 (1.00, 1.00)
M3	1	0.99 (0.99, 1.00)	1.00 (1.00, 1.01)
Carbohydrate (g)			
M1	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M2	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M3	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Protein (g)			
M1	1	0.99 (0.99, 1.00)	1.00 (1.00, 1.00)
M2	1	0.99 (0.99, 1.00)	1.00 (1.00, 1.00)
M3	1	0.99 (0.99, 1.00)	1.00 (1.00, 1.01)
NMES (g)			
M1	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M2	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
M3	1	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI.

6.11 Maternal adherence to dietary patterns during pregnancy and gestational weight gain status

Table 6.11 shows the mean maternal adherence to dietary patterns at 32 weeks. Across the weight gain groups, mean adherence to the 'health conscious' pattern was highest in those who gained weight within the IOM recommendations and lowest in those who gained more than recommended (p= <0.001). Those who gained less weight than recommended had the lowest adherence to the 'confectionary' pattern and those who gained more than recommended had the highest adherence (p= <0.001). All groups had negative scores (lower adherence) to both 'traditional' and 'processed' patterns, non-significantly. Adherence to the 'vegetarian' pattern was highest in women who gained less than recommended weight and lower in those who gained within and who gained more than recommended (p= 0.001).

Table 6.11 ANOVA of maternal adherence to PCA scores at 32 weeks and gestational weight status

PCA Scores	Less than recommended (n= 2442)	Within recommended (n= 2959)	More than recommended (n= 2074)	P value
PCA 1 'Health conscious'	0.12 (1.00)	0.18 (0.97)	0.03 (0.91)	<0.001
PCA 2 'Traditional'	-0.02 (0.96)	-0.02 (0.94)	-0.04 (0.96)	0.71
PCA 3 'Processed'	-0.09 (0.92)	-0.08 (0.86)	-0.04 (0.88)	0.17
PCA 4'Confectionery'	-0.05 (0.98)	0.03 (0.94)	0.099 (0.98)	<0.001
PCA 5 'Vegetarian'	0.03 (1.05)	-0.04 (0.97)	-0.06 (0.93)	0.001

Table 6.12 Multinomial logistic regression analysis of adherence to dietary patterns at 32 weeks gestation and gestational weight status

As shown in table 6.12, there was evidence of a negative association between the PCA group ‘health conscious’ and women with insufficient weight gain. This was attenuated when adjusted for maternal age and confounders only. There was evidence of a negative association between the PCA group ‘health conscious’ and women with excessive weight gain in model one, however, this was no longer significant when adjusted for confounders and mediators.

There was evidence of a negative association of the PCA group ‘confectionary’ and those with insufficient weight gain. There was evidence of a positive association of the ‘confectionary’ group and those with excessive weight gain, in the mediator adjusted model only.

There was evidence of a positive association between the PCA group ‘vegetarian’ and those with insufficient weight gain. This was not seen in those with excessive weight gain.

There was no evidence of associations between either the PCA group ‘traditional’ and ‘processed’ with either weight gain group.

Table 6.12 Multinomial logistic regression analysis of adherence to dietary patterns at 32 weeks gestation and gestational weight status

RRR (95% CI)[a]			
Maternal adherence to PCA scores at 32 weeks' gestation	**Recommended (n= 2959)** **Reference**	**Less than recommended (n= 2442)**	**More than recommended (n= 2074)**
PCA 1 'Health conscious'			
M1[b]	1	0.92 (0.87, 0.97)	0.90 (0.85, 0.96)
M2[c]	1	0.95 (0.89, 1.02)	0.93 (0.87, 1.00)
M3[d]	1	0.93 (0.87, 0.99)	1.04 (0.97, 1.12)
PCA 2 'Traditional'			
M1	1	0.99 (0.94, 1.05)	0.99 (0.94, 1.06)
M2	1	0.98 (0.93, 1.04)	1.00 (0.94, 1.06)
M3	1	0.99 (0.93, 1.04)	0.98 (0.92, 1.04)
PCA 3 'Processed'			
M1	1	1.00 (0.94, 1.06)	1.00 (0.94, 1.07)
M2	1	0.95 (0.89, 1.01)	0.99 (0.97, 1.06)
M3	1	0.96 (0.90, 1.02)	0.97 (0.90, 1.04)
PCA 4 'Confectionary'			
M1	1	0.92 (0.85, 0.97)	1.05 (0.99, 1.11)
M2	1	0.92 (0.86, 0.97)	1.05 (1.00, 1.12)
M3	1	0.90 (0.85, 0.96)	1.11 (1.05, 1.18)
PCA 5 'Vegetarian'			
M1	1	1.07 (1.01, 1.13)	0.98 (0.92, 1.04)
M2	1	1.08 (1.02, 1.14)	0.98 (0.92, 1.04)
M3	1	1.08 (1.01, 1.13)	1.00 (0.94, 1.06)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

Chapter 7 Discussion

7.1 Main findings

The findings suggest that both women with GDM and women with existing DM were more likely to consume a diet lower in percentage of energy from NMES and higher in percentage energy from protein when compared to women with no diabetes. These women were also less likely to consume the 'confectionary' dietary pattern. This differed from women with glycosuria, who were more likely to consume a diet higher in percentage energy from fat and less likely to consume the 'health conscious' and 'traditional' dietary pattern when compared to women with no diabetes.

There was a significant association between the 'health conscious' and 'confectionary' dietary patterns and inadequate GWG, suggesting women who had weight gain below the IOM recommendations were less likely to consume these patterns, compared to women who gained within the recommendations. The opposite association was seen in the 'confectionary' pattern and excessive GWG, suggesting women above the IOM recommendations were more likely to consume this pattern. A positive association was also found in greater adherence to the 'vegetarian' pattern and inadequate weight gain. However, there was no evidence for an association between energy and macronutrient intake and GWG.

7.2 Macronutrient and dietary intake and glycaemic status

Findings suggested differences in the mean energy, protein, carbohydrate and NMES intake across the groups, those with existing DM (grouped as both type 1 and type 2) and those with GDM consistently had the lowest intakes of energy, macronutrients and NMES. This result was in line expectations, as it was assumed that those with existing diabetes would have received extensive dietary management during and/or prior to their pregnancy, centred around monitoring the intake of carbohydrates (Sheard et al., 2004). It was further assumed that women who had planned their pregnancies would have aimed to achieve good glucose control prior to conceiving and those with unplanned pregnancies would be monitored closely throughout the pregnancy to try and achieve this. In line with the other results, those with existing DM were significantly less likely to consume the 'confectionary' pattern and when compared with those with no DM, this was also seen in the group of women who had GDM.

It was assumed that women with GDM would have a similar intake to those with existing diabetes, although, it is feasible that women with existing DM would have received a longer dietary counselling period than women with GDM. It was also assumed that the women who experienced glycosuria during the pregnancy would not have received any dietary counselling and therefore, may have had a similar intake to those with no diabetes. As they did not meet the criteria of a GDM diagnosis, these women would not have received any dietary counselling regarding the glycosuria; even though this

could indicate that hyperglycaemia is present and if ignored, may affect future diabetes status in subsequent pregnancies (Guariguata et al., 2014).

The exact timing and circumstance of GDM diagnosis is unknown for this sample; there is an indication that there was no national policy on GDM screening in the UK at the time of data collection and practices for testing differed around the country (Scott et al., 2002). However, during the Second International Workshop on GDM in 1984, it was determined that all pregnant women should be screened for glucose intolerance at 24-28 weeks; this recommendation did not change until the Fourth International Workshop on GDM, in 1997, deeming it unnecessary to screen women of a low risk (Negrato and Gomes, 2013). Therefore, if women in this sample were screened for GDM at 24-28 weeks and the dietary data used was collected at 32 weeks gestation; this could suggest that women with GDM had received dietary counselling and made changes to dietary intake from the time of diagnosis to data collection (Dornhurst and Frost, 2002). This reflects the similarity to the diets of women with existing DM and the differences in women with glycosuria.

Interestingly, previous studies have found that an increased intake of energy from fat is associated with increased risk of GDM (Saldana et al., 2004; Ley et al., 2011; Meinila et al., 2015). Although there is evidence that dietary fat influences insulin resistance in the general population and that substituting saturated fat for unsaturated fat is beneficial for insulin sensitivity (Rivellese et al., 2002), there is inconsistent evidence that dietary fat plays a role in the development of GDM/glycosuria (Bowers et al., 2012). In this sample, there was no evidence of an association of fat intake and both women with existing

DM and GDM, however women with glycosuria were found to have a significantly higher intake of percentage of energy from fat reflecting other research on energy, fat and adverse glycaemic status in pregnancy. This supports the assumption that women with glycosuria may not have received appropriate dietary counselling during their pregnancy to reduce hyperglycaemia, whereas women who received a diagnosis of GDM at 28 weeks gestation may have altered their diets according to the counselling received.

Similarly, there is debate in the role of low and high carbohydrate diets in the management of GDM and little is known about the effect of dietary carbohydrate in the prevention of GDM (Mulla, 2016). Findings from a systematic review of 9 RCTs suggests that low glycaemic index (GI) diets are associated with better outcomes in GDM pregnancies, including less insulin use and lower infant birthweight, but found no evidence for reduced total carbohydrate in the diet (Viana et al., 2014). In this sample, there was a significant association of lower carbohydrate intake and women with existing DM, there was evidence of lower carbohydrate in the women with GDM however this was not significant. This could suggest that women who had recently received a GDM diagnosis had not yet altered their carbohydrate intake according to dietary counselling. Women with glycosuria also had a lower intake of carbohydrates when compared to those with no diabetes, although this was not significant. There are no other studies that have shown this.

Conversely to the findings of this study, Radesky et al (2007) reported no significant associations of percentage macronutrient intake and GDM in a prospective study of 1733 women.

Unlike women with GDM and DM, women with glycosuria were significantly less likely to consume the ‘health conscious’ and the ‘traditional’ dietary patterns when compared to those with no diabetes, suggesting their diet could be less nutritionally balanced than those with no diabetes which could have contributed to hyperglycaemia. This supports the assumption that as GDM was diagnosed prior to dietary data collection, dietary counselling was received by women overt GDM.

Previous studies of dietary patterns and diabetes during pregnancy reported that GDM risk was lower with a higher adherence to a Mediterranean style diet (Schoenaker et al., 2015; Tryggvadottir et al., 2016). In the current study women with glycosuria were less likely to adhere to the ‘health conscious’ dietary pattern (similar to the Mediterranean diet). This could be a result of receiving little dietary counselling during the pregnancy, unlike women with GDM and women with existing diabetes.

To our knowledge there is a lack of studies on the influence of macronutrient and dietary intakes in women with hyperglycaemia but without overt GDM. However, current evidence suggests there are a number of adverse outcomes associated with maternal glycaemia (Metzger et al., 2008; Lawlor et al., 2010; Guariguata et al., 2014); suggesting the importance of providing dietary advice for women with glycosuria.

Findings from the Hyperglycaemia and Adverse Pregnancy Outcomes (HAPO) Study (2008) reported that maternal hyperglycaemia, that is less severe than levels of GDM diagnosis, was associated with macrosomia, foetal insulinaemia and increased admission to neonatal care (Metzger et al., 2008). Glycosuria during pregnancy was associated with greater offspring mean BMI and overweight at 9-11 years old, in a sample of 10, 591 ALSPAC mothers (Lawlor et al., 2010). A study of 8,515 ALSPAC mothers found that GDM, existing DM and glycosuria were positively associated with lower offspring IQ, at 8 years old, and educational attainment, at 16 years old (Fraser et al., 2012). Mothers with hyperglycaemia are at a higher risk of pre-eclampsia, caesarean section and hypertension; similar to women exposed to overt diabetes during pregnancy (Guariguata et al., 2014). Hyperglycaemia is also a strong predictor of future maternal T2DM and increases the risk of GDM in subsequent pregnancies (Guariguata et al., 2014).

The findings of the current study suggest that, in line with the assumptions, diets in women with glycosuria differ from those with diagnosed diabetes during pregnancy. As evidence suggests, maternal glycaemic status is associated with perinatal outcomes and the role of diet in this is unknown (Metzger et al., 2008). NICE provide robust guidelines for the management of women with diabetes during pregnancy, yet these are lacking in guidelines for the management of women with hyperglycaemia under the levels of overt GDM diagnosis (National Institute for Health Care and Excellence, 2015). It recommended that women with glycosuria (2+ on one occasion or 1+ on two or more occasions) are further tested for GDM, but no further instruction on

the management of glycosuria, including diet and activity advice, is provided (National Institute for Health Care and Excellence, 2015). This highlights the importance and implications for future research of the impact of dietary advice provided to all pregnant women, who do not receive an overt diagnosis of diabetes.

7.3 Dietary intake and adequacy of gestational weight gain according to IOM

The findings suggest no evidence of an association of energy and macronutrient intake with GWG. However, women who gained less than the recommended weight consumed significantly less energy per day than women who gained excessively and within the IOM guidelines.

As discussed in a review paper by Tobias and Bao (2014), the macronutrient composition of the diet and it's relation to weight management is not yet fully understood in non-pregnant populations, even though this has been extensively researched. As there is a lack of homogeneity in study design and assessment of exposures and outcomes in studies of pregnant populations, it creates difficulty in reaching conclusions in the relevance of macronutrient intake and GWG (Tielemans et al., 2016).

Unlike the current study, Diemert et al. (2016) reported that energy and free sugar intake, assessed using a 24-hour recall method, was positively associated with excessive GWG. This is supported by a systematic review of 12 studies examining energy and macronutrient intake and GWG, which reported increasing energy intake to be associated with increasing GWG

(Tielemans et al., 2016). However, a similar systematic review of 18 studies reported no evidence of an association between energy intake and GWG (Jebeile et al., 2016). Although these reviews examined similar areas, they differed in design; a meta-analysis was applied in one review (Jebeile et al., 2016) whereas narrative synthesis was carried out in the other (Tielemans et al., 2016). There were also methodological differences between these reviews, Jebeile et al. restricted the search dates from 1990-2015 whereas Tielemans et al. did not restrict search dates as is advised by Cochrane (Higgins and Green, 2011). This highlights the inconsistencies in the evidence surrounding the dietary intake and GWG.

The regression analyses for dietary patterns and GWG revealed a significantly lower adherence to the 'health conscious' and the 'confectionary' dietary patterns and a significantly higher adherence to the 'vegetarian' pattern in women who gained less than the recommended weight. There was also a positive association between adherence to the 'confectionary' pattern and excessive gain. Previous findings suggest inconsistent associations between dietary patterns and GWG (Uusitalo et al., 2009; Tielemans et al., 2016).

A study of PCA derived dietary patterns and GWG in Dutch pregnant women, reported a positive association of the 'vegetable, oil and fish' pattern with higher GWG in early pregnancy but only in women of normal weight. There was a positive association of adherence to the 'margarine, sugar and snacks' pattern and women who gained above the IOM recommendation. There were no consistent associations of any dietary pattern and inadequate weight gain, unlike the current study (Tielemans et al., 2015).

In another study examining dietary patterns of Finnish pregnant women and GWG, the ‘fast food’ dietary pattern (higher intakes of energy and sucrose) was significantly associated with a higher rate of gestational weight gain (Uusitalo et al., 2009). This is in contrast to the current study in which lower mean energy intake and adherence to a ‘vegetarian’ dietary pattern (negative loadings of red meat, poultry and fried foods) was associated with lower GWG.

Northstone et al. (2008) reported that dietary patterns were associated with nutrient and energy intake, in the ALSPAC sample. The ‘processed’ and ‘confectionary’ patterns were positively associated with increased fat, carbohydrate and sugar and decreased intakes of all other nutrient, including micronutrients. In contrast to this, the ‘health conscious’ and ‘traditional’ patterns were found to be associated with increased intakes of all nutrients other than fat, carbohydrates and sugar. This suggests that although no evidence of associations of nutrient intake and GWG was found in the current study; the nutrient composition of foods consumed together may provide some insight into GWG.

When examining studies of data-driven dietary patterns and GWG, the associations suggest that different dietary patterns are associated with different rates and adequacy of gain in pregnancy. This highlights the importance of reproducibility between studies of dietary patterns and GWG, as it is difficult to determine a specific recommended dietary pattern to reduce inadequate or excessive gain when methods used to assess GWG vary between studies. Considering *a priori* dietary patterns may help to provide more of an insight into habits and food which are consumed together

rather than looking at the effect single nutrients on weight gain status in pregnancy but also allow comparison between studies.

Weight gain during pregnancy is considered to be a result of positive energy balance and therefore may affected by altered physical activity (Streuling et al., 2011). A meta-analysis of the effects of physical activity interventions on GWG, which included 12 randomised controlled trials, reported that GWG was significantly lower in the physical activity intervention groups when compared with the control groups (Streuling et al., 2011). However, an important limitation of this systematic review is that due to heterogeneity in dietary assessment methods, energy intake was not considered. The suggestion that physical activity limits GWG is supported by a recent meta-analysis of 3203 pregnant women, in which women who enrolled into an intervention of diet and exercise during pregnancy gained significantly less weight when compared with control groups (da Silva et al., 2017). Of the weight gain sample used in the current analysis, 68.1% were physically active during pregnancy. The ALSPAC dataset contained only two questions regarding physical activity of women in this sample (if activity was undertaken at least once a week and how many hours a week, see appendix A) so although the effect of physical activity was adjusted for in these analyses, it was not possible to examine the effect of physical activity and GWG.

There is some evidence to suggest that pregnant women may actually decrease energy expenditure as pregnancy progresses by reducing the intensity and duration of leisure and work-related physical activity (Lof, 2011; Evenson et al., 2004). This may explain some of the excessive weight gain in

this sample, where there are no associations between macronutrient and dietary intake and GWG.

7.4 Strengths and Limitations

A major strength of this study is the consideration of both energy and macronutrient intake and data driven dietary patterns. Dietary pattern analysis is considered useful in describing the overall diet, foods, food groups and nutrients consumed rather than isolating and examining single nutrients (Cespedes and Hu, 2015). This approach provides a more realistic idea of the effects of multiple nutrients consumed together and provides easier translation of research into public health guidelines (Cespedes and Hu, 2015). Although PCA is considered a valuable approach in examining the relationship between dietary intake and disease, there has been some criticism of its use. The PCA approach relies on some subjective decisions and assumptions made by the analyst and dietary patterns vary across different populations, so many not be directly compared across studies (Hu, 2002). However, the combination of PCA and the macronutrient analysis in this study provides more of an insight into the overall dietary intake of this sample.

Another strength is that the dietary data was collected using a detailed FFQ, containing questions about 43 different food groups, which collected the data from the previous 4 weeks. As the FFQ was asking for dietary intakes over a shorted period of time recall bias would be lower compared to asking about intakes over an extended period of time. However, the FFQ did not include portion sizes so standard portion sizes were used; this may have resulted in some under or over-estimation of dietary intakes (Shim et al., 2014).

Although ALSPAC is a large prospective cohort of women who were recruited during pregnancy, there were very small numbers in the groups of women with existing and gestational diabetes. The prevalence of GDM in the sample was relatively low (0.5%) compared with other estimates (Patel et al., 2011), a systematic review examining the prevalence of GDM reported between 1-2% GDM in the UK population at the time of data collection (Farrar et al., 2016). Although it was assumed that the women in this sample were tested for GDM at 24-28 weeks gestation, it is possible that the lack of universal screening and diagnosis at the time resulted in under diagnosis of GDM (Scott et al., 2002).

The sample is considered representative of the UK population at the time (Golding et al., 2001). However, the majority of the ALSPAC sample was white (96.3%) when compared with the last UK census (Office for National Statistics, 2012); which reported 86% of the UK population as white, showing a decrease from the 1991 census in which 95% of the UK population were white (Owen, 1995). Therefore, the ALSPAC sample cannot be assumed to be representative for the current UK population.

It is important to consider the limitations of this study. A number of assumptions were made in the current study, with regards to glycaemic status in the participants. It was assumed that the women with existing diabetes would have received dietary and blood glucose management counselling throughout the pregnancy and prenatally, to maintain glycaemic control. It was assumed that GDM was diagnosed around 24-28 weeks gestation and following diagnosis, women with GDM would have received dietary and lifestyle counselling. It was also assumed that women without a

diagnosis of diabetes/glycosuria and women with glycosuria would have received little to no dietary advice related to glycaemic control during the pregnancy. However, the results presented in this study support these assumptions.

Another important limitation of this study was the use of maternal pre-pregnancy BMI as a mediator in the regression models. The data collected from the ALSPAC sample provided pre-pregnancy BMI as the only measure of weight status during pregnancy. It is recognised that adjusting for a variable which precedes the exposure and outcome can induce confounding into the model (Greenland, 2003). However, there is strong evidence suggesting that there is a relationship between pre-pregnancy weight status and incidence of GDM (Gaillard et al., 2013; Oteng-Ntim et al., 2013; Collier et al., 2016) and adequacy of GWG (Thornton et al., 2009; Heude et al., 2012; Zanardo et al., 2016), so it was considered important to include some form of maternal weight measurement. Pre-pregnancy BMI was included into a separate model and the results show little changes on the estimates.

Another limitation was that diet was measured only once by a single dietary assessment taken at 32 weeks, for intakes from the previous four weeks, so any dietary changes that may have occurred during the pregnancy were not observed. However, some studies have shown diet usually remains consistent throughout pregnancy trimesters, meaning food intake measured at one point is usually unchanged throughout the rest of the pregnancy; unless there has been a specific intervention such as dietary counselling after GDM diagnosis (McGowan and McAuliffe, 2013; Cuco et al., 2006). This can potentially be observed in the current sample, in the similarities of

intakes between the women with GDM and women with existing DM, while the women with glycosuria exhibited different intakes.

It is well recognised that self-reported measures of dietary and energy intake are subject to systematic bias and random variation and recall methods such as FFQ may result in underestimated intakes, particularly in obese subjects (Schoeller, 1995). However, the intakes of the women in this sample were found to be similar to those of a national dietary survey of non-pregnant women at the time and these are consistent with other reports of dietary intakes at the time (Rogers et al., 1998).

Finally, the representativeness of the sample in terms of weight status is an important consideration. According to Heslehurst et al. (2009) maternal obesity rates climbed from 7.6% to 15.6% between 1989 and 2007. The data collection from the current sample took place in 1991-1992 and the mean pre-pregnancy BMI of the sample was found to be 22.9 kg/m^2. Findings from the National Office of Statistics suggest that obesity in the general population was around 27% in 2015 (National Office of Statistics, 2017). It is possible that higher rates of obesity could result in higher rates of gestational weight gain, as pre-pregnancy BMI has been shown to track through the pregnancy (Marshall et al., 2010). Therefore, the current results may not be applicable to UK pregnant women today.

Chapter 8 Conclusions

8.1 Research findings and final conclusions

This research provides evidence of associations between macronutrient intake and specific dietary patterns and gestational diabetes and glycosuria in pregnant women. The findings suggest that women with glycosuria, who do not receive a diagnosis of GDM, may not receive the adequate dietary advice from health professionals aiming to reduce hyperglycaemia and the associated adverse outcomes during pregnancy. This highlights the importance of nutritional guidance for all pregnant women, to reduce the development of GDM rather than focussing only on the management of GDM once it has occurred.

The research has also identified associations of specific dietary patterns and weight gain lower and higher than the IOM weight gain recommendations, suggesting that diet does play a role in GWG

The UK is lacking in specific dietary guidelines to reduce the impact of negative pregnancy outcomes. The evidence presented adds to the evidence base for formulating specific dietary guidelines to avoid adverse glycaemic status and adverse GWG.

8.2 Contribution to existing knowledge

Existing literature demonstrates that adverse maternal conditions during pregnancy can influence maternal and offspring health outcomes in the perinatal period and beyond. Maternal obesity is thought to exacerbate the diabetogenic effects of pregnancy and thus increase health risks for mother and offspring, therefore entering pregnancy in good health and limiting gestational weight gain is important for risk reduction in future pregnancies and health.

The current literature suggests that diet plays a major role in the growth and development of the foetus and can have implications for the health of the mother, although maternal consequences are not as widely researched. Dietary intakes have been linked with characteristics such as adverse gestational weight and incidence of GDM, these conditions are linked with increased need for hospital care and future health care. Pregnancy is thought to provide a ‘teachable moment’ for mothers, in which lifestyle changes can be made to reduce negative pregnancy outcomes.

This research has given an insight into the associations of macronutrient, energy and free sugar intakes and dietary patterns of women at 32 weeks gestation and gestational weight gain and diabetes status during pregnancy. This research has also provided evidence of an association between free sugar intake and gestational weight gain. This research is unique in that it looks at the implications of energy, macronutrient and free sugar intake alongside dietary patterns in the ALSPAC cohort. This adds to the existing literature of the implications of diet in women with GDM and adverse GWG

and highlights some gaps in the research with regards to dietary intakes and these maternal health characteristics.

8.3 Recommendations for future research and practice

The findings of this research highlighted several important areas for future research and practice:

1. There is a lack of robust information on dietary and nutrient intakes during pregnancy (Bath et al., 2014). It is important that national nutritional surveys on the diet of pregnant women are carried out in the UK, to provide an insight into dietary habits and intakes of the whole population including adolescents and ethnic minorities. Prospective cohort studies, supported by well-designed RCTS, are required to deepen the knowledge base on the role of diet in the development of hyperglycaemia and weight gain during pregnancy. Improvements in the design and consistency of assessing exposures and outcomes in nutrition research are needed as it is difficult to build an evidence base when methodological limitations result in a lack of robust results.

2. This research highlighted the lack of studies examining the association between free sugar intake and GWG. As free sugar is a current concern for UK government and the SACN as an energy dense nutrient contributing to the rise in obesity and its comorbidities (SACN, 2015), further investigations of the contribution and effects of high sugar diets in pregnancy.

3. The UK is lacking guidelines for GWG. Evidence from well-designed intervention studies are needed in the UK population to draw an evidence

base for GWG guidelines, based on energy requirements during pregnancy. Maternal and child obesity has rapidly risen in the UK; more women are entering pregnancy as overweight or obese and therefore increasing the risks of weight retention, transgenerational obesity and its comorbid conditions such as T2DM (Heslehurst et al., 2010; Oteng-Ntim et al., 2013). Research in USA populations shows negative outcomes for mother and offspring in women who gain weight outside of the IOM recommendations (Institute of Medicine and Council, 2009). Although goal setting for GWG has been found to be useful in limiting GWG in USA populations (Tovar et al., 2011), it is impossible to set goals for pregnant women in UK when there are no evidence based GWG guidelines. NICE emphasise achieving a healthy weight before and after pregnancy, with no specific recommendations for what constitutes as healthy weight gain during pregnancy (National Institute for Health and Care Excellence, 2010). Yet with no guidelines it is impossible for pregnant women and health care professionals to understand what constitutes a healthy amount of weight gain during pregnancy and to feel empowered to make decisions regarding their pregnancy.

4. A national focus on achieving a healthy diet before and during pregnancy is an important consideration. In 2013, one in six pregnancies were unplanned (Wellings et al., 2013) so achieving optimum health before pregnancy is important. However, nutrition surveys in non-pregnant populations suggest that current UK diets do not meet recommendations for total fat intake, free sugars and fibre (Public Health England, 2016). There is a lack of specific information on the importance of glycaemic and weight control before and during pregnancy, for UK women (Lagan et al., 2011).

Both weight gain and hyperglycaemia, including diabetes during pregnancy, have been shown to have negative effects during and after pregnancy (Guariguata et al., 2014; Heslehurst et al., 2008). Women should be provided with detailed dietary counselling during their antenatal care to facilitate understanding of the importance of a healthy lifestyle.

5. Nutritional education in pregnant women is currently delegated to midwives in the UK (National Institute for Health and Care Excellence, 2008). However current research suggests that midwives feel there are a number of barriers to giving nutritional advice, including lack of time and resources and provision of limited nutrition education (Macleod et al., 2013; Arrish et al., 2017). A collaborative approach from nutrition health professionals, midwives and consultants should be considered, in which nutrition professionals play a defined and active role in the holistic health care of pregnant women in the UK.

9.0 References

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Chapter 9 Appendices

Appendix A Blank copy of the 'Your pregnancy' 32 weeks

YOUR PREGNANCY

This questionnaire asks about how you are now feeling and some questions about your background, and about your plans and preparations for the baby.
Your answers are confidential. Your name will not be on the questionnaire and none of the
doctors or nurses you see will know your answers.
Please answer all the questions you can. If there are any you cannot answer or do not wish to answer that is fine. Just leave them blank
THANK YOU VERY MUCH FOR YOUR HELP

06/02/92
Recycled Paper

FILLING IN THIS BOOKLET
Most of the questions can be answered by ticking the box beside the right answer
For example
How many times have you been to the supermarket in the past week?
None 1 1 2 2-6 3 7 or more 4
This means you went to the supermarket once in the past week
Sometimes there are questions with if in front of them
For example
a) Have you been to the supermarket today?
Yes 1 No 2
This means you didn't go to the supermarket and you don't
need to answer the next question
b) **If yes**, did you buy any carrots?
Yes 1 No 2
In general, though, each question needs an answer
In some questions you may be asked to describe something
It would be helpful if you wrote as clearly as possible
The small numbers in the squares are for office use only
3
SECTION A:PLANS AND EXPECTATIONS
Information about pregnancy
A1 a) Before you became pregnant this time did you read a lot about pregnancy and becoming a parent?
yes, a lot 1
yes, some 2
yes, a little 3
no, I didn't want to 4
no, I didn't have time 5
no, I didn't need to 6
b) Do you have friends or relatives who have children with whom you can discuss your pregnancy?
yes, many 1
yes, some 2
no 3
A2 How would you describe the knowledge you have about having a baby?

	I knew nothing	**I knew a little**	**I knew a lot**
i) before you became pregnant this time	1	2	3
	I know nothing	**I know a little**	**I know quite a lot**
ii) now	1	2	3

A3 a) Have you attended childbirth preparation classes in this pregnancy?
yes 1
no, but intend to 2

no, and don't intend to 3
haven't decided 4
b) Did you attend classes in a previous pregnancy?
Yes 1 No 2 Never been 7
pregnant before
A4 How much do you want to know about what might happen during
labour?
Yes No
i) I'd rather not know anything 1 2
ii) I just want to know the basics 1 2
iii) I want to know most things but
not things that will upset or 1 2
worry me
iv) I'm happy to let the staff
decide how much I ought to 1 2
know
v) I want to know as much as 1 2
possible

4

A5 Which of these options would you prefer ideally?
the most pain-free labour that drugs/ 1
epidural can give me
the minimum amount of drugs to keep 2
the pain manageable
no pain killers at all 3
don't have any opinion 9
other (please describe) 4
A6 Would you like someone you know (husband/partner/mother/friend)
with you at all times throughout your labour?
yes, I want this very much 1
yes, I would quite like this 2
I don't mind 3
no, I would prefer not to have this 4
no, I definitely do not want this 5
A7 Assuming that there are no complications, who do you
think should make the decisions about your labour?
(tick one only)
doctors 1
midwives 2
doctors and midwives 3
doctors, midwives and me together 4
me 5
midwives and me together 6
don't know 9
A8 How important is it to you that t giving birth will be a
wonderful experience?
very important 1
quite important 2
not very important 3
not at all important 4
I don't know 9
A9 a) Do you intend to start work after you have the baby?
Yes 1 No 2 **If no** go to B1
If yes,
b) about how old do you expect the baby will be when you go back to work?
less than 6 weeks 1
6 weeks - 5 months 2
6 months - 12 months 3
over 12 months 4

5

c) Have you decided what sort of child care you will have?
Yes 1 No 2
d) **If yes,** what sort of child care do you expect to use?
Yes No Don't know
i) nanny/childminder in 1 2 9
your home
ii) childminder outside 1 2 9
your home
iii) partner 1 2 9
iv) family 1 2 9
v) nursery/creche 1 2 9
vi) other (please describe) 1 2 9

6

SECTION B:YOUR PRESENT HEALTH
B1 How would you describe your health **in the last two weeks:**

always fit and well 1
usually fit and well 2
sometimes unwell 3
often unwell 4
always unwell 5
B2 **In the last 3 months** have you had any of the following:

	Yes, in last 3 months	**No, not in last 3 months**	**Don't know**
a) nausea	1	2	9
b) vomiting	1	2	9
c) diarrhoea	1	2	9
d) vaginal bleeding	1	2	9
e) jaundice	1	2	9
f) urinary infection	1	2	9
g) a cold	1	2	9
h) influenza (flu)	1	2	9
i) rubella (german measles)	1	2	9
j) thrush (candida)	1	2	9
k) genital herpes	1	2	9
l) other infection (please describe) …….	1	2	9
m) injury or shock to you (please describe) …… …….	1	2	9
n) sugar in urine	1	2	9
o) x-ray	1	2	9
p) amniocentesis (amnio)	1	2	9
q) chorionic villus sampling (CVS)	1	2	9
r) AFP test (spina bifida test)	1	2	9
s) ultrasound scan	1	2	9
t) headache	1	2	9
u) backache	1	2	9
v) varicose veins	1	2	9

B3 a) Have you been admitted to hospital in the last 3 months?
Yes 1 No 2 **If no,** go to B4

If yes, give reason for each admission:

b) **Reason admitted**	**Date**	**Number of days stayed**
i)	/ /199	
ii)	/ /199	
iii)	/ /199	
iv)	/ /199	
v)	/ /199	

B4 In the last 3 months have you used any medicines, pills or ointments for the following:

Medicine, pills, ointment for:	**Yes, in last 3 months**	**No, not in last 3 months**	**Don't know**
a) nausea	1	2	9
b) heartburn	1	2	9
c) vomiting	1	2	9
d) anxiety	1	2	9
e) infection	1	2	9
f) migraine	1	2	9
g) difficulty going to sleep	1	2	9
h) pain	1	2	9
i) allergies	1	2	9
j) skin condition	1	2	9
k) bleeding	1	2	9
l) depression	1	2	9
m) piles	1	2	9
n) constipation	1	2	9
o) cough	1	2	9
p) other reason (please describe)	1	2	9

B5 In the last three months have you been taking any of the following?

	Yes	**No**

a) iron 1 2
b) zinc 1 2
c) calcium 1 2
d) folic acid/folate 1 2
e) vitamins (please describe) 1 2
…… ……
f) other supplements or diet 1
foods (please describe)
…….
B6 Do you ever take homeopathic medicines?
Yes 1 Yes 2 No 3
often sometimes
8
If yes, please list any you have taken this pregnancy: ……
……..
B7 Please indicate how often you have taken the following pills in the last three months

	Every day	**Most days**	**Some- times**	**Not at all**
i) aspirin	1	2	3	4
ii) paracetamol	1	2	3	4
iii) codeine/anadin	1	2	3	4
iv) mogadon, or other sleeping tablets	1	2	3	4
v) valium, or other tranquillisers	1	2	3	4

B8 Please describe all pills, med icines and ointments you have taken or used **in the past 3 months**, including those listed above

	What did you take: (give exact name if you can) or use it?	**About how many days did you take it?**	**How many weeks pregnant were you?**
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

Check Have you included the contraceptive pill, iron tablets, laxatives, vitamins, sleeping tablets,
aspirin, cough mixture, pain killers, indigestion tablets, herbal medicine?
If you need more room continue on extra page
9
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
e) Liver, liver pate, kidney, heart	1	2	3	4	5
f) White fish (cod, haddock, plaice, fish fingers etc)	1	2	3	4	5
g) Other fish (pilchards, sardines, mackerel, tuna, herring, kippers, trout, salmon etc)	1	2	3	4	5
h) Shellfish (prawns, crab, cockles, mussels etc)	1	2	3	4	5
i) Eggs, quiche	1	2	3	4	5
j) Cheese	1	2	3	4	5
k) Pizza	1	2	3	4	5
l) Chips	1	2	3	4	5
m) Roast potatoes (cooked in fat)	1	2	3	4	5
n) Boiled, mashed, jacket potatoes	1	2	3	4	5

o) Rice (boiled) 1 2 3 4 5
p) Pasta (egspaghetti, Pot 1 2 3 4 5
Noodles, lasagna)
q) Crisps 1 2 3 4 5
r) Fried foods (egfried fish,
eggs, bacon, chops etc) 1 2 3 4 5
C2 Do you eat the fat on meat?
yes, all of it 1
yes, some of it 2
no 3
never eat meat 4

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C3 How many times a week nowadays do you eat:

Never or rarely | **Once in a week** | **1 - 3 times a week** | **4 - 7 times a week** | **More than once a day**

a) Baked beans 1 2 3 4 5
b) Peas, sweetcorn, broad 1 2 3 4 5
beans
c) Cabbage, brussel sprouts, 1 2 3 4 5
kale and other green leafy
vegetables
d) Other green vegetables 1 2 3 4 5
(cauliflower, runner beans,
leeks etc.)
e) Carrots 1 2 3 4 5
f) Other root vegetables 1 2 3 4 5
(turnip, swede, parsnip etc.)
g) Salad (lettuce, tomato, 1 2 3 4 5
cucumber etc.)
h) Fresh fruit (apple,
pear, banana, orange, 1 2 3 4 5
bunch of grapes etc.)
i) Tinned juice (including 1 2 3 4 5
tomato juice)
j) Pure juice not in tin 1 2 3 4 5
k) Pudding (e.g. fruit pie,
crumble, cheesecake, milk 1 2 3 4 5
pudding, mousse, gateaux)
l) Oat cereals (e.g. porridge, 1 2 3 4 5
Ready Brek, muesli)
m) Wholegrain or bran cereals
(e.g. All Bran, Bran Flakes, 1 2 3 4 5
Weetabix, Wheatflakes,
Fruit & Fibre)
n) Other cereals (e.g. Cornflakes,
Rice Krispies, 1 2 3 4 5
Special K, Frosties)
o) Cakes or buns (fruit cake,
sponge, teacake, buns, 1 2 3 4 5
doughnut, flapjack, scone,
custard tart, cream cake
etc.)
p) Crispbreads (Ryvita, 1 2 3 4 5
crackerbread etc.)
q) Biscuits (digestive,
shortcake, Hob Nobs, 1 2 3 4 5
Rich Tea, Nice, Marie,
chocolate biscuits,
Penguin, Club, Kit Kat etc.)
r) Chocolate bars (Mars,
Twix, Wispa, Bounty, 1 2 3 4 5
Creme Egg etc.)
s) Pulses - dried peas, 1 2 3 4 5
beans, lentils, chick peas
t) Nuts, nut roast 1 2 3 4 5
u) Bean Curd (e.g. Tofu, miso) 1 2 3 4 5
v) Tahini 1 2 3 4 5
w) Soya 'Meat', T V P , 1 2 3 4 5
Vegeburgers

11

Never or rarely | **Once in a week** | **1 - 3 times a week** | **4 - 7 times a week** | **More than once a day**

x) Chocolate (dairy milk

or plain, nut, fruit 1 2 3 4 5
filled etc.)
y) Sweets (peppermints,
boiled sweets, toffees 1 2 3 4 5
etc.)
C4 When you have a soft drink, how often do you choose low calorie or diet drinks?
always 1
sometimes 2
not at all 3
don't drink soft drinks 7
C5 How many pieces of bread, rolls or chappatis do you eat on a usual day ?
less than 1 1 1-2 2 3-4 3 5 or more 4
C6 How many times in a month do you eat take-away foods for your main meal?
never or rarely 1
1 - 2 2
3 - 4 3
5 - 9 4
10 or more 5
C7 What types of bread do you eat most days?

	Yes	**No**
a) white bread	1	2
b) brown/granary bread	1	2
c) wholemeal bread	1	2
d) chappatis, nan bread	1	2
e) don't usually eat any bread	1	2

C8 What sort of fat do you mainly use:

	(i) On bread or vegetables Yes	**(i) On bread or vegetables No**	**(ii) For frying Yes**	**(ii) For frying No**
a) Butter, Ghee, Dripping Lard, solid cooking fat	1	2	1	2
b) Hard or soft margarine e.g. Blue Band, Stork, supermarket own brand	1	2	1	2
c) Polyunsaturated margarine e.g. Flora, sunflower, Vitalite	1	2	1	2
d) Low fat spread e g Outline, Delight, St Ivel Gold	1	2	1	2
e) Sunflower, soya, corn, olive oil	1	2	1	2
f) Other vegetable oil	1	2	1	2

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g) Other (please describe)	1	2 1 2

C9 How many slices of bread (or rolls) spread with fat do you eat each day?(include bought sandwiches) slices
C10 What type(s) of milk do you use?

	Yes usually	**Yes sometimes**	**No not at all**
a) Full fat (silver or gold top)	1	2	3
b) Semi Skimmed (red stripe)	1	2	3
c) Skimmed (blue stripe)	1	2	3
d) Sterilised	1	2	3
e) Dried milk	1	2	3
f) Goat/sheep milk	1	2	3
g) Soya milk	1	2	3
h) Other (please describe)	1	2	3

C11 How often do you have milk:

	Yes usually	**Yes sometimes**	**No not at all**
a) In tea	1	2	3
b) In coffee	1	2	3
c) On breakfast cereal	1	2	3
d) As pudding (custard,rice)	1	2	3
e) To drink on its own	1	2	3
f) As a milky drink (Horlicks, cocoa, all milk coffee)	1	2	3

C12 a) How many cups of tea do you drink in a day? cups
(do not include herbal teas)
b) How many spoons of sugar in each cup? spoons
c) How many of the cups of tea you drink each day cups
are decaffeinated?

d) How many cups of coffee do you drink in a day? cups
e) How many spoons of sugar in each cup? spoons
f) How many of the cups of coffee you drink cups
each day are decaffeinated?
g) How many of the cups of coffee you drink each cups
day are made using real coffee (ienot instant)?
h) How many of these are decaffeinated? cups
C13 a) How many drinks of cola do you have **in a week**? drinks
b) How many of these drinks are decaffeinated? drinks
C14 a) Do you drink herbal teas at all?
yes, often 1 yes, occasionally 2 no, not at all 3
If no, go to C15

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If yes,
b) how many cups/mugs of herbal teas have you cups/mugs
drunk in the past week?
c) Please list the types of herbal teas you have drunk in the past 3 months:
C15 Do you buy organic foods?

	Yes, usually organic	**Yes, some- times organic**	**No, never organic**
a) fruit	1	2	3
b) vegetables	1	2	3
c) meat	1	2	3
d) other (please describe)	1	2	3

C16 Apart from herbal teas, are there any other health foods (whether or not
bought from a health food shop) that you often eat or drink?
Yes 1 No 2
If yes, please describe below:
C17 a) Have you been on a diet this pregnancy?
Yes 1 No 2
If yes, please describe the type of diet:
C17 b) Apart from this pregnancy have you ever gone on a diet to lose weight?
Yes 1 No 2
If yes,
c) how often?
1-2 1 3-5 2 6-10 3 more than 10 times 4
d) how long do your diets usually last?
under 1 month 1 1-3 months 2 more than 3 months 3
C18 a) Are you, or have you ever been a vegetarian?
yes, I am now 1 yes, in past not now 2 no, never 3
If yes,
b) how many years of your life have you been vegetarian?
years (If less than one year put 00)
C19 a) Are you, or have you ever been, a vegan (ie do not eat meat, poultry,
fish, eggs, butter, milk or cheese)?
yes, I am now 1 yes, in past not now 2 no, never 3
If yes,

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b) how many years of your life have you been vegan?
years (If less than one year put 00)

	Yes, most of the time	**Yes, occasionally**	**No, not at all**
C20 Do you now feel you've put on too much weight?	1	2	3
C21 Do you feel uncomfortable seeing your body in the mirror?	1	2	3
C22 Have you had a strong desire to lose weight at any time during this pregnancy?	1	2	3
C23 Do you feel dissatisfied about your shape?	1	2	3
C24 Have you experienced any loss of control over eating during this pregnancy?	1	2	3
C25 Are you concerned about losing any extra weight you've gained in this	1	2	3

pregnancy?
C26 How many days in the past month have you drunk the equivalent of 2 pints of beer, 4 glasses of wine or 4 pub measures of spirit?
everyday 5 more than 10 days 4
5-10 days 3 3-4 days 2
1-2 days 1 none 0
C27 At present how much of the following do you usually drink in a day:

At present	**Weekday**	**Weekend day**
a) beer or lager (half-pints)		
b) wine (glasses)		
c) spirits (pub-measures)		
d) other alcoholic drinks (pub measures)		

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SECTION D:YOUR OWN CHILDHOOD

Please indicate if any of the following events happened to you before you were 17 and how much it affected you.

Before you were 17:	**Yes, affected me a lot**	**Yes moderately**	**Yes mildly**	**Yes but did not affect me**	**No not happen**
D1 Your parent died	1	2	3	4	5
D2 A brother or sister died	1	2	3	4	5
D3 A relative died	1	2	3	4	5
D4 A friend died	1	2	3	4	5
D5 A parent had a serious illness	1	2	3	4	5
D6 A parent was in hospital	1	2	3	4	5
D7 You had a serious physical illness	1	2	3	4	5
D8 You were in hospital	1	2	3	4	5
D9 Brother or sister had a serious illness	1	2	3	4	5
D10 Brother or sister was in hospital	1	2	3	4	5
D11 A parent had a serious accident	1	2	3	4	5
D12 You had a serious accident	1	2	3	4	5
D13 Brother or sister had a serious accident	1	2	3	4	5
D14 You acquired a physical deformity	1	2	3	4	5
D15 You became pregnant	1	2	3	4	5
D16 A parent was imprisoned	1	2	3	4	5
D17 A parent was physically cruel to you	1	2	3	4	5
D18 Your parents separated	1	2	3	4	5

Before you were 17:	**Yes affected me a lot**	**Yes moderately**	**Yes mildly**	**Yes but did not affect me**	**No not happen**
D19 Your parents divorced	1	2	3	4	5
D20 A parent remarried	1	2	3	4	5
D21 A parent was emotionally cruel to you	1	2	3	4	5
D22 Your parents had serious arguments	1	2	3	4	5
D23 You were sexually abused	1	2	3	4	5
D24 A parent was mentally ill	1	2	3	4	5
D25 You discovered you were adopted	1	2	3	4	5

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Before you were 17:	**Yes affected me a lot**	**Yes moderately**	**Yes mildly**	**Yes but did not affect me**	**No not happen**
D26 Your family moved to a new district	1	2	3	4	5
D27 You were in trouble with the police	1	2	3	4	5
D28 You were expelled or	1	2	3	4	5

suspended from school
D29 You failed an important 1 2 3 4 5
exam
D30 Your family's financial 1 2 3 4 5
circumstances got worse
D31 You acquired a step- 1 2 3 4 5
brother or stepsister
D32 Other important happening 1 2 3 4 5
(please tick & describe)
D33 How many schools did you attend between the
ages of 5 and 16?
D34 Looking back would you call your childhood happy?
Please indicate for each age range:

	Yes very happy	**Yes moderately happy**	**Not really happy**	**No unhappy**	**No quite unhappy**	**No very unhappy**	**Can't remember**
i) 0-5 years	1	2	3	4	5	6	
ii) 6-11 years	1	2	3	4	5	6	
iii) 12-15 years	1	2	3	4	5	6	

D35 How many brothers and sisters did you have:

	Brothers	**Sisters**
a) older than you		
b) younger than you		

c) did you have a twin?
yes, twin brother 1
yes, twin sister 2
no 3
If you had a twin sister:
i) were you identical twins?
yes 1 no 2 not sure 3
ii) did you usually dress alike?
yes, usually 1 yes, sometimes 2 no, not at all 3

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SECTION E:YOUR ENVIRONMENT AND LIFESTYLE

E1 a) Are you living in the same home that you were in at the start of your pregnancy?
Yes 1 No 2
b) **If no,** how many times have you moved?
c) Have you been homeless at any time during this pregnancy?
Yes 1 No 2
d) Have we sent this questionnaire to your correct address?
Yes 1 No 2
If no, please telephone Bristol 256260 or send a card with your new address, quoting your contact number
e) Are you intending to move house in the near future?
Yes 1 No 2
If yes, please let us know your new address on the back cover
E2 Please indicate how often during the day you are in a room or enclosed place where other people are smoking:

	(i) Weekdays	**(ii) Weekends**
all the time	1	1
more than 5 hours	2	2
3-5 hours	3	3
1-2 hours	4	4
less than 1 hour	5	5
not at all	6	6

E3 How many cigarettes per day are you yourself smoking at the moment cigarettes
E4 a) Are you currently in paid work?
Yes 1 No 2
If yes, go to Question E5
b) Have you worked at all during this pregnancy?
Yes 1 No 2 **If no,** go to E6
c) What date did you stop work? / /19
d) What was the main reason?
ill health 1
tiredness 2
company rules 3
to prepare for the baby 4
other (please describe) 5
e) Are you now on paid maternity leave?
Yes 1 No 2

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E5 a) If you are working, how many hours per week do you work? hours

b) Do you do shift work?
Yes 1 No 2
c) **If yes**, does this include night shift?
Yes 1 No 2
E6 Which of the following statements best applied to you, in the last 3 months and now:

	Very energetic	**Quite energetic**	**Lacking in energy**
a) in the last 3 months	1	2	3
b) nowadays	1	2	3

E6 c) Compared with other pregnant women of your age, would you consider yourself to be:
much more active 1
somewhat more active 2
about the same 3
somewhat less active 4
much less active 5
d) Nowadays, at least once a week do you engage in any regular activity like brisk walking, gardening, housework, jogging, cycling, etc long enough to work up a sweat?
Yes 1 No 2
e) **If yes**, how many hours a week: hours
E7 In a normal day now, whether at home or not, do you:

	Yes often	**Yes sometimes**	**No not at all**
a) lift and carry young children	1	2	3
b) lift and carry heavy objects (more than 10kg or 20lb)	1	2	3
c) bend and stoop	1	2	3
d) have rest periods	1	2	3
e) use vibrating machinery	1	2	3

E8 How difficult at the moment do you find it to afford these items:

	Very difficult	**Fairly difficult**	**Slightly difficult**	**Not difficult**
a) Food	1	2	3	4
b) Clothing	1	2	3	4
c) Heating	1	2	3	4
d) Rent or mortgage	1	2	3	4
e) Things you will	1	2	3	4

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SECTION F:YOUR FEELINGS
The questions in this section ask you about your feelings and the way you behave nowadays Please indicate the way you feel

	Very Often	**Often**	**Not very often**	**Never**
F1 Do you feel upset for no obvious reason?	1	2	3	4
F2 Do you get troubled by dizziness or shortness of breath?	1	2	3	4
F3 Have you felt as though you might faint?	1	2	3	4
F4 Do you feel sick or have indigestion?	1	2	3	4
F5 Do you feel that life is too much effort?	1	2	3	4
F6 Do you feel uneasy and restless?	1	2	3	4
F7 Do you feel tingling or prickling sensations in your body, arms or legs?	1	2	3	4
F8 Do you regret much of your past behaviour?	1	2	3	4
F9 Do you sometimes feel panicky?	1	2	3	4
F10 Do you find that you have little or no appetite?	1	2	3	4
F11 Do you wake unusually early in the morning?	1	2	3	4
F12 Do you worry a lot?	1	2	3	4
F13 Do you feel tired or exhausted?	1	2	3	4
F14 Do you experience long				

periods of sadness? 1 2 3 4
F15 Do you feel strung-up
inside? 1 2 3 4
F16 Can you get off to
sleep alright? 1 2 3 4
F17 Do you ever have the
feeling you are 1 2 3 4
going to pieces?
F18 Do you often have
excessive sweating 1 2 3 4
or fluttering of
the heart?
F19 Do you find yourself 1 2 3 4
needing to cry?
F20 Do you have bad
dreams which upset 1 2 3 4
you when you wake up?
F21 Do you lose the
ability to feel 1 2 3 4
sympathy for others?
F22 Can you think as
quickly as you used 1 2 3 4

to?

Very Often Not very Never
often often

F23 Do you have to make
a special effort to 1 2 3 4
face up to a crisis
or difficulty?

Your feelings in the past week

F24 I have been able to laugh and see the funny side of things:
As much as I always could 1
Not quite so much now 2
Definitely not so much now 3
Not at all 4
F25 I have looked forward with enjoyment to things:
As much as I ever did 1
Rather less than I used to 2
Definitely less than I used to 3
Hardly at all 4

Your feelings in the past week

F26 I have blamed myself unnecessarily when things went wrong:
Yes, most of the time 1
Yes, some of the time 2
Not very often 3
No, never 4
F27 I have been anxious or worried for no good reason:
No, not at all 1
Hardly ever 2
Yes, sometimes 3
Yes, often 4
F28 I have felt scared or panicky for no very good reason:
Yes, quite a lot 1
Yes, sometimes 2
No, not much 3
No, not at all 4
F29 Things have been getting on top of me:
Yes, most of the time 1
Yes, sometimes 2
No, hardly ever 3
No, not at all 4

In the past week

F30 I have been so unhappy that I have had difficulty sleeping:
Yes, most of the time 1
Yes, sometimes 2
Not very often 3
No, not at all 4
F31 I have felt sad or miserable:
Yes, most of the time 1
Yes, quite often 2
Not very often 3
No, not at all 4
F32 I have been so unhappy that I have been crying:

Yes, most of the time 1
Yes, quite often 2
Only occasionally 3
No, never 4
F33 The thought of harming myself has occurred to me:
Yes, quite often 1
Sometimes 2
Hardly ever 3
Never 4

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SECTION G:INFANT FEEDING

Below are some attitudes about infant feeding often expressed by mothers
What do you feel?

Strongly Agree Unsure Disagree Strongly
agree disagree

G1 Breast-feeding stops a mother
from having the freedom to 1 2 3 4 5
do what she wants
G2 Breast-feeding gives the mother
a special relationship with 1 2 3 4 5
her baby
G3 Bottle-feeding allows the
father to share the child 1 2 3 4 5
more
G4 Breast milk is better for the 1 2 3 4 5
baby
G5 Bottle-feeding is more 1 2 3 4 5
convenient for the mother
G6 A mother who does not breast 1 2 3 4 5
feed is inferior
G7 Breast-feeding is difficult 1 2 3 4 5

G8 How are you going to feed your baby:

Breast Bottle Both Uncertain

a) in the first week 1 2 3 4
b) in the first month 1 2 3 4
c) in the next 3 months 1 2 3 4

G9 How does your partner want you to feed the baby?
don't know 1
no strong feelings 2
undecided 3 don't have a partner 7
wants me to breast feed 4
wants me to bottle feed 5

G10 Were you breast fed as a baby?
Yes 1 No 2 Don't know 9

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SECTION H:EDUCATION AND OCCUPATION

H1 What educational qualifications do you, your partner, your mother,
and your father have? Please tick all that apply

(i) (ii) (iii) (iv)
Your Your Your Your
self partner mother* father*

a) CSE or GCSE (D, E, F or G) 1 1 1 1
b) O-level or GCSE (A, B or C) 1 1 1 1
c) A-level 1 1 1 1
d) Qualifications in shorthand/
typing/or other skills, 1 1 1 1
e g hairdressing
e) Apprenticeship 1 1 1 1
f) State enrolled nurse 1 1 1 1
g) State registered nurse 1 1 1 1
h) City & Guilds intermediate 1 1 1 1
technical
i) City & Guilds final 1 1 1 1
technical
j) City & Guilds full 1 1 1 1
technical
k) Teaching qualification 1 1 1 1
l) University degree 1 1 1 1
m) No qualifications 1 1 1 1
n) Qualifications not known 1 1 1 1
o) Not applicable, no such 1 1 1 1
person
p) Other (please describe) 1 1 1 1

[* by this we mean the mother figure or father figure who was mostly responsible for bringing you up]

H2 What is the present employment situation of yourself and your partner?
Please tick all that apply

	(i) Yourself	(ii) Your partner
a) Working for an employer full-time (more than 30 hours a week)	1	1
b) Working for an employer part-time (one hour or more a week)	1	1
c) Self-employed, employing other people	1	1
d) Self-employed, not employing other people	1	1
e) On a government employment or training scheme	1	1
f) Waiting to start a job already accepted	1	1
g) Unemployed and looking for a job	1	1
h) At school or in other full-time education	1	1
i) Unable to work because of long- term sickness or disability	1	1

j) Retired from paid work	1	1
k) Looking after the home or family	1	1
l) Other (please describe)	1	1

H3 If your partner is not currently in paid employment w hen did his last job end?
Date your partner stopped working / /19
(If you are unsure, put an approximate date, e.g March 1988)
The questions below ask about your current occupation and that of your partner
H4 As far as you can, please describe the actual job, occupation, trade or profession (Use precise terms such as radio mechanic, woodworking machinist, tool-room foreman If the occupation is known by a special name, please use that name If in H M Forces, give the rank in addition to the actual job Please also describe the type of industry or service given: i.e. Give details of what is made, materials used, or services given)
a) **Your present job or last main job**
i) Actual job, occupation, trade or profession
ii) Hours worked per week:
iii) Please tick which of the following apply to you:
foreman 1
manager 2
supervisor 3
leading hand 4
self-employed 5
none of these 6
iv) Type of industry or service given (main things done in job):
…….
b) **Your partner** - present job or last main job
i) Do you currently have a partner?
Yes 1 No 2
If no, go to H5
ii) **If yes**, what is/was his actual job, occupation, trade or profession?
H4 b) ii) Hours worked per week:
iii) Please tick which of the following apply to him:
foreman 1
manager 2
supervisor 3
leading hand 4
self-employed 5
none of these 6
not known 9
iv) Type of industry or service given (main things done in job):

v) Is he in contact with particular fumes or chemicals in his job?
always1 often 2 sometimes 3
rarely4 never 5 don't 9
know
If yes, please describe:
H5 a) **The main job your mother or mother figure did at around the time you left school** (Please put HW if she was a housewife)
i) Actual job, occupation, trade or profession:
……..

ii) Type of industry or service given (main things done in job):
……..
H5 b) How old was your natural mother when you years were born? (If you don't know, put 99)
Yes No Don't know
c) Is your natural mother still alive? 1 2 9
H6 a) **The main job your father or father figure did at around the time you left school** (If not known put NK)
i) Actual job, occupation, trade or profession:
……..
ii) Please tick which of the following applied to him:
foreman 1
manager 2
supervisor 3
leading hand 4
self-employed 5
none of these 6
iii) Type of Industry or service given (main things done in job):
……..
b) How old was your natural father when you years were born? (If you don't know, put 99)
Yes No Don't know
c) Is your natural father still alive? 1 2 9
Problems
H7 Do you think you have been unfairly/unjustly treated in the last 12 months because of: **Yes Yes No not often sometimes at all**
a) your sex 1 2 3
b) your skin colour 1 2 3
c) the way you dress 1 2 3

d) your family background 1 2 3
e) the way you speak 1 2 3
Yes Yes No not often sometimes at all
f) your religion 1 2 3
g) other (please describe) 1 2 3
H8 How would you describe the race or ethnic group of yourself, your partner and your parents?
(i) (ii) (iii) (iv)
Yourself Partner Your mother* Your father*
white 01 01 01 01
black/Caribbean 02 02 02 02
black/African 03 03 03 03
black/other 04 04 04 04
(please describe below)
Indian 05 05 05 05
Pakistani 06 06 06 06
Bangladeshi 07 07 07 07
Chinese 08 08 08 08
any other ethnic group 09 09 09 09
(please describe)
(*by this we mean the mother or father figure who was mostly responsible for bringing you up)

SECTION I:BEING A PARENT
Below are a number of statements about how some people think a parent should behave with a baby Please indicate how much you agree with them
Yes, I I'm unsure I'm unsure No, I agree but probably but probably disagree agree disagree
I1 Babies should be picked up whenever they cry 1 2 3 4
I2 It is important to develop a regular pattern of feeding and sleeping with a baby 1 2 3 4
I3 Babies should be fed whenever they are hungry 1 2 3 4
I4 Babies need to be

stimulated if they 1 2 3 4
are to develop well
I5 Babies need quiet
secure surroundings 1 2 3 4
and should not be
disturbed too much
I6 Parents need to 1 2 3 4
adapt their lives
to the baby's demands
I7 A baby should fit into 1 2 3 4
its parents routine
I8 Babies should be
left to develop 1 2 3 4
naturally
I9 Talking, to even a
very young baby, is 1 2 3 4
important
I10 Cuddling a baby is 1 2 3 4
very important
I11 What is the youngest age at which you think it is alright for a mother to leave her child regularly in the care of another person during the day?
0 - 5 months1 6 - 11 months 2 1 - 2 years3
3 - 4 years 4 5 years or more 5 never 6
don't know9

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SECTION J

J1 Please put the date of completing this part of the questionnaire:
day month year
199
J2 Please give your date of birth:
day month year
19
Thank you for your help so far
These next pages are concerned with early sexual experience
IF YOU WOULD RATHER NOT ANSWER THEM, WE QUITE UNDERSTANDJUST
STOP NOW AND SEND THE QUESTIONNAIRE BACK AS USUAL
But it is possible that whether or not such events have taken place they may be a vital clue in understanding some of the problems we are trying to solve - even though they may appear to be unconnected. If you feel you can help, we would be very grateful

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SECTION K

As we are growing up we all have sexual experiences These are a normal part of development and learning Some people also have unwanted experiences to which they do not agree These experiences can be important and may affect how you feel about yourself, your partner and your baby Below are questions which ask about your sexual experiences from childhood until the present time
K1 Did anyone ever purposefully expose/flash themselves to you before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3
If yes,
(i) (ii)
Who was involved? **If yes,** did you want this to happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) girl friend 1 2 1 2 9
c) parent or parent 1 2 1 2 9
figure
d) brother or sister 1 2 1 2 9
e) other relative 1 2 1 2 9
f) family friend 1 2 1 2 9
g) stranger 1 2 1 2 9
h) other person 1 2 1 2 9
(please describe)
iii) how old were you when this first happened: years
K2 Did anyone masturbate in front of you before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3
If yes,
(i) (ii)
Who was involved? If yes, did you want this to

happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) girl friend 1 2 1 2 9
c) parent or parent 1 2 1 2 9
figure
d) brother or sister 1 2 1 2 9
e) other relative 1 2 1 2 9
f) family friend 1 2 1 2 9
g) stranger 1 2 1 2 9
h) other person 1 2 1 2 9
(please describe)
iii) how old were you when this first happened: years
30
31
K3 Did anyone ever touch or fondle your body, including your breast or genitals, or attempt to arouse you sexually before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3
If yes,
(i) (ii)
Who was involved? If yes, did you want this to happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) girl friend 1 2 1 2 9
c) parent or parent 1 2 1 2 9
figure
d) brother or sister 1 2 1 2 9
e) other relative 1 2 1 2 9
f) family friend 1 2 1 2 9
g) stranger 1 2 1 2 9
h) other person 1 2 1 2 9
(please describe)
iii) how old were you when this first happened: years
K4 Did anyone try to have you arouse them, or touch their body in a sexual way before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3
If yes,
(i) (ii)
Who was involved? If yes, did you want this to happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) girl friend 1 2 1 2 9
c) parent or parent 1 2 1 2 9
figure
d) brother or sister 1 2 1 2 9
e) other relative 1 2 1 2 9
f) family friend 1 2 1 2 9
g) stranger 1 2 1 2 9
h) other person 1 2 1 2 9
please describe)
32
iii) how old were you when this first happened: years
K5 Did anybody rub their genitals against your body in a sexual way before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3
If yes,
(i) (ii)
Who was involved? If yes, did you want this to happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) girl friend 1 2 1 2 9
c) parent or parent 1 2 1 2 9
figure
d) brother or sister1 2 1 2 9
e) other relative 1 2 1 2 9
f) family friend 1 2 1 2 9

g) stranger 1 2 1 2 9
h) other person 1 2 1 2 9
(please describe)
iii) how old were you when this first happened: years
K6 Did anyone have sexual intercourse with you before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3
If yes,
(i) (ii)
Who was involved? If yes, did you want this to happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) girl friend 1 2 1 2 9
c) parent or parent 1 2 1 2 9
figure
d) brother or sister 1 2 1 2 9
e) other relative 1 2 1 2 9
f) family friend 1 2 1 2 9
g) stranger 1 2 1 2 9
h) other person 1 2 1 2 9
(please describe)
iii) how old were you when this first happened: years
K7 Did anyone ever try to put their penis into your mouth before you were 16?
Yes, happened once only 1
Yes, happened more than once 2
No, did not happen 3

If yes,
(i) (ii)
Who was involved? If yes, did you want this to happen with this person?
No Yes No Yes Unsure
a) boy friend 1 2 1 2 9
b) father or father 1 2 1 2 9
figure
c) brother 1 2 1 2 9
d) other relative 1 2 1 2 9
e) family friend 1 2 1 2 9
f) stranger 1 2 1 2 9
g) other person 1 2 1 2 9
(please describe)
iii) how old were you when this first happened: years
Thank you for answering these questions which we realise may be difficult to answer If
there are any comments you'd like to make please write them below
VERY MANY THANKS FOR ALL YOUR HELP
When completed, put in the envelope provided and either bring to the clinic or post to:
Dr Jean Golding,
Children of the Nineties - ALSPAC,
Institute of Child Health,
24 Tyndall Avenue,
Bristol
BS8 1BR
Please remember, because this is strictly confidential, the people who look at this booklet will not know your name They will be unable to give you any help or contact anyone after reading what you have written If you feel you need advice, please feel free to contact our special information line (Bristol 256260 during office hours) Alternatively your Midwife or General Practitioner should be able to advise you

Appendix B Blank copy of data extraction form used in systematic review

DATA EXTRACTION FORM

Reviewer ID		First Author & contact	
Report ID		Year published	
Date Reviewed		Journal	
Title			

PICOS

Population	Pregnant women, >18 years, singleton pregnancies, term deliveries
Exposure	Free sugar intake
Outcome	Gestational weight gain
Study Design	RCT, ecological, cross sectional, cohort, case-control

STUDY DETAILS

Study aim			
Study design description			
How was the study randomised (if applicable)			
Who (if any) was blinded?			
Study Design		Recruitment year(s)	
Country of Study			
Source of Funding		Potential Conflict (Y/N)	

PARTICIPANTS:

Describe the participants:	
Participant inclusion criteria	
Participant exclusion criteria	
Number recruited	
Method of recruitment?	
Do participants meet PICOS criteria Yes ☐ No ☐ →**Exclude** Unclear ☐	

METHODS:

Describe methods:

Years of study duration	
Exposure – free sugar intake	
Dietary info collected at? (stage of pregnancy)	
Dietary collection tool (FFQ, 24hr recall etc)	
Validated or not validated?	
Period of time diet info collected for	
Measurement of dietary intake (% intake, kcal etc)	
Is free sugar collected? (Y/N)	
Write to authors? (Y/N)	
Date authors contacted	
Does study meet criteria Yes ☐ No ☐ →**Exclude** Unclear ☐	**Reason:**
Reviewer notes:	
Outcome – gestational weight gain	
Pre-pregnancy weight measured? (if yes method?)	
Total number of WG measurements	
Trimester/gestation of WG measurements	
WG during pregnancy measured or self-reported?	
Definition/Calculation of total GWG	
Further definition/calculation of GWG (i.e. in trimester, rate of)	
Was adequacy of GWG measured? How? (i.e. IOM etc)	
Do self-reported measurements correlate with measurements by practitioner?	
Reviewer notes:	
Does study meet criteria Yes ☐ No ☐ →**Exclude** Unclear ☐	**Reason:**

Intervention details (leave blank if N/A)	
Length/duration of intervention	
Characteristics of intervention group	
Describe key features of intervention	
Characteristics of control group	
Describe key features of control (if any)	

COVARIATES

Covariate info obtained from (questionnaires etc)	
Statistical analysis	
Model 1	
Model 2	
Model 3	
Missing data reported?	
Sensitivity analysis	
Notes	
Does study meet criteria Yes ☐ No ☐ →**Exclude** Unclear ☐	**Reason:**

RESULTS

Socio-demographics

Percentage of participants completed the study	
Age (median, mean and range)	
Pre-pregnancy BMI (km/m2)	
Race/ethnicity	
Social economic status	
Education level	
Parity	
Household income	
Energy (kcal, %, etc)	
Did the participants have GDM	
Did the participants have pre-eclampsia	
Were groups with missing data comparable?	
Subgroups to be reported	
Reviewer notes:	

Socio-demographics (intervention studies)

	Intervention	Control
Percentage of participants completed the study		
Age (median, mean and range)		
Pre-pregnancy BMI (km/m2)		
Race/ethnicity		
Social economic status		
Education level		
Parity		
Household income		
Energy intake (kcal, %, etc)		
Did the participants have GDM		
Did the participants have pre-eclampsia		
Were groups with missing data comparable to?		

Subgroups to be reported		
Reviewer notes:		

Outcome

Total number of participants					
Underweight BMI (% and n)		Normal BMI (% and n)			
Overweight BMI (% and n)		Obese BMI (% and n)			
Adequacy of weight gain					
Institute of Medicine categories (%, n etc)	Underweight	Normal BMI	Overweight	Obese	Overall
Inadequate					
Adequate					
Excessive					
Trimester of pregnancy	1st	2nd	3rd		
GWG g/week					
Total GWG (kg, lbs etc)					
Weight Change (n, %, etc)	Gain	Loss	No change		
[redacted]					
Mean GWG (KG, lbs etc)					
Rate of GWG (i.e. g/week from week 12-30 etc)					
Reviewer notes:					

Outcome (for intervention studies)

FOR INTERVENTION GROUP					
Total number of participants					
Underweight BMI (% and n)		Normal BMI (% and n)			
Overweight BMI (% and n)		Obese BMI (% and n)			
Adequacy of weight gain					
Institute of Medicine categories (%, n etc)	Underweight	Normal	Overweight	Obese	Overall
Inadequate					
Adequate					
Excessive					
Trimester of pregnancy	1	2	*3*		

Weight Change (n, %, etc)	Gain	Loss	No change
[redacted]			

FOR CONTROL GROUP					
Total number of participants					
Underweight BMI (% and n)		Normal BMI (% and n)			
Overweight BMI (% and n)		Obese BMI (% and n)			
Adequacy of weight gain					
Institute of Medicine categories (%, n etc)	Underweight	Normal	Overweight	Obese	Overall
Inadequate					
Adequate					
Excessive					

Trimester of pregnancy	1st	2nd	3rd
Weight Change (n, %, etc)	Gain	Loss	No change
[redacted]			

INTERVENTION AND CONTROL RESULTS		
GWG g/week		
Total GWG (kg, lbs etc)		
Mean GWG		
Rate of GWG (i.e. g/week from week 12-30 etc)		
Reviewer notes:		

Exposure – free sugar intake

Tertiles/Quartiles/Quintiles	1	2	3	4	5
g/day					
% of energy intake					

High or low intake (define)	
g/day	
% of energy intake	
Above or below median (define)	

Reviewer notes:	

Exposure (for intervention studies)

Tertiles/Quartiles/Quintiles	1	2	3	4	5
g/day					
% of energy intake					
Tertiles/Quartiles/Quintiles	1	2	3	4	5
g/day					
% of energy intake					
	INTERVENTION				
High or low intake (define)					
g/day					
% of energy intake					
Above or below median (define)					

Association of exposure (free sugar) and outcome (gestational weight gain)

Was energy adjusted for? (Y/N)		Attenuation of effect?		
Reported result (description)				
Measurement of reported statistic (tick)	Odds ratio	Relative risk	Mean difference	Absolute risk reduction
Reported statistic (as reported)				
95% Confidence interval				
P value				
Standard deviation				
Is this significant?				
Is this significant when adjusted for?				
Reviewer notes:				

CRUDE					
GWG g/week					
Tertiles/Quartiles/Quintiles	1 n (95% CI)	2 n (95% CI)	3 n (95% CI)	4 n (95% CI)	5 n (95% CI)
g/day (sugar)					
% of energy intake (sugar)					
Underweight					
Normal weight					
Overweight					
Obese					

ADJUSTED					
GWG g/week					
Tertiles/Quartiles/Quintiles	1 n (95% CI)	2 n (95% CI)	3 n (95% CI)	4 n (95% CI)	5 n (95% CI)
g/day (sugar)					
% of energy intake (sugar)					
Adjusted for					
Reviewer notes:					

E.G. Association= 1g intake sugar with 26g increase weight (CI 95% 8-44) (p=0.005) (still significant when adjusted for energy)

CONCLUSIONS:

Key conclusions	
Limitations:	
Correspondence required for further study information *(from whom, what and when)*	
Notes:	

Appendix C ANOVA and multinomial logistic regression analysis of energy adjusted macronutrient and free sugar residuals at 32 weeks gestation with or without DM/GDM/glycosuria (n= 8507)

Energy adjusted residual intakes	None (n= 8,185)	Existing DM (n= 33)	GDM (n= 35)	Glycosuria (n= 254)	P value
Fat (residual)	-0.20 (8.54)	1.21 (7.89)	-0.15 (8.79)	1.28 (8.83)	0.04
Carbohydrate (residual)	-0.37 (21.52)	-9.23 (17.94)	-7.25 (22.39)	-2.03 (21.6)	0.02
Protein (residual)	0.77 (10.99)	5.98 (7.42)	7.13 (10.11)	-0.88 (10.03)	<0.001
NMES (residual	-0.01 (0.40)	-0.45 (0.49)	-0.39 (0.50)	-0.03 (0.41)	<0.001

RRR (95% CI)[a]				
Energy adjusted residual intakes at 32 weeks gestation	**None (n= 8,185)**	**Existing diabetes (n= 33)**	**GDM (n= 35)**	**Glycosuria (n= 254)**
Fat **M1**[b] **M2**[c] **M3**[d] **M4**	 1 1 1	 1.0196 (0.9794, 1.0614) 1.0244 (0.9834, 1.0672) 1.0204 (0.9796, 1.0629) 1.0250 (0.9798, 1.0723)	 1.0008 (0.9626, 1.0406) 0.9997 (0.9604, 1.0407) 0.9904 (0.9517, 1.0307) 0.9909 (0.9515, 1.0320)	 1.0205 (1.0056, 1.0356) 1.0222 (1.0071, 1.0376) 1.0206 (1.0054, 1.0360) 1.0209 (1.0056, 1.0365)
Carbohydrate **M1** **M2** **M3** **M4**	 1 1 1	 0.9808 (0.9655, 0.9964) 0.9796 (0.9642, 0.9954) 0.9814 (0.9660, 0.9971) 0.9744 (0.9568, 0.9923)	 0.9854 (0.9702, 1.0008) 0.9856 (0.9700, 1.0014) 0.9895 (0.9740, 1.0052) 0.9881 (0.9718, 1.0045)	 0.9963 (0.9905, 1.0022) 0.9954 (0.9895, 1.0013) 0.9961 (0.9902, 1.0021) 0.9960 (0.9901, 1.0020)
Protein **M1** **M2** **M3** **M4**	 1 1 1	 1.0427 (1.0127, 1.0736) 1.0429 (1.0120, 1.0748) 1.0417 (1.0109, 1.0735) 1.0615 (1.0249, 1.0993)	 1.0498 (1.0211, 1.0793) 1.0509 (1.0212, 1.0815) 1.0484 (1.0192, 1.0785) 1.0538 (1.0224, 1.0863)	 0.9853 (0.9737, 0.9970) 0.9861 (0.9740, 0.9982) 0.9853 (0.9732, 0.9976) 0.9852 (0.9730, 0.9976)

NMES		0.9288 (0.0449,	0.1209 (0.0589,	0.8993 (0.6549,
M1	1	0.1919)	0.2491)	1.2349)
M2	1	0.0853 (0.0405,	0.1154 (0.0547,	0.8731 (0.6356,
M3	1	0.1794)	0.2437)	1.1992)
M4		0.0902 (0.0427,	0.1273 (0.0598,	0.9047 (0.6577,
		0.1904)	0.2710)	1.2443)
		0.1125 (0.5326,	0.1304 (0.0611,	0.9044 (0.6583,
		0.2378)	0.2783)	1.2427)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

Appendix D ANOVA and Multinomial regression analysis of energy-adjusted macronutrient and free sugar residuals at 32 weeks gestation in mothers categorised by measured gestational weight gain according to IOM recommendations.

Energy-adjusted residual intakes, mean (SD)	Less than recommended (n= 2442)	Within recommended (n= 2959)	More than recommended (n= 2074)	P value
Fat (residual)	-0.0869 (8.5569)	-0.2187 (8.4673)	-0.0069 (8.4978)	0.6700
Carbohydrate (residual)	-0.3963 (21.7693)	-0.6244 (21.1989)	-0.5651 (20.9369)	0.9233
Protein (residual)	0.5644 (11.3482)	1.0624 (10.7080)	0.5281 (10.8328)	0.1383
NMES (residual)	-0.0053 (0.4160)	-0.0150 (0.3829)	-0.0112 (0.3831)	0.6629

	RRR (95% CI)[a]		
Energy-adjusted residual intakes at 32 weeks	**Recommended (n= 2442) Reference**	**Less than recommended (n= 2959)**	**More than recommended (n= 2074)**
Fat			
M1[b]	1	1.0019 (0.9956, 1.0082)	1.0024 (0.9958, 1.0091)
M2[c]	1	0.9994 (0.9930, 1.0058)	1.0022 (0.9955, 1.0089)
M3[d]	1	0.9999 (0.9936, 1.0064)	0.9977 (0.9908, 1.0046)
Carbohydrate			
M1	1	1.0007 (0.9981, 1.0032)	0.9991 (0.9964, 1.0018)
M2	1	1.0010 (0.9985, 1.0036)	0.9987 (0.9960, 1.0014)
M3	1	1.0006 (0.9981, 1.0032)	1.0008 (0.9980, 1.0035)
Protein			
M1	1	0.9947 (0.9896, 0.9997)	0.9995 (0.9943, 1.0048)
M2	1	0.9965 (0.9913, 1.0017)	1.0015 (0.9961, 1.0070)
M3	1	0.9973 (0.9921, 1.0025)	0.9999 (0.9943, 1.0056)
NMES			
M1	1	1.0838 (0.9943, 1.2441)	0.9551 (0.8271, 1.1029)
M2	1	1.0774 (0.9367, 1.2391)	0.9176 (0.7931, 1.0617)
M3	1	1.0490 (0.9117, 1.2070)	1.0204 (0.8769, 1.1872)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

Appendix E ANOVA of maternal macronutrient and sugar intake at 32 weeks gestation in mothers with predicted inadequate, adequate or excessive gestational weight gain (n= 7475).

Unadjusted daily intakes, mean (SD)	Less than recommended (n= 946)	Within recommended (n= 2309)	More than recommended (n= 4734)	P value
Energy (kJ)	7072.5 (2017.1)	7235.3 (1933.1)	7323.1 (1909.0)	0.0008
Fat (g)	70.4 (23.3)	71.4 (23.8)	72.5 (22.4)	0.0136
Carbohydrate (g)	207.0 (63.0)	212.8 (59.8)	214.5 (58.8)	0.0019
Protein (g)	67.9 (19.5)	69.8 (18.7)	71.0 (18.9)	0.0000
NMES (g)	59.5 (35.1)	59.8 (32.3)	58.9 (30.6)	0.5768
Energy adjusted residuals				
Fat (residual)	0.4654 (8.2788)	-0.2660 (8.6015)	-0.1214 (8.5880)	0.0810
Carbohydrate (residual)	-0.9722 (21.7061)	0.1072 (21.3666)	-0.7931 (21.4835)	0.2087
Protein (residual)	-0.0907 (11.6775)	0.4752 (10.9340)	1.0031 (10.7961)	1.0086
NMES (residual)	0.0064 (0.4244)	0.0013 (0.4015)	-0.0206 (0.3871)	0.0316
Percentage of energy intake				
% of energy from fat	36.5 (4.5)	36.2 (4.6)	36.4 (4.5)	0.1784
% of energy from CHO	46.8 (4.8)	47.1 (4.8)	46.9 (4.7)	0.2175
% of energy from protein	16.5 (2.8)	16.6 (2.7)	16.6 (2.5)	0.5032
% of energy from NMES	13.1 (5.6)	12.9 (5.2)	12.6 (4.8)	0.0042

Appendix F Multinomial regression analysis of unadjusted energy, macronutrient and free sugar intake at 32 weeks gestation in mothers categorised by predicted gestational weight gain according to IOM recommendations.

	RRR (95% CI)[a]		
Dietary intakes at 32 weeks	**Recommended (n= 946)** **Reference**	**Less than recommended (n= 2309)**	**More than recommended (n= 4734)**
Energy (kJ)			
M1[b]	1	0.9999 (0.9999, 0.9999)	1.0000 (0.9999, 1.0000)
M2[c]	1	0.9999 (0.9999, 0.9999)	1.0000 (1.0000, 1.0000)
M3[d]	1	0.9999 (0.9999, 1.0000)	1.0000 (1.0000, 1.0000)
Fat (g)			
M1	1	0.9978 (0.9944, 1.0013)	1.0020 (0.9998, 1.0042)
M2	1	0.9971 (0.9937, 1.0006)	1.0027 (1.0005, 1.0050)
M3	1	0.9980 (0.9945, 1.0014)	1.0045 (1.0022, 1.0068)
Carbohydrate (g)			
M1	1	0.9982 (0.9969, 0.9995)	1.0003 (0.9995, 1.0012)
M2	1	0.9981 (0.9968, 0.9994)	1.0005 (0.9997, 1.0014)
M3	1	0.9985 (0.9972, 0.9998)	1.0015 (1.0006, 1.0024)
Protein (g)			
M1	1	0.9948 (0.9907, 0.9989)	1.0039 (1.0013, 1.0066)
M2	1	0.9955 (0.9914, 0.9997)	1.0047 (1.0020, 1.0074)
M3	1	0.9963 (0.9921, 1.0004)	1.0065 (1.0037, 1.0093)
NMES (g)			
M1	1	0.9994 (0.9971, 1.0018)	0.9987 (0.9971, 1.0003)
M2	1	0.9985 (0.9961, 1.0010)	0.9988 (0.9972, 1.0004)
M3	1	0.9994 (0.9970, 1.0019)	1.0006 (0.9989, 1.0022)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

Appendix G Multinomial regression analysis of energy-adjusted macronutrient and free sugar residuals at 32 weeks gestation in mothers categorised by predicted gestational weight gain according to IOM recommendations.

	RRR (95% CI)[a]		
Energy-adjusted residual intakes at 32 weeks	**Recommended (n= 2309) Reference**	**Less than recommended (n= 946)**	**More than recommended (n= 4734**
Fat			
M1[b]	1	1.0099 (1.0010, 1.0189)	1.0017 (0.9959, 1.0076)
M2[c]	1	1.0076 (0.9986, 1.0166)	1.0027 (0.9968, 1.0087)
M3[d]	1	1.0066 (0.9976, 1.0156)	1.0003 (0.9943, 1.0063)
Carbohydrate			
M1	1	0.9974 (0.9938, 1.0009)	0.9975 (0.9952, 0.9999)
M2	1	0.9973 (0.9938, 1.0009)	0.9972 (0.9948, 0.9995)
M3	1	0.9979 (0.9944, 1.0015)	0.9984 (0.9961, 1.0008)
Protein			
M1	1	0.9959 (0.9888, 1.0030)	1.0066 (1.0019, 1.0113)
M2	1	0.9994 (0.9921, 1.0068)	1.0070 (1.0021, 0.0119)
M3	1	0.9985 (0.9912, 1.0059)	1.0055 (1.0005, 1.0104)
NMES			
M1	1	1.0168 (0.8371, 1.2351)	0.8370 (0.7367, 0.9510)
M2	1	0.9690 (0.7975, 1.1773)	0.8140 (0.7150, 0.9267)
M3	1	1.0009 (0.8233, 1.2168)	0.8707 (0.7632, 0.9934)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

Appendix H Multinomial regression analysis of percentage of energy intake from macronutrient and free sugar residuals at 32 weeks gestation in mothers categorised by predicted gestational weight gain according to IOM recommendations.

	RRR (95% CI)[a]		
Percentage from energy intakes at 32 weeks	**Recommended (n= 2309) Reference**	**Less than recommended (n= 946)**	**More than recommended (n= 4734)**
Fat			
M1[b]	1	1.0148 (0.9981, 1.0317)	1.0066 (0.9957, 1.0176)
M2[c]	1	1.0099 (0.9932, 1.0270)	1.0090 (0.9979, 1.0202)
M3[d]	1	1.0091 (0.9923, 1.0262)	1.0065 (0.9952, 1.0179)
Carbohydrate			
M1	1	0.9882 (0.9727, 1.0039)	0.9897 (0.9794, 1.0000)
M2	1	0.9885 (0.9730, 1.0043)	0.9881 (0.9778, 0.9985)
M3	1	0.9910 (0.9753, 1.0068)	0.9936 (0.9830, 1.0042)
Protein			
M1	1	0.9949 (0.9962, 1.0244)	1.0144 (0.9951, 1.0340)
M2	1	1.0094 (0.9797, 1.0401)	1.0133 (0.9935, 1.0335)
M3	1	1.0033 (0.9736, 1.0340)	1.0017 (0.9817, 1.0221)
NMES			
M1	1	1.0046 (0.9900, 1.0194)	0.9842 (0.9746, 0.9940)
M2	1	0.9986 (0.9838, 1.0135)	0.9828 (0.9729, 0.9928)
M3	1	1.0026 (0.9877, 1.0178)	0.9907 (0.9805, 1.0010)

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI

Appendix I ANOVA of maternal adherence to PCA scores at 32 weeks gestation in mothers with predicted inadequate, adequate or excessive gestational weight gain.

PCA Scores	Less than recommended	Within recommended	More than recommended	P value
PCA 1 'Healthy'	-0.2714 (1.0025)	0.1491 (0.9744)	0.1256 (0.9567)	0.0000
PCA 2 'Traditional'	-0.0084 (1.0005)	-0.0647 (0.9055)	-0.0074 (0.9652)	0.0522
PCA 3 'Processed'	-0.0242 (0.9450)	-0.0825 (0.9034)	-0.0662 (0.8684)	0.2359
PCA 4'Confectionery'	-0.0933 (0.9678)	-0.0079 (0.9581)	0.0555 (0.9603)	0.0000
PCA 5 'Vegetarian'	0.0416 (1.0246)	-0.0013 (1.0227)	-0.0445 (0.9688)	0.0253

Appendix J Multinomial regression analysis of adherence to dietary patterns at 32 weeks gestation in mothers categorised by measured gestational weight gain according to IOM recommendations.

	RRR (95% CI)[a]		
PCA scores	**Recommended (n= 2309)** **Reference**	**Less than recommended (n= 946)**	**More than recommended (n= 4734**
PCA 1 'Healthy'			
M1[b]	1	0.8218 (0.7558, 0.8935)	1.0047 (0.9519, 1.0604)
M2[c]	1	0.8484 (0.7716, 0.9328)	1.0005 (0.9411, 1.0636)
M3[d]	1	0.8757 (0.7955, 0.9639)	1.0776 (1.0120, 1.1475)
PCA 2			
'Traditional'	1	1.0705 (0.9883, 1.1597)	1.0764 (1.0204, 1.1354)
M1	1	1.0677 (0.9847, 1.1578)	1.0909 (1.0336, 1.1514)
M2	1	1.0630 (0.9800, 1.1529)	1.0819 (1.0242, 1.1429)
M3			
PCA 3			
'Processed'	1	1.0669 (0.9786, 1.1632)	0.9977 (0.9416, 1.0571)
M1	1	1.0244 (0.9366, 1.1204)	1.0198 (0.9605, 1.0828)
M2	1	1.0155 (0.9285, 1.1106)	1.0017 (0.9426, 1.0645)
M3			
PCA 4			
'Confectionary'	1	0.8984 (0.8255, 0.9776)	1.0634 (1.0091, 1.1206)
M1	1	0.8989 (0.8262, 0.9781)	1.0626 (1.0081, 1.1202)
M2	1	0.9115 (0.8375, 0.9921)	1.0967 (1.0394, 1.1572)
M3			
PCA 5			
'Vegetarian'	1	1.0419 (0.9865, 1.1208)	0.9571 (0.9104, 1.0061)
M1	1	1.0421 (0.9668, 1.1231)	0.9516 (0.9047, 1.0010)
M2	1	1.0529 (0.9771, 1.1347)	0.9706 (0.9223, 1.0215)
M3			

[a] Reported as relative risk ratios and 95% confidence intervals
[b] Model 1: adjusted for maternal age
[c] Model 2: adjusted for maternal age, maternal parity maternal physical activity status, maternal smoking status, maternal social class and maternal education
[d] Model 3: adjusted for maternal age, maternal parity, maternal physical activity status, maternal smoking status, maternal social class, maternal education and maternal pre-pregnancy BMI