MATERNAL ETHNIC GROUP AND PREGNANCY ANTHROPOMETRICS IN THE DEVELOPMENT OF MATERNAL AND INFANT HEALTH OUTCOMES

Emma Louise Slack

A thesis submitted for the degree of Doctor of Philosophy
Faculty of Medical Sciences, Newcastle University
February 2019

Abstract

Aim: To investigate associations between pregnancy outcomes, South Asian ethnicity and pre-/early-pregnancy maternal anthropometrics (MA) and gestational anthropometric change (GAC).

Methods: A mixed methods approach was used to develop an evidence-based conceptual model of associations between outcomes and MA/GAC, involving: a systematic review, a framework-based synthesis and expert opinion. The conceptual model was tested using the Born in Bradford cohort data for Pakistani and White women. Regression models were used to investigate associations, adjusting for socio-demographic, behavioural and clinical factors.

Results: The evidence-based conceptual model hypothesised that gestational diabetes (GDM), hypertensive disorders of pregnancy (HDP), mode of delivery, maternal mortality, birth weight, gestational age at delivery, stillbirth, perinatal mortality, post-partum IGT, PPWR, breastfeeding, infant anthropometrics and maternal and child blood pressure in the longer term were associated with MA and GAC.

Pakistani women had significantly increased odds of GDM (Adjusted odds ratio (AOR) 1.08 (95%CI 1.06-1.11), HDP (AOR 1.11 (95%CI 1.08-1.15), Cesarean-section (AOR 1.05 (95%CI 1.01-1.08)), and induction (AOR 1.07 (95%CI 1.05-1.09)), and increased birth weight (adjusted coefficients; 13.77g (95%CI 9.24-18.30) associated with increasing BMI. With increasing GWG, birth weight increased for Pakistani women (adjusted coefficients; 22.92g (95%CI 18.07-27.78)). Significant interactions were identified for BMI and ethnicity on GDM (p=0.045), pre-term birth (p=0.049) following adjustment. There were no significant interactions between GWG and ethnicity on other pregnancy outcomes following adjustment. This was also true when using Asian-specific BMI criteria to calculate GWG.

Conclusion: There were ethnic differences in the shape of the association between BMI and GDM, and pre-term birth, following adjustment. In this cohort, there was no evidence of an ethnic difference in the association between any pregnancy outcome investigated and GWG following adjustment. More research is needed to investigate additional measures of GAC, and using other datasets looking at all South Asian subgroups.

Acknowledgements

This PhD has been a wonderful experience, but also the most challenging time of my life. During the PhD, I was diagnosed with chronic fatigue syndrome/Myalgiac Encephalomyelitis. Doing a PhD is hard enough, but learning to live with, and manage a chronic condition at the same time has been harder than I could have ever imagined. Without the love, help and support of my family, friends and colleagues I would not be where I am today- words are not enough to express my gratitude to you all.

Firstly, I would like to express my eternal gratitude to my supervisory team all of whom provided me with support and guidance throughout. I would particularly like to thank Dr Nicola Heslehurst and Prof Judith Rankin for always finding time to listen and advise, for challenging and supporting me, and for pushing me to get to where I am today; and Prof Steve Rushton for his expert guidance, both on statistical and theoretical matters, and on the importance of looking after myself. I would also like to thank my assessors Dr Ruth Bell and Prof Mark Pearce who have provided expert feedback, support and guidance. I would also like to express my gratitude to Dr Kate Best for always taking the time to explain and debate statistical issues with me.

I would like to thank my Mum; Dr Linda Turnbull, who has been my rock throughout, always supporting, inspiring and motivating me to continue. I would also like to thank my Husband, Alex, for his unconditional love, support and friendship, and for always making sure I remember to rest. I would like to thank my late father in law Anthony Redpath, who we miss dearly, and without whom I would not have been in a financial position to complete my studies. In addition, I would like to thank my Mother-in-law, Patricia Sutherland, my Dad, Bryan Slack and all of my friends, but in particular, Laura Watkins, Kate Best, Becca Watson, Emily Harkleroad, Kate Cullen, and Vishal Sharma who have always provided a listening ear.

I would like to thank the BiB research team, in particular those who gave up their time to attend the meeting to provide expert opinion on my conceptual model. I would also like to thank all the families who took part in the BiB project, without whom this research would not have been possible. Finally, I would like to thank the MRC and the Faculty of Medical Sciences for funding this studentship.

Publications from this studentship

Articles

- Slack E, Rankin J, Jones D, Heslehurst N. Effects of maternal anthropometrics on pregnancy outcomes in South Asian women: a systematic review. Obesity Reviews. 2018;19(4):485-500.
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Book Chapter

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Abbreviations

AOR: Adjusted odds ratio

ARR: Adjusted risk ratio

BiB: Born in Bradford

BMI: Body Mass Index

CI: Confidence interval

CMACE: Centre for Maternal and Child Enquiries

GAC: Gestational anthropometric change

GDM: Gestational diabetes mellitus

GOR: Government Office Region

GWG: Gestational weight gain

HDP: Hypertensive disorders of pregnancy

IMD: Index of multiple deprivation

IoM: Institute of Medicine

LSCS: lower segment caesarean section

LGA: Large for gestational age

MA: Maternal anthropometrics

MI: Multiple imputation

MOOSE: Meta-analysis of observational studies in epidemiology

MUAC: Mid upper arm circumference

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

NICU: Neonatal intensive care unit

PAF: Population attributable fraction

PICOS: Population, intervention, comparison, outcome, study type

PPH: Post-partum haemorrhage

PPWR: Post-partum weight retention

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCOG: Royal College of Obstetricians and Gynaecologists

RR: Risk Ratio

SEM: Structural equation modelling

SES: Socioeconomic status

SGA: Small for gestational age

SFT: Skinfold thickness

UK: United Kingdom

USA: United States of America

WHO: World Health Organisation

Chapter 1. Background

This chapter will discuss the background to this PhD project. It will summarise the existing evidence relating to obesity, maternal obesity, gestational weight gain (GWG) and maternal ethnicity, highlighting why this research is important and go on to state the aim and objectives.

1.1 Obesity

The increasing prevalence of people with overweight (body mass index (BMI) ≥25kg/m^2) and obesity (BMI≥30kg/m^2) is a global problem (1). Overweight and obesity are directly linked to a number of chronic diseases, including diabetes, cardiovascular diseases and cancer (1, 2). Risk of these associated diseases differs both by the amount of excess fat stored, and also in relation to the distribution of the excess fat (3). Excess abdominal (or central) fat alone is thought to be as great a risk factor for disease as is excess body fat (3). Obesity, and the diseases associated with it, have a major impact on human morbidity, mortality and quality of life, and place a large burden on healthcare resources (4). This section will give an overview of the existing evidence base on obesity in the general population, including international definitions of obesity, prevalence in the UK, related health inequalities and potential causes.

1.1.1 Defining obesity in adults

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines (Obesity: identification, assessment and management of overweight and obesity in children, young people and adults) published in 2014 (and checked by NICE in May 2018) state that BMI should be used primarily as an estimate of adiposity in adults (5). BMI is a measurement of weight for height and is calculated by dividing a person's weight (in kilograms) by their height (in meters squared) (1). BMI is a useful measure of population-level overweight and obesity (1). However, it may not correspond to the same degree of fatness in different individuals (1). Where BMI is <35kg/m^2, the use of waist circumference measurement should also be considered (5); this additional measurement enables both the amount and the distribution of body fat to be taken into account. Internationally, a BMI≥25kg/m^2, is considered to

indicate overweight and a BMI≥30kg/m^2 is considered to indicate obesity using the World Health Organisation (WHO) definitions (3). Obesity can be divided into a number of obesity subgroups as shown in Table 1.

Table 1 World Health Organisation BMI categories

Category	Body Mass Index (BMI) kg/m^2	Risk of comorbidities
Underweight	<18.5	Low (but the risk of other clinical problems increased)
Recommended weight	18.5-24.9	Average
Overweight	≥25.0	Increased
Obesity	≥30.0	-
Moderate obesity (class I obesity)	30-34.9	Moderate
Severe obesity (class II obesity)	35-39.9	Severe
Morbid obesity (class III obesity)	≥40.0	Very severe

Adapted from "World Health Organisation. Obesity: Preventing and Managing the Global Epidemic. 2000." (3)

Although the WHO BMI definitions are used by the NICE guidelines to identify obesity and the related health risks, it is recognised that BMI is not a direct measure of adiposity and that some level of clinical judgement is required (5). For example, it is recommended that BMI should be interpreted with caution, particularly in highly muscular adults where it may be a less accurate measure of adiposity (5). It is also emphasised that both waist circumference and the presence of comorbidities should play a role in determining the level of obesity related risk, and therefore the level of intervention required (5). The level of intervention required increases both with BMI and waist circumference: for men, a waist circumference of <94cm is low, 94-102cm is high and >102cm is very high; and for women <80cm is low, 80-88cm is high and >88cm is very high (5). Regardless of the waist circumference, the level of intervention should be higher for those with the presence of comorbidities as demonstrated in Table 2.

Table 2 Level of intervention required based on BMI, waist circumference level and presence of comorbidities.

BMI classification	Waist circumference			Comorbidities present
	Low	High	Very High	
Overweight	1	2	2	3
Moderate obesity	2	2	2	3
Severe obesity	3	3	3	4
Morbid obesity	4	4	4	4

Adapted from: National institute for Health and Care Excellence. Obesity: identification, assessment and management of overweight and obesity in children, young people and adults: National institute for Health and Care Excellence; 2014 [19th December 2014]. Available from: http://www.nice.org.uk/guidance/cg189/resources/guidance-obesity-identification-assessment-and-management-of-overweight-and-obesity-in-children-young-people-and-adults-pdf
1=General advice on healthy weight and lifestyle
2=Diet and physical activity
3=Diet and physical activity with the consideration of drugs
4=Diet and physical activity with the consideration of both drugs and surgery

It is also recognised that some ethnic groups may be at a higher risk of associated comorbidities at a lower BMI than the White population (5). The 2014 NICE guidelines recommend that lower BMI thresholds (23kg/m^2 to indicate increased risk and 27.5kg/m^2 to indicate high risk) should be used in Black African, African-Caribbean and Asian (South Asian and Chinese) populations to indicate the need for action to reduce the risk of obesity-related comorbidities such as type 2 diabetes (5). (A more detailed overview of obesity and ethnic groups is provided in Section 1.1.5, pgs.8-10).

1.1.2 **Defining obesity in children**

When defining overweight and obesity in children, age and sex need to be considered (1, 6). The WHO define childhood overweight and obesity (1). For children under the age of 5 years, overweight is a weight-for-height greater than two standard deviations above the WHO Child Growth Standards median (1). Obesity in children under 5 years of age is defined as weight-for-height greater than three standard deviations above the WHO Child Growth Standards median (1). For children aged 5-19 years, overweight is defined as a BMI-for-age greater than 1

standard deviation above the WHO Growth Reference median, and obesity is a BMI-for-age 2 standard deviations above the WHO Growth Reference median (1).

In the UK, children's BMI is categorised using variable thresholds that take into account the child's age and sex (7); these thresholds are known as a child growth reference. The child growth reference thresholds are calculated by measuring and weighing a large sample of children (the reference population) to identify how BMI varies by age and sex across the population (7). These data provide an average BMI for a girl and a boy at a particular age, as well as the distribution of measurements above and below the average (7). Therefore, individual children can be compared to the reference population, and from this the degree of variation from an expected value can be calculated (7). The National Obesity Observatory states z-scores[1] or centiles are used to define BMI thresholds on a child growth reference (7).

1.1.3 **Prevalence of, and risks associated with, obesity in the general population**

The most recent WHO factsheet (2018) on obesity states that since 1975 the number of people who have obesity has nearly tripled worldwide (1). Today, most of the world's population live in countries where overweight and obesity kill more people than underweight (1). In 2016, more than 1.9 billion adults ages 18 years and older who were overweight, 650 million of whom had obesity (1). This equates to 39% of adults aged 18 years or over who had overweight (38% of men and 40% of women), and 13% who had obesity (11% of men and 15% of women) (1). In high income countries, around half the women of childbearing age (sometimes referred to as reproductive age; age 15-49 years (8)) have either overweight or obesity (9); for example in England in 2015-16, 37% of women age 16-24, 49% of women age 25-34 years, and 59% of women age 35-44 had a BMI≥25kg/m^2 (10). In 2016, 41 million children under the age of five years worldwide were classified as either overweight or obese, and over 340 million children and adolescents aged five to 19 had overweight or obesity (1).

[1] A BMI z score or standard deviation score indicates how many units (of the standard deviation) a child's BMI is above or below the average BMI value for their age group and sex. For instance, a z score of 1.5 indicates that a child is 1.5 standard deviations above the average value.

A raised BMI is a major risk factor for non-communicable disease and it is thought that the more increased BMI is, the higher the risk (1). Non-communicable diseases that have been associated with BMI include cardiovascular disease, diabetes, musculoskeletal disorders such as osteoarthritis and also some cancers including endometrial, breast, kidney and colon (1). Childhood obesity is also associated with adverse health outcomes; this relates both to the long and short term (1). Children with obesity have an increased risk of breathing difficulties, fractures, hypertension, insulin resistance, early markers of cardiovascular disease and also psychological effects (1). They also have an increased risk of obesity in the future, premature death and disability in adulthood (11).

Obesity prevalence is increasing in the UK. Between 1993 and 2013, the proportion of men who were categorised as having obesity increased from 13.2% to 26% (12), this was still the same at 26% in 2016 (13) and the proportion of women rose from 16.4% to 23.8% (12), this had increased further to 27.0% in 2016 (13). In 2016/17, results from the National Child Measurement Program[2] found that 9.6% of reception-aged children (aged 4-5 years; 10.0% of boys and 9.2% of girls) were classified as having obesity according to the British 1990 population monitoring definition of obesity (≥95th centile) (14); this was a slight decrease from 9.9% in 2006/7 (10.07% in boys and 9.0% in girls) (15). For year six children (aged 10-11 years), 20.0% (21.8% of boys and 18.0% of girls) were classified as having obesity (14), this was an increase from 2006/7 where 17.5% were classified as having obesity (19.0% of boys, and 15.8% of girls) (15). By 2050, it is predicted that 60% of adult men, 50% of adult women and 25% of children will have obesity (16).

1.1.4 **Economic impact of obesity**

A systematic review published in 2017 included 23 studies (from Canada, USA, Brazil, Germany, Thailand, Mexico, Korea, Czech Republic, Republic of Ireland, Spain and Sweden) (17). The review found that when considering adults aged 18 years or older, obesity accounted for substantial economic burden, both in developed and developing countries despite considerable heterogeneity in methodological approaches, study populations and time frames (17). Poor health associated with

[2]National Child Measurement Program measures the height and weight of around one million school children in England each year

obesity is related to increased work absenteeism, mortality and decreased employment, personal income and quality of life (18). Statistical modelling of economic implications of obesity in the USA has found that relative to a matched normal weight population, adults with obesity average $3900 higher medical expenditures in an initial year, this increased to $4600 more in the tenth year (18). This excess cost differed by obesity class. Over a ten-year period, the excess expenditure relating to obesity averaged $4280 per year; this was $2820 for those with obesity class I, $5100 for those with obesity class II and $8710 for those with obesity class III (18). Additional simulation evidence has looked at predicted economic burden of obesity in the UK and USA to 2030 (19). Current trends project that 11 million more adults will have obesity in the UK and 65 million more adults will have obesity in the USA by 2030. The combined medical costs associated with treatment of associated preventable diseases are estimated to increase by $48–66 billion/year in the USA and by £1·9–2 billion/year in the UK by 2030 (19).

1.1.5 **Obesity related health inequalities**

Health inequalities are defined by WHO as “differences in health status, or in the distribution of health determinants between different population groups” (20). Health inequalities are strongly related to obesity in the general population, both worldwide and in the UK (21). This means that obesity levels differ across different populations, for example; across different ethnic groups, or different levels of socioeconomic status (SES). These inequalities relate to potentially modifiable factors such as education, SES (e.g. income and employment) and to non-modifiable factors such as age, ethnicity and gender. Identification of groups particularly at risk of obesity and the associated comorbidities is important to inform the development of targeted interventions, and where relevant the development of public health guidelines.

Age and sex

Obesity prevalence differs by both age and sex in the UK (22, 23). In adults aged 16 and over, prevalence of obesity is higher in men compared with women. In England between 2013 and 2015, the three-year average of those with overweight or obesity was 66.8% for men and 57.8% for women (22). However, there was very little

difference in three-year average for those with just obesity; 25.7% for men and 25.8% for women (22). Among both men and women, overweight and obesity prevalence is lowest between the ages of 16-24 years, generally higher in the older age groups and decreases in the oldest age group (75+ years); this final decrease in prevalence is most apparent for men (22). In England in 2015, at all ages there was a higher proportion of men with overweight or obesity compared with women (22). The sex and age differences can also be seen in children; in 2016/17 10.0% of boys and 9.2% of girls aged 4-5 were classified as having obesity (14). However, for children aged 10-11 years, 21.8% of boys and 18.0% of girls were classified as having obesity (14).

Ethnicity

Obesity and overweight has been found to vary by ethnicity in both adults and children (21, 24). In England in 2016/17, 22.6% of 4-5 year olds had overweight. This was 34.2% in 10-11 year olds (24). In 4-5 year olds, Black African children had the highest proportion with overweight (31.1%) and Indian children had the lowest (14.9%) (24). In 10-11 year olds, this had changed. Although Black African children still had the highest proportion with overweight (46.2%), White British children now had the lowest (31.6%) (24). In 2016/17, 61% of all adults had obesity; this was highest for Black adults (69%) and lowest for Chinese adults (32%).

The relationship between obesity and ethnicity is a complex one (25). This is due to an interplay of factors affecting health in different ethnic groups (26). For example, health behaviors may differ by ethnic group in accordance with religious, cultural and socioeconomic factors, as well as by geography (25, 26). In the UK, it is thought that some ethnic minority groups have a healthier diet than that of the White majority population (26, 27). However, for some ethnic minority groups, particularly those of South Asian origin, low physical activity levels and unhealthy diets are known to be of concern (26, 27). In addition, members of minority ethnic groups in the UK are often found to have lower SES then the majority White population (27), and low SES has also been associated with a greater risk of obesity, particularly in women and children (26). More information on the interrelationship between ethnicity and SES is given in section 1.7.1, pg.30.

Deprivation

Until the 1960s, it is thought that socioeconomic inequalities in obesity prevalence were largely absent (28). As obesity rates have increased over time, inequalities have strengthened; obesity rates in both adults and children have increased most in those with the poorest background (21, 29). In England in 2016/17, 13% of children aged 4-5 who had obesity lived in most deprived areas, compared with 7% in the least deprived areas (30). At age 10-11, the difference was more marked; 26% of children had obesity compared with 13% in the least deprived areas (30). In 2016/1, adults living in the most deprived parts of England were 46% more likely to have obesity compared with adults living in the least deprived parts (30). Data from England in 2014 showed that obesity prevalence in women increases with greater levels of deprivation, independent of the measure of deprivation used (22). For men, on the other hand, obesity prevalence has only been found to be associated with occupation, education and qualification-based measures of deprivation (22).

Disability

Obesity has also been associated with disability (31). Although there is limited data available, it has been observed that adults with disabilities are more likely to have obesity and lower physical activity levels than those without disabilities in the general population (31). This association has been found to vary with both age and gender (26). Children with a disability have also been found to have a higher risk of obesity; one report found that children who have a limiting illness (the meaning of limiting illness was not defined in the report) were also more likely to have overweight or obesity; this association was found to be stronger in those children who also had a learning disability (32). Another study found that children with chronic conditions (asthma, hearing or vision condition, learning disability, autism and attention-deficit/hyperactivity disorder) had a higher risk of obesity compared to those children without a chronic condition (33).

1.1.6 **Determinants of obesity**

All aspects of our health, including whether or not we have obesity, are dependent on a number of complex factors including our individual genetics, lifestyle and

environment. This idea has been depicted in a model developed by Dhalgren and Whitehead (34) which places the social determinants of health in order of factors relating to the wider environment, to factors that only affect the individual. In Dhalgren and Whitehead's model, these factors are (from wider environment to individual level factors); General socioeconomic, cultural and environmental conditions; Living and working conditions including agriculture and food production, education, work environment, unemployment, water and sanitation, health care services, housing; Social and community networks; Individual lifestyle factors and Age, sex and constitutional factors. Factors are both fixed and unchangeable for example; genetics, ethnicity, sex and age, and potentially modifiable for example smoking, diet and physical activity.

Biologically, obesity is caused through energy imbalance leading to excess fat deposition when the energy intake from the consumption of food and drink is greater than the energy expended through the body's metabolism and through physical activity over a prolonged period of time (1, 35). In 2007, the Foresight report highlighted that the causes of obesity are more complex and multifaceted than a simple positive energy imbalance (16). This complexity was depicted by the report's systems map of obesity (Figure 1) which shows that there are a large number of interrelated factors contributing to obesity development (16).

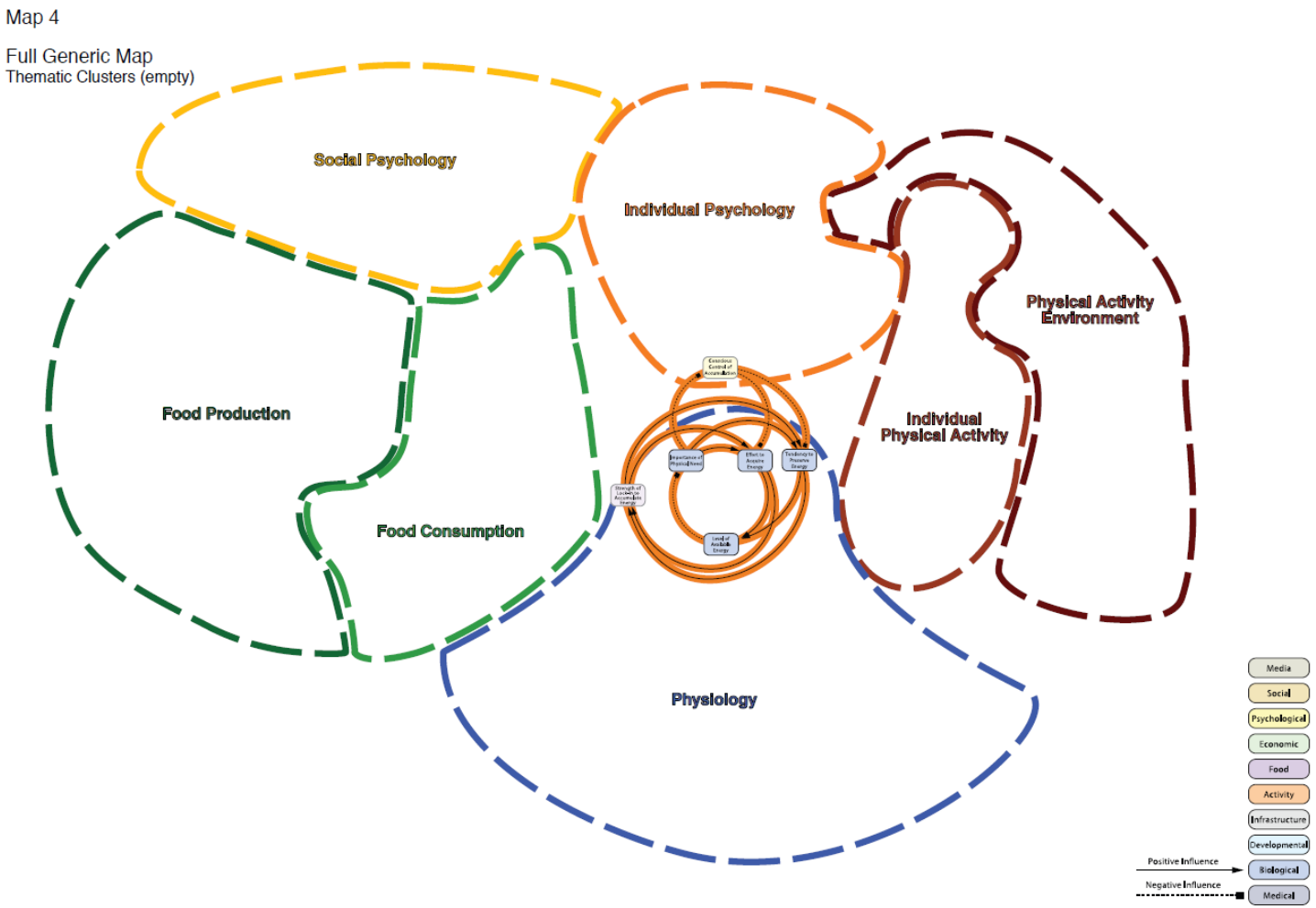


Figure 1 Foresight obesity systems map: thematic clusters of obesity determinants
(Source: Government Office for Science. FORESIGHT Tackling Obesities: Future Choices–Obesity System Atlas. 2007.) Please note this is available under the Open Government Licence for Public Sector Information available at https://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/

The factors thought to influence the development of obesity include an individual's genetics and ill health which relates to any conditions which may pre-dispose an individual to obesity (35). There are also a number of other potential causes of obesity which vary both by population and also across a person's life course (16). These include behaviour; particularly physical activity and eating, and how these behaviours influence energy imbalance within the body (16). A positive energy imbalance (i.e. too much energy in) leads to the development of excess adipose tissue and subsequent obesity (16). Individual psychology and motivation may also contribute to obesity development, for example motivation for physical activity or particular foods and food consumption patterns (35). Type, level and frequency of physical activity may also be involved. This in turn may be influenced by opportunities for physical activity and the obesogenic environment we live in (35). For example, one may want to walk to work; however, this decision may be dictated by whether or not there is a safe route with street lighting. Another influencing factor is the quality, quantity and frequency of food consumption; and also access to food and drink; the availability and affordability of healthy food products such as fruit and vegetables may influence consumption (35).

In the UK, it is thought that obesity is primarily caused by people's latent biological susceptibility to develop obesity interacting with the changing environment which increasingly includes lower physical activity and more dietary abundance (16). However, evidence from epidemiological studies and animal models suggests that the development of obesity and the related metabolic disorders lies both in the interactions between genes and adult risk factors such as low physical activity level and unbalanced diet, and also the interaction between genes and the embryonic, fetal and early postnatal environment (4).

The idea that maternal health may influence the future health of the infant is not a new concept (4). The social and geographical health inequalities have been debated since Victorian times (4). However, it was not until 1977 that epidemiological evidence in Norway led to the suggestion of a causal link between environmental factors in early life and subsequent disease (36). Years later in the UK, Barker and Osmond put forward the suggestion that it was poverty, poor nutrition and the general health of the mother producing both high infant mortality rates and a lifetime risk of coronary heart disease (37). This suggestion was followed with studies of UK

cohorts looking at fetal and placental size and the risk of hypertension in adult life (38), fetal nutrition and cardiovascular disease in adult life (39) and the fetal origins of coronary heart disease (40). This research led to the hypothesis that adverse environmental factors in early life cause disruption of normal growth and development of an adult phenotype prone to the development of cardiovascular disease; also known as the developmental origins of health and disease hypothesis. Both under- and over-nutrition in utero are thought to influence risk of obesity in later life, this is suggested by the U- or J-shaped association which has been observed between birth weight and subsequent obesity (41, 42). Two factors that are thought to influence nutrition in utero are maternal pre-pregnancy BMI; whether the mothers BMI is in the underweight, overweight or recommended range (18.5-24.9kg/m^2), and also how much weight a women gains during pregnancy, known as gestational weight gain (GWG).

1.2 Maternal obesity

This section will give an overview of how maternal obesity is defined using current guidelines, the existing evidence base on maternal obesity including prevalence in the UK and also the associated risks for both mother and infant.

1.2.1 Defining maternal obesity

While there is an absence of pregnancy-specific BMI criteria to define maternal weight status during pregnancy, research, guidelines and clinical practice use the WHO BMI classification categories which reflect the risk of type 2 diabetes and cardiovascular disease in the non-pregnant population (3, 43). As in the non-pregnant population, maternal obesity (≥30kg/m^2) can be divided into a number of subgroups. An additional BMI category is often used in pregnancy which includes women with a BMI≥50kg/m^2 and is termed “extreme obesity” (or sometimes referred to as “super-morbid obesity”) (44) (Table 3).

Table 3 Maternal BMI categories

Category	Body Mass Index (BMI) kg/m^2
Underweight	<18.5
Recommended weight	18.5-24.9
Overweight	≥25.0
Pre-obese	25.0-29.9
Obese	≥30.0
Moderate obesity (class I obesity)	30.0-34.9
Severe obesity (class II obesity)	35.0-39.9
Morbid obesity (class III obesity)*	40.0-49.9
Extreme obesity	≥50.0

*Maternal morbid obesity is also sometimes defined as a BMI ≥40.0, therefore including those women who have extreme obesity

As these criteria were developed based on risk information for the non-pregnant population, their use is limited in the later stages of pregnancy due to naturally incurred weight gain including fetus, placenta, fluid and adipose tissue (44). Current UK guidelines state that weight and height at the booking appointment (first antenatal appointment with a health care professional recommended to be within 13 weeks (45)) should be used to calculate maternal BMI, and plan subsequent care during pregnancy (45). UK and international maternal obesity guidelines (46-50) have been developed which state that women with a pre-pregnancy BMI≥30kg/m^2 should be advised at the booking appointment that their weight poses a risk to the health of both themselves and their unborn child (47, 51). Unlike obesity guidelines for the non-pregnant population (5), these guidelines do not differentiate between subgroups of maternal obesity, making recommendations only for all women with a BMI≥30kg/m^2 (45). While the CMACE/RCOG joint guidelines for the clinical management of obesity in pregnancy (46) do provide some recommendations by obesity subgroup, they do not make recommendations for women with a booking BMI≥50kg/m^2 who are considered to be at significantly increased risk in terms of adverse outcomes during pregnancy (44).

1.2.2 **Maternal obesity prevalence**

As with obesity in the general population, maternal obesity has been increasing over time internationally. In the 1980s, data from Europe, USA and Australia show that between 2% and 8% of women had obesity in pregnancy, by the 2000s, this had increased to 20-30% in the USA, and 10-15% in Australia and Europe (52-57). In the UK, prevalence of overweight and obesity in females age 16-44 years increased between 1993 and 2013 from 25% to 29%, and 12% to 19%, respectively (12). Findings from the 2010 The Centre for Maternal and Child Enquiries (CMACE) national project report (58) identified that the UK prevalence of women with a known BMI≥35kg/m^2 at any point in pregnancy was 4.99% which translating to approximately 38,478 maternities each year in the UK. The prevalence of women with a pregnancy BMI≥40kg/m^2 in the UK was 2.01%, while having a BMI≥50kg/m^2 affected 0.19% of all women giving birth. In addition, a retrospective epidemiological study of a nationally representative dataset looking at first trimester obesity in England found that maternal obesity doubled between 1989 and 2007 from 7.6% to 15.6% (59). This increasing trend has also been observed in Cardiff where the incidence of maternal obesity more than doubled from 3.2% to 8.9% between 1990 and 1999 (60), and also in Glasgow where maternal obesity rose from 9.4% to 18.9% between 1990 and 2002/4 (52). Recent data from the Maternal and Perinatal Audit from the 1st April 2015 to the 31st March 2016 in England, Scotland and Wales showed that only 47.3% of pregnant women had a BMI in the recommended range (BMI≥18.5 to <25.0kg/m^2) and 21.3% of pregnant women have a BMI in the obese range (≥30kg/m^2) (61).

Regional variation in the prevalence of maternal obesity in the UK has also been reported (59). Heslehurst *et al.* (59) mapped nationally representative data on first trimester obesity from 2007 using the Ordinance Survey Government Office Region (GOR) boundaries, Table 4 shows the geographical distribution of first trimester obesity in England by GOR compared to the national average for 2007 which was 15.6% (59).

Table 4 Geographical distribution of maternal first trimester obesity in England 2007* using Ordinance Survey Government Office Region boundaries

Region	Maternal first trimester obesity in England (%)
North East	17.3
North West	15.7
Yorkshire	18.2
East Midlands	18.8 (+/-2.5)**
West Midlands	21.6
East of England	15.8
London	13.3
South East	13.8
South West	15.6

*Including data from 32 maternity units for 2007 deliveries, and two maternity units for 2006 deliveries where 2007 data were not available.
**No data provided for East Midlands; the proportion was modelled based on the HSE 2006 data for women and GOR, and the differences in proportions for all other GORs pregnancy data compared with the HSE data.
Source: Heslehurst N, Rankin J, Wilkinson JR, Summerbell CD. A nationally representative study of maternal obesity in England, UK: trends in incidence and demographic inequalities in 619 323 births, 1989–2007. International Journal of Obesity. 2010;34(3):420-8.

1.2.3 **Risks associated with maternal obesity**

International research has highlighted that maternal obesity has implications for both mother and child (62-64). CMACE reported that 49% of all maternal deaths between 2006-2008 occurred in women with an overweight or obese BMI, and 27% in women with an obese BMI (65). The mother is also at increased risk of preeclampsia (46, 64, 66, 67), thromboembolic complications (66, 68), both elective and unplanned caesarean section (C-section) (62, 69, 70) and gestational diabetes mellitus (GDM) (66, 71, 72) which has been linked to an increased risk of the future development of type 2 diabetes (73).

It has been observed that infants born to women with obesity have an increased risk of adverse health outcomes including macrosomia (62), shoulder dystocia (62), late fetal death (a fetal death which occurs after 28 weeks completed gestation) (62, 74), prolonged pregnancy (>41 weeks gestation), post-term birth (>42 weeks gestation) (75-84) and congenital anomalies (62, 85, 86). There is also some evidence to suggest an increased risk of pre-term birth (<37 weeks gestation) (87, 88), however evidence is inconsistent, and complicated by the use of different definitions for both pre-term birth and maternal obesity. Maternal obesity has also been associated with longer term outcomes for the infant such as subsequent obesity (89).

There are also associations between maternal obesity and complications during labour and the need for more induced and operative deliveries (62). As a result, women with obesity may experience limited choices relating to where and how they can give birth; there may be restrictions on home births, the use of a birthing pool and also the type of pain relief that can be administered (47). More pain relief may be required due to reduced mobility during labour; as pain relief is difficult to administer in women with obesity, there is an increased need for general anaesthesia which is also associated with higher risk (47). There are also complications associated with maternal obesity after birth (64). Compared to women of recommended weight, wound healing can be slower in women with obesity, with an increased risk of infection (90), there is a higher likelihood that extra support will be required in establishing breastfeeding (64, 90), and there is also an increased risk of depression both during pregnancy (91) and following delivery (64, 91). Furthermore, due to the increased morbidity during pregnancy and labour associated with increased maternal weight, women with obesity are also more likely to be hospitalised and to spend longer in hospital following pregnancy than women of recommended BMI (64, 90).

In addition to the increased health risks for both mother and infant associated with maternal obesity, there is also a demand for additional care and resources from health service providers (90). Although the exact cost of maternal obesity in the UK is hard to quantify due to the absence of a national information strategy relating to the collection of maternal obesity data in the UK (90). A qualitative study of the perceived impact of maternal services identified by healthcare professionals caring for obese women in the North East of England identified that healthcare professionals caring for women in pregnancy feel that maternal obesity has major implications for service delivery (90). This included resource and cost implications, additional care requirements due to the complications associated with maternal obesity, restriction in care options for the mother, difficulty carrying out certain procedures and also the impact on the psychological wellbeing of the mother (90). Managing and minimising the risks of these complications, therefore, has a major impact on maternity services (79, 90, 92).

1.3 Gestational weight gain

This section will give an overview of the existing evidence base on GWG, including how it is defined, the associated risks for both mother and infant and also a discussion of current GWG guidelines.

1.3.1 Defining gestational weight gain

The weight a woman gains between the time of conception and the onset of labour is known as GWG (93). GWG is a complex and unique biological phenomenon which supports the growth and development of the fetus (94). This section will provide a brief background on normal physiologic and metabolic changes, which take place during pregnancy and are related to GWG in singleton pregnancies. Firstly, I will consider the components of GWG. There are maternal, placental and fetal components of GWG. The maternal components are made up of total body water accretion, fat free mass, or protein accretion and fat mass accretion (94). Placental components are made up of placental weight, placental growth, placental development and placental composition (94). Fetal components are made up of fetal growth including fat free mass and fat mass, and also amniotic fluid composition (94). In general, water, protein and fat in the fetus, amniotic fluid, placenta, uterus, mammary gland, maternal blood volume and maternal adipose tissue make up GWG (95). The minimal amount of GWG thought to be sufficient for both fetal growth, and maternal post-partum lactation is 8kg (17.6lbs) (95).

The total amount of weight gained in normal-term pregnancies differs from woman to woman (94). However, some generalisations can be made about the tendencies and patterns of GWG (94). Evidence from the USA between 1985 and 2009 suggested that in singleton pregnancies, the mean total GWG of adult women with a recommended weight, giving birth to term infants ranged from 10.0kg to 16.7kg. Evidence also found that adolescents gained more weight during pregnancy compared with adult women (means ranged from 14.6 to 18.0kg in the studies examined) (94), and there was an inverse association between maternal BMI and GWG; the higher the BMI, the lower the amount of GWG (94). The pattern of GWG is generally higher in the second trimester and is related to maternal BMI (94). However, this may differ according to maternal age and ethnicity (94).

1.3.2 **Determinants of gestational weight gain**

As with obesity, there are thought to be multiple causes of GWG. The Institute of Medicine (IoM) discussed the determinants of GWG in detail when they reviewed their GWG guidelines in 2009 (94), a summary of the is shown in Table 5.These determinants interact to determine the energy balance of the individual, and so, the total and overall pattern of GWG.

Table 5 Factors influencing GWG according to the Institute of Medicine

Social and environmental factors	• Societal/Institutional: media, culture and acculturation, health services, policy • Environment: altitude, environmental toxicants, natural and man-made disasters • Neighbourhood/community: access to healthy foods, opportunities for physical activity • Interpersonal/Family: family violence, marital status, partner and family support
Maternal factors	• Genetic characteristics • Developmental programming • Socio-demographic characteristics e.g. ethnicity, socioeconomic status, food insecurity • Anthropometric and physiological characteristics including maternal BMI, hormonal milieu, basal metabolic rate • Medical factors including pre-existing co-morbidities, hyperemesis gravidarum, anorexia nervosa and bulimia nervosa • Psychological factors such as depression, stress and attitude towards weight gain • Behavioural factors including dietary intake, physical activity, substance abuse and unintended pregnancy

(Adapted from Institute of Medicine. Weight Gain During Pregnancy: Reexamining the Guidelines. Yaktine A, Rasmussen K, editors. Washington DC: National Academic Press; 2009 (94))

1.3.3 **Prevalence of excessive gestational weight gain**

There is limited evidence in the UK on the prevalence of excessive GWG. In Europe and the United States, 20-40% of women gain more than the recommended weight during pregnancy (96). A systematic review and meta-analysis of 1,309,136 women

from 23 international studies; four from China, two from Korea, and one each from Taiwan and Japan, Norway, Belgium, Italy, Denmark, and Sweden found that 23% of women had low GWG, 30% had recommended GWG, and 47% had high GWG (97). Analysis of live singleton births in 46 states, using the 2013 USA National Vital Statistics System birth data, found that the prevalence of recommended GWG was 32.1%, inadequate GWG was 20.4% and excessive GWG was 47.5%. Women with an underweight BMI had the highest prevalence of inadequate and recommended GWG (32.2% and 44.3%, respectively), and women with a BMI in the obese range had the highest prevalence of excessive GWG (55.8%) (98).

1.3.4 **Risks associated with gestational weight gain**

Both excessive and inadequate GWG have been associated with adverse pregnancy outcomes for mother and infant. Excessive GWG has been associated with short-term pregnancy outcomes for the mother including abnormal (99) and impaired glucose tolerance (IGT) (94, 100), pregnancy induced hypertension (94, 101, 102), caesarean delivery (94, 101-103), increased risk of unsuccessful breastfeeding (94), and increased length of hospital stay (104). Excessive GWG has also been associated with short-term outcomes for the infant; fetal growth (94, 103, 105, 106), increased birth weight (93, 107-110), large for gestational age (LGA) (103, 111), macrosomia (102, 112, 113), very pre-term birth (114), low five minute Apgar score (115), hypoglycaemia (115), meconium aspiration syndrome, (115) and polycythaemia (115).

Excessive GWG has also been associated with longer term pregnancy outcomes for the mother; post-partum weight retention (PPWR) (93, 94, 103, 105, 116-121) which may contribute to the increasing prevalence of overweight and obesity in women (117, 119) and in the infant; offspring obesity (103, 108, 111, 121-124), which in turn may partially explain the increasing prevalence of childhood obesity. A recent systematic review of the evidence relating to GWG and offspring obesity carried out by Lau *et al.* in 2014 concluded that current findings indicate that GWG is a modifiable risk factor for childhood obesity (123). In addition, some of the short-term pregnancy outcomes for the infant associated with excess GWG have also been linked to long-term adverse outcomes. For example, increased birth weight is thought to predict higher BMI (125, 126) and adverse health outcomes later in life (127, 128).

When considering the evidence related to GWG and adverse pregnancy outcomes, it is important to take into consideration that the observed association may be affected by how GWG is measured and also how excessive and inadequate GWG are defined. There is no singular clear way to measure GWG and therefore methods differ between studies. Measurement methods include maternal weight measurements taken at antenatal appointments throughout pregnancy to calculate GWG (120), maternal self-reported GWG (108, 122, 129), self-reported pre-pregnancy weight and weight at delivery (103), GWG reported on birth records (106, 110), and GWG calculated from the last weight recorded before delivery and measured pre-pregnancy weight (116, 121). Use of different GWG measurement methods and definitions for excessive or inadequate gain makes comparing results across different studies complex. Despite this, there appears to be a consensus that GWG is a modifiable risk factor that may influence both long- and short-term health outcomes for both mother and infant.

1.3.5 **Gestational weight gain guidelines**

Currently evidence-based weight management in pregnancy guidelines in the UK do not provide recommendations for GWG (47). In the USA, the IoM first published GWG in 1990 (72) shown in Table 6.

Table 6 1990 Institute of Medicine GWG recommendations

Pre-pregnancy weight category	**Pre-pregnancy BMI (kg/m^2)**	**Reccomended total gain**	
		Kg	lb
Underweight	<19.8	12.5-18	28-40
Recommended weight	19.8-26.0	11.5-16	25-35
Overweight	26.0 to 29.0	7-11.5	15-25
Obese	>29.0	At least 6.8	At least 15

Adapted from Institute of Medicine. Nutrition During Pregnancy: Part I: Weight Gain, Part II: Nutrient Supplements. Washington: National Academy Press; 1990. (72)

In 2009, the USA reviewed the 1990 IoM GWG guidelines focusing on the trade-off between maternal and child outcomes (94). This trade off was the focus of the review as evidence suggested lower GWG was associated with a decreased risk of adverse outcomes for the mother and increased risk for the infant, and higher GWG was associated with increased risk for the mother but generally decreased risk for the

infant (94). The 2009 review therefore prioritised making recommendations that minimised risk for both mother and infant (94). Outcomes considered were PPWR, caesarean delivery, fetal size (small for gestational age (SGA) and large for gestational age (LGA)) and childhood obesity. However, evidence was limited as all of the studies included in the review (94) considered GWG as a categorical rather than continuous variable, with no agreement on the definitions of the GWG groups used (94). In addition, none of the included studies provided information on obesity in childhood as an outcome, or provided information on the consequences of variation among women of different ethnic subgroups (94). The 2009 review resulted in the development of BMI specific GWG guidelines, which are independent of age, parity, smoking history, and ethnicity based on observational evidence shown in Table 7.

Table 7 2009 Institute of Medicine GWG recommendations

Pre-pregnancy weight category	**BMI (kg/m^2)**	**Recommended range of total weight kg (lbs)**	**Recommended rates of weight gain in the second and third trimesters (Mean range (kg/week))**
Underweight	<18.5	12.5-18 (28-40)	0.51 (0.44-0.58)
Recommended weight	18.5-24.9	11.5-16 (25-35)	0.42 (0.35-0.50)
Overweight	25.0-29.9	7.5-11.5 (15-25)	0.28 (0.23-0.33)
Obese	≥30.0	5-9 (11-20)	0.22 (0.17-0.27)

(Adapted from Institute of Medicine. Weight Gain During Pregnancy: Re-examining the Guidelines. Yaktine A, Rasmussen K, editors. Washington DC: National Academic Press; 2009. (94))

The American College of Obstetricians and Gynaecologists Committee Opinion on the updated IoM guidelines states that the guidelines have come under some criticism from physicians who believe that the weight targets are too high especially for women with a BMI≥25kg/m^2, and also that they do not address concerns in relation to PPWR (130). The guidelines also do not differentiate between the subgroups of obesity (moderate 30-34.9kg/m^2, severe 35-39.9kg/m^2, morbid obesity ≥40kg/m^2 and extreme obesity ≥50kg/m^2) due to a lack of evidence of the short- and long-term outcomes for both mother and infant (130). As the risks of adverse pregnancy outcomes may differ across obesity subgroups as they do for conditions outside of pregnancy such as diabetes, heart disease and hypertension (131), a

single GWG recommendation for all obesity classes may warrant some concern, particularly in women in the highest obesity subgroups.

A systematic review and meta-analysis by Kapadia *et al.* in 2015 considered whether it would be safe to recommend GWG below the 2009 IoM guidelines in obese women (132). The review included 18 cohort studies primarily from developed countries, 13 of which were representative of an average pregnant population, five focused on low-income populations, high risk pregnant population and in an African American population through subscribers to a popular ethnic magazine (132). Results from the analysis of primary outcomes showed that GWG below the 2009 IoM guidelines was associated with increased adjusted odd ratios (AOR) of pre-term birth (<37 weeks) and SGA (defined as a birth weight less than the 10th percentile of weight for infant sex and gestational age at delivery) but decreased AORs of LGA (defined as a birth weight more than the 90th percentile for infant sex and gestational age at delivery), macrosomia (>4000 and >4500g), gestational hypertension, pre-eclampsia and caesarean delivery (132). The review concluded that although GWG below the IoM 2009 guidelines may be beneficial for some people if individualized taking into account their existing co-morbidities. Routine recommendation cannot be advised without better risk prediction models to identify women who were at risk of adverse pregnancy outcomes below the 2009 IoM GWG guidelines (132).

In the UK, NICE highlight that the 2009 IoM BMI specific GWG guidelines (94) have not been validated by intervention studies and there is no evidence from large scale trials (47). Therefore, although the UK weight management in pregnancy guidelines have recently been reviewed (51), NICE have not adopted the IoM GWG guidelines. NICE state that the lack of evidence-based GWG guidelines in the UK remains an urgent research need, in particular considering the long term outcomes for the child and also relating to ethnic diversity (47, 51).

1.4 The combined effect of maternal body mass index and gestational weight gain

It is also important to consider whether there is a combined effect of BMI and GWG on pregnancy outcomes. This information could be used in the development of BMI

specific GWG guidelines and potentially to inform future research which furthers understanding of the mechanisms linking GWG and maternal BMI to adverse pregnancy outcomes. Current evidence suggests that, in addition to the independent effects of BMI and GWG, there is also a combined effect (67, 102, 133, 134). The association between GWG and adverse pregnancy outcome is thought to vary by maternal pre-pregnancy BMI, although the exact association is different for different outcomes. Risk of adverse pregnancy outcomes including C-section and PPWR have been found to increase with level of obesity and be amplified by excess GWG (64, 66, 135); GWG and high maternal BMI decreased the risk of growth restrictions, LGA and low Apgar score (135).

While there is some evidence to suggest that limited or no weight gain in women with obesity would have favourable pregnancy outcomes (134, 136), inadequate GWG has been associated with an increased risk of infants being born SGA (93, 103, 115). As weight loss during pregnancy is not advised (45), BMI specific GWG guidelines may help to decrease the risk in women who are already pregnant, in order to inform whether there is a need for the development of such guidelines. The combined effect of maternal BMI and GWG should be investigated within UK populations.

1.5 Potential mechanisms linking maternal obesity and gestational weight gain to adverse pregnancy outcomes

This section will consider the evidence relating to the potential mechanisms, which link maternal obesity and GWG to adverse pregnancy outcomes. Currently, the mechanisms by which maternal obesity and excess GWG cause adverse pregnancy outcomes are unclear and are likely to be different for different pregnancy outcomes. One theory suggests that rather than being a result of either maternal obesity or GWG individually, adverse pregnancy outcomes occur due to the excess adipose tissue (fat) and consequential insulin resistance (137). Both maternal obesity and excess GWG are associated with a greater risk of GDM (66, 72, 94, 100, 138) which in turn is associated with the subsequent development of type 2 diabetes (73). This increased insulin resistance in the mother is also thought to effect fetal outcomes. During pregnancy, insulin resistance develops in the mother in order to provide the

growing fetus with vital nutrients (137). It has been suggested that in mothers with greater amounts of adipose tissue during pregnancy, either as a result of having overweight at the start of pregnancy or through excessive GWG (or both), delivery of nutrients to the fetus is exaggerated through further increased insulin resistance and possible interference with maternal hormones that regulate placental nutrient transporters (137). Greater concentrations of glucose and fatty acids cross the placenta to the fetus as it develops (4, 139, 140) leads to increased fetal production of insulin, and consequently, increased fetal growth (4, 110, 139). This is known as the fetal over nutrition hypothesis (110, 140).

It is also thought that this increased fetal insulin may influence longer-term outcomes for the infant including greater adiposity in adult life through permanent changes to pancreatic islet cells, hypothalamus and adipose tissue in the fetus (4, 139). It is, however, also possible that the association between maternal BMI and GWG and offspring obesity may be explained by shared genetic and environmental exposures between the mother and her offspring (124). However, Lawlor *et al.* found that, in women with a maternal BMI in the recommended range, most of the association between BMI and GWG and offspring obesity could be explained by shared familial characteristics such as lifestyle and environment (124). When considering women with a maternal BMI in either the overweight or obese categories, there was evidence to suggest that there was a contribution from mechanisms in utero (124).

1.6 Effect of interventions on maternal obesity and gestational weight gain

"*Pregnancy is thought to be a teachable period that can have positive, long term outcomes*" (141).

Phelan suggests that the concern women have for the health of their unborn infant can provide significant motivation in itself to promote lifestyle change (141). This idea has led to the development of interventions in an attempt to reduce maternal obesity, and excessive GWG. These interventions have consisted of weight management using various types of diets, increased physical activity and behaviour modification (142). Review evidence shows that healthy eating or physical activity interventions

have had moderate success in reducing excessive GWG (143); on average in 21 randomised controlled trials, 1.81kg of GWG was limited in pregnant women with overweight and obesity compared with those not receiving intervention. Despite this, randomised controlled trials have had little effect on pregnancy outcomes investigated to date, including GDM, pre-eclampsia or macrosomia (142). Some of the lack of success in these trials has been attributed to poor compliance with protocols, and low statistical power (142). However, research suggests that pre-and early pregnancy metabolic condition effect early gene expression and placental function (142). Therefore, the lack of success in these interventions may also be due to when the interventions started in pregnancy. Catalano suggests that for these interventions to be more successful, they need to start prior to pregnancy (142). It is also possible that the lack of effectiveness of these interventions could be high heterogeneity between participants for example in ethnicity. It might be that interventions tailored to target populations, for example, specific ethnic groups may have more success than less specific interventions targeted at wider populations with many ethnic groups.

1.7 Ethnic groups, maternal obesity and gestational weight gain

This section will discuss ethnic differences in patterns of childbirth, maternal obesity, GWG, and evidence relating to the associated outcomes, it will then go on to discuss the suitability of current guidelines for weight management during pregnancy in the UK for ethnic minority groups. Globally, in 2017, the average fertility rate (births per woman) was 2.4 children (144). However, there are different patterns of childbirth for different countries. The highest fertility rate in 2017 was for women in Niger at 7.2 children per woman, followed by Somalia at 6.2 children per woman (144). Korea, Puerto Rico and Hong Kong had the lowest fertility at 1.1 children per woman, this was followed by Singapore and Moldova at 1.2 children per woman(144). Patterns of childbirth also differ within countries by ethnicity. For example; in the USA, in 2017, 52% of births were to White women, 14% to Black women, 7% to Asian women and 23% to Hispanic women (145). While in England and Wales in 2017, 59.5% of all live births were to women of White British ethnicity and 11.6% were born to women who described themselves as “White Other”. “All other” ethnic groups had 11.5% of live births, South Asian women had 8.76%, the majority of whom were Pakistani (1.49% Bangladeshi, 3.12% Indian and 4.15% Pakistani), Black women had 4.19% of live

births (Black African women 3.35% and Black Caribbean 0.84%), 4.52% of live births in England and Wales were born to women who did not specify their ethnicity (146).

Ethnic differences also exist both in the prevalence of obesity and also with regard to obesity related illness (5). Like obesity in the general population, maternal obesity has been associated with ethnic minority groups in the UK (59, 81, 147). Heslehurst *et al.* (59) and Knight *et al.* (81) found that Black ethnic group was associated with increased maternal obesity compared to White ethnic group when using the WHO BMI criteria to diagnose weight status during pregnancy. In another study, Heslehurst *et al.* (147) identified that Black and South Asian women have a higher incidence of first trimester obesity compared to White women, and that this was most pronounced for Pakistani women.

GWG has also been found to vary by ethnic group; the evidence available is predominantly from the USA (148-151). Studies found that White women tended to have higher GWG than other ethnic groups (including Black, Hispanic and Asian (primarily East Asian populations i.e. Chinese, Japanese, Philippine)), and so White women were less likely to have inadequate GWG and more likely to have excessive GWG (148-151). There is also one study from Europe by Kinnunen *et al.* who considered GWG in a population of 632 healthy pregnant women in Groruddalen, Oslo, Norway (152). Findings showed that there were no ethnic differences in GWG at 15 weeks gestation, by 28 weeks, Eastern European and Middle Eastern European women had gained significantly more weight than their western European counterparts had, and there was no significant difference for the other ethnic groups (South Asian, East Asian and African). However, when considering fat mass gain, both South and East Asian women gained significantly more than the White European reference group, with South Asian women having the highest fat mass gain at both 15 and 28 weeks gestation (152).

Headen *et al.* (153) found in a cohort study of 6,849 pregnancies in Black, Hispanic and White mothers that both inadequate and excessive GWG (defined using the IoM GWG recommendations (94)) differed by ethnicity. Black and Hispanic women were observed to have an increased risk of inadequate GWG which remained significant following adjustment for potentially confounding variables (pre-pregnancy BMI, mother's age at birth, parity, marital status, smoking during pregnancy, gest age of child, and infant's birth year). This finding has also been observed for Black and

Hispanic women who were also found to have an increased risk of excessive GWG compared to White women. However, the association was no longer significant when analysis adjusted for confounding variables. Current evidence on GWG and ethnicity primarily considers Black and Hispanic ethnic groups; there is very little evidence which considers GWG, and whether GWG is affected by maternal BMI in Asian populations in particular those which reflect ethnic groups in the UK.

In addition to the difference in incidence of obesity, both the independent and combined effects of maternal pre-pregnancy BMI and GWG on adverse pregnancy outcome are also thought to differ by ethnic group (153). Research in the USA has identified disparities in obstetric risk among African American and Hispanic women (154-157). Compared to White women with obesity, Hispanic women with obesity have been found to have an increased rate of GDM (155, 156), macrosomia (155), pre-eclampsia (156) and C-section (155, 157). African American women also had increased rates of C-section (155-157), and were the ethnic group most likely to have adverse pregnancy outcomes overall compared to White women (154).

Outside pregnancy, people of Asain origin have been found to have a particularly increased risk of obesity related comorbidites when compared to the White population. For example, a review of the international evidence relating to obesity in Asian populations found that people of Asian origin had an increased cardiometabolic risk and all-cause mortality at a lower BMI compared with White populations (158). However, this conclusion was limited by the use of varying definitions for different ethnic groups. Since the review was published in 2009, further evidence has associated the increased risk in Asian populations with a greater total fat mass, which leads to more rapid and earlier accumulation of fat in the key organs linked to diabetes (such as muscle and the liver), and a lesser ability to metabolise fat versus carbohydrates which may increase their susceptibility to associated morbidities (159). Maternal pre-pregnancy BMI has been found to have a significantly greater effect on insulin resistance among Asian women compared with White women (155, 160, 161). Results of another study carried out by Shen *et al.* (154) showed that insulin sensitivity in Asian women with a pre-pregnancy BMI of 23kg/m^2 was comparable to that of a White woman with a BMI of 30kg/m^2 (154). These finding suggest that these Asian women were at a higher risk of insulin sensitivity at a lower BMI than their White counterparts during pregnancy (154). As this was a cross-sectional study,

and the sample size was relatively small (n=116 White, n=28 Asian), the results should be interpreted with caution. However, current evidence suggests that ethnicity may modulate the effects of obesity on insulin resistance during pregnancy.

1.7.1 Ethnicity and socioeconomic status

While biological mechanisms are thought to account for some of the observed association between maternal BMI, GWG and increased adverse pregnancy outcomes in ethnic minority groups, there may also be some influence from the interaction between SES and ethnicity. The association between ethnicity and both obesity in the general population and also with maternal obesity is complicated by the interrelationship between ethnicity and socioeconomic group. It has been identified that health status varies by ethnicity, and also by SES (162). Maternal obesity is no exception, and has been found to be associated with both ethnic minority groups and socioeconomic deprivation in the UK (58, 59). The association shows higher levels of maternal obesity in the most deprived socioeconomic groups (using the 2007 IMD classification system) and also in ethnic minority groups (59). In the UK, ethnic minority groups are usually among the most deprived social groups (27), although the degree to which SES and ethnicity are confounded is dependent on the measure of SES used (162). Investigations into whether disparities in health status are due to either “ethnicity and social class”, or “ethnicity or social class” are complicated by this overlap between ethnicity and SES (162).

1.7.2 Suitability of guidelines for ethnic minority groups in the UK

If the risk of adverse pregnancy outcomes related to obesity does indeed differ by ethnicity, using the WHO BMI categories for the general population may not be suitable in pregnancy or for all ethnic groups. In particular, they were not suitable for Asians who are thought to have an increased susceptibility to the metabolic effects of adiposity when compared with European Whites of a similar BMI (43, 45). The WHO has defined Asian-specific BMI classification criteria for the non-pregnant population to determine weight-related risk (43) which are lower than those for the general population (3) (Table 8). The difference between the two classification categories

reflects that Asian populations are at increased risk of obesity related diseases at a lower BMI.

Table 8 Comparison of the World Health Organisation BMI criteria for the general population and specific to the Asian population

	General population BMI (kg/m^2)	**Asian-specific BMI (kg/m^2)**
Underweight	<18.5	<18.5
Recommended weight	18.5-24.9	18.5-23
Overweight	25-29.9	23-27.5
Obese	≥30	>27.5

The evidence base for developing BMI criteria specific to Asian populations was not pregnancy-related (43), and while there is some evidence relating to ethnic disparities in pregnancy in the USA (154), there is little comparative research representing UK ethnic diversity to inform UK weight management guidelines. Therefore, current UK guidelines for weight management (47) and the clinical management of maternal obesity (46, 138) do not differentiate between the internationally agreed BMI criteria for the general population and Asian populations (43). In their guidelines, NICE advises that the BMI criteria for the general population are used to define obesity as a risk factor for antenatal intervention (47).

In addition, evidence shows that the reason Asian populations have higher obesity related risk at lower BMI values is due to differences in body composition (25, 163). Asian populations tend to have more visceral fat (fat that is stored in the abdominal cavity, surrounding organs such as the liver, pancreas and intestines (164)), at the same BMI as White populations (25, 165). South Asian populations in particular, are more likely to have higher levels of visceral fat, lower levels of muscle mass and increased insulin resistance (166). Studies show ethnic differences in body composition can be observed from birth, both when investigating infants born in South Asia, and South Asian infants born in the UK. Compared to White infants born in the UK; Indian infants have been found to have higher levels of body fat and insulin (167), and Pakistani infants born in the UK have been found to have lower birth weight, and higher fat mass compared with their white British counterparts (168). Ethnic differences in weight related risk are unlikely to be explained fully by differences in body composition. This is due to the complex nature of the issue, and

the number of different risk factors involved (for example genetics, life history (e.g. growth), proteomics, behaviour, physiology, education, physical environment, values and beliefs) (25). However, body composition is a valuable measure that reflects a number of these factors including genetics and proteomics along with behavioural and environmental factors (25).

Guidelines, which include recommendations based on lean and fat mass distribution in addition to the relevant BMI cut offs for specific ethnic groups, may be advantageous, and allow better prediction of weight related risk in pregnancy in different ethnic groups. Such guidelines would need to include measures which better reflect body composition. These would include measures of maternal anthropometrics (MA) such as; waist to hip ratio, and anthropometric measures such as tricep skinfold thickness (SFT), subscapular SFT, mid upper arm circumference, and thigh circumference, along with the gestational change in these anthropometric measurements; gestational anthropometric change (GAC).

1.8 Rationale

Variations in obesity related risk by ethnicity and SES lead to health inequalities (26). These health inequalities also apply to maternal obesity and GWG making them significant public health issues in the UK. Attempts to rectify ethnicity-related health inequalities should begin with an accurate account of epidemiology (157). Asians are the second largest ethnic group in the UK (7.5% of the population) after White ethnic group (86.0% of the population). Within the Asian population, the majority are South Asian; Indian (2.5%), Pakistani (2.0%) and Bangladeshi (0.8%) (169, 170). Recent data from England and Wales show that the largest proportion of live births to a minority ethnic group were to women of South Asian ethnicity 8.76%, the majority of whom were Pakistani (1.49% Bangladeshi, 3.12% Indian and 4.15% Pakistani) (146). In addition, 28.4% of live births were to women who were born outside the UK In the England and Wales (146). Pakistan and Poland are the most common countries of birth for women born outside the UK (2.5% and 3.1% of all live births, respectively in 2017), with other South Asian born women contributing 3.2% of all live births (Indian women 2.0% and Bangladeshi women 1.1%). Therefore, South Asians make up a large percentage of those accessing maternity services in some areas (147) and inefficient care for such ethnic minority groups may widen the gap in health

inequalities (147). National data from England shows that the incidence of maternal obesity in South Asian populations doubles when using ethnic group specific BMI criteria (147). Therefore, a large proportion of South Asian women are potentially being wrongly assigned to low risk care using current UK guidelines (147).

Additional evidence from a UK study carried out by Bryant *et al.* (171), using data on 8478 women from the Born in Bradford (BiB) project, shows that the prevalence of maternal obesity in a Pakistani population rose from 18.8% when using the WHO BMI criteria for the general population to 30.9% when the WHO Asian specific BMI criteria were applied (171). Although this study found that the prevalence of maternal obesity increased, application of the Asian specific BMI threshold was not found to increase the predictive ability of those at risk of adverse pregnancy outcomes related to obesity: caesarean section, hypertensive disorders of pregnancy (HDP), macrosomia, GDM and pre-term births (171). The results of this study apply only to maternal pre-pregnancy BMI and therefore do not take into account GWG and the risk associated with it, or the combined effect of BMI and GWG on pregnancy outcomes. In addition, the study did not consider long-term pregnancy outcomes such as obesity in the offspring and PPWR for the mother. These outcomes may influence future obesity prevalence and be of particular public health importance in Asian populations, such as the Pakistani population, who are thought to have an increased susceptibility to the metabolic effects of adiposity when compared with European Whites of a similar BMI (43, 45).Research which furthers understanding of both the short- and long-term outcomes, associated with MA and excessive GAC in at risk populations could be used to inform the development of guidelines to improve risk management and clinical care. Evidence shows that managing and minimising risks associated with maternal obesity and excessive GWG has a major impact on maternity services (70, 79, 90, 92), and may play a role in minimising future obesity risk for both mother and infant. Epidemiological evidence has indicated that exposures in early life are important for obesity development and later health but there are gaps in the knowledge regarding the impact of factors during pregnancy and early life, particularly in South Asian children (172). Further population-based, epidemiological research is therefore required to identify relationships between UK ethnic groups, MA, GAC, and the short- and long-term outcomes of pregnancy for the

mother and the child to ensure the best quality of care is provided for women irrespective of their ethnicity.

1.9 Aim

The aim of my PhD was to investigate the relationship between UK ethnic groups (White and South Asian), maternal anthropometrics (MA), gestational anthropometric change (GAC), and short- and long-term pregnancy outcomes for mother and child.

1.10 Objectives

1. To develop a conceptual model of the association between maternal ethnicity, maternal anthropometrics (MA), gestational anthropometric change (GAC),, and the development of short- and long-term health outcomes for women and their offspring using the existing evidence base and systematic review methodology.

2. To use this conceptual model to inform the selection of both short- and long-term pregnancy outcomes to be investigated in this project.

3. To carry out an analysis of the association between pregnancy outcomes (maternal and child) and maternal body mass index (BMI) among White and Pakistani women using data from the Born in Bradford (BiB) cohort.

4. To carry out an analysis of the association between pregnancy outcomes (maternal and child) and gestational weight gain (GWG) among White and Pakistani women using data from the BiB cohort.

5. To carry out an analysis of the combined effect of maternal body mass index (BMI) and gestational weight gain (GWG) on pregnancy outcomes (maternal and child) among White and Pakistan women using data from the Born in Bradford (BiB) cohort.

6. To investigate the impacts of direct and indirect risk factors for gestational weight gain (GWG) using Structural Equation Modelling.

Chapter 2. Methodology

This chapter discusses the methodological approach used for my PhD research (individual methods are described in Chapter 3, Section 3.4 pgs.46-53; Chapter 4, Section 4.4, pgs.117-127; Chapter 5, Section 5.4, pgs.176-177; and Chapter 6, all sections, pgs.183-208) how this process has informed the study design used, and the need for a mixed methods approach.

2.1 Structural equation modelling[3]

SEM refers not to a single statistical technique, but to a family of related procedures (173). Other terms which are also used interchangeably in the literature are "covariance structure analysis", "covariance structure modelling" and "analysis of covariance structures" (173). Another term which has also been associated with SEM is "causal modelling", however, this is a dated expression as the results of SEM cannot generally be used as evidence of a causal association (173). Figure 2 gives an overview of the SEM process (174).

[3]The term SEM will be used but this also refers to path analysis, which uses the same process as SEM, but does not include latent variables. For more information on SEM, please see Section 6.2.3 in Chapter 6, pgs.196-199).

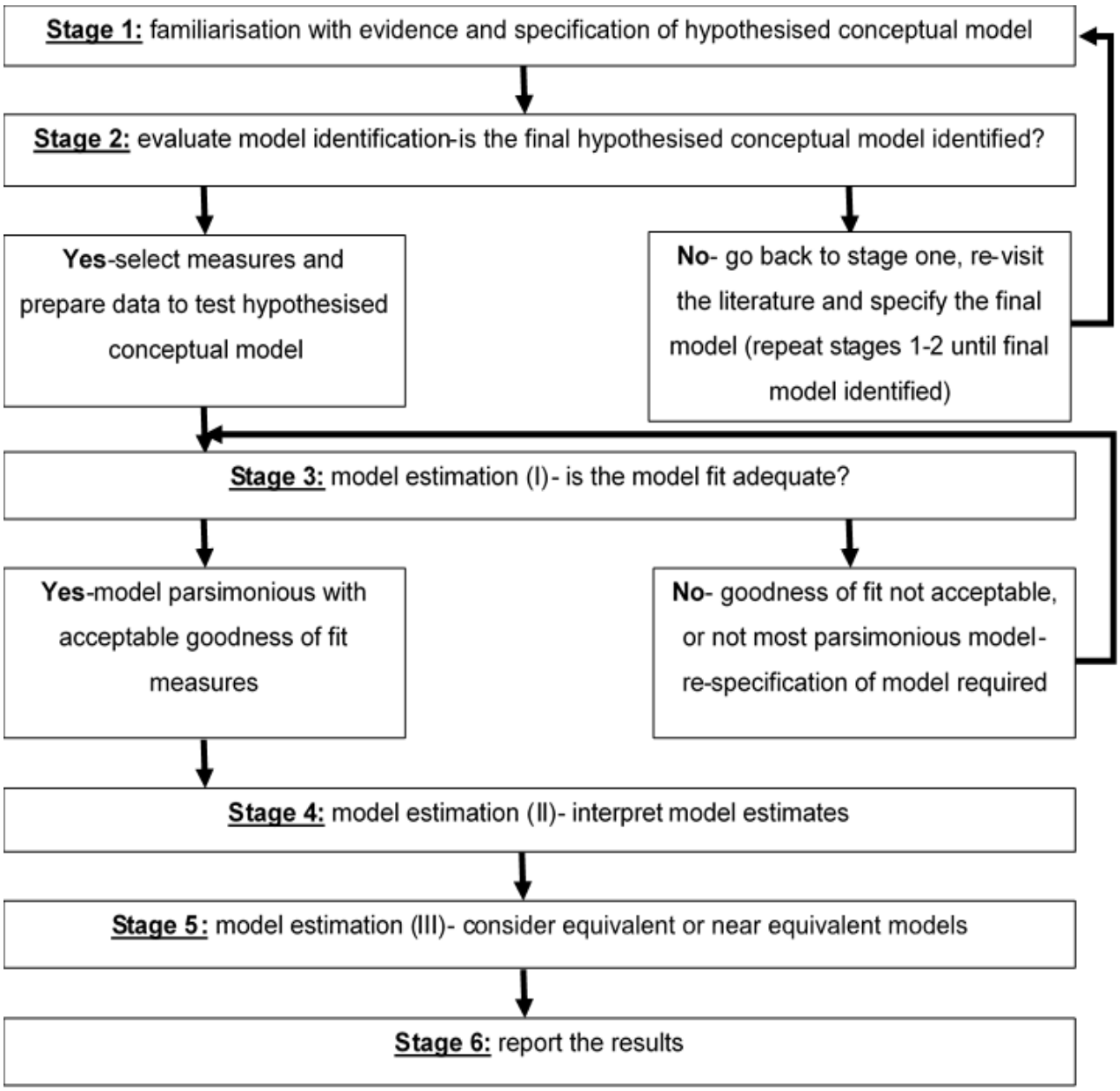


Figure 2 The SEM process

(Adapted from Kline RB. Specification. Principles and Practice of Structural Equation Modelling. Methodology in Social Science. Third ed: The Guilford Press; 2011. p. 91-123.)

Note: Identification refers to whether it is theoretically possible for the computer to estimate all parameters in the model, generally the degrees of freedom should be more than or equal to zero, and all latent variables must be assigned a scale e.g. standard deviations (175)

The SEM process was used to inform the structure of my PhD research which investigates the association between maternal ethnicity, MA, GAC and pregnancy outcomes for mother and infant. The key focus of SEM is to develop a conceptual model of hypothesised associations between variables, using existing evidence and theory, and then to test this model using real data. I have used both theoretical and empirical evidence to develop an evidence-based conceptual model of pregnancy outcomes, which were associated with MA or GAC, and also variables which mediated or confounded these associations. I used the hypothetical conceptual models for each pregnancy outcome to inform data analysis using data from the BiB cohort to investigate these associations in a UK South Asian population[4].
The goal of the SEM process is to generate a model that:

- Makes theoretical sense.
- Is reasonably parsimonious[5].
- Has an acceptably close correspondence, or "fit", with the data (173).

The most important phase of the SEM process is model specification, as later phases of the SEM process assume that the specified model is fundamentally correct (173). While in variable selection methods based on statistical significance, such as stepwise regression, the computer selects predictors for entry based on statistical significance (173). The selection of variables for SEM requires the use of theoretical and empirical evidence for the provision of information relating to which variables are assumed to be associated with other variables and also the directionalities of these associations (173). The most important thing that is required for SEM is a strong familiarity with the theoretical and the empirical literature in the research area (173). This knowledge guides each step in SEM, from initial model specification, model modification and reanalysis through to result interpretation (173)

To ensure that I had a strong familiarity with the literature in this research area, and was able to develop an evidence-based conceptual model for data analysis, it was

[4] Please note that while not all associations have been investigated using SEM, I have used the SEM process, and the conceptual model developed from this, to inform which associations have been investigated, and which variables have been included in adjusted analysis.
[5] A parsimonious model has the minimum number of predictor variables which achieves the desired level of explanation; i.e. if you have two models with a similar fit to the data, the simpler model, with less variables, would be preferred (172)

necessary for a mixed methods approach to be used. There was no review evidence which considers the association between MA, GAC and specific pregnancy outcomes in South Asian women that I could use or update to develop a relevant, evidence-based conceptual model.

2.2 Mixed methods

"Mixed methods research means adopting a research strategy employing more than one type of research method. The methods may be a mix of qualitative and quantitative methods, a mix of quantitative methods or a mix of qualitative methods" (176).

There are multiple reasons to choose a mixed-methods (or multimethod (177)) approach, described in detail by Green, Caraceli and Graham (178) and Bryman (179). A summary of these reasons is given in Table 9. This PhD has included both quantitative and qualitative research to provide a comprehensive account and richness in detail to inform the development of a conceptual model. The reasons for choosing mixed methods that are particularly important for this PhD are highlighted in grey in Table 9.

Table 9 Summary of reasons for conducting mixed methods research

Greene, Caracalla, and Graham (1989) (176)	Bryman (2006) (179)
Triangulation- convergence, corroboration and correspondence of results from the different methods	**Triangulation or greater validity**- that the qualitative and quantitative research may be combined together to triangulate findings so that they can be mutually corroborated
Complementarity- elaboration, enhancement, illustration and clarification of the results of one method from the results of the other method	**Offset**- that both qualitative and quantitative research have their own strengths and weaknesses, combining them together is thought to allow the researcher to offset the weaknesses and draw on the strengths of both
Development- use of the results from one method to help develop or inform the other method	**Process**- when quantitative research provides an account of structures in social life but qualitative research provides a sense of process
Initiation- discovery of paradox and contradiction, new perspectives of frameworks, the recasting of questions or results from one method with the questions or results from the other method	**Completeness**- Mixed methods research enables the researcher to bring together a more comprehensive account of the area of research
Expansion- seeks to expand the range of inquiry by using different methods for different components of inquiry	**Different research question**- Qualitative and quantitative research methods are both thought to be able to answer different types of research questions
	Explanation- when one method is used to help explain the findings of the other
	Unexpected results- unexpected results of one methodology (qualitative or quantitative) may be explained by the other
	Instrument development- qualitative research may be employed to help with the development of questionnaires for example to improve wording
	Sampling- where one approach is used to facilitate the sampling of cases or participants
	Credibility- refers to the suggestion that employing both approaches is thought to enhance the credibility of the findings
	Context- qualitative research may provide contextual understanding of the quantitative findings
	Illustration- this refers to the use of qualitative research to illustrate the quantitative findings
	Utility- Combining the two approaches may be more useful to practitioners or others
	Confirm and discover- when using qualitative (and in the case of this PhD project, quantitative also) data to develop a hypothesis and using quantitative data to test the hypothesis
	Diversity of views- combining researchers' and participants' views through both qualitative and quantitative research methods, uncovering relationships between variables with quantitative inquiry and revealing meanings through qualitative inquiry
	Enhancement- making more of either qualitative or quantitative findings by gathering data using the alternative methodology

Mixed methods designs can either be simultaneous or sequential in arrangement (177). Simultaneous designs are where both types of methods are applied at the same time, and sequential designs are where one method is followed by another (177). This PhD utilises a sequential design to fulfil all stages of the SEM process, focusing on the importance of conceptual model development and specification. The sequential design consists of the following phases (relating back to Figure 2, pg.37; phases 1-3 of this thesis make up Stage 1 and phase 4 makes up stages 2-6).

Phase 1: Systematic review

A quantitative systematic review relating to associations between MA, GAC and short- and long-term maternal and infant outcomes in migrant and descendant South Asian women was carried out (Chapter 3). This identified evidence to support inclusion or exclusion of pregnancy outcomes in the conceptual model.

Phase 2: Mixed research synthesis

Systematic reviews aim to provide a high-level comprehensive overview of primary research relating to a particular research question through the identification, evaluation and summarisation of all relevant research (180-182). However, they often conclude that not enough good quality evidence is available to answer the research question, or to inform policy and practice (182). In addition, Dixon-Woods *et al.* suggest that excluding any type of evidence based on the grounds of its methodology could have potentially important implications (183). For example, a preoccupation with methodology may divert attention away from understanding the nature and content of research findings, and the fact that methodologically diverse primary studies may yield similar findings (184). Mixed-methods systematic reviews (which include both quantitative and qualitative evidence), also known as mixed research syntheses, attempt to increase significance and relevance (182, 185). This is done by maximising findings, and the ability of these findings to inform policy and practice through the inclusion and integration of evidence from different types of research (182, 185).

While the Phase 1 systematic review (Chapter 3) identified associations between MA, GAC and pregnancy outcomes, it did not identify variables that influenced these

associations (i.e. mediating and confounding variables) in Pakistani women. Therefore, a mixed methods framework-based synthesis was also carried out to synthesize variables that may influence the associations, i.e. confounding and mediating variables, between MA, GAC and pregnancy outcomes in Pakistani women. Qualitative evidence was included in addition to quantitative evidence to ensure exploration of potentially mediating and confounding variables relating to women's individual feelings, thoughts and experiences.

Phase 3: Validation study

Using any form of systematic review requires research to have been carried out, evidence to have been published and available for inclusion in the synthesis. In under-researched fields, this can be problematic and key factors could be missed. The model specification and modification was driven by existing evidence and theory. In order to limit the effect this had on the model, I consulted with experts in the field at the BiB project about whether:

1. They agreed with the variables that had been identified through phases 1 and 2.
2. There were any other variables that they thought were relevant and should be included.

Phase 4: Secondary data analysis of prospective cohort

The final phase was to use data from the BiB cohort to investigate the conceptual model using data for White and Pakistani women. Analysis aimed to investigate ethnic differences in the following associations:

- MA and pregnancy outcomes.
- GAC and pregnancy outcomes.
- Combined effect of MA and GAC on pregnancy outcomes.

It also aimed to investigate how the application of WHO Asian specific BMI cut offs influenced these associations, compared with application of WHO cut offs for the general population and finally to investigate the contribution of mediating and confounding variables in the association between MA and GAC using SEM. Information on the BiB cohort is given in Appendix 1 (pgs.306-319).

Evidence from the two systematic reviews, and validation study was used to identify variables for inclusion in the conceptual model including: all possible associations between exposures of interest and pregnancy outcomes; and evidence of confounding or mediating variables. Evidence of associations were included in the conceptual model (irrespective of the strength or consistency of the evidence supporting them). Associations within the model were only removed if not supported by the data from the BiB cohort.

Chapter 3. Systematic review of the effects of maternal pre-/early pregnancy anthropometrics and anthropometric change during pregnancy on short- and long-term pregnancy outcomes in South Asian women (Phase 1)

This chapter is a systematic review of the effects of MA and GAC on short- and long-term pregnancy outcomes in South Asian women. An update of this systematic review has been published in Obesity reviews (186).

3.1 Introduction

Although existing reviews consider the association between maternal BMI and pregnancy outcomes (187), GWG and pregnancy outcomes within the 2009 IoM GWG guidelines (94), and also of the evidence of adverse outcomes according to the IoM guidelines (105); none of this review evidence related specifically to South Asian women, or considered different measures of body composition other than BMI and weight (kg). This chapter describes the rationale and process of conducting a systematic review to identify pregnancy outcomes associated with MA and GAC during pregnancy in migrant[6] and descendant South Asian women.

Outcomes considered in the development of the IoM GWG recommendations were: PPWR, caesarean delivery, fetal size (SGA and LGA) and childhood obesity (Figure 3).

[6] The term migrant is defined as “a person who moves from one country to another to live there on a permanent or semi-permanent basis” (186).

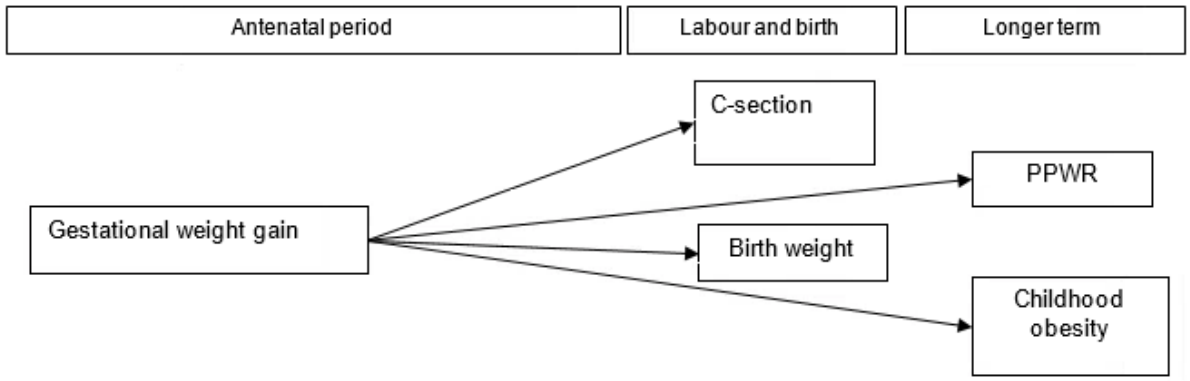


Figure 3 Pregnancy outcomes identified as associated with GWG, and used in the development of the 2009 IoM guidelines

Note: PPWR=post-partum weight retention, C-section=caesarean section.

The 2009 IoM guidelines are based on evidence from ethnic minority groups which may not be relevant to those in the UK (94). For example Hispanic, Black and Asian populations where the definition of Asian relates primarily to East Asian populations such as Filipino, Chinese and Japanese (188). Although Asians are the second largest ethnic group in the UK (7.5% of the population) after White ethnic group (86.0% of the population), the majority are South Asian: Indian (2.5%), Pakistani (2.0%) and Bangladeshi (0.8%) (169, 170).

3.2 Aim

To undertake a systematic review of the international evidence to investigate the associations between MA[7], GAC[8] and short- and long term pregnancy outcomes in South Asian[9] women compared with White women.

[7] MA is used here to refer to both pre-pregnancy and early pregnancy weight measurements e.g. BMI, skinfold thickness measures, body fat percentage etc.
[8] GAC refers to weight gained during pregnancy, and also other measurement of weight gain e.g. skinfold thickness, body fat percentage etc.
[9]Ideally this search would have focused only on Pakistani women, however searches undertaken in the scoping phase of this review identified insufficient evidence in this ethnic group and the search criteria were broadened to all migrant and descendant South Asian women

3.3 Objectives

- To systematically identify and synthesise the current evidence base relating to MA and GAC among South Asian women compared with White women.
- To identify associations between MA and short-term pregnancy outcomes for the mother and offspring.
- To identify associations between MA and long-term pregnancy outcomes for the mother and offspring.
- To identify associations between GAC and short-term pregnancy outcomes for the mother and offspring.
- To identify associations between GAC and long-term pregnancy outcomes for the mother and offspring.
- To identify the combined effect of MA and GAC on short- and long-term pregnancy outcomes for the mother and offspring.
- To use the results of this systematic review to contribute to the development of the conceptual model.

3.4 Methods

3.4.1 Inclusion and exclusion criteria

- **Inclusion criteria:**
  - Peer reviewed, full published studies (i.e. not editorials, abstracts, position pieces, research letters or posters).
  - Studies on humans.
  - Any study date.
  - Studies involving observational quantitative research methods; cross sectional, case control and cohort study designs.
  - Published in the English language (however, any studies identified in the search strategy published in languages other than English have been recorded).
  - Published results for migrant and descendant South Asian women and White women.

- Studies considering:

  Any measure of MA and pregnancy outcomes

  And/ or

  Any measure of GAC and pregnancy outcomes.

- **Exclusion criteria:**
  - Includes only women using assisted reproductive techniques as these pregnancies may have a different risk profile, for example assisted reproductive techniques have been associated with both short-term adverse pregnancy outcomes such as gestational hypertension and pre-term birth, and also longer term adverse outcomes such as increased risk of childhood illness (189).
  - Only presents results for multiple pregnancies as these may also have a different risk profile, for example a higher risk of low birth weight (190).

3.4.2 **Definitions of included ethnic groups**

The inclusion criteria were broadened to include all migrant and descendant South Asian women, rather than Pakistani women only, because during the development of the search strategy, searches carried out during the scoping phase of this review identified limited papers relating to the systematic review topic and migrant and descendant Pakistani women. For the purposes of this systematic review, the Asian population was defined as South Asian in accordance with the definition used in the 2013 NICE guidelines (191) and include people who are:

"immigrants and descendants from Bangladesh, Bhutan, India, Indian-Caribbean (migrants of South Asian family origin), Maldives, Nepal, Pakistan and Sri Lanka" (192).

Studies were also included if they were carried out in the UK and referred to an Asian population. This was decided, as in the UK, the term Asian is used to refer to people with ancestry in the Indian subcontinent whereas in other countries the meaning is much broader, particularly in the USA where the term Asian is mainly used to describe East Asian populations e.g. Chinese, Japanese and Filipino (188). The restriction to South Asian populations is due to the fact that the evidence synthesis

from this systematic review was to be used to inform the development of a conceptual model of MA, GAC and pregnancy outcomes among Pakistani women living in the UK.

White ethnic groups considered were those referring to White women e.g. White European, Caucasian, or White British women. In studies which reported UK data and more than one White or European ethnic group, the data for White British were included in this systematic review.

3.4.3 **Searches**

Searches were carried out using keywords developed with advice from an information specialist in accordance with the PICOS framework (Table 10) (193). PICOS refers to the patient, population or disease being addressed; the interventions or exposure; the comparator group; the outcome or endpoint; and the study design to be included (193). PICOS framework was used to give structure to search term development, and ensure no aspect of the search was left out. Scoping searches were carried out using the terms in Table 10 to inform the development of a final search strategy for each database searched. All final search strategies are given in Appendix 2 (pgs.320-328).

Table 10 Search term development using PICOS

	P: Patient, population or disease being addressed		I: Intervention or exposure	C: Comparator group	O: Outcome/ endpoint	S: Study design
	AND					
OR	**Ethnic group terms:** • Ethnicity • Race • Racial • Asian • Pakistan • Bangladesh • Sri Lanka • Nepal • Bhutan • Maldives • India • Migrant • Immigration • Acculturation • Black and minority ethnic groups	**Pregnancy terms:** • Pregnancy • Maternal • Gravidity • Mother • Parent	• Obesity • Body composition • BMI • Body mass index • Weight gain • Weight • Fat • Adiposity • Fatness • Waist circumference • W:H ratio • Waist to hip ratio • Waist-hip ratio	South Asian women must be compared to White women	Will not be restricted to specific pregnancy outcomes	Observational studies only

Note: PICOS stands for patient, population or disease being addressed; the interventions or exposure; the comparator group; the outcome or endpoint; and the study design to be included (193)

Systematic reviews of epidemiological studies require comprehensive search strategies to supplement database searching. This is due to the limited ability of database searches alone to systematically identify the body of relevant observational research (194). The search strategy for this review was designed to maximise the identification of relevant epidemiological studies.

Electronic databases were searched between 1st December 2015 and 31st July 2016 using keywords. Search terms and subject headings were converted into the relevant format for twelve databases: MEDLINE (Fig.1), Embase, Scopus, PsychInfo, British Nursing Index (BNI) and Cumulative Index to Nursing and Allied Health Literature (CINAHL), AMED (Allied and Complementary Medicine), Joanna Briggs Institute database, PROSPERO, CRD database (DARE), Cochrane database of systematic reviews and the federated search engine Epistemonikos which provides access to systematic reviews, and primary articles included in these reviews (all searches other than MEDLINE given in Appendix 2; pgs. 320-328). The reference lists of relevant studies, or related reviews, identified by the database search were hand searched for any relevant studies which had been cited by the studies. Each

study which met the inclusion criteria was subjected to citation searches using Google Scholar to identify any published studies that had cited the included studies. Authors of any relevant published abstracts were contacted to identify any subsequent full publications of the research. Any studies identified by the supplementary searches were also subject to reference list and citation searching until no further eligible studies were identified. Authors of the final included studies were contacted for additional data to include in the analyses when required.

After excluding duplicate studies using the function in Endnote, two researchers screened all the studies identified by the search strategy. Study selection occurred in two stages. First, the initial screening of titles and abstracts was carried out against the pre-determined inclusion criteria to identify potentially relevant studies. Exclusion at this stage occurred if both reviewers made the decision to exclude independently because the study did not meet this review's inclusion criteria. This stage was followed by screening the full studies identified as potentially relevant in the initial screening. Two researchers independently screened all full studies. Disagreements regarding eligibility were resolved through discussion between the reviewers, and where necessary, a third independent review by a member of the supervisory team (this was not required). Where access to the full study was not available online through Newcastle University Library, copies were requested using inter library loans. References were managed and recorded in Endnote x7. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (193) was used to record the flow of studies through the review.

3.4.4 **Data extraction and quality assessment**

Data extraction and quality assessment for all included studies were carried out by myself and another researcher independently; two of my supervisors (Nicola Heslehurst and Judith Rankin) and a research assistant (Daniel Jones) supported me with this process. All independent analyses were combined and any discrepancies were resolved through discussion, and if necessary, by a third independent review by an additional member of the supervisory team; this was not required for this review.

Data extraction

The Cochrane cohort study data extraction form was adapted to the context of the research question for my review. This data extraction form was piloted by myself, one of my supervisors and the research assistant to check for consistency in data extraction between reviewers, and used to extract relevant information (The final data extraction template is given in Appendix 3, pgs.329-332). The following study information was extracted:

- Title of the paper, author, year of study.
- Setting.
- Data collection time period, and methodology.
- Information on ethnic groups included, how ethnicity was assigned.
- Information on the outcome(s).
- Information on the exposure(s).
- The number of participants identified, included and excluded, and whether all participants had been accounted for in each group.
- Inclusion and exclusion criteria.
- Whether baseline characteristics had been reported by ethnicity, and if they had, data for the baseline characteristics by ethnic group.
- Study results; all relevant results associated with maternal weight, GWG and pregnancy outcomes, the factors that had been adjusted for in the analysis and the data analysis methods.

Quality assessment

There are few validated quality assessment tools applicable to observational studies. Three quality assessment tools were considered for this review; the NICE methodology checklist (195), the National Heart Lung and Blood Institute for National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (196) and the Newcastle-Ottawa quality assessment scale for cohort studies (197). While all three quality assessment tools had limitations, the Newcastle-Ottawa scale was found to be the most appropriate for the research question and study design following piloting of the three tools by myself, a member of the supervision team and a research assistant. The Newcastle-Ottawa scale had also

been used previously in a topic-related systematic review of observational studies investigating maternal BMI and post-term birth (84). The final quality assessment form is given in Appendix 4 (pgs.333-336). The maximum quality score a paper can receive is eight. For the purposes of this review, studies with a quality score above four were deemed to be of reasonable quality.

3.4.5 **Data synthesis**

The type of data synthesis carried out was dependent on the studies included in the review, and whether it was considered appropriate and useful to pool the results of these studies (198). Primarily, the appropriateness of pooling the results of the individual studies identified for inclusion in the systematic review was assessed. It was decided that results would only be pooled where results for one pregnancy outcome were available for two or more studies as this is the minimum recommended number for meta-analysis (199), and the study methodology and measures of exposure and outcome used in each study were sufficiently similar to support pooling of the results. Pooling of the data was not appropriate due to the diversity of exposure measures, and pregnancy outcomes used. Therefore, meta-analysis is not possible, and data was synthesised to provide a narrative summary of the evidence. This summary was structured around the subgroups of MA, GAC, the combined effect of MA and GAC and type of pregnancy outcome. This review was interested in two types of comparison:

1. Within each ethnic group i.e. exposed South Asian women compared with control South Asian women in the reference group; and exposed White women compared with control White women in the reference group. This comparison would allow estimates of risk to be produced, for example, for South Asian women with obesity compared with South Asian women of recommended BMI, and also for White women with obesity compared with White women of recommended BMI.
2. Between ethnic groups i.e. exposed South Asian women compared with White women of the same exposure category, for example South Asian women with obesity compared with White women with obesity. This comparison would

allow estimates of risk at each exposure level in South Asian women compared with White women.

Where effect sizes were not presented for these comparisons the data presented in studies (or provided when authors were contacted) were used to calculate unadjusted odds ratios (OR) for the associations between MA/GAC and pregnancy outcomes when possible. If mean and standard deviation (SD) for weight were provided at baseline and at time points during pregnancy, then difference in means and 95% confidence intervals (CI) were calculated to show the gain in exposure to that time point. Where studies presented a summary statistic of an anthropometric measure (e.g. mean weight or weight gained during pregnancy) of South Asian and White women in a population with an outcome (e.g. GDM), these were also included. All calculations were carried out using STATA 14.

Conceptual model

The results identified by this systematic review have been used to inform the development of a conceptual model which represents the associations between MA, GAC, the combined effect of MA and GAC, and pregnancy outcomes in South Asian women. This has been done by considering whether or not there is evidence to support the association between an exposure and an outcome. The model was developed in three stages; including evidence relating to MA and pregnancy outcomes, additionally including evidence for GAC and pregnancy outcomes, and finally additionally including the evidence for the combined effect of MA and GAC and pregnancy outcomes. Each stage of model development has been represented using a diagram where the arrows represent associations between variables, and the colour of the arrow represents the stage of descriptive synthesis. This diagram has been expanded at each stage of the descriptive synthesis based on the findings of the review.

3.5 Results

Searches identified 24,671 studies, of which 19 met the inclusion criteria, which included a total of 346,319 births (306,254 White and 40,065 South Asian). A

PRISMA flow diagram (193) shows the studies which have been excluded and the reasons for exclusion (Figure 4).

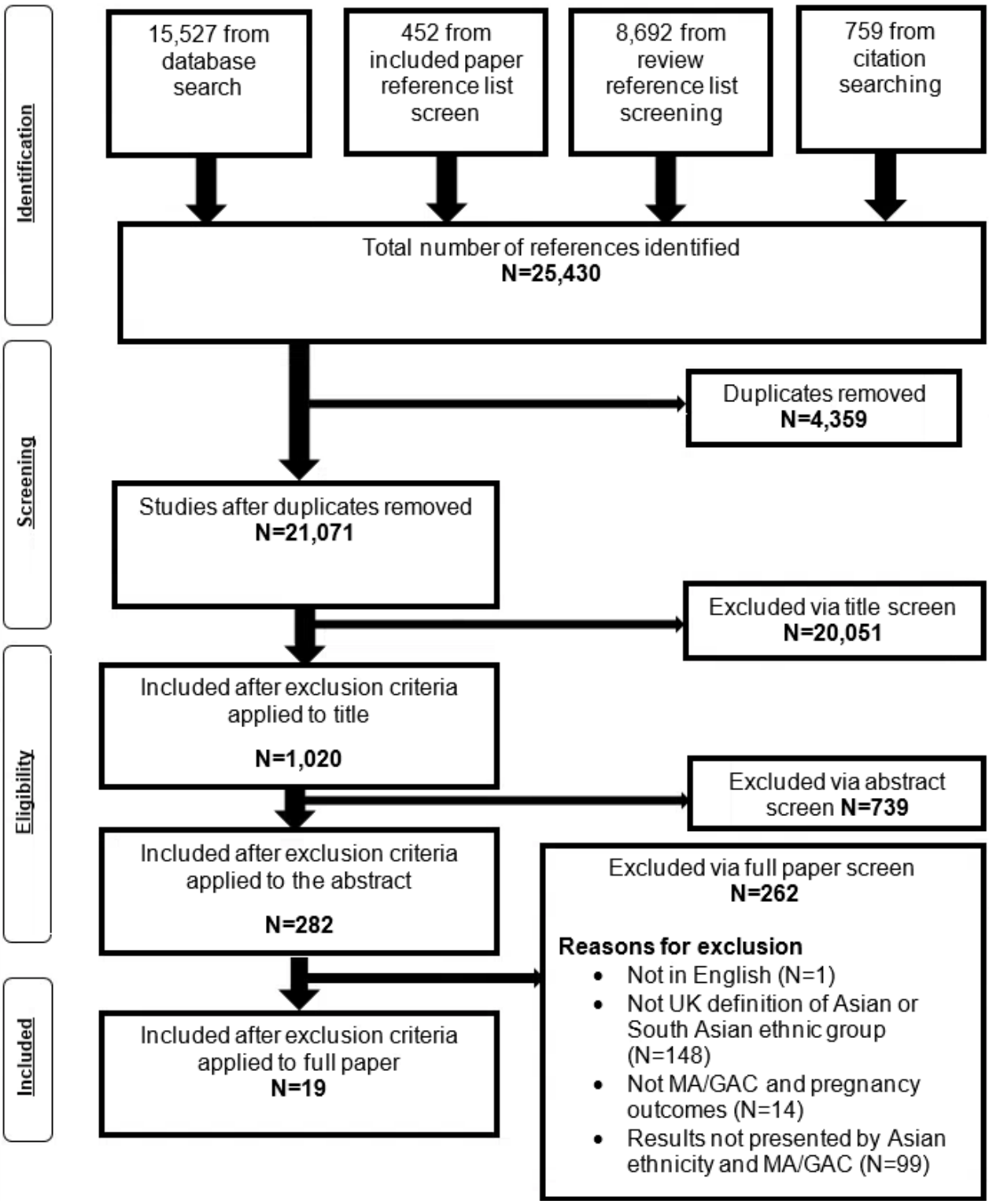


Figure 4 PRISMA flow diagram for systematic review searching and screening

Of the included 19 studies, there were 12 from the UK (171, 200-210) (two using data from BiB (171, 200); the studies did not present results for the same outcomes), two each from Norway (211, 212) and Australia (213, 214), and one each from Spain (215), California (216), and Canada (161). Some studies used more than one exposure; there were 18 studies which used MA measurements as the exposure (161, 171, 200-210, 212-216), three that considered GAC as the exposure (203, 211, 215), one that considered the combined effect of both MA at baseline and GAC (211)) and one that presented the trend in weight throughout pregnancy, considering both MA and GAC, in relation to a pregnancy outcome (212).

There were 14 outcomes identified by the review: four antenatal outcomes (GDM, HDP, and GAC); nine pregnancy outcomes for mother and infant (mode of delivery, distance from skin to epidural space, congenital anomaly, gestational age at delivery, stillbirth, admission to the neonatal intensive care unit, perinatal death, PPH and birth weight); and two longer term maternal outcomes (PPWR and IGT).

Ten of the included studies received a quality score of more than four, and nine scored less than four (Table 11). None of the studies included in this review received a score of eight, the maximum that can be achieved when using the Newcastle Ottawa quality assessment tool. The quality of the evidence for all exposures and outcomes appears to be well distributed; although there is very little evidence available for some of the pregnancy outcomes, that which is available is mostly of reasonable quality (above four).

Table 11 Summary of included studies

Author, publication year, region and country, Study design	**Ethnic groups** (terms used in article, definition, and sample size, n)	**Data collection time period**	**Exposure**	**Outcome**	**Quality score (out of 8)**
Bissenden *et al.*, 1981, Birmingham, UK, Prospective cohort (203)	European n=28 Asian; Pakistani or Bangladeshi, n=11 Total n=39	Not specified	• Incremental changes per week in body measurements in the second trimester • Maternal weight • Mid upper arm circumference • Triceps, biceps and subscapular skinfold thickness	• Well grown babies	2
Bissenden *et al.* 1981 Birmingham, UK, Prospective cohort (202)	European, n=31 Asian; Pakistani or Bangladeshi, n=39 Total n=70	Not specified	• Maternal weight • Triceps, biceps and subscapular skinfold thickness • Incremental change from booking to 29 weeks was also calculated	• Anthropometric change: Incremental changes per week in body measurements in the second trimester in Maternal weight Mid upper arm circumference Triceps, biceps and subscapular skinfold thickness	2
Bryant *et al.*, 2014, Bradford, UK, Prospective cohort (171)	White British n=4547 Pakistani n=4547 Total n=8478	March 2007 to December 2010	• Maternal BMI (Defined using WHO classification (BMI≥30kg/m^2) and South Asian specific category (BMI≥27.5kg/m^2))	• Mode of birth • Hypertensive disorders of pregnancy • GDM • Macrosomia • Pre-term birth	5
Dornhorst *et al.* 1992 London, UK, Prospective cohort (207)	White; Northern European and Caucasian n=6109 Indian; from the Indian subcontinent n=1164 Total n=7273	1984 to 1988	• Maternal BMI (kg/m^2, <27 and ≥27)	• GDM	5

Author, publication year, region and country, Study design	**Ethnic groups** (terms used in article, definition, and sample size, n)	**Data collection time period**	**Exposure**	**Outcome**	**Quality score (out of 8)**
Dunne *et al.* 2000 Birmingham, UK, Retrospective cohort (210)	Caucasian n=312 Indo-Asian women; Pakistan, India, Bangladesh, n=128 Total n=440	1990 to 1998	• Maternal BMI (kg/m^2)	• GDM and IGT	3
Hernandez-Rivas *et al.* 2013 Barcelona, Spain, Prospective cohort (215)	Caucasian n=190 South Central Asian; Pakistan, India, Bangladesh n=81 Total n=271	January 2004 to April 2011	• Maternal BMI (kg/m^2) • Weight gain during pregnancy (kg)	• GDM	4
Makgoba *et al.* 2011, London, UK, Retrospective cohort (205)	White woman, n=131201 South Asian women, n=2749 Total n=134150	1988 to 2000	• Maternal BMI (kg/m^2)	• GDM	5
Makgoba *et al.* 2012 London, UK, Retrospective cohort (206)	White woman, n=107901 South Asian women, n=15817 Total n=123718	1988 to 2000	• Maternal BMI (kg/m^2)	• GDM • Birthweight	5
Oteng-Ntim *et al.* 2013 London, UK, Cross sectional (204)	White; White British, White Irish and Other White, n=12418 Asian; Bangladeshi, Indian, Pakistani, other Asian and Asian British, n=1162 Total n=13580	Jan 1st 2004 to Dec 31st 2008	• Maternal BMI (kg/m^2)	• GDM • Mode of delivery • PPH • Pre-term birth • Macrosomia • Low birthweight • Admission to neonatal intensive care/special care nursery • Perinatal death	7
Penn *et al.* 2014 London, UK, Retrospective cohort (201)	White; British, Irish, White Other, n=26390 Asian; Indian, Pakistani, Bangladeshi, Asian Other, n=2857 Total n=29347	January 2004 to May 2012	• Maternal BMI (kg/m^2) • Also created a second BMI variable for South Asian women only.	• Stillbirth	6
Pu *et al.* 2015 Northern California, Retrospective cohort (216)	White; Non-Hispanic White, n=9011 Asian Indian, n=5069 Total n=14080	2007 to 2012	• Maternal BMI (kg/m^2) (Also WHO categories relevant to South Asian women)	• GDM	7

Author, publication year, region and country, Study design	**Ethnic groups** (terms used in article, definition, and sample size, n)	**Data collection time period**	**Exposure**	**Outcome**	**Quality score (out of 8)**
Retnakaran *et al.* 2006 Canada, Cross sectional (161)	Caucasian n=116 South Asian; India, Pakistan, Sri Lanka and Bangladesh, n=31 Total n=147	Not specified	• Maternal BMI (kg/m^2) • Weight gain in pregnancy (kg) • Adiponectin concentration (measure of hypoadiponectinemia)	• GDM • IGT • Normal glucose tolerance	3
Sharma *et al.* 2011 Oxford, UK, Prospective cohort (208)	White; British, Irish and any other White Background, n=709 Asian or Asian British; Indian, Pakistani, Bangladeshi or any other Asian background, n=249 Total n=958	February 2009 to December 2009	• Maternal BMI (kg/m^2)	• Distance from Skin to lumbar epidural space	4
Sheridan *et al.* 2013 Bradford, UK, Prospective cohort (200)	White British n=4488 Pakistani n=5127 Total n=9615	2007 to 2011	• Maternal BMI (kg/m^2)	• Congenital anomalies	5
Sinha *et al.* 2003 Birmingham, UK, Retrospective cohort (209)	Caucasian n=91 Indo Asian; Predominantly Muslim women from the Punjab Region, n=89 Total n=180	Not specified	• Booking weight (kg) (Booking defined as 16 weeks gestation)	• GDM • Post-partum IGT	4
Sommer *et al.* 2015 Groruddalen, Oslo, Norway, Prospective cohort (212)	European; Europeans of whom 82% were Norwegian (Three women born in North America were categorised as Europeans) n=353 South Asian; 63% Pakistani and 31% Sri Lankan n=190 Total n=543	May 2008 to May 2010	• Maternal BMI (kg/m^2) • Subcutaneous fat (mm, at 14 and 28 weeks gestation, and 14 weeks after delivery) • Serum Leptin level (ug/l at 14 and 28 weeks gestation, and 14 weeks after delivery)	• GDM • Anthropometric change during pregnancy • PPWR	5
Sommer *et al.* 2014 Groruddalen, Oslo, Norway, Prospective cohort (211)	European n=348 South Asian n=181 Total n=529	May 2008 to May 2010	• Maternal BMI (kg/m^2) • Body weight (kg) and truncal fat • Subcutaneous fat • Weight gain, and gain of total fat, truncal fat and mean skinfold gain	• GDM	6

Author, publication year, region and country, Study design	**Ethnic groups** (terms used in article, definition, and sample size, n)	**Data collection time period**	**Exposure**	**Outcome**	**Quality score (out of 8)**
Wong *et al.* 2011 New South Wales, Australia, Retrospective cohort (213)	Anglo-European n=215 South Asian; Indian, Pakistani, Sri Lankan and Fiji Indian n=160 Total n=375	July 2007 to July 2010	• Maternal BMI (kg/m^2)	• GDM	4
Yue *et al.* 1996 Sydney, Australia, Retrospective cohort (214)	Anglo-Celtic n=2412 Indian n=114 Total n=2526	Not specified	• Maternal BMI (kg/m^2)	• GDM	4

*Quality assessment scores for each question on the Newcastle-Ottawa scale reported in Appendix 5, pg.337
IGT=Impaired glucose tolerance, GDM=Gestational diabetes, PPWR=Post-partum weight retention, PPH=Post-partum haemorrhage, BMI=Body mass index, WHO=World Health Organisation

3.5.1 **Quality of included studies**

The quality of the evidence identified was varied. Scores ranged from two to seven out of a possible score of eight. Overall, 58% of studies had a quality score of either four or five out of eight, two out of the 19 included studies; 11% scored seven out of eight. There were no studies that scored eight out of eight.

Reasons for low study quality varied (for full details of quality score for individual studies please see Appendix 5; pg.337). All studies scored highly for selection of the non-exposed cohort (i.e. it was drawn from the same sample as the exposed cohort), and length of follow up (i.e. the length of follow up was sufficient) (161, 171, 200-216). Eight studies scored highly for the representativeness of the exposed cohort, this meant that the exposed cohort was truly representative (171, 201, 204, 205, 207, 214, 216); the other studies either did not describe the exposed cohort (n=2) (202, 203) or used a selected group which was not truly representative (n=9) (161, 200, 206, 208-213, 215). Ascertainment of the exposure scored low overall; four studies scored highly by obtaining data on the exposure from secure records (171, 211, 212), or by structured interview (200), the others (n=15), either did not describe how exposure was obtained (n=13) (161, 201-204, 207-210, 213-216) or obtained by written self-report (n=2) (205, 206). When considering the comparability of the cohorts on the basis of study design or statistical adjustment; three studies scored highly by controlling for a measure of SES and additional factors (204, 206, 216), four studies controlled for additional factors only (201, 209, 211, 212); 12 studies did not control for any factors and therefore scored poorly (161, 171, 200, 202, 203, 205, 207, 208, 210, 213-215). Assessment of pregnancy outcome scored well overall; 17 studies scored highly using either independent blind assessment (161, 200, 201, 204, 205, 207-209, 211-216) or record linkage (171, 206, 210). Only two studies scored poorly due to not providing a description for ascertainment of pregnancy outcome (202, 203). Quality scores also varied for management of missing data in the studies; ten scored highly by either having complete follow up (n=2) (201, 207) or <20% loss to follow up (n=8) (200, 204, 205, 208, 211, 213, 215, 216). Nine studies scored poorly; four studies had a follow up rate <80% (171, 206, 209, 212) and five provided no statement about exclusions or loss to follow up (161, 202, 203, 210, 214).

The majority of evidence was available for GDM; the quality of studies considering GDM as an outcome ranged from three to seven out of eight, the majority of studies

for this outcome had a quality score of four or five. The next largest number of included studies presenting results for an outcome was for birth weight; the quality of these studies ranged from two to seven out of eight. Where there were two included studies that presented results for a pregnancy outcome, the study quality ranged from two to seven out of eight. Quality was lowest for anthropometric change during pregnancy (two and five out of eight) and was higher for gestational age at delivery and mode of birth (five and seven out of eight). Where only one included study presented results on an outcome, the quality of studies ranged from two to seven out of eight; the study for maternal mental health in pregnancy had the lowest quality score, and studies for admission to NICU, perinatal death and postpartum IGT all scored seven out of eight.

3.5.2 **Maternal pre-/early pregnancy anthropometry and pregnancy outcomes**

There were 18 studies that used MA measures as the exposure (161, 171, 200-210, 212-216). There were 16 studies that used maternal BMI (161, 171, 200, 201, 204-208, 210, 212-216). Two of these studies used Asian specific criteria in addition to general population criteria (201, 216), and one used ≥27kg/m^2 as a definition of obesity in both South Asian and White women (207). Nine of the studies used maternal BMI (kg/m^2) as a continuous variable (161, 171, 206, 210, 212-215) and seven used it as a categorical variable (200, 201, 204, 205, 207, 208, 216). There were three studies that used maternal weight (kg) as an exposure variable; all three presented it as a continuous variable (202, 203, 209). There were two studies that used maternal skinfold thickness (SFT) as the exposure variable, both presented it as a continuous variable (202, 212). In addition, one study presented maternal serum leptin level, this was used as a continuous exposure variable (212).

There were 14 outcomes identified when MA were considered the exposure. These outcomes were; GDM, HDP of pregnancy, change in anthropometrics, mode of delivery, distance from skin to epidural space, congenital anomaly, gestational age at delivery, stillbirth, birth weight, post-partum haemorrhage (PPH), admission to the neonatal intensive care unit (NICU), perinatal death, post-partum IGT and PPWR (Table 12 and Table 13).

Antenatal outcomes

There were 14 studies which presented information on GDM; six studies that presented information regarding BMI in a population of women with GDM (206, 210, 212-215), three studies presented unadjusted results for the association between maternal BMI and GDM (171, 205, 207), two studies which presented adjusted results for the association between maternal BMI and GDM (207, 216), one that considered both pre-existing diabetes and GDM as one outcome variable (204) and one that carried out multivariate analysis of factors affecting insulin sensitivity in pregnancy (161). Only one study presented unadjusted results for HDP (171), and only one for anthropometric change (202) (Table 12 and Table 13).

Maternal and infant birth outcomes

One study presented unadjusted results for distance from skin to epidural space (208), and one for congenital anomaly (200). There were two studies that presented results relating to both mode of delivery and gestational age at delivery; one presenting unadjusted results (171) and one adjusted results (204). Only one study presented unadjusted and adjusted results for stillbirth (201). One study presented information regarding BMI in a population of women with well grown babies (babies born above the 90th percentile (203)), one study presented unadjusted results for the association between maternal BMI and birth weight (171), and two studies which presented adjusted results for the association between maternal BMI and birth weight (204, 206). Adjusted results were presented for PPH, admission to the NICU and perinatal death by one study (204) (Table 12 and Table 13).

Longer term maternal outcomes

One study presented the mean weight of a population of women with post-partum IGT (209). There was one study that presented the significance in the change in weight from 14 weeks gestation to 14 weeks post-partum (212).

Table 12 Effects of maternal BMI on pregnancy outcomes in South Asian and White women

Author and study year	Ethnic groups	Exposure	Control group	Pregnancy outcome	Odds ratio (95% confidence interval)		Adjusted odds ratio (95% confidence interval)	
					White ethnic group	South Asian ethnic group	White ethnic group	South Asian ethnic group
Bryant *et al.* 2014 (171)	White British women (n=4547) Pakistani women (n=4547)	5kg/m^2 increase in BMI	n/a	GDM	1.25 (1.12, 1.40)*	1.55 (1.43, 1.69)*	-	-
				Pre-term birth	0.87 (0.77, 0.98)*	0.98 (0.87, 1.11)	-	-
				Macrosomia	1.36 (1.27, 1.47)*	1.57 (1.41, 1.75)*	-	-
				Hypertensive disorder	1.60 (1.46, 1.76)*	1.54 (1.39, 1.71)*	-	-
				C-Section	1.34 (1.26, 1.42)*	1.36 (1.27, 1.45)*	-	-
Dornhorst *et al.* 1992 (207)	White women; Northern European and Caucasian (n=6109) Indian women; from the Indian subcontinent (n=1164)	BMI≥27 kg/m^2	BMI<27 kg/m^2	GDM	4.6 (2.1,10.4)*	3.5 (2.0, 4.2)*	4.3 (1.9, 9.8)*	2.0 (0.9, 4.2)
Makgoba *et al.* 2011 (205)	White woman (n=131201) South Asian women (n=2749)	25.0-29.9 kg/m^2 ≥30kg/m^2	15.5-24.9kg/m^2	GDM	1.77 (1.50, 2.09)$^{\infty *}$ 4.70 (3.98, 5.55)$^{\infty *}$	2.57 (2.02, 3.23) $^{\infty *}$ 5.80 (4.36, 7.71) $^{\infty *}$	- -	- -

Author and study year	Ethnic groups	Exposure	Control group	Pregnancy outcome	Odds ratio (95% confidence interval)		Adjusted odds ratio (95% confidence interval)	
					White ethnic group	South Asian ethnic group	White ethnic group	South Asian ethnic group
Oteng-Ntim 2013 (204)	White women; White British, White Irish and Other White (n=12418) Asian women; Bangladeshi, Indian, Pakistani, other Asian and Asian British (1162)	≥30kg/m^2	<30kg/m^2	Diabetes (GDM and pre-existing diabetes)	-	-	4.97 (3.39, 7.28)* **PAF** 20.3 (15.46, 24.53)	5.48 (2.43, 12.35)* **PAF** 17.37 (13.07, 21.09)
				Elective C-section	-	-	1.41 (1.08, 1.84)* **PAF** 4.24 (2.43, 6.00)	1.52 (0.73, 3.14) **PAF** 4.02 (2.31, 5.70)
				Emergency C-section	-	-	1.98 (1.69, 2.33)* **PAF** 3.48 (2.65, 4.30)	0.65 (0.32, 1.31) **PAF** 2.93 (2.23, 3.63)
				Instrumental Delivery	-	-	0.78 (0.63, 0.96)* **PAF** -1.84 (-2.71, -0.98)	1.04 (0.50, 2.16) **PAF** -1.57 (-2.30, -0.84)
				PPH	-	-	1.75 (1.49, 2.06)* **PAF** 3.55 (2.67, 4.41)	0.77 (0.40, 1.48) **PAF** 3.28 (2.47, 4.09)
				Pre-term delivery	-	-	1.66 (1.30, 2.11)* **PAF** 2.66 (1.06, 4.23)	1.25 (0.61, 2.56) **PAF** 2.39 (0.96, 3.81)
				Macrosomia	-	-	1.54 (1.27, 1.89)* **PAF** 5.15 (3.64, 6.64)	0.98 (0.30, 3.20) **PAF** 5.52 (3.84, 7.18)
				LBW	-	-	0.75 (0.58, 0.98)* **PAF** -0.01 (-0.10, 0.08)	0.92 (0.47, 1.37) **PAF** -0.03 (-0.20, 0.14)
				NICU	-	-	1.92 (1.52, 1.42)* **PAF** 3.75 (2.05, 5.41)	1.12 (0.52, 2.42) **PAF** 3.52 (1.94, 5.07)
				Perinatal death	-	-	2.19 (0.96, 4.98) **PAF** 3.17 (-2.96, 8.93)	2.00 (0.46, 8.71) **PAF** 3.02 (-2.78, 8.50)

Author and study year	Ethnic groups	Exposure	Control group	Pregnancy outcome	Odds ratio (95% confidence interval)		Adjusted odds ratio (95% confidence interval)	
					White ethnic group	South Asian ethnic group	White ethnic group	South Asian ethnic group
Penn *et al.* 2014 (201)	White women; British, Irish, White Other (n=26390)	≥30kg/m^2	<30kg/m^2	Stillbirth	1.38 (0.72, 2.66)$^{\infty}$	4.84 (1.97, 11.91)$^{\infty *}$	1.32 (0.68, 2.57)	4.64 (1.84, 11.70)*
	Asian women; Indian, Pakistani, Bangladeshi, Asian Other (n=2857)	≥27.5kg/m^2	<27.5kg/m^2					2.83 (1.17, 6.85)*
Pu *et al.* 2015 (216)	Non-Hispanic White (n=9011)	≥25kg/^{2}	<25kg/m^2	GDM	-	-	2.0 (1.74, 2.4)*$ **PAF** 28.9 (22.4, 35.1)	1.17 (1.5, 2.0)*$ **PAF** 25.5 (17.4, 33.3)
	Asian Indian women (n=5069)	≥23kg/m^2	<23kg/m^2		-	-	-	1.9 (1.7, 2.2)*$ **PAF** 39.0 (29.7, 47.6)
Sheridan *et al.* 2013 (200)	White British (n=4488)	<18.5kg/m^2	18.5-24.9kg/m^2	Congenital anomalies	1.50 (0.47-4.18)$	0.96 (0.54,1.73)$	-	-
	Pakistani (n=5127)	25-29.9 kg/m^2			1.00 (0.59,1.70)$	1.03 (0.76,1.39)$	-	-
		≥30kg/m^2			1.22 (0.73, 2.04)$	0.69 (0.45,1.03)$	-	-

$^{\infty}$Effect size calculated from data provided in published paper using STATA 14
*Significant as 95% confidence interval does not cross 1.00
$Relative risk
PAF: population attributable fraction % and 95%CI (PAF is the reduction in population disease risk or mortality that would occur if the exposure to a risk factor was eliminated or reduced to an ideal exposure scenario, where the distributions of other risk factors in the population remain unchanged (217, 218)), PPH=postpartum haemorrhage, GDM=gestational diabetes, NICU=neonatal intensive care unit, LBW= low birth weight, C-section=caesarean section

Table 13 Effects of maternal BMI on pregnancy outcomes in South Asian women compared with White women

Author and study year	Ethnic groups	Exposure	Control group	Pregnancy outcome	Odds ratio (95% confidence interval)	
					White ethnic group	South Asian ethnic group
Dornhost *et al.* 1992 (207)	White women; Northern European and Caucasian (n=6109) Indian women; from the Indian subcontinent (n=1164)	Indian women: <27kg/m^2 ≥27kg/m^2	White women: <27kg/m^2 ≥27kg/m^2	GDM	Ref Ref	10.18 (4.82-21.49)$^{\infty *}$ 13.38 (7.13-25.13)$^{\infty *}$
Makgoba *et al.* 2011(205)	White woman (n=131201) South Asian women (n=2749)	South Asian women: 15.5-24.9kg/m^2 25.0-29.9kg/m^2 ≥30kg/m^2	White European women: 15.5-24.9kg/m^2 25.0-29.9kg/m^2 ≥30kg/m^2	GDM	Ref Ref Ref	3.00 (2.52-3.58)$^{\infty *}$ 4.20 (3.33-5.29)$^{\infty *}$ 3.70 (2.79-4.89)$^{\infty *}$
Penn *et al.* 2014 (201)	White women; British, Irish, White Other (n=26390) Asian women; Indian, Pakistani, Bangladeshi, Asian Other (n=2857)	South Asian women: <30kg/m^2 ≥30kg/m^2	White women: <30kg/m^2 ≥30kg/m^2	Stillbirth	Ref Ref	1.71 (0.95-3.07)$^{\infty}$ 6.13 (2.39-15.73)$^{\infty *}$
Sheridan *et al.* 2013 (200)	White British (n=4488) Pakistani (n=5127)	Pakistani women: <18.5kg/m^2 18.5-24.9kg/m^2 25-29.9kg/m^2 ≥30kg/m^2	White British women: <18.5kg/m^2 18.5-24.9kg/m^2 25-29.9kg/m^2 ≥30kg/m^2	Congenital anomalies	Ref Ref Ref Ref	1.30 (0.73-2.31)$^{\infty}$ 2.48 (1.68-3.67)$^{\infty *}$ 2.55 (1.57-4.14)$^{\infty *}$ 1.33 (0.77-2.30)$^{\infty}$

$^{\infty}$ Effect size calculated from data provided in published paper using STATA 14

* Significant as 95% confidence interval does not cross 1.00

GDM=gestational diabetes, ref=reference group

3.5.3 **Antenatal outcomes associated with maternal pre-/early pregnancy anthropometry**

Gestational diabetes

Differences in means and trends in maternal anthropometrics in women with gestational diabetes

Seven studies presented results on mean MA in a population of women with GDM (MA is considered the exposure here due to temporality; GDM occurs after MA in this instance). One study presented results for maternal weight (kg) (213), and a further six presented information on BMI (206, 210, 212-215), one of which also presented results for maternal skinfold thickness and serum leptin levels (212) (Table 14). The one study that provided the mean weight of women with GDM found that mean weight was only slightly lower in South Asian women (213). Four studies presented the mean BMI of a population of women with GDM (210, 213, 215). Two of these studies found that there was very little difference in mean BMI between South Asian and White women with GDM (210, 215), and the other two found that South Asian women had a lower mean BMI than White women with GDM (206, 213). There was one additional study by Yue *et al.* which did not present any data but did contain a graph showing that BMI was higher in women with GDM in both Indian and Ango-Celtic[10] women than those without GDM (214). It also showed that BMI was very slightly higher in Indian women with GDM compared to Anglo-Celtic women with GDM, and that Indian women without GDM had slightly lower BMI than Anglo-Celtic women without GDM (214).

[10] Definition not specified by author. Definition from Collins English Dictionary “Australian: of or relating to an inhabitant of Australia who was or whose ancestors were born in the British Isles”

Table 14 MA measurements of women in population of women with pregnancy outcome.

Author and study year	Ethnic group	Exposure	Exposure mean (Standard deviation)		P value	Pregnancy outcome
			White ethnic group	South Asian ethnic group		
Dunne *et al.* 2000 (210)	Caucasian women (n=312) Indo-Asian women (Pakistan, India, Bangladesh) (n=128)	BMI (kg/m^2)	29.2 (8.5)	29.1 (5.7)	-	GDM
Hernandez-Rivas *et al.* 2013 (215)	Caucasian (n=190) South Central Asian; Pakistan, India, Bangladesh (n=81)	BMI (kg/m^2)	27.4 (6.18)	27.0 (4.65)	0.630	GDM
Makgoba *et al.* 2012 (206)	White European (n=707) South Asian (n=304)	BMI (kg/m^2)	26.7 (5.8)	25.3 (4.9)	<0.001	GDM
Wong *et al.* 2011 (213)	Anglo-European women (n=215) South Asian women; Indian, Pakistani, Sri Lankan, Fiji Indian (n=160)	BMI (kg/m^2)	30.6 (8.1)	26.8 (5.2)	-	GDM
Sinha *et al.* 2003 (209)	Caucasian women (n=91) Indo Asian women; Predominantly Muslim women from the Punjab Region (n=89)	Weight (kg)	69.8 (4.2)	68.3 (6.45)	-	GDM

GDM=gestational diabetes, BMI=Body mass index

Sommer *et al.* considered the development of BMI, skinfold thickness and serum leptin during and after pregnancy in women with and without GDM (212). In both women with and without GDM, at all time points, including baseline, South Asian women had lower BMI values, higher SFT and serum leptin values than White European women. In addition, women with GDM appeared to have higher measurements of BMI, SFT and serum leptin at all time points compared to women without GDM (healthy women) (212).

Unadjusted effect size for the association between maternal anthropometrics and gestational diabetes

Three studies presented unadjusted results for the association between maternal BMI and GDM (171, 205, 207). Bryant *et al.* found that per 5kg/m^2 increase in BMI, Pakistani women had a higher OR of GDM than White British women (Pakistani: OR 1.55, 95%CI 1.43-1.69 and White: OR 1.25, 95%CI 1.12-1.40) (171) (Table 12). Makgoba *et al.* presented odds for GDM in White women with a BMI 25.0-29.9kg/m^2 and ≥30kg/m^2 compared with women of BMI 15.5-24.9kg/m^2, and presented the raw data to calculate these results for South Asian women (205). Results showed that South Asian women had higher odds of GDM than White women in both BMI groups (BMI 25.0-29.9kg/m^2, South Asian: OR 2.57, 95%CI 2.02-3.23, White: OR 1.77, 95%CI 1.50-2.09 and BMI≥30kg/m^2 South Asian: OR 5.80, 95%CI 4.36-7.71 and White: OR 4.70, 95%CI 3.98-5.55) (205) (Table 12). Dornhorst *et al.* found that when women with a BMI≥27 kg/m^2 are compared with women of BMI<27kg/m^2, White women had a higher OR of GDM than women from the Indian subcontinent (White: OR 4.6, 95%CI 2.1-10.4 and Asian Indian: OR 3.5, 95%CI 2.0-4.2) (207) (Table 12).

Using the data presented in two of the included studies, unadjusted ORs were calculated for GDM in a specified BMI group in South Asian women, compared with White women (205, 207). The results from both studies showed that South Asian women had an increased risk of GDM at all levels of BMI (205, 207). Dornhorst *et al.* considered two BMI groups; BMI≥27kg/m^2 and BMI<27kg/m^2 and showed that when compared with White women, South Asian women had a higher risk of GDM in both BMI groups, and the OR was highest in the higher BMI group (BMI<27kg/m^2, OR 10.18, 95%CI 4.82-21.49 and BMI≥27kg/m^2 OR 13.38 95%CI 7.13-25.13) (207) (Table 13). Data from Makgoba *et al.* allowed the calculation of ORs for three BMI groups; 15.5-24.9 kg/m^2, 25.0-29.9 kg/m^2 and ≥30kg/m^2 (205). When compared with White women of the same BMI, South Asian women in the BMI group 25.0-29.9kg/m^2 had the highest risk of GDM (OR 4.20, 95%CI 3.33-5.29) followed by those with a BMI≥30kg/m^2 (OR 3.70 95%CI 2.79-4.89) with a BMI 15.5-24.9kg/m^2 (OR 3.00 95%CI 2.52-3.58) (205) (Table 13).

Adjusted effect size for the association between maternal anthropometrics and gestational diabetes

There were four studies which also presented adjusted results for the association between maternal BMI and GDM (161, 204, 207, 216), one that considered both pre-existing diabetes and GDM as one outcome variable (204), two that considered GDM as an outcome variable (207, 216) and one that carried out multivariate analysis of factors affecting insulin sensitivity in pregnancy (161). Oteng-Ntim *et al.* found that when Asian women with a BMI≥30kg/m^2 were compared to Asian women with a BMI<30kg/m^2, the AOR for pre-existing diabetes and GDM was higher than that for White women with a BMI≥30kg/m^2 compared to White women with a BMI<30kg/m^2 (South Asian: AOR 5.48, 95%CI 2.43-12.35 and White: AOR 4.97 95%CI 3.39-7.28). The AORs were adjusted for age, parity and deprivation (204) (Table 12). Oteng-Ntim *et al.* also presented PAFs (referred to in Table 12) which are the percentage reduction in outcome (here this is GDM) if the exposure (maternal BMI≥30kg/m^2) was reduced to the ideal (maternal BMI<30kg/m^2). PAFs can be interpreted as the proportion of disease cases (GDM) that would be prevented following the reduction of the exposure to an ideal, assuming that the exposure is causal (218). Results showed that South Asian women had a lower reduction than White women (17.37% 95%CI 13.07, 21.09 in South Asian women and 20.3% 95%CI 15.46, 24.53 in White women) (204) (Table 12).

Two studies provided adjusted results which suggested the effect size for GDM was lower in South Asian women compared with White women (207, 216). Dornhorst *et al.* considered the AOR of GDM in White (Northern European and Caucasian) women and women from the Indian subcontinent, living in the UK, comparing those with a BMI≥27 kg/m^2 with those with a BMI<27 kg/m^2 (207). Findings showed that women from the Indian subcontinent had a lower AOR of GDM than White women (AOR 2.0 (95%CI 0.9-4.2) and 4.3 (95%CI 1.9-9.8), respectively), AORs were adjusted for age and parity (207) (Table 13). Pu *et al.* provided relative risks (RR), adjusted for maternal education, parity, smoking, insurance status for the risk of GDM associated with overweight and obesity in Asian Indian and Non-Hispanic White women (216). They compared women with a BMI≥25kg/m^2 with women with a BMI<25kg/m^2 (216). Results showed Asian Indian women had a lower adjusted RR

(ARR) than Non-Hispanic White women (Asian Indian ARR 1.17, 95%CI 1.5-2.0 and White: ARR 2.0 95%CI 1.74-2.4) (216) (Table 12).

Pu *et al.* also considered the ARR in Asian Indian women using the Asian specific BMI criteria, comparing women with a BMI≥23kg/m^2, with women of BMI<23kg/m^2 (216). Results showed that although the ARR increased, it remained lower than that for the White population with a BMI≥23kg/m^2 (ARR 1.9 95%CI 1.7-2.2) (216) (Table 12). Pu *et al.* also presented PAFs for GDM in South Asian and White women, including a PAF for South Asian women at the lower BMI cut off. Results showed that although at ≥25kg/m^2 the PAF was lower in South Asian women (25.5% 95%CI 17.4, 33.3) than in White women (28.9% 95%CI 22.4, 35.1), when using the equivalent Asian specific BMI criteria ≥23kg/m^2 for the South Asian population, the PAF increased to above that of White women with a BMI 25kg/m^2 (39.0 95%CI 29.7, 47.6) (216) (Table 12).

Retnakaran *et al.* carried out multivariate analysis of factors affecting insulin sensitivity adjusted for age, weeks gestation, parity, pre-pregnancy BMI, weight gain in pregnancy, previous history of GDM, family history of diabetes, glucose intolerance and ethnicity (161). Results showed that BMI in South Asian women had only a modest effect on insulin sensitivity compared with Caucasian women (slope of -0.4 (95%CI -0.22 to -0.13) in South Asians compared with -0.17 (95%CI -0.15 to 0.08) in Caucasians). When adiponectin[11] was added into the model as a covariate, it replaced South Asian ethnicity (161).

Hypertensive disorders of pregnancy

Bryant *et al.* found that per 5kg/m^2 increase in BMI, the odds of HDP was significantly increased for both White and South Asian women (White OR 1.60 95%CI 1.46-1.76 and South Asian OR 1.54 95%CI 1.39-1.71) (171) (Table 12). There was no information relating to differences in means and trends in weight or adjusted effect sizes or the association between MA and HDP.

[11] Adiponectin is a protein that is produced, and secreted by fat cells and has reduced expression in people with obesity and insulin resistance (217)

Anthropometric change

Two studies provided results for the association between MA and GAC (202, 212). Both considered MA as continuous variables, Bissenden *et al.* presented mean difference in gain of maternal weight and SFT (bicep, triceps and subscapular SFT) (202) while Sommer *et al.* presented the change in BMI, triceps, subscapular, suprailiac SFT measures and the sum of all these, and also serum leptin levels from 14 to 28 weeks gestation (212).

Differences in means and trends in maternal anthropometrics in women with gestational anthropometric change

Bissenden *et al.* provided baseline measurements for maternal weight and SFT and the amount of each of these measures gained at 29, 33 and 37 weeks gestation for Asian and European women in four groups (202). The four groups were; Group A: normal pregnancy, Group B: those with unexplained fetal growth retardation, Group C: those with pregnancy pathology and normal fetal growth, and Group D: those with pregnancy pathology and normal fetal growth (202). A pregnancy pathology was defined as either hypertension (a diastolic blood pressure of more than 90 mmHg at any stage during pregnancy outside labour or vaginal bleeding during labour (threatened abortion or antepartum haemorrhage) (202). Fetal growth retardation was defined as a baby born below the 10th centile in weight in accordance with data from Thompson *et al.* 1968 (219).

Bissenden *et al.* presented results for weight measurements at different time points during pregnancy (202) (Table 15). The baseline weight measurements (booking 8-18 weeks) and the measurements at 29 (29-31) weeks, 33 (32-34) weeks and 37 (35-39) weeks gestation were used to calculate the mean difference in GAC from baseline to each time point. In women who had normal pregnancies (group A), weight at baseline was lower, all measurements of SFT were higher and at all-time points, weight gain was slightly lower in South Asian women. Bicep and triceps SFT were found to be higher in South Asian women, although subscapular SFT gain was lower. In women who had a pregnancy pathology and normal fetal growth (Group C), weight at baseline was lower in South Asian women, and all SFT measurements were higher. Weight gain was lower in South Asian women at all time points, as were

gains in all SFT measurements. Data were not available for European women in group B (those with unexplained fetal growth retardation), or South Asian women in Group D (those with pregnancy pathology and normal fetal growth) so no comparisons could be made.

Within the ethnic groups, those with pregnancy pathologies (groups C and D) seemed to have a higher weight and SFT measurements at baseline than those with a normal pregnancy. In the European group, those women that had a pregnancy pathology and a light for gestational age baby appeared (group D) to gain more weight and SFT than those without a light for gestational age baby (group C). The results of this study were limited by both small sample size and the fact that there was no data available for group B in European women and group D in South Asian women, limiting the comparisons that could be made. There was no information presented relating to differences in means and trends in weight or adjusted effect sizes (Table 15).

Table 15 GAC in women with different pregnancy complications

Exposure (measured at booking visit (8-18 weeks)	Exposure Mean ±SD (n)						Outcome	Outcome Mean difference (95%CI) ∞					
	European groups*			Asian groups*				European groups*			Asian groups*		
	A	C	D	A	B	C		A	C	D	A	B	C
Weight (kg)	56.3 ±6.1 (23)	65.2 ±10.5 (10)	66.3 ±8.2 (6)	53.0 ±7.7 (11)	49.9 ±7.7 (5)	60.6 ±11.1 (9)	**Weight gain (g) to:**						
							29 (29-31) weeks	6.2 (2.7 to 9.7)	8.4 (-1.6 to 18.4)	8.5 (-2.9 to 19.9)	6.2 (<0.0 to 12.8)	3.8 (-4.3 to 11.9)	6.1 (-6.2 to 18.4)
							33 (32-34) weeks	8.3 (4.5 to 12.1)	10.1 (0.3 to 19.9)	10.4 (0.3 to 20.5)	6.8 (0.2 to 13.4)	3.5 (-4.7 to 11.7)	7.2 (-3.7 to 18.1)
							37 (35-39) weeks	10.4 (6.8 to 14.0)	8.9 (-1.3 to 19.1)	12.7 (0.7 to 24.8)	9.3 (2.7 to 15.9)	3.5 (-6.4 to 13.4)	6.9 (-3.8 to 17.6)
Bicep SFT (mm)	7.18 ±3.2 (23)	10.1 ±3.2 (10)	9.12 ±4.0 (6)	8.8 ±3.2 (10)	9.9 ±6.2 (5)	11.7 ±7.9 (9)	**Bicep SFT gain (mm) to:**						
							29 (29-31) weeks	2.14 (>0.0 to 4.3)	3.4 (-2.0 to 8.8)	3.6 (-2.9 to 10.0)	2.9 (-1.2 to 7.0)	-1.1 (-8.5 to 6.3)	2.3 (-3.9 to 8.5)
							33 (32-34) weeks	3.2 (1.1 to 5.3)	3.33 (-1.4 to 8.1)	5.5 (0.7 to 10.4)	4.2 (0.3 to 8.1)	-1.5 (-9.3 to 6.3)	2.3 (-3.9 to 8.5)
							37 (35-39) weeks	2.45 (0.5 to 4.4)	2.3 (-2.0 to 6.7)	4.9 (-2.2 to 12.0)	4.1 (0.1 to 8.1)	-2.0 (-8.5 to 4.5)	1.8 (-4.3 to 7.9)
Tricep SFT (mm)	12.69 ±3.9 (23)	17.89 ±5.2 (10)	15.73 ±5.5 (6)	16.2 ±3.6 (10)	14.2 ±5.5 (5)	20.5 ±10.8 (9)	**Triceps SFT gain (mm) to:**						
							29 (29-31) weeks	1.1 (-1.3 to 3.4)	1.3 (-4.3 to 6.81)	3.9 (-3.9 to 11.6)	3.1 (-1.8 to 8.0)	-0.9 (-7.5 to 5.7)	-0.2 (-9.00 to 8.6)
							33 (32-34) weeks	1.5 (-0.9 to 3.9)	-0.1 (-5.3 to 5.1)	3.7 (-2.7 to 10.0)	3.5 (-0.9 to 7.9)	-1.8 (-7.6 to 4.0)	-1.6 (-8.8 to 5.6)
							37 (35-39) weeks	0.9 (-1.4 to 3.3)	-1.3 (-6.1 to 3.6)	4.2 (-3.7 to 12.0)	3.5 (-1.2 to 8.2)	-1.9 (-7.4 to3.6)	-1.3 (-8.6 to 6.00)
Subscapular SFT (mm)	11.49 ±4.6 (23)	17.47 ±8.1 (10)	16.43 ±11.0 (6)	17.5 ±5.1 (10)	15.1 ±8.1 (5)	21.4 ±12.9 (9)	**Subscapular SFT gain (mm) to:**						
							29 (29-31) weeks	3.0 (0.6 to 5.3)	1.6 (-5.9 to 9.2)	2.07 (-11.1 to 15.2)	4.6 (>0.0 to 9.2)	1.4 (-9.4 to 12.2)	0.7 (-9.3 to 10.7)
							33 (32-34) weeks	3.6 (1.1 to 6.1)	2.4 (-5.5 to 10.3)	2.5 (-8.8 to 13.8)	3.4 (-1.3 to 8.1)	0.4 (-7.8 to 8.6)	-0.4 (-8.5 to 7.7)
							37 (35-39) weeks	4.01 (1.2 to 6.8)	0.5 (-7.4 to 8.4)	4.1 (-9.1 to 17.)	-4.5 (-11.5 to 2.5)	0.7 (-7.8 to 9.2)	0.1 (-8.8 to 9.0)

∞Calculated in STATA 14 from data provided in Bissenden JG, Scott PH, King J, Hallum J, Mansfield HN, Wharton BA. Anthropometric and biochemical changes during pregnancy in Asian and European mothers having light for gestational age babies. BJOG: An International Journal of Obstetrics & Gynaecology. 1981;88(10):999-1008. *Groups: A=normal pregnancy; B=unexplained light for gestational age baby; C=pregnancy pathology and normal fetal growth; and D=pregnancy pathology and light for gestational age baby (there were no European women B and no Asian women D due to small study sample size).

Notes: Pregnancy pathology either hypertension (a diastolic blood pressure of more than 90 mmHg at any stage during pregnancy outside labour or vaginal bleeding during labour (threatened abortion or antepartum haemorrhage). Fetal growth retardation is a baby born below the 10th centile in weight in accordance with data of Thompson *et al.* 1968

Sommer *et al.* presented the GAC (BMI, triceps, subscapular, suprailiac SFT measures and the sum of all these, and also serum leptin levels) between 14 weeks gestation and 28 weeks gestation (212). Results showed that despite having a significantly lower BMI at 14 weeks gestation (p=0.015), South Asian women had significantly higher BMI at 28 weeks gestation (p=0.023) (212) (Table 16). Triceps SFT was not significantly different between the two ethnic groups at 14 weeks gestation (p=0.83), and there was no significant difference in the SFT gained to 28 weeks (p=0.085) (212). South Asian women had significantly higher subscapular SFT at both 14 and 28 weeks gestation compared with European women (p=0.002 and p<0.001 respectively), gaining significantly more from 14 weeks gestation to 28 weeks (p=0.12) (212). At 14 weeks gestation there was no significant difference in suprailiac SFT between the two ethnic groups (p=0.960); this was also true at 28 weeks gestation (p=0.240) (212). There was no significant difference in the sum of SFT at 14 weeks gestation between the two ethnic groups (p=0.200), however by 28 weeks gestation South Asian women had gained a significantly higher sum of SFT (p=0.001) (212) (Table 16). There was no information relating to unadjusted or adjusted effect sizes for the association between MA and GAC.

A summary of the evidence identified for outcomes which occur during pregnancy associated with MA is given in Table 17. This information has then been depicted in the form of a conceptual model diagram (Figure 5). Arrows represent evidence of an association between two variables.

Table 16 GAC from 14 to 28 weeks gestation

Ethnic group (European n=309 and South Asian n=158)	Weight measure	14 weeks gestation Mean (SD)	P value for difference between ethnic groups	28 weeks gestation Mean (SD)	P value for difference between ethnic groups	P value for change in parameters 14 weeks gestation to 28 weeks gestation between ethnic groups
European	BMI (kg/m²)	25.4 (4.9)	0.015	27.8 (4.8)	0.023*	0.630
South Asian		24.3 (4.1)		26.8 (4.1)		
European	Triceps (mm)	24.1 (6.9)	0.83	24.9 (6.6)	0.045*	0.085
South Asian		24.2 (7.0)		26.3 (6.8)		
European	Subscapular (mm)	19.2 (7.8)	0.002	20.8 (7.6)	<0.001*	0.120
South Asian		21.7 (7.1)		24.3 (7.1)		
European	Suprailiac (mm)	27.1 (7.6)	0.96	30.0 (6.8)	0.240	0.330
South Asian		27.1 (7.3)		30.8 (6.3)		
European	Sum of skinfolds	70.4 (19.8)	0.20	75.4 (18.4)	0.001*	0.053
South Asian	(mm)	72.9 (18.5)		81.5 (17.5)		
European	S-leptin (µg/L)	1.35 (0.17)	0.002	1.71 (0.18)	<0.001*	<0.004*
South Asian		1.65 (0.14)		2.20 (0.15)		

Data from table 2 Sommer C, Jenum AK, Waage CW, Mørkrid K, Sletner L, Birkeland KI. Ethnic differences in BMI, subcutaneous fat, and serum leptin levels during and after pregnancy and risk of gestational diabetes. European Journal of Endocrinology. 2015;172 (6):649-56.

Table 17 Summary table of the results relating to MA and outcomes during pregnancy

Author and year	Anthropometric exposure	Outcome		
		Anthropometric change during pregnancy	GDM	HDP
Bissenden *et al.* 1981 (202)	Weight (kg)	*Weight gain (kg), UA, No p value		
	Bicep SFT (mm)	*Bicep skinfold gain (mm), UA, No p value		
	Tricep SFT (mm)	*Tricep skinfold (mm), UA, No p value		
	Subscapular SFT (mm)	*Subscapular skinfold gain (mm), UA, No p value		
Bryant *et al.*, 2014, (72)	5kg/m^2 increase in BMI		*** UA, P=0.003 White OR 1.25 (95% CI1.12, 1.40) Pakistani OR 1.55 (95% CI1.43, 1.69)	*** UA, p=0.60
Dornhorst *et al.* 1992 (207)	Maternal BMI (kg/m^2)		*** A, No P value	
			** UA, No P value	
Dunne *et al.* 2000 (210)	Maternal BMI (kg/m^2)		*UA, P value non-significant (value not given)	
Hernandez-Rivas *et al.* 2013 (215)	Maternal BMI (kg/m^2)		*UA, P=0.630	
Makgoba *et al.* 2011 (77)	Maternal BMI (kg/m^2)		*** UA , No P value	
			** UA, No P value	
Makgoba 2012 (206)	BMI (kg/m^2)		*UA P<0.001	
Oteng-Ntim *et al.* 2013 (76)	BMI≥30kg/m^2 vs <30kg/m^2		*** A, No P value	
Pu *et al.* 2015 (88)	BMI≥25kg/m^2 vs <25kg/m^2 and BMI≥23kg/m^2 vs <23kg/m^2		*** A , No p value	
Retnakaran *et al.* 2006 (90)	Maternal BMI (kg/m^2)		** UA, No p value	
Sommer *et al.* 2015 (84)	Maternal BMI (kg/m^2)	*UA, p=0.63 at 14 to 28 weeks	*UA, No p value	
	Serum leptin (µg/l)	*UA, p=0.085 at 14 to 28 weeks	*UA, No p value	
	Tricep SFT (mm)	*UA, p=0.12 at 14 to 28 weeks		
	Subscapular SFT (mm)	*UA, p=0.33 at 14 to 28 weeks		
	Suprailiac SFT(mm)	*UA, p=0.053 at 14 to 28 weeks		
	Sum of SFT (mm)	*UA, p=0.004 at 14 to 28 weeks	*UA, No p value	
Yue *et al.* 1996 (214)	Maternal BMI (kg/m^2)		*UA, No p value	
Wong *et al.* 2011 (85)	Maternal BMI (kg/m^2)		*UA, No p value	

Green= Increased association between exposure and outcome in South Asian women; Red= Non-significant or no difference between ethnic groups; Grey= No data available
*= Difference in mean of exposure in a population with pregnancy outcome between two South Asian and White women (e.g. mean weight (kg) in South Asian and White women with GDM), **= Where South Asian women of an exposure category are compared with White women in the same exposure category (e.g. South Asian women with obesity compared with White women with obesity), ***= Where South Asian women in the exposure category are compared with South Asian women in the reference category, and White women in the exposure category compared with White women in the reference group (e.g. South Asian women with obesity compared to South Asian women with recommended BMI, and White women with obesity compared with White women with recommended BMI). UA= unadjusted; A=Adjusted; GDM= Gestational diabetes mellitus; HDP= Hypertensive disorders of pregnancy; OR=odds ratio; Note: all ORs presented with 95% confidence interval e.g. OR (95% CI)

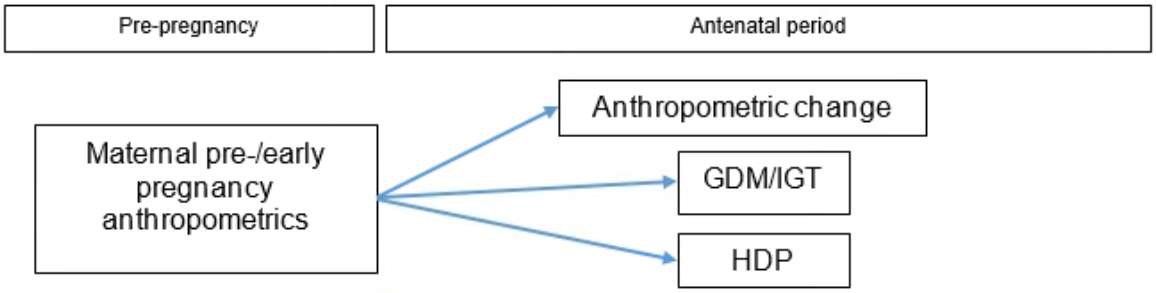


Figure 5 Diagram representing associations between MA and pregnancy outcomes where evidence from this systematic review suggests weight related risk differs between South Asian and White women and/or is significantly increased for South Asian women

GDM=gestational diabetes mellitus, IGT=impaired glucose tolerance
HDP=hypertensive disorders of pregnancy

3.5.4 Maternal and infant birth outcomes associated with maternal pre-/early pregnancy anthropometry

Mode of delivery

Bryant *et al.* found that per 5kg/m^2 increase in BMI, Pakistani and White women had very similar ORs for C-section (White: OR 1.34 95%CI 1.26-1.42 and Pakistani: AOR 1.36 95%CI 1.27-1.45) (171) (Table 12).

Oteng-Ntim *et al.* presented ORs and PAFs adjusted for age, parity and deprivation. Results showed that White women with a BMI≥30 kg/m^2 had a significantly increased AORs, and of elective and emergency lower segment C-section (LSCS) compared with White women with a BMI<30 kg/m^2 (Elective LSCS: AOR 1.41 95%CI 1.08-1.84 and emergency LSCS: AOR 1.98 95%CI 1.69-2.33) (Table 12).South Asian women with a BMI≥30kg/m^2 on the other hand, did not have a significantly increased ORs (elective lower segment caesarean section: AOR 1.52 95%CI 0.73, 3.14 and emergency lower segment caesarean section: AOR 0.65 95%CI 0.32, 1.31) (204) (Table 12).PAFs for both elective and emergency LSCS were higher for White women (4.24 95%CI 2.43-6.00 and 3.48 95%CI 2.65-4.30, respectively) than they were in South Asian women (4.02 95%CI 2.31-5.70 and 2.93 95%CI 2.23-3.63). White women also had significantly decreased odds of instrumental delivery when

South Asian women did not (White: AOR 0.78 95% CI 0.63-0.96 and South Asian: AOR 1.04 95%CI 0.50-2.16), PAFs for instrumental delivery were higher in White women than South Asian (3.48 95%CI 2.65, 4.30 and -1.57 95%CI -2.30,-0.84, respectively) (204) (Table 12).There was no evidence which provided difference in means of MA in women with certain modes of delivery.

Distance from skin to epidural space

The systematic search identified only one study which investigated the distance from skin to epidural space at a range of BMI values (204). Results showed that at each BMI, the distance was higher for White women compared with South Asian, although no p-values were available to indicate statistical significance of the ethnic difference (208) (Table 18).

Table 18 Ethnic difference in distance from skin to lumbar epidural space by maternal BMI

Author and study year	**Exposure: BMI (kg/m^2)**	**Pregnancy outcome**: Distance from skin to lumbar epidural space (cm)	
		White ethnic group	**South Asian ethnic group**
Sharma *et al.* 2011	20 25 30 35 40	4.7 5.3 6.0 6.6 7.2	4.5 5.1 5.7 6.2 6.8

BMI: Body mass index

Congenital anomaly

Sheridan *et al.* found that when women with a BMI<18.5kg/m^2 were compared with women of BMI18.5-24.9kg/m^2, there was no significant increase in the risk of congenital anomaly for either White or Pakistani women (White: RR 1.50, 95%CI 0.47-4.18 and Pakistani: RR 0.96, 95%CI 0.54-1.73) (200) (Table 12).This was also the case for women with a BMI 25-29.9 kg/m^2 (White: RR 1.00 95%CI 0.59-1.70 and Pakistani: RR 1.03, 95%CI 0.76-1.39) and those with a BMI≥30kg/m^2 (White: RR 1.22 95%CI 0.73-2.04 and Pakistani RR 0.69 95%CI 0.45-1.03) (200) (Table 12).

Raw data presented by Sheridan *et al.* allowed the ORs for congenital anomalies in Pakistani women compared with White women to be calculated for the following BMI groups; <18.5kg/m^2, 18.5-24.9kg/m^2, 25-29.9kg/m^2 and ≥30kg/m^2. Results showed that there was a significantly increased risk of congenital anomalies for South Asian women in the 18.5-24.9kg/m^2 and 25-29.9 kg/m^2 BMI groups (OR 2.48, 95%CI 1.68-3.67 and OR 2.55 95%CI 1.57-4.14, respectively), but not the <18.5kg/m^2 or ≥30kg/m^2 group (OR 1.30 95%CI 0.73-2.31 and OR 1.33 95%CI 0.77-2.30, respectively) (200) (Table 12). There was no evidence identified that presented either difference in means in women whose pregnancies were affected by congenital anomalies or adjusted findings for the association between MA and congenital anomalies.

Gestational age at delivery

Bryant *et al.* found that per 5kg/m^2 increase in BMI, the OR of pre-term birth (<37 weeks) was significantly decreased for White women (OR 0.87, 95%CI 0.77-0.98), and decreased for Pakistani women although the result did not reach statistical significance (OR 0.98 95%CI 0.87-1.11) (171) (Table 12).

Oteng-Ntim *et al.* presented ORs and PAFs adjusted for age, parity and deprivation (204). Results showed that when women with a BMI≥30kg/m^2 were compared with women of a BMI<30kg/m^2, White women had a significantly increased AOR (1.66, 95%CI 1.30-2.11), while Asian women did not (AOR 1.25, 95%CI 0.61-2.56) (204) (Table 12).The PAF for White women was slightly higher than for South Asian women (2.66, 95%CI 1.06-4.24 and 2.39 95%CI 0.96-3.81, respectively) (204) (Table 12). There were no studies identified by the searches that presented difference in means for women delivering at different gestational ages.

Stillbirth

One study presented results on stillbirth (201). Women with a BMI≥30kg/m^2 were compared with women of a BMI<30kg/m^2, South Asian women had a higher increase in stillbirth than White women (White: OR 1.38, 95%CI 0.72-2.66 and Asian: OR 4.84, 95%CI 1.97-11.91) (201) (Table 12).Using the raw data presented by Penn *et*

al., unadjusted ORs for the risk of stillbirth were calculated comparing Asian women to White women of the same BMI. Results showed that while there was no significant increase in risk of stillbirth when South Asian women with a BMI<30kg/m^2 were compared with White women of the same BMI (OR 1.71, 95%CI 0.95-3.07), at a BMI≥30kg/m^2 South Asian women had a significantly higher risk (OR 6.13, 95%CI 2.39-15.73) (Table 13).

Penn *et al.* also presented ORs which were adjusted for maternal age, hypertension and parity (201). When women with a BMI≥30kg/m^2 were compared with women of a BMI<30kg/m^2, South Asian women had a higher increase in stillbirth than White women, although in both White and Asian women the effect size was reduced following adjustment (White AOR 1.32, 95%CI 0.68-2.57 and Asian AOR 4.64, 95%CI1.84-11.70) (201) (Table 12). Asian specific BMI criteria were also applied and showed that South Asian women with obesity had an AOR of stillbirth of 2.83 (95%CI 1.17-6.85). While this is lower than the AOR when using the BMI criteria for the general population, it is still higher than the AOR for the White population and the confidence interval is narrower suggesting that it is a more precise estimate (201) (Table 12). There were no studies identified by the review that presented difference in means for women who had a stillbirth.

Birth weight

Bissenden *et al.* presented a graph that showed that in a population of women having well grown babies (babies above the 10th centile according to Thomson *et al.* 1968 (219)), Asian women delivering well grown babies have mean weight (kg), middle upper arm circumference and bicep SFT (mm) that was not significantly different than that of White women delivering well grown babies (non-significant, no p-values specified) South Asian women in this study did, however, have significantly higher mean triceps and subscapular SFT (mm) than White women ($p<0.025$, and $p<0.005$, respectively) (203).

Bryant *et al.* found that per 5kg/m^2 increase in BMI, Pakistani women had a higher OR for macrosomia than White British women (White British: OR 1.36, 95%CI 1.27-1.47 and Pakistani: OR 1.57, 95%CI 1.41-1.75) (171) (Table 12).

Oteng Ntim *et al.* presented ORs and PAFs adjusted for age, parity and deprivation for macrosomia and low birth weight (defined as <2.5kg) (204). Findings showed that when women with a BMI≥30kg/m^2 were compared with women of BMI<30kg/m^2, White women had a higher AOR of macrosomia than South Asian women (White: AOR 1.54, 95%CI 1.27-1.89 and Asian AOR 0.98, 95%CI 0.30-3.20), the PAF was slightly higher in South Asian women than in White women (5.52, 95%CI 3.84-7.18 and 5.15, 95%CI 3.64-6.64, respectively) (204). White women with a BMI≥30kg/m^2 also had significantly reduced AOR of low birth weight (AOR 0.75, 95%CI 0.58-0.98), the reduction in AOR for South Asian women did not reach statistical significance (AOR 0.92, 95%CI 0.47-1.37), the PAF was very similar in White women and South Asian (-0.01, 95%CI -0.10-0.08 and -0.03, 95%CI -0.20-0.14, respectively) (204) (Table 12).

Makgoba *et al.* suggested that pregnancy comorbidities, in particular GDM, may influence the association between maternal weight and pregnancy outcomes (206). Makgoba *et al.* presented a graph but no raw data or data from analysis, showing that there were differences in birth weight between women with and without GDM at different BMI values (206). The graph suggested that in both ethnic groups, independent of whether or not GDM was present, birth weight increased with increasing maternal BMI (206). In women without GDM, South Asian women had lower birth weights at all BMI values compared with White European women (206). However, when comparing women with GDM, at the lower BMI values, birth weights in South Asian women started lower than those for White European women (206). As BMI increased, however, birth weight z-scores for South Asian women increased to the same level as White European women. In both ethnic groups, birth weight was significantly higher in women with GDM (206).

Post-partum haemorrhage

Oteng-Ntim *et al.* presented ORs and PAFs adjusted for age, parity and deprivation (204). Results showed that when women with a BMI≥30kg/m^2 were compared with women with a BMI<30kg/m^2, White women had significantly increased risk of PPH while South Asian women did not (White: AOR 1.75, 95%CI 1.49-2.06 and South Asian: AOR 0.77, 95%CI 0.40-1.48) (204) (Table 12).The PAF for PPH was higher in

White women than South Asian (3.55%, 95%CI 2.67, 4.41 and 3.28%, 95%CI 2.47, 4.09, respectively) (204) (Table 12).There were no studies identified which presented either difference in means in women with PPH, or the unadjusted effect size for the association between MA and PPH.

Admission to neonatal intensive care unit

Oteng-Ntim *et al.* presented ORs and PAFs for admission to the NICU adjusted for age, parity and deprivation (204). Results showed that when women of BMI≥30kg/m^2 were compared with women of BMI<30kg/m^2, White women had a significantly increased AOR of admission to the NICU (White AOR 1.92, 95%CI 1.52-1.42 and South Asian AOR 1.12, 95%CI 0.52-2.42), the PAF was higher in White women than South Asian women (3.75%, 95%CI 2.05, 5.41 and 3.52%, 95%CI 1.94, 5.07, respectively) (204) (Table 12).The searches did not identify any studies which presented difference in means in women with admission to the NICU, or the unadjusted effect size for the association between maternal pre-/early pregnancy anthropometrics and admission to the NICU.

Perinatal death

Oteng-Ntim *et al.* presented ORs for perinatal death adjusted for age, parity and deprivation (204). Results showed that when women with a BMI≥30kg/m^2 were compared with women with a BMI<30kg/m^2,both White and South Asian women with a BMI≥30kg/m^2 had an increased AOR of perinatal death, neither AOR reached statistical significance (White: AOR 2.19, 95%CI 0.96-4.98 and South Asian: AOR 2.00, 95%CI 0.46-8.71), the PAF was slightly higher in White women than South Asian women (3.17%, 95%CI -2.96, 8.93 and 3.02%, 95%CI -2.78, 8.50, respectively) (204) (Table 12).There were no studies identified which presented either difference in means in women with perinatal death, or the unadjusted effect size for the association between MA and perinatal death.

A summary of the evidence identified for birth outcomes associated with MA is given in Table 19. This information has then been depicted in the form of a conceptual

model diagram (Figure 6). Arrows represent evidence of an association between two variables.

Table 19 Summary table of the results relating to MA and birth outcomes for model development

Author and year	Anthropo-metric exposure	Outcome								
		Distance to epidural space	**Stillbirth**	**PTB**	**Congenital anomalies**	**Birth weight**	**Mode of delivery**	**PPH**	**Perinatal death**	**Admission to NICU**
Bissenden *et al.* 1981 (203)	Weight (kg)					Well grown babies *UA, P value non-significant (value not given)				
	Middle upper arm (mm)					**Well grown babies** *UA, P value non-significant (value not given)				
	Tricep SFT (mm)					**Well grown babies** *UA, P value <0.025				
	Subscapular SFT (mm)					**Well grown babies** *UA, P value <0.005				
	Bicep SFT (mm)					**Well grown babies** *UA, P value non-significant (value not given)				
Bryant *et al.*, 2014, (72)	5kg/m^2 increase in BMI			*** UA P=0.17		**Macrosomia** *** UA P=0.04	**C-section** *** Unadjusted P=0.78			
Makgoba 2012 (206)	BMI (kg/m^2)					**Birth weight z-scores** ***A, No P value given				
Oteng-Ntim *et al.* 2013 (76)	BMI≥30kg/m^2 vs <30kg/m^2			*** A No P value		**LBW** *** A No P value	**C-section and instrumental delivery** *** A No P value	*** A No P value	*** A No P value	*** A No P value
Penn *et al.* 2014 (73)	Maternal Obesity BMI≥30kg/m^2 vs <30kg/m^2 and BMI≥27.5kg/m^2 vs <27.5kg/m^2		*** A P=0.001 (0.02 using Asian specific BMI) for South Asian P=0.41 for White ** UA No P value							
Sharma *et al.* 2011 (76)	Maternal BMI (kg/m^2)	*UA No P value								

Author and year	Anthropo-metric exposure	Outcome								
		Distance to epidural space	**Stillbirth**	**PTB**	**Congenital anomalies**	**Birth weight**	**Mode of delivery**	**PPH**	**Perinatal death**	**Admission to NICU**
Sheridan *et al.* 2013 (71)	Maternal BMI (kg/m^2)				*** UA Compared with normal BMI, for underweight, overweight and obese P =1.00, 0.65, 0.17, for White and P=0.96, 0.87 and 0.07 and for South Asian ** UA No P value					

Green= Increased association between exposure and outcome in South Asian women
Red= Non-significant or no difference between ethnic groups
Grey= No data available
*= Difference in mean of exposure in a population with pregnancy outcome between two South Asian and White women (e.g. mean weight (kg) in South Asian and White women with GDM)
**= Where South Asian women of an exposure category are compared with White women in the same exposure category (e.g. South Asian with obesity women compared with White women with obesity)
***= Where South Asian women in the exposure category are compared with South Asian women in the reference category, and White women in the exposure category compared with White women in the reference group (e.g. South Asian women with obesity compared to South Asian women with recommended BMI, and White women with obesity compared with White women with recommended BMI)
UA= unadjusted, A=Adjusted, GDM= Gestational diabetes mellitus, HDP= Hypertensive disorders of pregnancy, PTB= Pre-term birth, PPH= Post-partum haemorrhage, NICU= neonatal intensive care unit

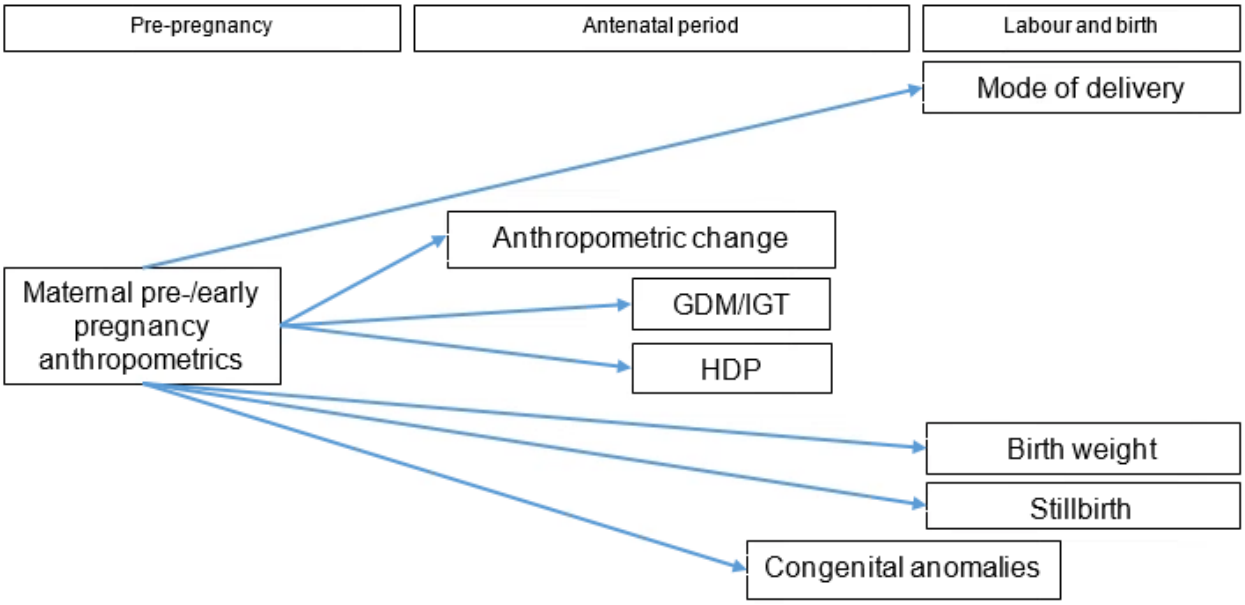


Figure 6 Diagram representing associations between MA and pregnancy outcomes where evidence from this systematic review suggests weight related risk differs between South Asian and White women and/or is significantly increased for South Asian women.

HDP=Hypertensive disorders of pregnancy, GDM= Gestational diabetes mellitus, IGT= Impaired glucose tolerance
Note: Although congenital anomalies can be detected in the antenatal period (reflected by placement in conceptual model), they have been considered as a birth outcome for the purpose of this thesis

3.5.5 Longer term maternal outcomes associated with maternal anthropometrics

Postnatal impaired glucose tolerance

One study provided the mean weight of women with postnatal IGT finding that Asian women had a lower weight (68.3kg) compared with White women (79.7kg); no p value was given. There were no studies identified which presented either the adjusted or unadjusted effect size for the association between maternal pre-/ early pregnancy anthropometrics and postnatal IGT.

Post-partum weight retention

There was one study that provided GAC (BMI, triceps, subscapular, suprailiac SFT measures and the sum of all these, and also serum leptin levels) between 14 weeks gestation and 14 weeks post-partum (212). Results showed that despite having a significantly lower BMI at 14 weeks gestation ($p=0.015$), the change in BMI from 14 weeks gestation to 14 weeks post-partum was significantly higher for South Asian women ($p<0.001$) leaving them with a mean BMI that was not significantly different to that of European women ($p=0.830$) (Table 20). Triceps SFT was not significantly different between the two ethnic groups at 14 weeks gestation ($p=0.830$). However, at 14 weeks post-partum, triceps SFT was significantly higher for South Asian women compared with European women ($p<0.001$) (212) (Table 20).

South Asian women also had significantly higher subscapular SFT at both 14 weeks gestation and 14 weeks post-partum compared with European women ($p=0.002$ and $p<0.001$, respectively), gaining significantly more from 14 weeks gestation to 14 weeks post-partum ($p=0.022$) (212) (Table 20). At 14 weeks gestation, there was no significant difference in suprailiac SFT between the two ethnic groups ($p=0.96$). However, at 14 weeks post-partum South Asian women had significantly higher suprailiac SFT ($p= 0.001$) and had gained significantly more than European women ($p=0.016$) (212) (Table 20). There was no significant difference in the sum of SFT at 14 weeks gestation between the two ethnic groups ($p=0.20$). However, by 14 weeks post-partum, South Asian women had gained significantly more sum of SFT ($p<0.001$), leading to a significantly higher sum of SFT ($p<0.001$) compared with European women (212) (Table 20). There were no studies identified which presented either the adjusted or the unadjusted effect size for the association between MA and admission to the NICU.

A summary of the evidence identified for long-term outcomes associated with MA is given in Table 21, and the information has then been depicted in the form of a conceptual model diagram (Figure 7).

Table 20 Change in anthropometric measures from 14 weeks gestation to 14 weeks post-partum

Ethnic group (European n=309 and South Asian n=158)	**Weight measure**	**14 weeks gestation Mean (SD)**	**P value for difference between ethnic groups**	**14 weeks post-partum Mean (SD)**	**P value for difference between ethnic groups**	**P value for change in parameters 14 weeks gestation to 14 weeks post-partum between ethnic groups**
European	BMI (kg/m²)	25.4 (4.9)	0.015	25.7 (5.1)	0.83	<0.001
South Asian		24.3 (4.1)		25.6 (4.2)		
European	Triceps (mm)	24.1 (6.9)	0.83	24.8 (6.7)	<0.001	<0.001
South Asian		24.2 (7.0)		27.5 (6.1)		
European	Subscapular (mm)	19.2 (7.8)	0.002	20.8 (7.9)	<0.001	0.022
South Asian		21.7 (7.1)		25.7 (6.9)		
European	Suprailiac (mm)	27.1 (7.6)	0.96	27.1 (7.8)	0.001	0.016
South Asian		27.1 (7.3)		30.0 (6.9)		
European	Sum of skinfolds (mm)	70.4 (19.8)	0.20	72.6 (19.6)	<0.001	<0.001
South Asian		72.9 (18.5)		83.1 (16.5)		
European	S-leptin (µg/L)	1.35 (0.17)	0.002	0.90 (0.18)	<0.001	<0.001
South Asian		1.65 (0.14)		1.53 (0.16)		

Data from Table 2 Sommer C, Jenum AK, Waage CW, Mørkrid K, Sletner L, Birkeland KI. Ethnic differences in BMI, subcutaneous fat, and serum leptin levels during and after pregnancy and risk of gestational diabetes. European Journal of Endocrinology. 2015;172(6):649-56.

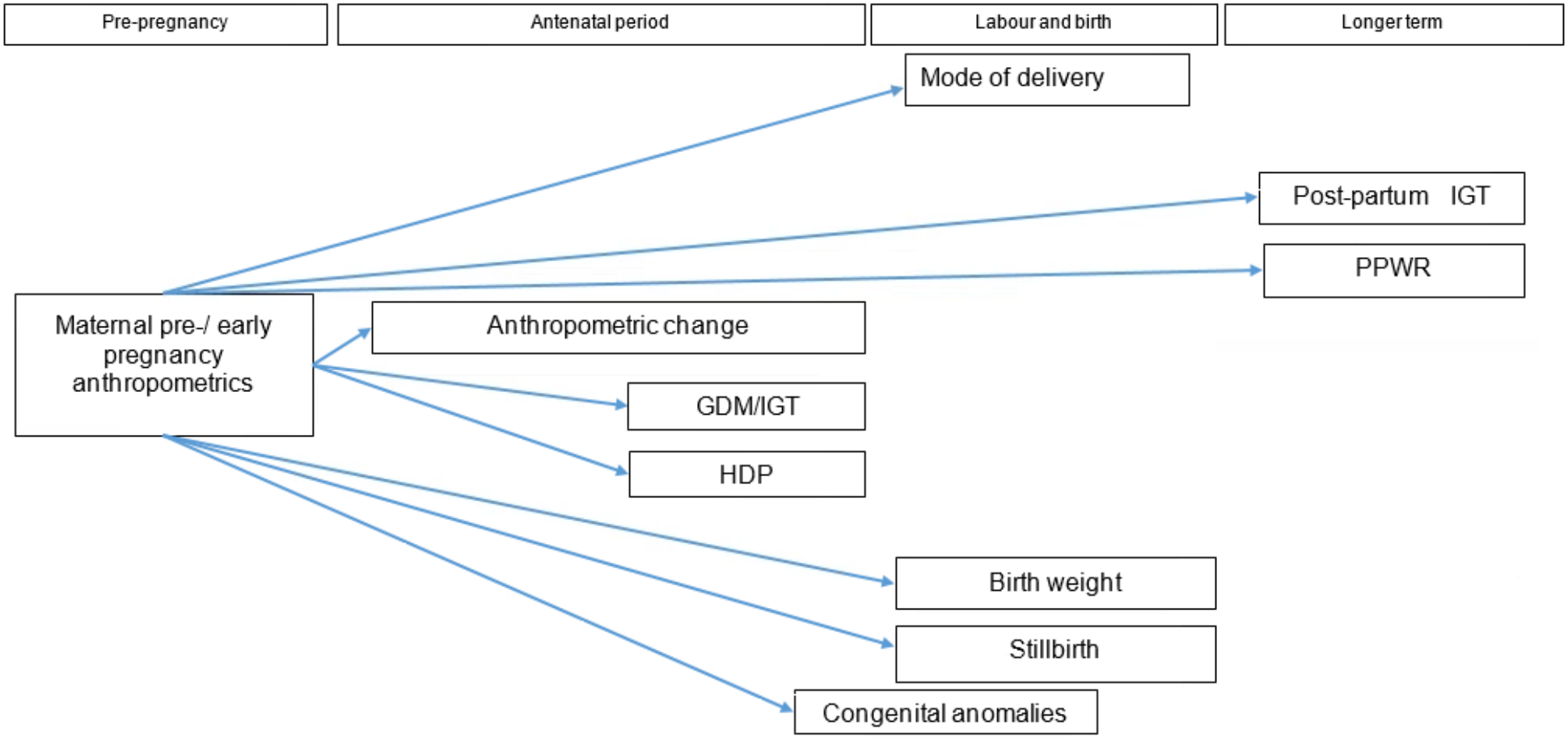


Figure 7 Diagram representing associations between MA, GAC and pregnancy outcomes where evidence from this systematic review suggests weight related risk differs between South Asian and White women and/or is significantly increased for South Asian women

HDP=Hypertensive disorders of pregnancy, GDM=gestational diabetes mellitus, IGT=impaired glucose tolerance, PPWR=post-partum weight retention

Table 21 Summary table of the results relating to MA and post-partum outcomes for model development

Author and year	Anthropometric exposure	Outcome	
		Post-partum IGT	**PPWR**
Sinha *et al.* 2002 (81)	Maternal BMI(kg/m^2)	***UA, no P value**	
Sommer *et al.* 2015 (84)	Maternal BMI (kg/m^2)		**14 weeks PPWR,** *UA, P<0.001
	Serum leptin (µg/l)		**14 weeks PPWR,** *UA, P<0.001
	Tricep SFT (mm)		**14 weeks PPWR,** *UA, P<0.001
	Subscapular SFT (mm)		**14 weeks PPWR,** *UA, P=0.003
	Suprailiac SFT (mm)		**14 weeks PPWR,** *UA, P<0.001
	Sum of SFT (mm)		**14 weeks PPWR,** *UA, P<0.001

Green=Increased association between exposure and outcome in South Asian women
Grey=No data available
*=Difference in mean of exposure in a population with pregnancy outcome between two South Asian and White women (e.g. mean weight (kg) in South Asian and White women with GDM)
UA=unadjusted, PPWR=Post-partum weight retention, IGT=Impaired glucose tolerance

3.5.6 **Change in gestational anthropometric change during pregnancy and pregnancy outcomes**

Two studies presented results for GAC and pregnancy outcomes; both studies considered GAC as a continuous variable (212, 215). One presented total weight gain (kg) (215), and the other presented weight gain (kg per week), fat mass gain (kg per week), truncal fat gain (kg per week), and mean skinfold gain (mm per week) (212). Results were only available for the association between GWG and GDM.

Gestational diabetes

One study presented the mean GWG in a population of women with GDM (215). Results showed that there was lower average weight gain in South Asian women with GDM. However there was no significant difference between the two groups (p=0.163) (215) (Table 22).

Sommer *et al.* calculated AORs for the association between measures of GAC (weight gain (kg per week), fat mass gain (kg per week), truncal fat gain (kg), mean skinfold gain (mm)) and GDM (211). When adjusting for ethnic origin, gestational week at inclusion, age and parity, results showed that, compared to the White ethnic group, South Asian women had an increased risk of GDM for all measures of GAC (weight gain: AOR 2.43, 95%CI 1.62-3.65, fat mass gain: AOR 2.46, 95%CI 1.64-3.69, truncal fat gain AOR 2.44, 95%CI 1.62-3.65, mean skinfold gain: AOR 2.50, 95%CI 1.62-3.84) (211) (Table 23).When additionally adjusting for maternal BMI (model 2), the risk of GDM development increased (weight gain: AOR 2.77, 95%CI 1.83-4.21, fat mass gain: AOR 2.80, 95%CI 1.84-4.26, truncal fat gain AOR 2.78, 95%CI 1.83-4.22, mean skinfold gain: AOR 2.72, 95%CI 1.75-4.23) (211) (Table 23). This suggests that when controlling for the effects of maternal BMI, the effect of GWG, gain in SFT and truncal fat gain on the development of GDM was increased. Maternal homeostatic model assessment (HOMA, also HOMA-IR), a method for assessing β-cell function and insulin resistance (IR) from basal (fasting) glucose and insulin or C-peptide concentrations, was also added into the model (model 3). Here, the risk of GDM in South Asian women decreased, but remained significantly higher than that for White women (weight gain: AOR 1.84 95%CI 1.16-2.90, fat mass gain: AOR 1.86, 95%CI 1.18-2.95, truncal fat gain AOR 1.82, 95%CI 1.15-2.89, mean

skinfold gain: AOR 1.88, 95%CI 1.16-3.04) (211) (Table 23).There was no information presented on unadjusted effect size for the association between change in MA during pregnancy and GDM.

Birth weight

Bissenden *et al.* presented the incremental GAC from 9-20 weeks to 27-31 weeks gestation in South Asian and White women having well grown babies (babies above the 10th centile according to Thomson *et al.* 1968 (219)) (203). Results showed that there was no significant difference in weight (kg) or mid upper arm muscle circumference (mm) in South Asian women and White women delivering well grown babies (no p values given) (Table 22) (203). Tricep and bicep SFT gain (mm) were significantly higher in South Asian women than White ($p<0.001$ and $p<0.050$, respectively), the difference in subscapular SFT was increased in South Asian women although the difference did not reach statistical significance ($p=0.070$) (203) (Table 22). There was no information presented on either the unadjusted or adjusted effect size for the association between change in anthropometrics during pregnancy and birth weight.

A summary of the evidence identified for outcomes associated with GAC is given in Table 24, and depicted in the form of a conceptual model diagram in Figure 8.

Table 22 Summary statistics of GAC in a group with pregnancy outcome for White and South Asian women

Author and study year	Pregnancy outcome	Exposure	Exposure mean (SD)		p value
			White ethnic group	South Asian ethnic group	
Hernandez-Rivas *et al.* 2013 (215)	GDM	GWG (kg)	9.41 (4.96)	8.34 (4.23)	0.163
Bissenden *et al.* (203)	Birth weight (well grown babies)	GWG (kg) from 9-20 to 27-31 weeks	0.42 (0.03)	0.42 (0.04)	Non-significant (no p value given)
		Gain in triceps skinfold (mm) from 9-20 to 27-31 weeks	0.00 (0.03)	0.22 (0.03)	<0.001*
		Gain in bicep skinfold (mm) from 9-20 to 27-31 weeks	0.10 (0.02)	0.21 (0.07)	<0.050*
		Gain in subscapular skinfold (mm) from 9-20 to 27-31 weeks	0.15 (0.04)	0.25 (0.07)	0.070
		Gain in mid upper arm muscle circumference (mm) from 9-20 to 27-31 weeks	0.03 (0.01)	-0.01 (0.02)	Non-significant (no p value given)

*significant p value (p<0.05)
GDM=gestationa diabetes, GWG=gestational weight gain, SD=standard deviation

Table 23 Effect of GAC (using z scores) on the onset of GDM as defined by International Association of Diabetes and Pregnancy Study Groups criteria

Author and study year	**Exposure**	**Control group**	**Pregnancy outcome**	**AOR (95%CI)**	
				White ethnic group	**South Asian ethnic group**
Sommer *et al.* 2014 (211)	Weight gain (kg per week)	White ethnic group	GDM	1	**Model 1** 2.43 (1.62, 3.65) **Model 2** 2.77 (1.83, 4.21) **Model 3** 1.84 (1.16, 2.90)
	Fat mass gain (kg per week)			1	**Model 1** 2.46 (1.64, 3.69) **Model 2** 2.80 (1.84, 4.26) **Model 3** 1.86 (1.18, 2.95)
	Truncal fat gain (kg)			1	**Model 1** 2.44 (1.62, 3.65) **Model 2** 2.78 (1.83, 4.22) **Model 3** 1.82 (1.15, 2.89)
	Mean skinfold gain (mm)			1	**Model 1** 2.50 (1.62, 3.84) **Model 2** 2.72 (1.75, 4.23) **Model 3** 1.88 (1.16, 3.04)

Notes: Model 1 adjusted for ethnic origin, gestational week at inclusion, age and parity; Model 2 additionally adjusted for pre-pregnant BMI; Model 3 additionally adjusted for homeostatic model assessment (HOMA-IR). GDM=gestational diabetes

Table 24 Summary table of the results relating to GAC and pregnancy outcomes

Author and year	Anthropometric exposure	Outcome		
		Anthropometric gain	GDM	Birth weight
Hernandez-Rivas *et al.* 2013 (87)	Maternal BMI (kg/m^2)		*UA, P=0.163	
Sommer *et al.* 2014 (211)	Weight gain (kg/week)		** A, No P value	
	Fat mass gain (kg/week)		** A, No P value	
	Truncal fat gain (kg/week)		** A, No P value	
	Mean SFT gain (mm/week)		** A, No P value	
Bissenden *et al.* 1981 (203)	Weight (kg)			*Well grown babies
	Middle upper arm (mm)			*Well grown babies
	Tricep skinfold (mm)			*Well grown babies
	Subscapular skinfold (mm)			*Well grown babies
	Bicep skinfold (mm)			*Well grown babies

Green= Increased association between exposure and outcome in South Asian women
Red= Non-significant or no difference between ethnic groups
Grey= No data available
*= Difference in mean of exposure in a population with pregnancy outcome between two South Asian and White women (e.g. mean weight (kg) in South Asian and White women with GDM)
**= Where South Asian women of an exposure category are compared with White women in the same exposure category (e.g. South Asian women with obesity compared with White women with obesity)
UA= unadjusted, A=Adjusted, GDM= Gestational diabetes mellitus

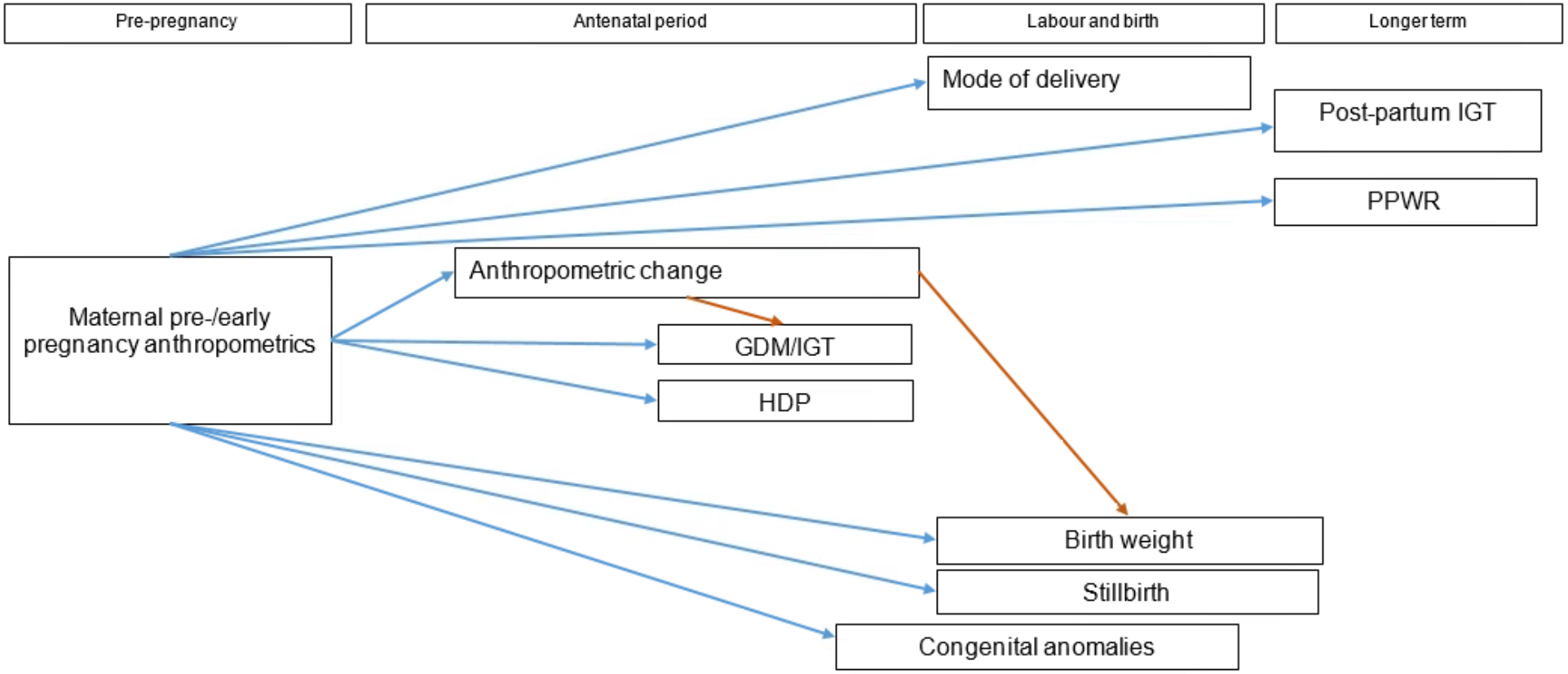


Figure 8 Diagram representing associations between MA, GAC and pregnancy outcomes where evidence from this systematic review suggests weight related risk differs between South Asian and White women and/or is increased for South Asian women

HDP=hypertensive disorders of pregnancy, GDM=gestational diabetes mellitus, IGT=impaired glucose tolerance, PPWR= post-partum weight retention

3.5.7 **Combined influence of maternal anthropometrics, gestational anthropometric change and pregnancy outcomes**

Two studies considered the combined influence of MA and GAC on pregnancy outcomes. One study investigated maternal BMI (kg/m^2) and truncal fat gain (kg) on the odds of GDM (211); in this study anthropometric measurements were considered as continuous variables (83). The other study provided change in weight (BMI, tricep, subscapular, suprailiac SFT measures and the sum of all these, and also serum leptin levels) between 14 weeks gestation and both 28 weeks gestation and 14 weeks post-partum (212).

Gestational diabetes

Sommer *et al.* considered the combined influence of maternal BMI and truncal fat gain on GDM in White and South Asian women (211). The results showed that South Asian women had a higher odds of GDM compared with White women (211) (Table 25). When ethnic origin was combined with a one standard deviation (0.14kg per week) truncal fat gain, the risk of GDM increased in both ethnic groups and remained higher in the South Asian women, the same was true when ethnic origin was combined with a one standard deviation ($4.7kg/m^2$) increase in maternal BMI Across both ethnic groups, the increase in risk of GDM was more with an increase in BMI than truncal fat gain. The risk of GDM was highest in both ethnic groups when there was both an increase in truncal fat gain and maternal BMI. It should be noted that the confidence intervals appear wide in the South Asian ethnic group (Table 25).

Table 25 Combined effects of ethnic origin, truncal fat gain, BMI on the risk of GDM

Exposure	European or South Asian	Odds ratio for GDM	95% confidence interval	
Single effect of ethnic origin	European	1 (reference)	-	
	South Asian	2.86	1.88	4.34
Combined effect of ethnic origin and 0.14kg/week increase in truncal fat	European	1.30	1.10	1.60
	South Asian	3.80	2.40	6.00
Combined effect of ethnic origin and having 4.8kg/m² higher pre-pregnant BMI	European	1.66	1.40	1.97
	South Asian	4.75	2.96	7.6
Combined effect of ethnic origin, 0.14kg/week increase in truncal fat and having 5 kg/m² higher pre-pregnant BMI	European	2.21	1.68	2.89
	South Asian	6.30	3.74	10.63

(Source: Sommer C, Mørkrid K, Jenum AK, Sletner L, Mosdøl A, Birkeland KI. Weight gain, total fat gain and regional fat gain during pregnancy and the association with gestational diabetes: a population-based cohort study. International Journal of Obesity. 2014;38 (1):76-81. Data from graph in article was provided by the authors)

Post-partum weight retention

One study provided GAC (BMI, tricep, subscapular, suprailiac SFT measures and the sum of all these, and also serum leptin levels) between 14 weeks gestation and both 28 weeks gestation and 14 weeks post-partum (212). Although this study didn't discuss the combined influence of MA and GAC explicitly, it provides a picture of the average anthropometric trends during pregnancy and to 14 weeks post-partum in the two ethnic groups. Results showed that despite having a significantly lower BMI at 14 weeks gestation ($p=0.015$), South Asian women had significantly higher BMI at 28 weeks gestation ($p=0.023$) and the change in BMI from 14 weeks gestation to 14 weeks post-partum was significantly higher for South Asian women ($p<0.001$), leaving South Asian women with a mean BMI that was not significantly different to that of European women ($p=0.83$) (Table 26).

Triceps SFT was not significantly different between the two ethnic groups at 14 weeks gestation ($p=0.830$), and there was no significant difference in the SFT gained to 28 weeks ($p=0.085$). However, at 14 weeks post-partum, triceps SFT was significantly higher for South Asian women compared with European women ($p<0.001$) (212) (Table 26). South Asian women had significantly higher subscapular SFT at all three time points compared with European women ($p=0.002$, $p<0.001$ and

p<0.001, respectively), gaining significantly more from 14 weeks gestation to both 28 weeks (p=0.120) and also to 14 weeks post-partum (p=0.022) (212) (Table 26). At 14 weeks gestation, there was no significant difference in suprailiac SFT between the two ethnic groups (p=0.960). This was also true at 28 weeks gestation (p=0.240). However, at 14 weeks post-partum South Asian women had significantly higher suprailiac SFT (p= 0.001) and had gained significantly more than European women (p=0.016) (212). There was no significant difference in the sum of SFT at 14 weeks gestation between the two ethnic groups (p=0.200). However, by 28 weeks gestation, South Asian women had gained a significantly higher sum of SFT (p=0.001), although the gain between the two ethnic groups was not significantly different (p=0.053) (212). By 14 weeks post-partum, South Asian women had gained significantly more (p<0.001), leading to a significantly higher sum of SFT (p<0.001) compared with European women (Table 26).

A summary of the evidence identified for outcomes associated with MA, and GAC is given in Table 27, and depicted in the form of a conceptual model diagram in Figure 9. Arrows represent evidence of an association between two variables.

Table 26 MA at 14 and 28 weeks gestation, and 14 weeks post-partum

Ethnic group (European n=309 and South Asian n=158)	Weight measure	14 weeks gestation Mean (SD)	P value for difference between ethnic groups	28 weeks gestation Mean (SD)	P value for difference between ethnic groups	P value for change in parameters 14 weeks gestation to 28 weeks gestation between ethnic groups	14 weeks post-partum Mean (SD)	P value for diff-erence between ethnic groups	P value for change in parameters 14 weeks gestation to 14 weeks post-partum between ethnic groups
European	BMI (kg/m²)	25.4 (4.9)	0.015	27.8 (4.8)	0.023	0.630	25.7 (5.1)	0.830	<0.001
South Asian		24.3 (4.1)		26.8 (4.1)			25.6 (4.2)		
European	Triceps (mm)	24.1 (6.9)	0.830	24.9 (6.6)	0.045	0.085	24.8 (6.7)	<0.001	<0.001
South Asian		24.2 (7.0)		26.3 (6.8)			27.5 (6.1)		
European	Subscapular (mm)	19.2 (7.8)	0.002	20.8 (7.6)	<0.001	0.120	20.8 (7.9)	<0.001	0.022
South Asian		21.7 (7.1)		24.3 (7.1)			25.7 (6.9)		
European	Suprailiac (mm)	27.1 (7.6)	0.960	30.0 (6.8)	0.24	0.330	27.1 (7.8)	0.001	0.016
South Asian		27.1 (7.3)		30.8 (6.3)			30.0 (6.9)		
European	Sum of skinfolds (mm)	70.4 (19.8)	0.200	75.4 (18.4)	0.001	0.053	72.6 (19.6)	<0.001	<0.001
South Asian		72.9 (18.5)		81.5 (17.5)			83.1 (16.5)		
European	S-leptin (µg/L)	1.35 (0.17)	0.002	1.71 (0.18)	<0.001	<0.004	0.90 (0.18)	<0.001	<0.001
South Asian		1.65 (0.14)		2.20 (0.15)			1.53 (0.16)		

Data from Table 2 Sommer C, Jenum AK, Waage CW, Mørkrid K, Sletner L, Birkeland KI. Ethnic differences in BMI, subcutaneous fat, and serum leptin levels during and after pregnancy and risk of gestational diabetes. European Journal of Endocrinology. 2015;172(6):649-56

Table 27 Summary of results for MA, GAC and pregnancy outcomes

Author and year	**Anthropometric exposure**	**GDM**	**PPWR**
Sommer *et al.* 2014 (211)	Maternal BMI (kg/m²) and truncal fat gain (kg/week)	** UA, No P value	
Sommer 2015			Suggests that amount of weight gained during pregnancy contributes to PPWR

Green= Increased association between exposure and outcome in South Asian women
Grey= No data available
**= Where South Asian women of an exposure category are compared with White women in the same exposure category (e.g. South Asian women with obesity compared with White women with obesity)
UA=unadjusted, GDM=gestational diabetes mellitus, PPWR=post-partum weight retention

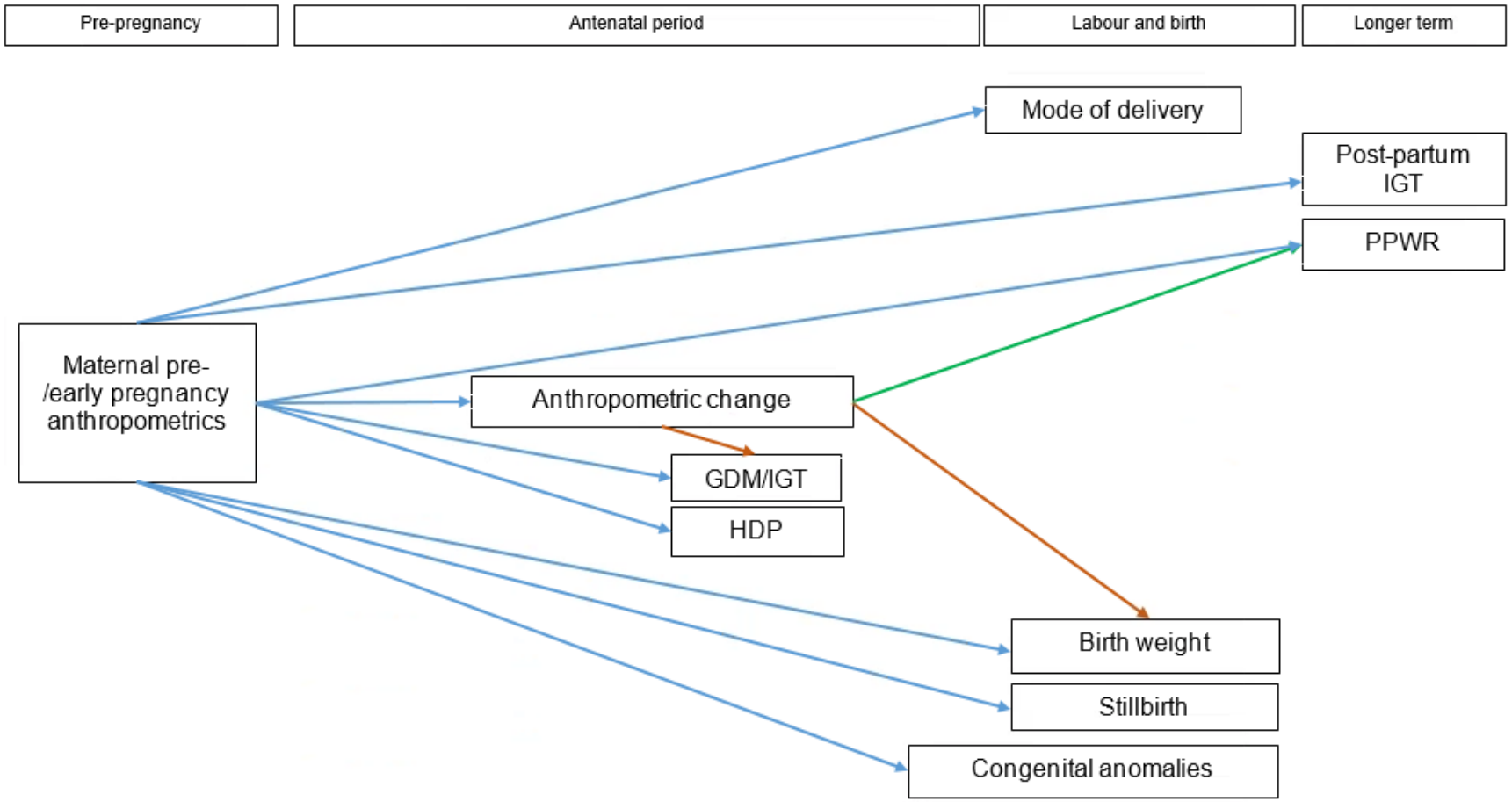


Figure 9 Diagram representing pregnancy outcomes associated with MA (blue), GAC (orange) and the accumulative effect of both (green), from this systematic review suggests weight related risk differs between South Asian and White women and/or is significantly increased for South Asian women
HDP=hypertensive disorders of pregnancy, GDM=gestational diabetes mellitus, IGT=impaired glucose tolerance, PPWR=post-partum weight retention, MA=maternal anthropometrics and GAC= maternal anthropometric change

3.6 Discussion

This section summarises key findings from the systematic review, discusses the strengths and limitations of the included evidence (both generally, and in terms of conceptual model development), and compares outcomes identified by the evidence in the in the systematic review with those identified by evidence in the 2009 IoM guidelines.

This systematic review included 19 studies and data from 346,319 births (306,254 White and 40,065 South Asian) to compare the association between pregnancy anthropometrics and pregnancy outcomes. This was the first review to consider the association between pregnancy outcomes, MA and GAC in South Asian women. The strongest evidence from included studies suggested that South Asian women have a higher risk of GDM associated MA compared with White British women. There was also evidence to suggest that South Asian women had a higher risk of GDM associated with GAC compared with White British women. The review also found that, when considering South Asian women alone (i.e. not comparing to White British women), there was evidence to suggest an increased association between MA and birth weight, C-Section and GDM. There was also evidence that suggested an increased association between GAC and GDM in South Asian women. There was limited evidence to suggest that there may be associations between MA and HDP, congenital anomalies, PPWR and postnatal IGT. There was also limited evidence to suggest that there was a combined effect of MA and GAC on GDM and PPWR.

One of the aims of this review was to use the results to contribute to the development of the conceptual model. This was done by identifying pregnancy outcomes associated with MA and GAC in South Asian women. Associations were included in the conceptual model where there was evidence of an association between exposure and outcome in South Asian women. Results from this review show that in South Asian women, GAC, HDP, GDM, mode of delivery, birth weight, stillbirth, congenital anomalies, weight retention and postnatal IGT are all associated with MA, and should be included in the conceptual model. The review also identified that GDM was associated with GAC, and MA and GAC appeared to have a combined effect on GDM and PPWR. The evidence also suggests that there was no significant

association between gestational age at delivery, PPH, admission to the NICU, perinatal death, and MA or GAC.

As this step was exploratory (i.e. to develop a conceptual (hypothetical) model that I would then go on to test using data), associations were included independent of the amount and quality of evidence. Had there been more evidence available, it may have been beneficial to take into account study quality when deciding whether or not to include an association in the conceptual model. Poor quality studies may be more prone to bias compared with high quality studies. For example; by not adjusting for relevant confounding variables in study design or analyses, observed results may be biased. Biased results are those which do not reflect the true results for a population under study. For conceptual model development, this was less of an issue for significant associations as these were included at this stage, and if not true could be removed from the model using evidence from analysis of the BiB cohort. This was more of an issue where results were not significant, and therefore not included in the conceptual model; it may have been that a significant association was not identified due to poor study quality and not because there wasn't actually an association.

This review found that there the majority of evidence was available for MA as an exposure (18 studies), and the majority of these studies provided results for maternal BMI (16 studies). The review also highlighted that the evidence relating to GAC as an exposure was limited. There were three studies, which provided evidence for GAC as an exposure, and only one considering the combined effect of MA and GAC. Although nine of the 16 studies looking at maternal BMI as the exposure considered BMI as a continuous variable (161, 171, 206, 210, 212-215), of the seven which used categorical BMI (200, 201, 204, 205, 207, 208, 216), only two considered Asian-specific BMI cut offs (201, 216). There was also one study which used ≥27kg/m^2 as a definition of obesity in both South Asian and White women (207). However, this does not reflect the difference in weight related risk between the two ethnic groups and so was not considered as application of Asian-specific BMI criteria. No studies considered level of GWG for BMI using the Asian specific BMI criteria for South Asian women.

In terms of pregnancy outcomes identified by the review, the majority of evidence was available for GDM (14 studies). There was limited evidence for other outcomes; four studies considered birth weight, two studies considered each GAC, mode of

delivery and gestational age at delivery (pre-term birth) and only one study was available for each HDP, congenital anomalies, distance from skin to epidural space, stillbirth, admission to the neonatal intensive care unit, perinatal death, PPH, PPWR and post-partum IGT. Despite limited evidence for a number of pregnancy outcomes, and for GAC as both an exposure and outcome, this systematic review has provided evidence to facilitate the first stage of conceptual model development. It has also highlighted gaps in the research, and areas for future research, in particular that there is more research needed considering GAC as both and exposure and outcome in South Asian women. To the best of my knowledge, this is the first systematic review to consider the association between MA and GAC on pregnancy outcomes in migrant and descendant South Asian women. The studies identified for inclusion for this systematic review also allowed me to consider three levels of exposure; MA, GAC and the combined effects of these on a number of different pregnancy outcomes. Therefore, the review provides evidence for the association between these exposures and outcomes in an ethnic group that is relevant to the UK.

Despite providing evidence to enable me to start to develop a conceptual model, there are a number of limitations to the evidence identified by this systematic review. The main limitation is that only two of the studies reporting BMI as a categorical variable considered the BMI criteria suggested by the WHO that are specific to the Asian population and compared the results in a White population using the WHO BMI criteria for the general population. As a result, it is possible that the results from studies that did not explore BMI cut offs for the Asian population, reflecting the increased risk of obesity-related adverse outcomes at a lower BMI, may have underestimated the effect size; this may have led to conclusions that there was not an association, when in fact there may have been (i.e. a false negative, or type 2 error (220)). In terms of model development, this meant that I may have excluded a variable from the conceptual model that may be relevant to Pakistani women living in Bradford. In order to minimise the effect of this limitation on the model development, I have also included all pregnancy outcomes identified by this review where the effect size was increased but statistical significance was not detected (e.g. $p>0.05$ or the 95%CI included 1.00) and Asian specific BMI criteria were not applied. The associations that this identified were between MA and both perinatal death and gestational age at delivery.

This systematic review also highlighted a gap in the evidence; there was a lack of evidence relating to GAC and pregnancy outcomes in South Asian women; more research is needed considering this association; particularly whether there is higher risk at lower weight gain for South Asian women compared with White women. In order to minimise this limitation, I will compare the associations identified by the systematic review with those found to be significantly associated with GWG in the 2009 IoM guidelines. Although the associations identified by the IoM guidelines may not be directly relevant to South Asian women, this systematic review has highlighted that, to date, these associations have not been investigated in this population. Therefore, in order to determine whether these outcomes are also associated with GAC in South Asian women living in the UK, they will also be included in the conceptual model (Figure 10).

Another limitation of the included evidence is that I was unable to consider South Asian subgroups. The South Asian population is thought to be very heterogeneous and results that are applicable to the Pakistani population may not be applicable to the Indian population. In addition, it is possible that while the South Asian population as a whole may not have an increased risk of a particular outcome, a subgroup (Indian/Pakistani/Bangladeshi) may do. For example; where an association is increased for Pakistani women and decreased for Indian and Bangladeshi women, by looking at all South Asian women together, the effect in Pakistani women is masked by including Bangladeshi and Indian women. This is a gap in the research, and in future I would recommend possible, research should focus on investigating risk in South Asian subgroups separately, rather than considering South Asian women as a whole.

There were also no studies that considered obesity subgroups using the Asian specific BMI criteria (≥27·5 to <32·5, ≥32·5 to <37·5, and ≥37·5 kg/m^2 (43)). Although some did look at continuous BMI (171), this does not enable investigation of the difference in risk when applying the WHO BMI cut offs for the general population, and Asian population. When using the WHO BMI criteria for the general population, obesity is a heterogeneous group. Evidence suggests that obesity related risk in pregnancy risk is different at different obesity cut offs. That is, the risk of a particular outcome at a BMI of 30kg/m^2 is likely to be different compared with a BMI of 45kg/m^2. For example; a systematic review of the association between maternal BMI and post-

term birth found in linear analysis that at midpoint of obese class I group, BMI 32.5kg/m^2, the odds of post-term birth (≥42 weeks gestation) were 1.38 (95%CI 1.31 to 1.46), while in obese class II, BMI 42.5kg/m^2, the odds of post-term birth were 1.95 (95%CI 1.88 to 2.02) (84). This risk difference within the pregnancy population with obesity may also be present in South Asian women when applying the appropriate BMI cut offs. However, it was not investigated by any of the included studies and is therefore a gap in the evidence base. Future research should investigate the risk of pregnancy outcomes for South Asian women, ideally within Pakistani, Bangladeshi, and Indian populations, within each of the obesity subgroups and using Asian specific BMI criteria.

There were also strengths and limitations of the systematic review methods used. The search strategy for this systematic review was extremely comprehensive. I used a gold standard duplicate screening approach and followed all stages on the PRISMA protocol (193). I conducted a thorough search of 12 databases. Once all references were in an endnote file, titles, abstracts and full papers were screened by myself and another researcher. We also searched the reference lists of all studies included and reviews that were related to the topic area. I also carried out citation searching through Google Scholar and contacted authors of relevant abstracts and posters to find out if there had been any further related studies and also for additional information where possible. Despite how rigorous the review process was, grey literature was not included in the searches. This was a limitation as including grey literature can be important in adding up to date literature to a review; it includes research which is ongoing but not published (for example ongoing but unpublished systematic reviews and RCTs). It also includes published literature which are not in journals, for example PhD theses and conference proceedings. By not including grey literature in this review, it is vulnerable to publication bias. Publication bias occurs as negative results are less likely to be published in peer reviewed journals, were this occurs research in the published literature is systematically unrepresentative of all completed studies (published and unpublished) (221).

In conclusion, this systematic review has been an important phase of conceptual model development. It has identified pregnancy outcomes associated with MA and GAC that are relevant to South Asian women. It has also highlighted the lack of evidence in particular relating to GAC and pregnancy outcomes in South Asian

women. It is essential that the extent to which GAC influences pregnancy outcomes, both independently and the combined effects with MA, should be investigated in migrant and descendant South Asian women (and indeed all other UK ethnic groups) to enable development of guidelines for weight management during pregnancy that are appropriate for all women living in the UK.

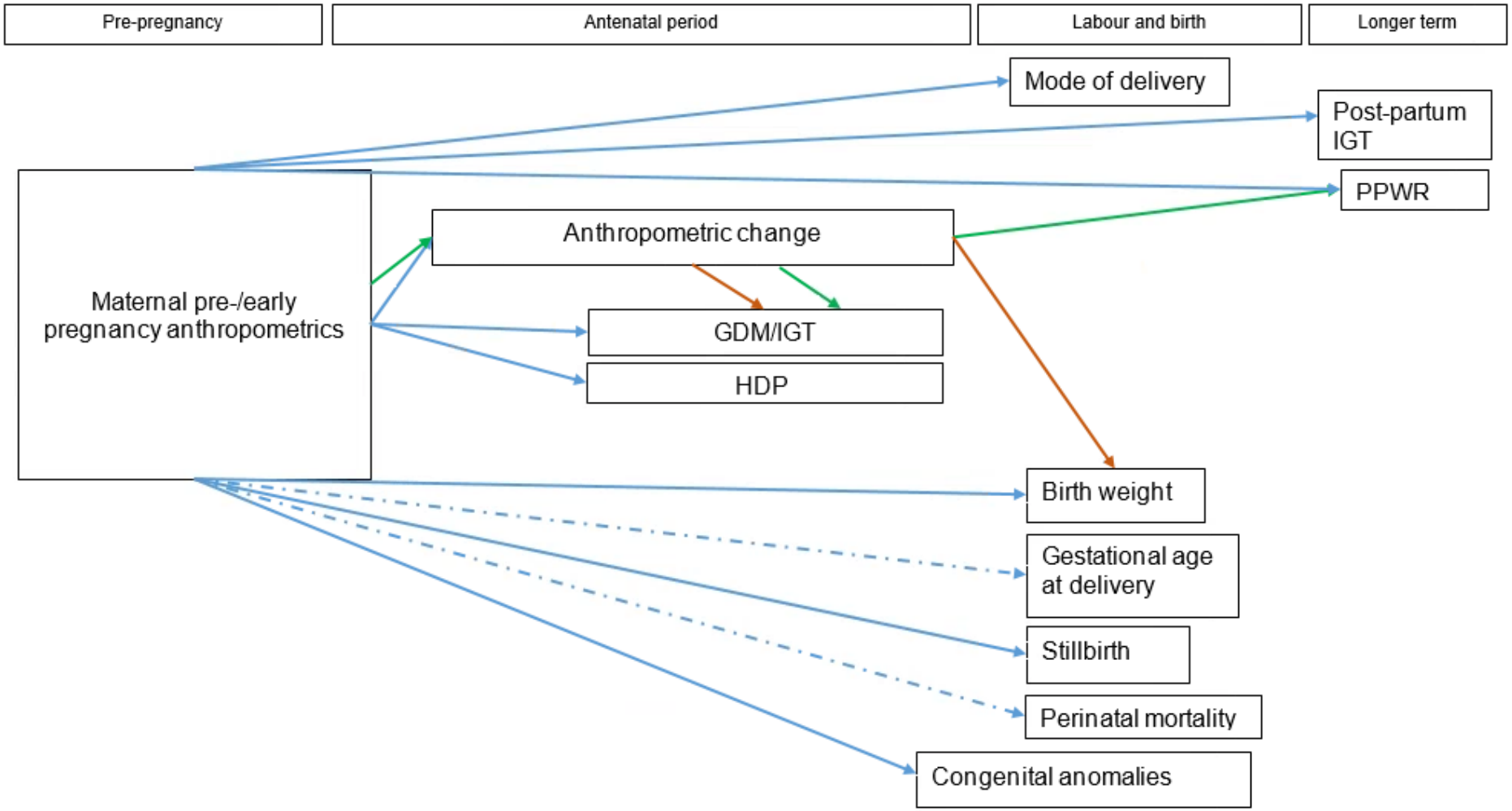


Figure 10 Diagram representing pregnancy outcomes associated with MA (blue), GAC (orange) and the accumulative effect of both (green), from this systematic review suggests weight related risk differs between South Asian and White women and/or is significantly increased for South Asian women.

Note: HDP=Hypertensive disorders of pregnancy, GDM=Gestational diabetes mellitus, IGT=Impaired glucose tolerance, PPWR=post-partum weight retention

3.6.1 **Comparison with outcomes Institute of Medicine guidelines for weight gain during pregnancy**

The IoM developed guidelines for GWG during pregnancy using evidence on the association between GWG and the following pregnancy outcomes; PPWR, caesarean delivery, SGA, LGA and childhood obesity. GDM and pre-eclampsia were also identified by the literature review phase of the report. However, the committee decided not to include these outcomes due to a lack of evidence for GWG as a cause:

"The committee considered the incidences, long-term sequelae, and baseline risks of several potential outcomes associated with GWG. Post-partum weight retention, caesarean delivery, gestational diabetes mellitus (GDM), and pregnancy-induced hypertension or preeclampsia emerged from this process as being the most important maternal health outcomes. The committee removed preeclampsia from consideration because of the lack of sufficient evidence that GWG was a cause of preeclampsia and not just a reflection of the disease process. The committee also removed GDM from consideration because of the lack of sufficient evidence that GWG was a cause of this condition. Post-partum weight retention and, in particular, unscheduled primary caesarean delivery were retained for further consideration. Measures of size at birth (e.g., small-for-gestational age [SGA] and large-for-gestational age [LGA]), pre-term birth and childhood obesity emerged from this process as being the most important infant health outcomes." (94) (pg. 242)

While findings from this systematic review agree that GWG, or GAC, is associated with PPWR and birth weight, and also found no evidence for the causal association between GAC and HDP, there were also some discrepancies. The evidence from the IoM guidelines suggested that childhood obesity is associated with GWG. However, childhood obesity was not a pregnancy outcome reported by any of the studies included in my systematic review, and so it is still unclear to what extent MA and GAC may influence this pregnancy outcome in South Asian women. The IoM guidelines also found that GWG was associated with mode of delivery (in particular C-section), and although these pregnancy outcomes were identified as associated with MA by my systematic review, the associations with GAC were not identified by the literature included in the systematic review relating to South Asian women.

In the evidence identified by my systematic review, GDM was found to be associated with both MA and GAC (including GWG) in South Asian women. In the 2009 IoM guidelines, although GDM was included as an outcome potentially associated with GWG in the review of the literature, it was not included as a pregnancy outcome in the development of the recommendations as there was insufficient evidence to support GWG as a cause of GDM (94). The lack of inclusion of GDM in the GWG guidelines is of particular relevance to women of South Asian origin for whom GDM appears to be significantly associated with MA change during pregnancy. This suggests that the 2009 IoM guidelines may not be applicable to South Asian women, and more research is needed to investigate to what extent MA at baseline, GAC, and the combined effect influence pregnancy outcomes, including GDM. This would provide information regarding whether the current IoM guidelines are indeed applicable to all ethnic groups as suggested, or need to be revised in order to be relevant for UK ethnic groups.

The evidence identified by this systematic review has been used to develop the conceptual model shown in Figure 11. This shows the associations between MA and pregnancy outcomes (blue), GAC (orange), the combined effects of MA and GAC (green), and finally the additional associations identified by the IoM guidelines for which there was no data available for in my systematic review (black).

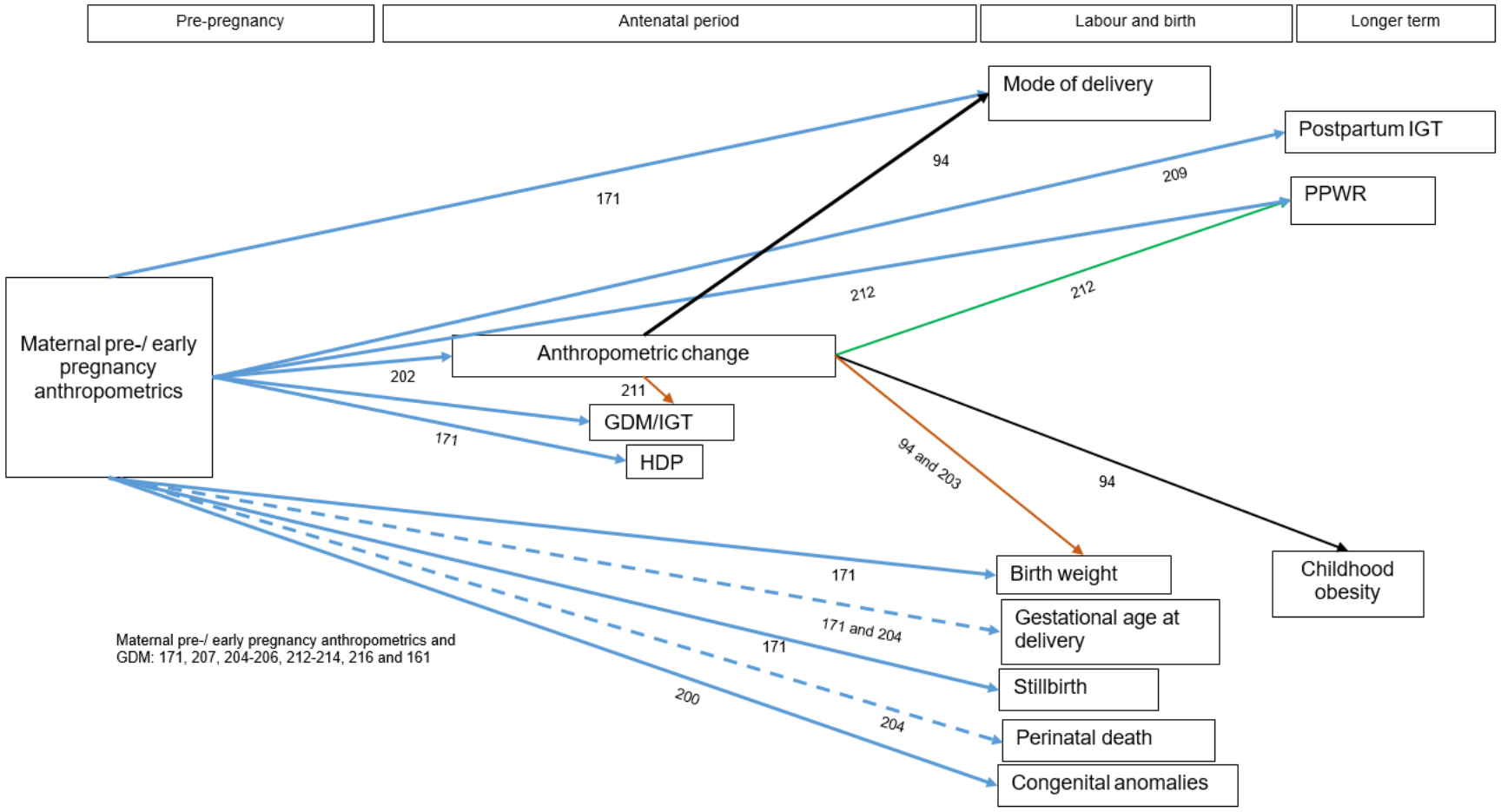


Figure 11 Diagram representing pregnancy outcomes associated with MA (blue), GAC (orange) and the combined effect of both (green), from this systematic review and additional pregnancy outcomes considered in the development of 2009 IoM GWG guidelines, that were not highlighted by my review (black).
Note: HDP=Hypertensive disorders of pregnancy, GDM=Gestational diabetes mellitus, IGT=Impaired glucose tolerance, PPWR=post-partum weight retention, MA= maternal anthropometrics and GAC=gestational anthropometric change

Chapter 4. A mixed methods systematic literature search and framework-based synthesis of qualitative and quantitative literature to identify the confounding and mediating variables (Phase 2)

This chapter is a systematic literature search and framework based synthesis to identify confounding and mediating variables of the associations between of MA and GAC on short- and long-term pregnancy outcomes in Pakistani women.

4.1 Introduction

The purpose of this review was to further develop the conceptual model specific to Pakistani women and add information on confounding and mediating variables. The results of the systematic review (Chapter 3) ,and evidence from the 2009 IoM guidelines (94), provided evidence for the associations to start developing the conceptual model (Shown in Figure 11, Chapter 3, Section 3.6.1, pg.114). However, the evidence of variables that may influence MA, GAC and pregnancy outcomes in Pakistani women (i.e. confounders and mediators such as maternal age, parity and conditions in pregnancy such as GDM, depending on where they occur on the causal pathway) were not considered. To explore the confounding and mediating variables which may influence the associations between exposures and the outcomes identified in Phase 1 (Chapter 3), a mixed methods research synthesis was carried out.

4.1.1 Defining confounding and mediating variables

When considering which variables to adjust for statistical analysis, it is important to consider the variables that might influence the association you are investigating; these variables can either be confounding, or mediating.

A confounding variable is a variable that influences the outcome in a population unexposed to the exposure of interest, a variable that influences the exposure, and must also be unaffected by the exposure and thus not a mediator (222). As an example of this I have considered the association between maternal BMI and GDM

(Figure 12). A confounding variable of this association is maternal age, as maternal age effects both maternal BMI and GDM (205).

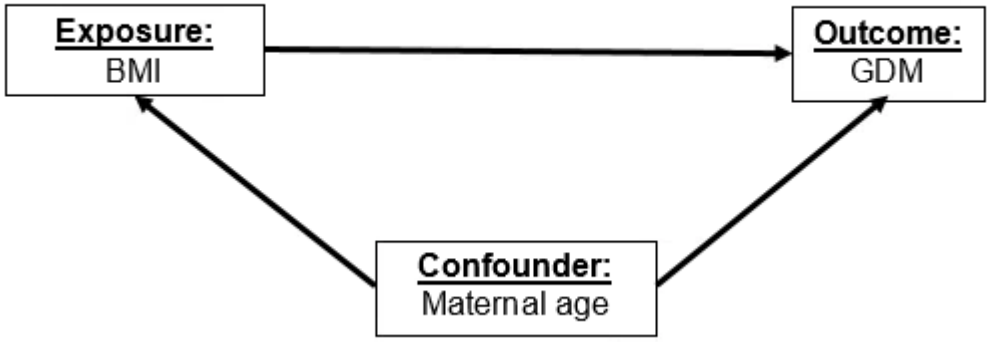


Figure 12 Visual representation of an example of a confounding variable

Mediating variables are those which are affected by the exposure, and also affect the outcome of interest (Figure 13) (223). For example; a mediator of the association between maternal BMI and GDM is GWG as maternal BMI effects the amount of weight a woman gains (or loses) during pregnancy, and GWG is associated with GDM (102).

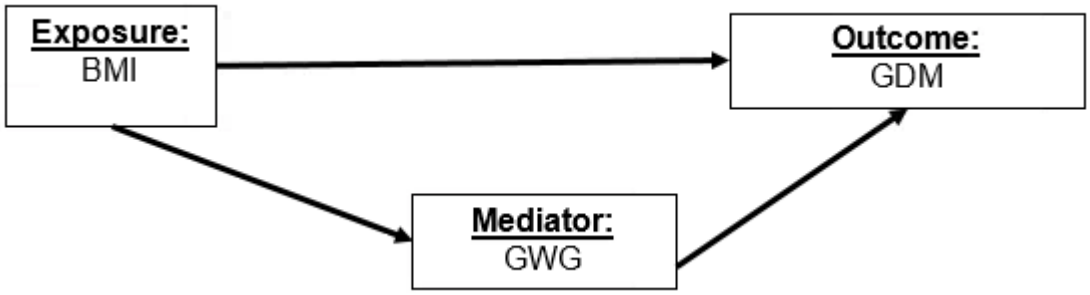


Figure 13 Visual representation of an example of a mediating variable

4.2 Aim

To identify confounding and mediating variables of the association between MA, GAC and pregnancy outcomes in migrant and descendant Pakistani women using both qualitative and quantitative published evidence.

4.3 Objectives

To carry out a systematic search of the existing evidence base in order to:

- Identify any variables that may influence MA and GAC in Pakistani women.
- Identify additional pregnancy outcomes that may be associated with MA or GAC that may not have been found by the systematic review (for example; where the association between maternal Pakistani ethnicity and a pregnancy outcome has been adjusted for maternal BMI. This adjustment for maternal BMI as a confounder suggests that BMI is associated with both ethnicity (the exposure) and the specified pregnancy outcome).
- Consider variables affecting pregnancy outcomes that have been identified either in my systematic review, the 2009 IoM guidelines for GWG (94), or this research synthesis in Pakistani women.
- Use a broad review of the literature carried out as part of the literature search to discuss ethnic differences between variables (mediators and confounders) identified, and whether there might be any associations between variables of interest.

4.4 Methods

This review followed the four steps for reporting mixed methods systematic reviews suggested by Hong *et al.* (224). These are:

1. Stating the review includes both qualitative and quantitative evidence in the title.
2. Providing clear justification for why a mixed methods systematic review has been used, and what synthesis design (i.e. segregated, integrated or contingent) has been used.
3. Clear description of synthesis methods used (i.e. qualitative or quantitative synthesis methods) with methodological references.
4. Description of how qualitative and quantitative data were integrated; and discussing insight gained from doing so (the discussion should clearly reflect

on the added value and insight of combining qualitative and quantitative evidence).

4.4.1 **Synthesis design**

Sandelowski *et al.* (185) proposed three general frameworks for mixed-research syntheses; segregated, contingent and integrated methodologies:

Segregated methodology: Maintains a clear distinction between quantitative and qualitative evidence requiring individual synthesis to be carried out prior to the final mixed-research synthesis (185). The qualitative and quantitative findings may either support each other (confirmation), contradict each other (refutation), or add to each other (complementarity) (185). Provided that the individual qualitative and quantitative syntheses focus on the same general phenomenon, confirmation, refutation and complimentarily can all be used to inform the research question (185).

Integrated methodology: Direct combination of identified evidence into a single mixed methods synthesis (185). Integrated methodologies require that the quantitative and qualitative evidence is similar enough to be aggregated into a single synthesis (185). This aggregation process requires that either the qualitative data is converted into a numerical format and included with quantitative data in the statistical analysis, or the quantitative data is converted into themes, coded and presented alongside the qualitative data (185).

Contingent methodology: Two or more syntheses which are conducted sequentially and based on the results from the previous synthesis (185). The process starts by asking an initial research question and then conducting a qualitative, quantitative or mixed methods research synthesis of which the results are used to generate a second research question and research synthesis, and so on (185). Multiple syntheses, either integrated and/or segregated, are carried out until the final result addresses the researcher's review objective (185).

I decided that because quantitative and qualitative evidence would be analysed together to answer the same research question, an integrated design would be used. This allowed both quantitative and qualitative evidence to be analysed together using

framework-based synthesis (225), a method that allows the systematic reviewing of diverse literature (226).

4.4.2 **Synthesis methods**

This literature review used a qualitative synthesis method; framework-based synthesis, to identify variables of interest to conceptual model development. Framework-based synthesis has been adapted from framework analysis; a data analysis method for conducting primary qualitative research (183, 227). While framework analysis has been developed and refined over time, the core principals of the approach have been found to be versatile across a number of different studies (227). Framework analysis has been adapted for the synthesis of primary evidence in a review by Oliver *et al.* (226). In framework synthesis, Oliver *et al.* use the principles of framework analysis and apply them to a systematic review in order to label the data of studies in meaningful and manageable sections, so later they can be retrieved and explored (183). Framework-based synthesis involves the reviewers choosing a conceptual model which is likely to be suitable for the review question; this model is used for the basis of the initial coding (183). This model is then modified in response to the evidence reported in the studies identified by the review (183). The revised framework then includes both variables from the original conceptual model hypothesised by the reviewers, along with any modified and additional variables identified by the evidence in the review. While framework-based synthesis has predominantly been used to synthesise qualitative research, here it will be applied to a mixed methods research synthesis including quantitative, qualitative and mixed methods evidence to modify an a priori framework (i.e. the conceptual model developed in Chapter 3; final version shown in section 3.6.1, pg.114). The findings from this mixed methods research synthesis will then be used to further develop the conceptual model which will be used to inform later data analysis using the BiB dataset.

As Framework-based synthesis is based on the core principles of framework analysis, I have developed this mixed methods review using the five key stages for

framework analysis highlighted by Ritchie and Spencer (227), with the addition of a literature searching stage as used by Oliver *et al.* (226). The stages used were:

1. Familiarisation and literature searching.
2. Identifying a thematic framework.
3. Indexing.
4. Charting.
5. Mapping and interpretation.

4.4.3 **Familiarisation and literature searching**

In framework analysis, familiarisation is the process of gaining an overview of the material gathered before sifting and sorting any data, it also involves the beginning of the process of abstraction and conceptualisation (227). As this mixed research synthesis was complex and exploratory, with no specific outcome, I combined familiarisation and literature searching stages together in order to ensure that all relevant literature was included. A systematic literature search was carried out to identify qualitative and quantitative studies that could be used to inform my knowledge on the following topics in Pakistani women, or comparing Pakistani women with White women:

- Pregnancy and birth.
- Pregnancy anthropometrics (both MA and GAC).
- Pregnancy outcomes.

Methods for the search were as follows; those studies identified by the search for the systematic review (Chapter 3, Section 3.4.3, pgs.48-50) were also screened for inclusion in this mixed research synthesis. An additional search was carried out to ensure that no relevant qualitative research was missed. Studies identified by both searches were combined in Endnote prior to deduplication. The qualitative searches were carried out using keywords developed using SPICE (228) (Table 28). SPICE refers to the Setting, Perspective, Intervention or exposure, Comparator group, and Evaluation to be included (228). Scoping searches were carried out to inform the

development of a final search strategy for each database searched (final search terms are attached as Appendix 6, pgs.338-347).

Table 28 Search term development using SPICE

	SPICE				
	S: Setting	**P:** Perspective	**I:** Intervention or exposure	**C:**Comparator group	**E:** Evaluation
	AND				
OR	Pregnancy Maternal Gravidity Mother Parent	Ethnic Culture Race Racial Asian Pakistan Migrant Immigration generation status	Obesity Body composition. BMI Body mass index Weight Gain Weight Fat Adiposity Fatness Waist circumference W:H ratio Waist to hip ratio	None	Views Opinions Perspectives Experience Voice Feelings Thoughts Beliefs

This review included results from studies that were included in my systematic review reported in Chapter 3, and new studies that were not included in your systematic review. The aim of study selection was to ensure that all relevant papers are included in the review. Once search terms had been developed, the same six-stage search strategy and methods of study selection used in the systematic review were used to identify relevant literature (detail provided in Chapter 3, Section 3.4.3, pgs.48-50).

To summarise, these included:

Stage 1: Electronic database searches.

Stage 2: Reference list searches.

Stage 3: Citation searches.

Stage 4: Contacting authors of published abstracts.

Stage 5: Repeating stages 1-4 for any new studies identified.

Stage 6: If required, authors of the included studies were contacted for additional data (this was not required).

Study selection included screening titles and abstracts followed by screening the full papers of potentially relevant studies.

Once I had thoroughly familiarised myself with the literature available, I applied more specific inclusion and exclusion criteria to the studies identified by the initial search. This allowed me to limit the studies to only those relevant for inclusion in the framework synthesis i.e. those considering variables influencing MA, GAC or pregnancy outcomes in Pakistani women, in addition to those studies included in the systematic review.

Inclusion criteria

- Qualitative, quantitative and mixed-methods research studies.
- Peer reviewed, full published studies (i.e. not editorials, abstracts etc.).
- Studies on humans.
- Any publication date.
- Must present evidence of variables which may influence MA, GAC or pregnancy outcomes (GDM, HDP, mode of delivery, birth weight, stillbirth, perinatal death, congenital anomalies, gestational age at delivery, post-partum IGT, PPWR and infant anthropometrics) in Pakistani women (or South Asian in a study using data from BiB cohort, or study already included in my systematic review in Chapter 3).
  Or/
  Presents evidence of a potential association between MA and a pregnancy outcome not identified by my systematic review or the IoM guidelines e.g. where adjustment made for maternal weight in the association between Pakistani ethnicity (or South Asian in a study using data from BiB cohort, or study already included in my systematic review in Chapter 3) and a pregnancy outcome (e.g. birth weight).

Exclusion criteria

Studies were excluded if:

- Includes only women using assisted reproductive techniques as these pregnancies may have a different risk profile, for example assisted reproductive techniques have been associated with both short pregnancy outcomes such as gestational hypertension and pre-term birth, and also longer term outcomes such as increased risk of infant illness (189).
- Only presents results for multiple pregnancies as these may also have a different risk profile, for example a higher risk of low birth weight (190).
- Not English language

4.4.4 **Identifying a thematic framework**

The conceptual model of pregnancy outcomes shown in Figure 11, Chapter 3, Section 3.6.1, pg.114, has been used as an *a-priori* thematic framework for this mixed research synthesis. This initial *a priori* framework has been built upon by identifying variables associated with the variables identified in my systematic review (Chapter 3) and 2009 IoM guidelines (94). It also allowed me to look for any other pregnancy outcomes which are potentially associated with MA, or GAC. For example, where an association between one variable and a pregnancy outcome has adjusted for MA. This would suggest that there is evidence of an association between both the exposure and outcome variable in the analysis, but also the potential confounder which has been controlled for.

4.4.5 **Indexing**

Indexing is the process where the thematic framework is systematically applied to the data (227). Here, this meant that papers identified as relevant for inclusion were read and evidence of a variable influencing either an exposure or an outcome in the *a-priori* framework was indexed using headings relevant to the variable e.g. “maternal age”, “parity”, “SES” and so on. This was done for both quantitative and qualitative studies. For quantitative studies, this related to statistical effect size, for qualitative research this related to discussion of a particular variable (topic area; for example parity, diet, physical activity). In addition, where analysis for the association between

maternal ethnicity and a pregnancy outcome was adjusted for MA or GAC, the variable was indexed with the name of the additional pregnancy outcome e.g. “breastfeeding”, “maternal death” and so on.

4.4.6 **Charting**

Charting is the stage where data is lifted from its original transcript and rearranged into an appropriate thematic reference (227). This stage allowed a picture of the data as a whole to be constructed (227). For this framework-based synthesis, charting occurred once the thematic framework had been applied to the included primary studies. I created a chart by applying the thematic framework of outcomes (e.g. birth weight) and confounding/mediators variables (e.g. maternal age, maternal education, IMD, parity). I also identified in this stage which studies were quantitative, qualitative or mixed methods, and whether or not they used data from the BiB cohort (the dataset that I went on to use for the final stage of my PhD). In this stage, data was lifted from the original studies and placed in the relevant cell for that study and the exposure/outcome of interest, along with the index given to the section e.g. “age”, “parity” and so on, and where possible for quantitative studies, the direction and statistical significance of the association (i.e. evidence of statistical significance for the association between the identified confounding/mediating variable (e.g. parity/age/SES) and exposure/outcome of interest (e.g. BMI/GDM) in Pakistani women[12]). For qualitative studies, it was my interpretation of data in the included studies, for example if there was a discussion relating to exercise and gestational weight gain, I would extract the variable “physical activity” and place it in the cell for qualitative evidence in the row for GWG. I carried out all the stages in the charting process for all included studies. In order to validate the charting process, a random 20% sample of the included studies were reviewed and charted by two members of the supervisory team independently (NH and JR). All independent analyses were combined, and any discrepancies were resolved through discussion, and if necessary, by a third independent review by an additional member of the supervisory

[12] This could also be South Asian if the evidence was included in the phase 1 systematic review, or using data from the BiB cohort.

team (this was not required). An example of the chart structure used is given in Table 29.

Table 29 Example chart for identifying variables associated with anthropometric exposures and pregnancy outcomes in Pakistani women using dummy data and explaining abbreviations that may be used in these charts

Exposure/ outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis (or direction of association unclear)	Qualitative evidence
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	U-shaped (S/NS/NP)*	No association (S/NS/NP)*		
Maternal BMI	*Study A (Quant, SR)*	*Maternal age (S)*	*Food outlet availability (S)*	-	*Fathers education (NS)*	*Maternal age, parity, smoking, family history of diabetes and insulin*	-
	Study B (FS, Qual)	-	-	-	-	-	*Marriage and parity*

-No evidence identified
SR= Evidence included in systematic review, FS= Evidence identified through systematic search
Qual= Qualitative study not BiB data, QualB= Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data, MM= Mixed methods not using BiB data and MMB= mixed methods study using BiB data.
*S= statistically significant association, NS=association not statistically significant, or NP= Evidence of statistical significance not available

4.4.7 **Mapping and interpretation**

Mapping and interpretation is the final stage in which all the variables identified by the review were combined, allowing the data to be mapped and interpreted as a whole (227). The aim of this review was to identify confounding and mediating variables that may influence MA, GAC and pregnancy outcomes, and to find the associations between these variables. Therefore, any additional pregnancy outcomes identified by this review were added to the conceptual model diagram. All potentially confounding and mediating variables identified for each exposure and outcome of interest are summarised in tables. Based on the aim of this review, to identify variables to inform conceptual model development, and to enable completion of the project within the specified timeframe, a pragmatic, *a-priori* decision was made that no detailed analysis of the qualitative data alone would be carried out.

4.5 Results

4.5.1 **Familiarisation**

Evidence from the systematic review, the 2009 IoM guidelines and this initial systematic search which identified 92 studies, provided me with an overview of the available evidence for familiarisation (here papers were still included if they identified an ethnic difference in outcome but did not provide evidence of mediators or confounders). The evidence was interrogated for variables which differed between White and Pakistani women and might influence the association between MA, GAC and pregnancy outcomes in Pakistani women. These variables were used to create a diagram (Figure 14), informed by evidence and diagram structure used in the 2009 IoM guidelines; the original diagram used for familiarisation, adapted from the diagram in the 2009 IoM guidelines is shown in Appendix 7 (pg.348). This diagram gave a representation of the overall topic and allowed me to familiarise myself with the research area.

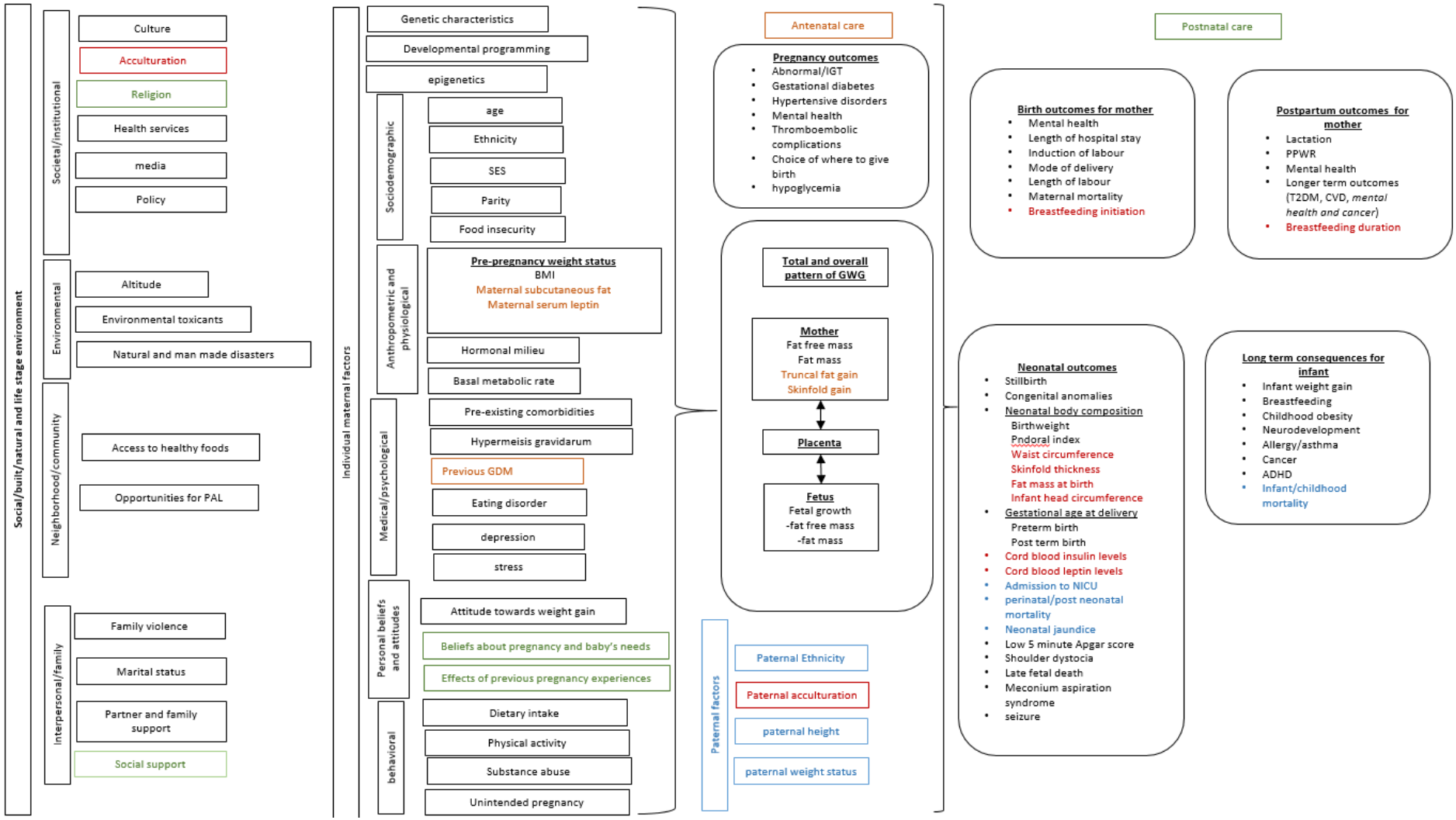


Figure 14 Diagram representing familiarisation stage
(Adapted from Institute of Medicine. Weight Gain During Pregnancy: Re-examining the Guidelines. Yaktine A, Rasmussen K, editors. Washington DC: National Academic Press; 2009. Key: Black=information from the 2009 IoM guidelines, orange=evidence from the systematic review, red=evidence from BiB cohort, blue= quantitative evidence not using data from BiB cohort, and green=qualitative evidence not using data from BiB cohort)

4.5.2 **Refining the inclusion criteria**

In total, there were 75 studies (out of the 92 referred to in the Familiarization section 4.5.1, pg.127) 19 of the studies used for initial familiarization step did not meet the inclusion criteria for this systematic review (i.e. did not have evidence of variables which may affect the associations between MA, GAC and pregnancy outcomes)) relevant for inclusion in this mixed methods review (Figure 15): all 19 from the systematic review[13] described in Chapter 3 (161, 171, 200-216) (two using data from the BiB cohort (171, 200)); 18 new[14] studies which used data from the BiB cohort (168, 229-245); 29 quantitative studies not using BiB data (246-274); eight qualitative studies (275-282); and one study that reported data for Pakistani and White British women from both the BiB cohort and another UK cohort study (283) (the Millennium cohort study) (Figure 15). A summary table for these studies is included in Appendix 8 (pgs.349-354). Firstly, I will discuss all the variables that were identified by the framework-based synthesis. I will then go on to describe further model development using these variables.

[13] These studies were included in my systematic review (Chapter 3), and also identified as relevant for inclusion in this framework based synthesis.

[14] New studies are those which were identified as relevant for inclusion by the search for this framework based synthesis, and were not already included in my systematic review (Chapter 3).

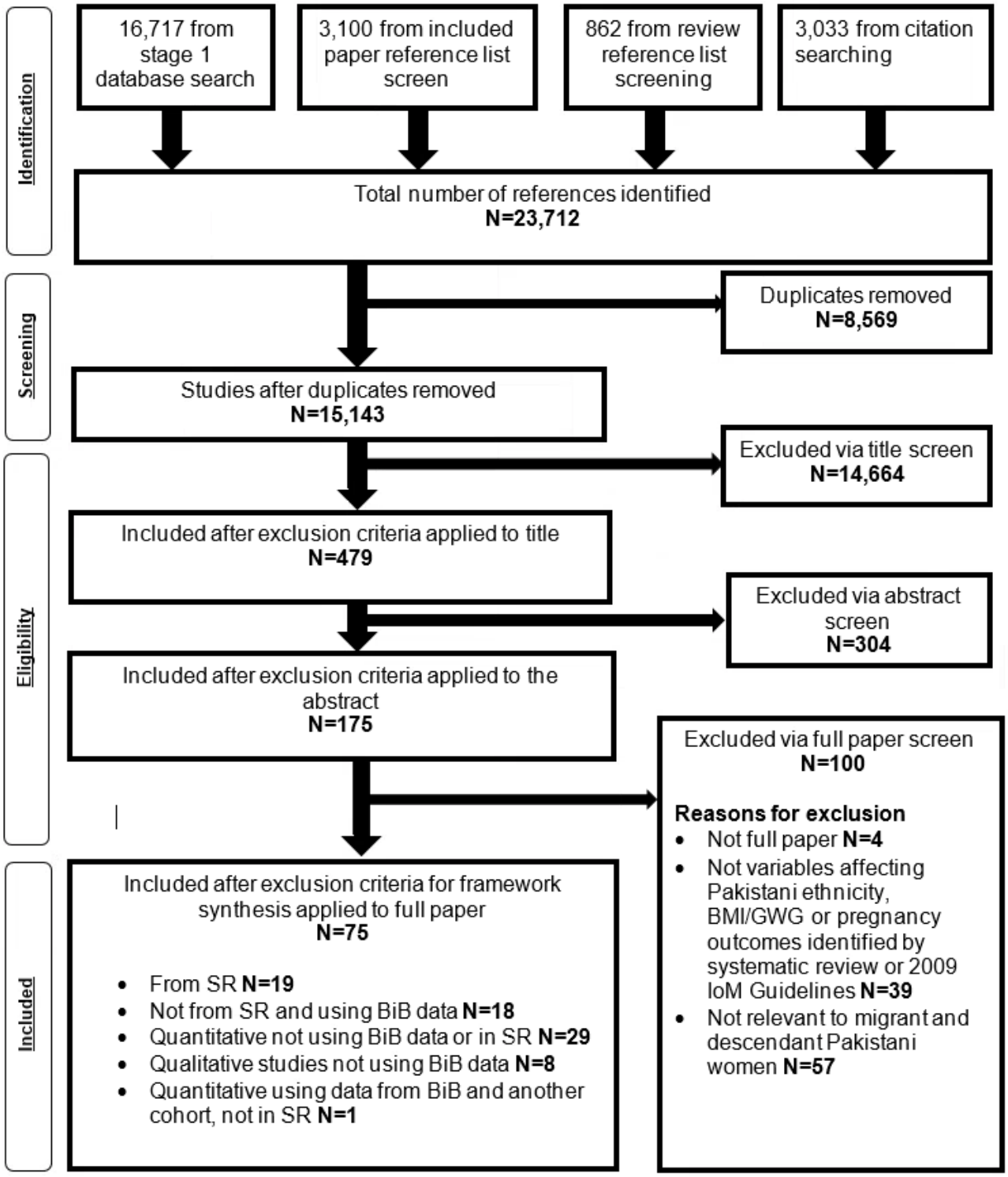


Figure 15 PRISMA flow diagram for mixed methods review searching and screening

4.5.3 **Maternal anthropometric measurements**

Maternal weight

Results for variables that could influence maternal weight are shown in Table 30. Two studies provided evidence suggesting variables that may influence maternal weight; neither study used data from the BiB cohort. One was quantitative and included in my systematic review (209). This study adjusted for age, parity, smoking, family history of diabetes and insulin when considering the association between maternal weight and postnatal glucose tolerance (209).The other was a new qualitative study (275). Evidence from this study suggested that both being married and having a higher parity may be associated with higher maternal weight (275).

Maternal BMI

Results for variables that could influence maternal BMI are shown in Table 30. Nine quantitative studies provided evidence of variables that might influence maternal BMI (168, 204, 205, 207, 212, 216, 232, 240, 241). There were six included in my systematic review; one using data from the BiB cohort (240), and five using other sources of data (204, 205, 207, 212, 216). The other three studies were new and used data from the BiB cohort (168, 232, 241). Significant positive associations were identified between maternal age (232) and general health questionnaire score in pregnancy (240) and maternal BMI. Positive associations (without significance reported) were identified for maternal BMI and parity (212) and partners place of birth being South Asia (168, 241). A negative association (without significance reported) was identified between maternal BMI and food outlet availability (232). There was no association identified between maternal BMI and deprivation (232).

The quantitative studies which investigated associations between maternal BMI and pregnancy outcomes included the following variables in their adjusted analyses; maternal age (204, 207, 216, 241), parity (204, 207, 216, 241), employment (241), education (216, 241), receipt of means tested benefits (241) and housing tenure (241), smoking (216), insurance status (216), family history of type 2 diabetes (216), foreign born status (216) and deprivation (204).

Skinfold thickness

One quantitative study included in my systematic review, not using data from the BiB cohort, provided evidence of variables that might be associated with maternal SFT (212). A positive association was identified between parity and tricep, subscapular and sum of skinfold thickness, although there were no indicators of significance (p values or confidence intervals) reported (212). There was also no association identified between parity and suprailliac SFT, although no p value was provided (212) (Table 30).

Serum leptin

Results for variables that could influence serum leptin levels are shown in Table 30. One quantitative study included in my systematic review, not using data from the BiB cohort, provided evidence of variables that might be associated with maternal serum leptin (212). This study suggested that there was a positive association between parity and maternal serum leptin, although no p value or confidence interval was available for the association (212).

Other anthropometric measures

There was no evidence available for variables that might influence either mid upper arm circumference, total body fat or truncal fat.

Table 30 Evidence for variables which could influence MA in Pakistani women

Exposure	Study	Evidence available in study to support type of association with outcome (statistical significance)			Variables used in adjusted analysis for association between exposure of interest and an outcome in relevant ethnic group (*or direction of association unclear* [a])	Qualitative evidence
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	No association (S/NS/NP)*		
Weight	Sinha *et al.* 2003 (209) (Quant, SR)	-	-	-	Maternal age, parity, smoking, family history of diabetes and insulin	-
	Bandyopadhyay *et al.* 2011 (275) (FS, Qual)	-	-	-	-	Marriage and parity
BMI	Dornhorst *et al.* 1992 (207) (SR, Quant)	-	-	-	Maternal age and parity	-
	Makgoba *et al.* 2011 (205) (SR, Quant)	-	-	-	"all significant confounders"-unclear which these are	-
	Oteng-Ntim 2013 (204) (SR, Quant)	-	-	-	Maternal age, parity and deprivation	-
	Pu *et al.* 2015 (216) (SR, Quant)	-	-	-	Maternal education, parity, smoking, insurance status, maternal age, family history of diabetes and foreign-born status (place of birth)	-
	Sommer *et al.* 2015 (212) (SR, Quant)	Parity (NP)	-	-	-	-
	Fraser *et al.* 2012 (232) (FS, QuantB)	Maternal age (S)	Food outlet availability (S) -	Deprivation (IMD) (NS)	-	-
	Traviss *et al.* 2012 (240) (FS, QuantB)	GHQ score in pregnancy (S)	-	-	-	-
	West *et al.* 2013 (168) (FS, QuantB)	Partners place of birth South Asian (NP)	- -	-	-	-

Exposure	Study	Evidence available in study to support type of association with outcome (statistical significance)			Variables used in adjusted analysis for association between exposure of interest and an outcome in relevant ethnic group (*or direction of association unclear* [a])	Qualitative evidence
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	No association (S/NS/NP)*		
BMI	West *et al.* 2014 (FS, QuantB) (241)	Partners place of birth South Asian (NP) -	- -	-	Maternal age; parity; maternal employment; maternal education, receipt of means tested benefits; housing tenure. *Maternal place of birth*	-
Tricep skinfold	Sommer *et al.* 2015 (212) (SR, Quant)	Parity (NP)	-	-	-	-
Subscapular skinfold	Sommer *et al.* 2015 (212) (SR, Quant)	Parity (NP)	-	-	-	-
Suprailiac skinfold	Sommer *et al.* 2015 (212) (SR, Quant)	-	-	Parity (NP)	-	-
Sum of skinfolds	Sommer *et al.* 2015 (212) (SR, Quant)	Parity (NP)	-	-	-	-
S-leptin	Sommer *et al.* 2015 (212) (SR, Quant)	Parity (NP)	-	-	-	-

-No evidence identified
SR= Evidence included in systematic review, FS= new study i.e. evidence identified through systematic search and not in the systematic review
Qual= Qualitative study not BiB data, QualB= Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB= Quantitative study using BiB data and MMB= mixed methods study using BiB data.
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available
[a]*Text in italics means direction of the association unclear*

4.5.4 **Gestational anthropometric change**

Results for variables that could influence GAC are shown in Table 31. Three studies provided evidence of variables that might influence GAC (211, 275, 278). One was quantitative, and included my systematic review (211), and two were new qualitative studies (275, 278); no studies used data from the BiB cohort. The quantitative study adjusted for gestational week at inclusion, age, parity, BMI and HOMA-IR (insulin resistance) when considering the association between gain in weight, fat mass, truncal fat and mean skinfold thickness and GDM (211). The two qualitative studies reported that diet and physical activity may influence the amount of gestational weight gain (275, 278) and one also reported that personal beliefs may play a role (275). There was no evidence identified for variables that might influence gain in mid upper arm circumference during pregnancy.

Table 31 Evidence for variables which could influence GAC in Pakistani women

Exposure	**Study**	**Variables used in adjusted analysis**	**Qualitative evidence**
Weight gain	Bandyopadhyay *et al.* 2011 (275) (FS, Qual)	-	Marriage, parity, Beliefs (religious), weight issues and exercise
	Greenhalgh *et al.* 2015 (278) (FS, Qual)	-	Exercise, Diet
Fat mass gain	Sommer *et al.* 2014 (211) (SR, Quant)	Gestational week at inclusion, maternal age, parity, BMI and Insulin resistance (HOMA-IR)	-
Truncal fat gain	Sommer *et al.* 2014 (211) (SR, Quant)	Gestational week at inclusion, maternal age, parity, BMI and Insulin resistance (HOMA-IR)	-
Mean skinfold gain	Sommer *et al.* 2014 (211) (SR, Quant)	Gestational week at inclusion, maternal age, parity, BMI and Insulin resistance (HOMA-IR)	-

-No evidence identified
SR=Evidence included in systematic review, FS=new study i.e. evidence identified through systematic search and not in the systematic review, BMI=body mass index, HOMA-IR=homeostatic model assessment-insulin resistance, Qual=Qualitative study not BiB data, Quant=Quantitative study not using BiB data

Antenatal outcomes

This section will discuss the following outcomes: GDM and HDP; both of which were identified by my systematic review as relevant outcomes. Estimated fetal measurements and cord blood leptin and insulin measurements were identified as potential outcomes of interest in a Pakistani population by the framework-based synthesis (through including maternal weight as a variable in statistical adjustment (as a confounder), and therefore suggesting that it is associated with each outcome).

Gestational diabetes and impaired glucose tolerance during pregnancy

Results for variables that could influence gestational diabetes and glucose tolerance are shown in Table 32. Fifteen studies provided evidence of variables that might influence GDM (161, 171, 204, 205, 207, 211, 212, 214, 216, 233, 241, 275, 278). There were 11 quantitative studies; nine were included in my systematic review (161, 171, 204, 205, 207, 211, 212, 214, 216) (one of which used data from the BiB cohort (171)), there also were four new studies; two quantitative studies which used data from the BiB cohort (233, 241), and two qualitative studies which did not use data from the BiB cohort (275, 278).

Positive associations were identified between the following variables and GDM; maternal BMI (161, 171, 204, 205, 207, 211, 212, 214, 216), maternal age (205, 214, 216), family history of diabetes (216), sum of skinfold thickness (212), serum leptin (212), truncal fat gain (211), cord blood insulin and leptin (233), place of birth of the mother and father (241) and generation status (246). There was no association identified between foreign born status and GDM (216). Quantitative studies also adjusted for the following variables when GDM was considered as a pregnancy outcome; maternal age (161, 204, 207, 211, 214, 216, 241, 262), parity (161, 204, 207, 211, 216, 241, 262), maternal education (216, 241, 262), deprivation (IMD) (204), smoking (216, 241, 262), health insurance (216, 262), family history of diabetes (161, 216), foreign borne status (216), number of weeks gestation (161), pre-/early pregnancy BMI (161, 211, 214, 241), weight gain in pregnancy (161), history of GDM (161), glucose intolerance (161), gestational week at inclusion (211), insulin resistance (211), age gap between GDM and type 2 diabetes (214), employment (241), receipt of means tested benefits (241), housing tenure (241), drinking habits (262), and timely initiation of prenatal care (262).

Qualitative evidence suggested that GDM was influenced by maternal diet (275, 278), maternal exercise (278), maternal obesity (278) and history of diabetes (including gestational diabetes) (278).

Table 32 Evidence for variables which could influence GDM or measures of glucose tolerance in pregnancy

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance) **Positive (S/NS/NP)***	Variables used in adjusted analysis	Qualitative evidence
GDM or measures of glucose tolerance in pregnancy (e.g. gestational fasting glucose)	Bryant *et al.*, 2014 (171) (SR, QuantB)	BMI (S)	-	-
	Dornhorst *et al.* 1992 (207) (SR, Quant)	BMI (NP)	Maternal age and parity	-
	Makgoba *et al.* 2011 (205) (SR, Quant)	Maternal age (S), BMI (S)	-	-
	Oteng-Ntim *et al.* 2013 (204) (SR, Quant)	BMI (S)	Maternal age parity and deprivation (IMD)	-
	Pu *et al.* 2014 (216) (SR, Quant)	BMI (S), Family history of diabetes (S), maternal age (S), foreign borne status (NS)	Maternal education, parity, smoking, insurance status, maternal age, family history of type 2 diabetes and foreign borne status	-
	Retnakaran *et al.* 2006 (161) (SR, Quant)	BMI (NS)	Maternal age, number of weeks gestation, parity, pre-pregnancy BMI, weight gain in pregnancy, previous history of GDM, family history of diabetes, glucose intolerance and ethnicity	-
	Sommer *et al.* 2015 (212) (SR, Quant)	BMI (NP), Sum of skinfold thickness (NP) and s-leptin (NP)	-	-
	Sommer *et al.* 2014 (211) (SR, Quant)	Truncal fat gain (S), BMI (S)	Gestational week at inclusion, maternal age parity, BMI and HOMA-IR	-
	Yue *et al.* 1996 (214) (SR, Quant)	BMI (NP) and maternal age (NP)	BMI, maternal age and the age gap between GDM and development of type 2 diabetes	-
	Lawlor *et al.* 2014 (233) (FS, QuantB)	Cord blood leptin and Insulin (S)	-	-
	West *et al.* 2014 (241) (FS, QuantB)	Place of birth of the mother and father South Asia (NP for trend)	Maternal age; parity; maternal employment; maternal education, receipt of means tested benefits; housing tenure; early pregnancy BMI; smoking in pregnancy.	-
	Bakken *et al.* 2015 (246) (FS, Quant)	Maternal place of birth South Asia (NS)	-	-

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)	Variables used in adjusted analysis	Qualitative evidence
		Positive (S/NS/NP)*		
	Sanchalika *et al.* 2015 (262) (FS, Quant)	-	Maternal age, maternal education, parity, health insurance coverage, smoking and drinking habits and timely initiation of prenatal care	-
GDM or measures of glucose tolerance in pregnancy (e.g. gestational fasting glucose)	Bandyopadhyay *et al.* 2011 (275) (FS, Qual)	-	-	Diet
	Greenhalgh *et al.* 2015 (278) (FS, Qual)	-	-	Diet, exercise, maternal obesity and previous DM/GDM

-No evidence identified
SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review, DM= diabetes mellitus, GDM= gestational diabetes mellitus, IMD=index of multiple deprivation, BMI=body mass index, HOMA-IR=homeostatic model assessment-insulin resistance, Qual=Qualitative study not BiB data, Quant=Quantitative study not using BiB data and QuantB= Quantitative study using BiB data
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Hypertensive disorders of pregnancy

Results for variables that could influence HDP are shown in Table 33. Two studies provided evidence of variables that might influence HDP (171, 241). Both were quantitative studies using data from the BiB cohort; one was in my systematic review (171), and the other was a new study (241). A significant positive association was identified between maternal BMI and HDP (171). There was also a positive association between maternal and paternal place of birth and HDP; the risk of HDP was also found to be highest when both the mother and father were south Asian born, and lowest when both were UK born (241). Statistical adjustments were also carried out for the following variables when HDP was considered as a pregnancy outcome: maternal age, parity, employment, education, receipt of means tested benefits, housing tenure, maternal BMI and smoking in pregnancy (241).

Table 33 Evidence for variables which could influence HDP

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance) Positive (S/NS/NP)*	Variables used in adjusted analysis
HDP	Bryant *et al.*, 2014 (171) (SR, QuantB)	BMI (S)	-
	West *et al.* 2014 (241) (FS, QuantB)	Place of birth of the mother and father South Asia (NS)	Maternal age; parity; maternal employment; maternal education, receipt of means tested benefits; housing tenure; BMI; smoking in pregnancy.

-No evidence identified
SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review, BMI=body mass index,
QuantB=Quantitative study using BiB data
*S=statistically significant association, NS=association not statistically significant

Mental health during pregnancy

Results for variables that could influence mental health during pregnancy are shown in Table 34. Two new studies provided evidence of variables that might influence mental health during pregnancy (240, 283). Both were quantitative and used data from the BiB cohort (240, 283); one of these studies also presented evidence using data from the Millennium cohort study, in addition to the evidence using data from the

BiB cohort (283). One study provided evidence that maternal BMI might be associated with mental health during pregnancy as analysis adjusted for maternal BMI (240). Both studies identified SES as a factor that may influence maternal mental health during pregnancy (235, 240, 283). Traviss *et al.* found that lower SES was more strongly associated with depression in pregnancy (240) and Uphoff *et al.* found that in the BiB cohort maternal mental health was associated with maternal education, means tested benefits and employment of the father (283). There was also one study not using the BiB cohort that commented on SES and mental health finding that maternal mental health was associated with both maternal education and employment (283). Evidence also suggested that mental health during pregnancy was associated with whether or not the women were married or cohabiting; Traviss *et al.* found that being unmarried increased the GHQ score by around 3 points (240).

Table 34 Evidence for variables which could influence mental health in pregnancy

Outcome	**Study**	**Evidence available in study to support type of association with outcome (statistical significance)**			**Variables used in adjusted analysis (*or association unclear*)**
		Positive (S/NS)*	**Negative (S/NS)***	**U-shaped (S/NS)***	
Mental health during pregnancy (GHQ score; higher GHQ suggests poorer mental health)	Traviss *et al.* (240) (FS, QuantB)	-	-	-	Maternal BMI, Marriage/ cohabiting status
	Uphoff *et al.*$ (283) (FS, QuantB)	Financial situation (S)	Receipt of means tested benefits (S)	Maternal education (S),	
	Uphoff *et al.*$ (283) (FS, Quant)	Financial situation (S)	Maternal education (NS), Receipt of means tested benefits (NS), Employment of father (S)		

-No evidence identified
FS=Evidence identified through systematic search and not in the systematic review
Qual=Qualitative study not BiB data, QualB=Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data
*S=statistically significant association, NS=association not statistically significant
$Please note that this study presents evidence from two different cohorts; BiB and MCS

Estimated fetal measurements

Results for variables that could influence estimated fetal measurements are shown in Table 35. One new quantitative study, using data from the BiB cohort provided evidence of variables that might influence fetal measurements (235). When

considering fetal adiposity as an outcome associated with maternal ethnicity, this study adjusted for maternal weight, maternal height, maternal age, parity, smoking during pregnancy and IMD, which is a measure of SES (235). When considering fetal weight as a pregnancy outcome associated with maternal ethnicity, the study adjusted for maternal weight, maternal height, maternal age, maternal education, parity, smoking during pregnancy and IMD (235). Finally, when considering fetal head circumference as a pregnancy outcome associated with maternal ethnicity, the study adjusted for maternal weight, maternal height, maternal age, maternal education and smoking during pregnancy (235). This suggests that the estimated fetal measurements of weight, adiposity and head circumference may be associated with all these variables, including maternal weight. Estimated fetal measurements have been included as an outcome in the updated conceptual model for further investigation.

Cord blood insulin and leptin

Results for variables that could influence cord blood insulin and leptin are shown in Table 35. One new quantitative study, using evidence from the BiB cohort presented evidence of variables that may influence cord blood insulin and leptin; the associations between ethnicity and cord blood insulin and leptin were adjusted for maternal height, maternal weight, maternal age, maternal education, gestational age and infant sex (233).

Table 35 Evidence for variables which could influence fetal measurements

Outcome	Study	Variables used in adjusted analysis
Fetal adiposity	Norris *et al.* 2014 (235) (FS, QuantB)	Maternal height, maternal weight, maternal age, parity, smoking during pregnancy and IMD
Fetal weight	Norris *et al.* 2014 (235) (FS, QuantB)	Maternal height, maternal weight, maternal age, maternal education, parity, smoking during pregnancy and IMD.
Fetal head circumference	Norris *et al.* 2014 (235) (FS, QuantB)	Maternal height, maternal weight, maternal age, maternal education and smoking during pregnancy.
Cord blood insulin	Lawlor *et al.* 2014 (233) (FS, QuantB)	Maternal height, maternal weight, maternal age, maternal education, gestational age and infant sex
Cord blood leptin	Lawlor *et al.* 2014 (233) (FS, QuantB)	Maternal height, maternal weight, maternal age, maternal education, gestational age and infant sex

FS=Evidence identified through systematic search and not in the systematic review
QuantB=Quantitative study using BiB data

4.5.5 **Maternal and infant pregnancy outcomes**

This section will discuss the following pregnancy outcomes: infant anthropometric at birth, stillbirth, mode of delivery, gestational age at delivery and congenital anomalies; all of which were identified by my systematic review as relevant outcomes. Additionally, maternal mortality was identified as a potential outcome of interest in a Pakistani population by the framework-based synthesis (through including maternal BMI as a variable in statistical adjustment (as a confounder), and therefore suggesting that it is associated with maternal mortality).

Maternal mortality

Results for variables that could influence maternal mortality are shown in Table 36. One new quantitative study, not using data from the BiB cohort, identified variables that might influence maternal death (259). In the analysis of the association between Pakistani ethnicity and maternal death, adjustments were carried out for BMI, age, parity, multiple pregnancy, GDM, HDP, anaemia, antenatal care, smoking status, substance misuse, previous pregnancy problems, pre-existing medical problems and employment (259). This suggests that maternal death may be associated with all these variables, including maternal BMI. Therefore, maternal death should be included in the conceptual model suggesting that further investigation is required.

Table 36 Evidence for variables which could influence maternal mortality

Outcome	Study	Variables used in adjusted analysis
Maternal mortality	Nair *et al.* 2014 (259) (FS, Quant)	Pre-/early pregnancy maternal BMI, maternal age, parity, multiple pregnancy, GDM, HDP, anaemia, antenatal care, smoking status, substance misuse, previous pregnancy problems, pre-existing medical problems and maternal employment

FS=Evidence identified through systematic search and not in the systematic review
Quant=Quantitative study not using BiB data

Birth weight

Results for variables that could influence birth weight are shown in Table 37. Eighteen quantitative studies provided evidence of variables that may influence birth weight (202, 203, 206, 230, 231, 233, 236, 241, 242, 246, 247, 253, 255, 257, 258, 261, 262, 265, 283). One study was in my systematic review and did not use data from the BiB cohort (206). Seventeen studies were new; seven studies used data from the BiB cohort (230, 231, 233, 236, 241, 242, 283) (one also presented evidence using data from another cohort (283)), and the final ten studies did not use data from the BiB cohort (202, 246, 247, 253, 255, 257, 258, 261, 262, 265).

Significant positive associations were identified between the following variables and birth weight: GDM (206), maternal age (206), BMI (206), cord blood leptin (233), maternal education (283), consanguinity (255), infant sex (265) and skinfold thickness gain during pregnancy (bicep, tricep and subscapular) (202). Positive associations were also identified between birth weight and place of birth of the mother and father; birth weight was higher where mother and father were South Asian born as opposed to UK born. This association was non-significant in two studies (246, 253) and there was no p value provided by two studies (241, 258). Both marriage (258) and infant sex (male) (253) were found to be positively associated with birth weight, although no p values were provided. Weight gain during pregnancy was also found to be associated with birth weight, although the association did not reach significance (202). Significant negative associations were identified between GDM and birth weight (262). No other significant negative associations were identified. However, birth weight was also found to be non-significantly, negatively associated with SES (measured using Carstairs index which is a summary measure

of deprivation; primarily material disadvantage, based on census information (284)) (206), smoking (206), financial situation (283) and means tested benefits (283). One study suggested a U-shaped association between birth weight and fathers employment, although this did not reach statistical significant (283) and finally Ramadan fasting was not associated with birth weight (236).

In analyses of birth weight outcomes, statistical adjustments were made for maternal characteristics, maternal medical history and comorbidities, behavioural variables and social variables. Maternal characteristics included maternal age (206, 230, 242, 246, 247, 253, 257, 258, 262), maternal BMI (206, 230, 242) and maternal height (231, 242, 255, 257). Maternal medical history and comorbidities included highest diastolic blood pressure in pregnancy (206), maternal hypertension (242), year of first birth (253), gestational age at delivery (230, 242, 246, 247, 255, 257, 258, 261), parity (230, 242, 246, 255, 257, 261, 262), conception year and season (230, 261), number of previous live and stillbirths (258), complications during pregnancy (257), receipt of antenatal care (257), and infant sex (231, 242, 253, 255, 257, 258, 261). Behavioural variables included smoking during pregnancy (206, 230, 231, 242, 247, 257, 262), exposure to environmental tobacco smoke during pregnancy (230), maternal fasting glucose (242), cohabiting status of mother (242), alcohol consumption during pregnancy (230, 242, 257). Social variables included measures of SES; Carstairs index (206), paternal employment (206), IMD (230), maternal education (230, 242, 247, 262), housing tenure (242, 247, 257), receipt of means tested benefits (242), health insurance coverage (262), individual and neighbourhood SES (230), annual household income (257), highest educational qualification in the household (257), highest occupational class in the household (257), and socio-economic circumstances of the mother (253).

Abdominal circumference at birth

Results for variables that could influence abdominal circumference at birth are shown in Table 37. One new quantitative study using data from the BiB cohort suggested an association between maternal weight at booking and abdominal circumference at birth through adjustment (240). Abdominal circumference at birth was also found to be effected by infant sex, IMD and gestational age at delivery (240).

Table 37 Evidence for variables which could influence birth weight

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***	
Birth weight	Makgoba *et al.* 2012 (206) (SR, Quant)	GDM (S), maternal age (S), pre-/early pregnancy maternal BMI (S)	SES (Carstairs index) (NS) Smoking (NS)	-	-	Maternal age, pre-/early pregnancy maternal BMI, highest diastolic blood pressure, smoking status in pregnancy, Carstairs index (neighbourhood deprivation) and paternal unemployment
	Dadvand *et al.* 2014 (230) (FS, QuantB)	-	-	-	-	Gestational age at delivery, maternal age, pre-/early pregnancy maternal BMI, smoking during pregnancy, exposure to environmental tobacco smoke during pregnancy, parity, alcohol consumption during pregnancy, conception year and conception season, maternal education, IMD and individual and neighbourhood SES
	Fairley *et al.* 2013 (231) (FS, QuantB)	-	-	-	-	Infant sex, smoking during pregnancy and maternal height.
	Lawlor *et al.* 2014 (FS, QuantB) (233)	Cord blood leptin (S)	-	-	-	-
	Petherick *et al.* 2015 (236) (FS, QuantB)	-	-	-	Fasting (S)	-
	Uphoff *et al.* 2015 (283) (FS, QuantB)	Maternal education (S)	Financial situation (NS), Means-tested benefits (NS)	Employment father (NS)	-	-
	Uphoff *et al.* 2015 (283) (FS, Quant)	-	-	-	-	-

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***	
	West *et al.* 2013 (168) (FS, QuantB)	-	-	-	-	Smoking, alcohol consumption during pregnancy, maternal age, maternal hypertension, maternal fasting glucose, maternal height, pre-/early pregnancy maternal BMI, parity, gestational age at delivery, infant sex, socioeconomic position (maternal education, housing tenure, receipt of means tested benefits), and living with partner.
	West *et al.* 2014 (241) (FS, QuantB)	Place of birth of mother and father South Asia (NP)	-	-	-	-
	Bakken *et al.* 2015 (246) (FS, Quant)	Place of birth of mother South Asia (NS)	-	-	-	age, parity, and gestational age
	Bansal *et al.* 2014 (247) (FS, Quant)	-	-	-	-	gestational age, age, education, smoking and housing tenure
	Honeyman *et al.* 1987 (255) (FS, Quant)	Consanguinity (S)	-	-	-	sex, gestational age, parity, and maternal height
	Kelly *et al.* 2009 (257) (FS, Quant)	-	-	-	-	Gender, gestational age, parity, age at birth, maternal height, pre-pregnancy weight, any complications during pregnancy. Drinking during pregnancy, smoke during pregnancy, received anti-natal care. Annual household income, housing tenure, lone parenthood, highest educational qualification in the household, highest occupational class in the household.
	Leon *et al.* 2012 (258) (FS, Quant)	Marriage (NP) and maternal place of birth South Asia (BW higher if born in Pakistan rather than UK i.e. “first generation”) (NP)	-	-	-	Sex, gestational age, age and number of previous live and stillbirths

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***	
Birth weight	Harding *et al.* 2004 (253) (FS, Quant)	Place of birth South Asia (NS), infant sex (NP)	-	-	-	age at birth registration and socio-, economic circumstances of mother, year of first birth, and gender of infant
	Sanchalika *et al.* 2015 (262) (FS, Quant)	-	GDM (S)	-	-	age, education, health insurance coverage, parity, and smoking and drinking habits
	Pedersen *et al.* 2012 (261) (FS, Quant)	-	-	Length of residence in the country (S)	-	year of delivery, gestational age, infant sex and parity
	Terry *et al.* 1980 (265) (FS, Quant)	Infant sex (S)	-	-	-	-
	Bissenden *et al.* 1981 (202) (SR, Quant)	Weight gain (NS), bicep (S), tricep (S) and subscapular (NS) skinfold thickness gain	-	-	-	-
Abdominal circum-ference at birth	Traviss *et al.* 2012 (240) (FS, QuantB)	Baby is male (S)	IMD (S), gestational age at delivery (S)	-	-	Mother's weight at booking

-No evidence identified

SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review

Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data

*S=Statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Stillbirth

Results for variables that could influence stillbirth are shown in Table 38. Four quantitative studies not using data from the BiB cohort provided information for variables influencing stillbirth; one was in my systematic review (201), and three were new (249, 251, 264). The evidence from the systematic review in Chapter 3 suggested that maternal obesity may influence the risk of stillbirth (201). Evidence from the quantitative literature not using the data from the BiB cohort found that stillbirth may be influenced by consanguinity as the proportions of stillbirth were lower in unrelated parents compared with first cousin marriages (264). Maternal education was also found to be associated with stillbirth as the proportions of stillbirth were low in mothers with more than 12 years education (264). Stillbirth was also found to differ by generation status, both Sorbye *et al.* and Gardosi *et al.* found that risk of stillbirth was higher in first generation Pakistani women than second generation (251, 264).

Perinatal mortality

Results for variables that could influence perinatal mortality are shown in Table 38. One study identified in my systematic review, not using data from the BiB cohort found that maternal BMI was positively associated with perinatal mortality, although the association was not significant (204) .

Table 38 Evidence for variables which could influence stillbirth and perinatal mortality

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)		Variables used in adjusted analysis
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	
Stillbirth	Penn *et al.* 2014, (201) (SR, Quant)	BMI (S)	-	
	Bundey *et al.* 1991 (249) (FS, Quant)	Consanguinity (NP), congenital anomalies (NP)	-	
	Sorbye *et al.* 2014 (264) (FS, Quant)	Consanguinity (NP), SES, Mothers place of birth (Pakistan; yes) (NP)	Mothers education (NP)	Year of birth, maternal age, parity and SES
	Gardosi *et al.* 2013 (251) (FS, Quant)	Place of birth South Asia (S)	-	Parity, Smoking, BMI, Maternal place of birth
Perinatal mortality	Oteng Ntim *et al.*, 2014 (204) (SR, QuantB)	BMI (NS)	-	-

-No evidence identified
SR=Evidence included in systematic review, FS= Evidence identified through systematic search and not in the systematic review
Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Mode of delivery

Results for variables that could influence mode of delivery are shown in Table 39. Four quantitative studies provided evidence on mode of delivery; one in my systematic review (204), and three new studies; two not using data from the BiB cohort (246, 256), and one using data from the BiB cohort (171). Evidence using data from the BiB cohort found that maternal BMI was associated with an increased risk of C-section (171). The evidence from the systematic review in Chapter 3 suggested that maternal obesity may influence the risk of both elective C-section, and instrumental delivery, although no indication of statistical significance was provided. Evidence from one study not using data from the BiB cohort found that maternal place of birth affects mode of delivery (both vaginal and operative), Instrumental delivery was found to be higher in second generation Pakistani women in Norway (born in Norway) and both C-section (overall, and both elective and emergency independently) and spontaneous delivery were found to be lower in second generation Pakistani women (246). Evidence from the other study not using data

from the BiB cohort suggested that odds of C-section might be affected by age, attendance to antenatal classes, booking >20 weeks, birth weight, fetal sex, IUGR, year of birth and hospital of birth and that odds of delivery by forceps or ventouse (instrumental delivery) might be affected by age, ethnic group, birth weight, hospital of birth, induction, year of birth, baby's sex and augmentation by including these variables in adjustments for the association between maternal BMI and the mode of delivery (256).

Table 39 Evidence for variables which could influence mode of delivery

Outcome	**Study**	**Evidence available in study to support type of association with outcome (statistical significance)**		**Variables used in adjusted analysis**
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	
Mode of delivery	Oteng-Ntim *et al.* 2013 (204) (SR, Quant)	**Elective and emergency C-section and instrumental delivery:** BMI (NP)	-	-
	Bryant *et al.* 2014 (171) (SR, QuantB)	**C-section** (S): BMI	-	-
	Bakken *et al.* 2015 (246) (FS, Quant)	**Instrumental delivery:** Maternal place of birth (second generation higher prevalence) (NP)	**C-section (overall, and both elective and emergency independently) and spontaneous delivery:** Maternal place of birth (second generation lower prevalence) (NP)	-
	Ibison *et al.* 2005 (256) (FS, Quant)	-	-	**Odds for C-section**: age, attendance to antenatal classes, booking>20 weeks, birthweight, fetal sex, IUGR, year of birth and hospital of birth **Odds for delivery by forceps or ventouse:** age, ethnic group, birthweight, hospital of birth, induction, year of birth, baby's sex and augmentation.

-No evidence identified
SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review
Quant=Quantitative study not using BiB data
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Gestational age at delivery

Results for variables that could influence gestational age at delivery are shown in Table 40. Twelve studies presented evidence of variables that might influence gestational age at delivery; one was from my systematic review (204), and eleven were new; five used data from the BiB cohort only (231, 236, 239-241), one study used data from the BiB cohort in addition to data from the Millennium Cohort study (283), and five used other quantitative data (246, 247, 258, 261, 262).

One study identified through the search for my systematic review adjusted for maternal age, parity and deprivation in the association between maternal ethnicity and gestational age at delivery suggesting that these three variables might be associated with the outcome (204). Evidence using data from the BiB cohort suggested that gestational age is associated with infant sex (231, 239). Mother's mental health during pregnancy was also found to be associated with gestational age at delivery; a higher general heal questionnaire (GHQ) score was associated with an earlier gestational age at delivery (240). Evidence also found that there was no association between gestational age at delivery and fasting (236), air pollution (239) and measures of SES; maternal education, financial situation, means tested benefits and employment of the father (283). Three studies found that gestational age at delivery was positively associated with generation status (241, 246, 258), one additional study found that there was a U-shaped association between gestational age at delivery (pre-term birth) and length of residence in the country (261). GDM was found to be positively associated with gestational age at delivery; if GDM was present, gestational age at delivery was later (262). Marital status was also found to be positively associated with gestational age at delivery (258).

In analyses of the outcome gestational age at birth, statistical adjustments were made for maternal age (204, 246, 247, 261, 262), parity (204, 246, 261, 262), deprivation (204), housing tenure (247), individual education (247), health insurance coverage (262), year of delivery (261), smoking (261, 262) and drinking habits (261).

Table 40 Evidence for variables which could influence gestational age at delivery

Outcome	**Study**	**Evidence available in study to support type of association with outcome (statistical significance)**				Variables used in adjusted analysis (*or association unclear*)
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***	
Gestational age at delivery	Oteng Ntim *et al.* 2013 (204) (SR, Quant)	-	-	-	-	Maternal age, parity, and deprivation (IMD)
	Fairley *et al.* 2013 (231) (FS, QuantB)	Infant sex (NP)	-	-	-	-
	Petherick *et al.* 2015 (236) (FS, QuantB)	-	-	-	Fasting during Ramadan	-
	Schembari *et al.* 2015 (239) (FS, QuantB)	Infant sex (NP)	-	-	Air pollution	-
	Traviss *et al.* 2012 (240) (FS, QuantB)	-	Mother's GHQ score	-	-	-
	Uphoff *et al.* 2015 (283) (FS, QuantB)	-	No benefits (higher OR of PTB) (NS), Employment father (higher OR of PTB for employment)	Maternal education (NS), Financial situation (NS)	-	-
	Uphoff *et al.* 2012 (283) (FS, Quant)	Maternal education (NS), No benefits (lower OR of PTB) (NS), Employment father (lower OR of PTB for employment) (NS)	-	Financial situation (NS)	-	-
	Bakken *et al.* 2015 (246) (FS, Quant)	-	-	-	-	Maternal age and parity *Maternal place of birth*
	West *et al.* 2014 (241) (FS, QuantB)	-	-	-	-	*Place of birth of mother and father*

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis (*or association unclear*)
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***	
Gestational age at delivery						
	Bansal *et al.* 2014 (247) (FS, Quant)	-	-	-	-	Maternal age, housing tenure, maternal education and smoking during pregnancy
	Leon *et al.* 2012 (258) (FS, Quant)	Marriage (NP)	Place of birth South Asia (South Asian born higher gestational age) (NP)	-	-	-
	Sanchalika *et al.* 2015(262) (FS, Quant)	-	GDM (GDM decreased OR of PTB)(S)	-	-	Maternal age, maternal education, health insurance coverage, parity, and smoking during pregnancy and alcohol consumption during pregnancy
	Pedersen *et al.* 2012 (261) (FS, Quant)	-	-	Length of residence in the country (NP for trend but S for certain categories of length of residence)	-	Year of delivery, maternal age an parity

-No evidence identified
PTB=pre-term birth
SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review
Qual= Qualitative study not BiB data, QualB= Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data and MMB= mixed methods study using BiB data.
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Congenital anomalies

Results for variables that could influence congenital anomalies are shown in Table 41. Two studies identified by the search for the framework synthesis provided evidence of variables that may influence congenital anomalies; one using the data from the BiB cohort (200), and one other quantitative study not using data from the BiB cohort (271). Both studies found that consanguinity was associated with a higher risk of congenital anomalies (200, 271). Additional analysis carried out in the systematic review (Chapter 3) of data presented by Sheridan *et al.* also found that a higher maternal BMI may also be associated with a higher risk of congenital anomalies. SES was found to be negatively associated with congenital anomalies; the risk of congenital anomaly was highest in the least deprived group (200). Stoltenberg *et al.* also adjusted analysis of the association between Pakistani ethnicity and risk of congenital anomalies for consanguinity, mothers and fathers years of education, age, parity, period and place of birth (271).

Table 41 Evidence for variables which could influence congenital anomalies

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)		Variables used in adjusted analysis (*or association unclear*)
		Positive (S/NP)*	Negative	
Congenital anomalies	Sheridan *et al.* 2013 (200) (SR, QuantB)	Consanguinity (S) (BMI- only from additional analysis in the SR (NP))	Deprivation (IMD) (S for least deprived group)	-
	Stoltenberg *et al.* 1997(271) (FS, QuantB)	Consanguinity (NP)	-	Consanguinity, mothers and fathers years of education, maternal age, parity, period and place of birth of mother

-No evidence identified
SR= Evidence included in systematic review, FS= Evidence identified through systematic search and not in the systematic review
Qual=Qualitative study not BiB data, QualB=Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data and MMB= mixed methods study using BiB data.
*S=statistically significant association, NP=Evidence of statistical significance not available

4.5.6 **Longer term outcomes**

This section will discuss the following pregnancy outcomes: Breastfeeding, PPWR, post-partum IGT, and infant anthropometric measurements (those identified were; BMI, and skinfold thickness). PPWR and post-partum IGT were identified by the

literature from the search for my systematic review, breastfeeding and childhood anthropometrics on the other hand were identified as potential outcomes of interest in a Pakistani population by the evidence identified by the updated literature search for this framework-based synthesis (through including maternal BMI as a variable in statistical adjustment (as a confounder), and therefore suggesting that it is associated with breastfeeding and measured of childhood anthropometrics).

Breastfeeding

Results for variables that could influence breastfeeding are shown in Table 42. Eleven studies were identified that provided evidence of the variables which may influence breastfeeding (229, 234, 237, 238, 250, 252, 268, 276, 277, 279, 281). There were three quantitative studies using data from the BiB cohort (234, 237, 238), one mixed methods study using data from the BiB cohort (229), three quantitative studies not using data from the BiB cohort (250, 252, 268), and four qualitative studies not using data from the BiB cohort (276, 277, 279, 281). Positive associations were identified between the following variables and breastfeeding: education (234), income (268), maternal age (250), maternal education (250), paternal education (250), and paternal employment (250). Negative associations were identified between breastfeeding and maternal employment (250), household income (250), and generation status (250). There also appeared to be U-shaped associations between both parity and age of migration and breastfeeding (250). Quantitative studies which investigated breastfeeding as a pregnancy outcome adjusted for the following variables in their analysis; age (237, 238, 250, 252), maternal education (229, 237, 238, 250, 252), paternal education (250), marital and cohabiting status (237, 238), smoking (237, 238), maternal pre-/early pregnancy BMI (237, 238), parity (237, 238, 250, 252), gestational age at delivery (237, 238), birth weight (237, 238), mode of delivery (237, 238), means tested benefits (229), maternal employment (250, 252), paternal employment (250), household income (250), lone mother status (252), introduction to solid foods before four months (252). Kelly *et al.* adjusted for gender of the baby, parity, maternal age, housing tenure, household income, maternal education, maternal employment, smoking, mothers occupational social class, 1 or 2 parent household, infant care arrangements and language spoken at home (268).

The qualitative evidence also identified a number of variables that might influence breastfeeding. These were; previous breastfeeding experience (229), perceived health benefits of breastfeeding (229), perceived quality of breastmilk (276, 277, 280), convenience (229, 280), emotional reasons (229), family (277, 279, 280), peer support (276, 279), culture (277, 281), privacy (276, 277, 280, 281), SES (276), gestational age at delivery (276), returning to work (276), support from hospital staff (276), support at home (276), and the belief that extra food may increase maternal weight (276). One qualitative study reported no association between breastfeeding and maternal age, marital/cohabiting status, ability to pay the bills, current financial status and parity (276).

Table 42 Evidence for variables which could influence breastfeeding

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis (*or association unclear*)	Qualitative evidence
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	U-shaped (S/NS/NP)*	No association (S/NS/NP)*		
Breast-feeding	Santoreli *et al.* 2014 (237) (FS, QuantB)	-	-	-	-	Maternal age, maternal education, marital status, smoking during pregnancy, pre-/early pregnancy maternal BMI, parity, pre-term birth (gestational age at delivery), low birth weight (birthweight) and mode of delivery.	-
	Santoreli *et al.* 2013 (238) (FS, QuantB)	-	-	-	-	Maternal age, maternal education, marital status, smoking during pregnancy, pre-/early pregnancy maternal BMI, parity, gestational age at delivery, birthweight and mode of delivery.	-
	Cabieses *et al.* 2014 (229) (FS, QuantB)	-	-	-	-	Maternal education and means testes benefits	Previous breastfeeding experience, health benefits, convenience, emotional reasons, and confidence
	Lawton *et al.* 2012 (234) (FS, QuantB)	Education (S)	-	-	-	-	-

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis (*or association unclear*)	Qualitative evidence
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***		
Breast-feeding	Griffiths *et al.* 2007 (252) (FS, Quant)	-	-	-	-	Age at first motherhood, maternal age at cohort baby's birth, parity, socio-economic status, maternal education, maternal employment, lone mother status, introduction of solids before 4 months if discontinuing breastfeeding before 4 months (and discontinuing breastfeeding before 4 months if introducing solids <4 months)	-
	Kelly *et al.* 2006 (268) (FS, Quant)	Income (S)	-	-	-	Gender of the baby, parity, maternal age, housing tenure, household income, maternal education, maternal employment, smoking, mothers occupational social class, 1 or 2 parent household, infant care arrangements and language spoken at home	-
	Busck-Rasmussen 2014 (250) (FS, Quant)	**Suboptimal breastfeeding :** Parental employment (NP), Length of residence (NP), age at migration to Denmark (NP).	**Suboptimal breastfeeding:** Place of birth South Asia (descendant of migrants had higher odds of suboptimal breastfeeding than migrants to Denmark) (NP), Maternal age (higher age, decreased odds of suboptimal breastfeeding) (NP), Maternal and paternal education (higher education, decreased odds of suboptimal breastfeeding) (NP).	**Sub-optimal breastfeeding**: Parity (NP) and household income (NP).	-	Maternal age, parity, maternal and paternal education, maternal and paternal attachment to labour market and household income.	-

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)				Variables used in adjusted analysis (*or association unclear*)	Qualitative evidence
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	**U-shaped (S/NS/NP)***	**No association (S/NS/NP)***		
Breast-feeding	Ingram *et al.* 2003 (281) (FS, Qual)	-	-	-	-	-	Religion and privacy
	Ingram *et al.* 2008 (279) (FS, Qual)	-	-	-	-	-	Culture, religion, family, family and peer support
	Choudhry *et al.* 2012 (277) (FS, Qual)	-	-	-	-	-	Culture, Privacy, perceived quality of breastmilk, religion and culture, family
	Bowes and Domokos 1998 (276) (FS, Qual)	-	-	-	Maternal age, place of birth, fluency in English or proximity of relatives (Qualitative evidence)	-	SES, gestational age at delivery, privacy, returning to work, support from hospital staff, support at home, peer support, perception that extra food may increase maternal weight, and perceived quality of breastmilk
	Twamley *et al.* 2011 (280) (FS, Qual)	-	-	-	-	-	Convenience, family, privacy and perception of quality of breastmilk

-No evidence identified
SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review
Qual=Qualitative study not BiB data, QualB=Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data MMB=mixed methods study using BiB data.
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Post-partum impaired glucose tolerance

Results for variables that could influence post-partum IGT are shown in Table 43. One study identified by the literature search for my systematic review found that post-partum IGT was positively associated with insulin requirement during pregnancy (209). This study adjusted for age, parity, booking weight, smoking and family history of diabetes, although no significant association was identified between post-partum IGT and any of these variables in South Asian women.

Post-partum weight retention

Results for variables that could influence PPWR are shown in Table 43. One study identified by the literature search for my systematic review provided evidence on variables that might influence PPWR (212). There was a positive association between GDM and PPWR; women who had GDM on average retained more weight at 14 weeks post-partum than those without GDM (212). This study carried out statistical adjustments for weeks of gestation at inclusion, number of weeks post-partum, age and parity (212).

Table 43 Evidence for variables which could influence post-partum IGT and PPWR

Outcome	**Study**	**Evidence available in study to support type of association with outcome (statistical significance)**		**Variables used in adjusted analysis (*or association unclear*)**
		Positive (S/NS/NP)*	**Negative (S/NS/NP)***	
Post-partum IGT	Sinha *et al.* 2003 (209) (SR, Quant)	Insulin requirement during pregnancy (S), parity (NS), Age (NS),	booking weight (NS), family history of diabetes (NS)	Maternal age, parity, booking weight, smoking, family history and insulin
PPWR	Sommer *et al.* 2015 (212) (SR, Quant)	GDM (NP)	-	weeks of gestation at inclusion, number of week's post-partum, maternal age, and parity

-No evidence identified
SR=Evidence included in systematic review
Quant=Quantitative study not using BiB data
*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

Infant anthropometrics

Infant waist circumference

Results for variables that could influence Infant waist circumference are shown in Table 44. Three studies identified by the updated search for this framework-based synthesis were identified providing evidence of variables influencing infant waist circumference; one using data from the BiB cohort (240) and two quantitative studies not using data from the BiB cohort (254, 267). One found that there was a positive association between maternal alcohol consumption since birth, mothers BMI at six months post-partum and mothers self-reported smoking after pregnancy (240). This study also reported a U-shaped association between infant waist circumference and maternal mental health in pregnancy (Mothers GHQ subscale D score) (240). One study found that maternal BMI was positively associated with infant obesity and also adjusted for the following variables; age of the infant, survey year, mothers BMI, fathers BMI mother's employment status, mother's social class, mothers highest educational qualification, mothers immigration status, mothers current smoking status, lone parent family indicator, and household income (254). One other study adjusted for the following variables; mother’s highest academic qualification, maternal SES and number of infants in household (267).

Infant skinfold thickness

Results for variables that could influence Infant SFT are shown in Table 44. One study using data from the BiB cohort was identified that provided evidence of variables that might influence infant SFT (168). This study found that both birth weight and generation status (place of birth of babies parents) were positively associated with infant skinfold thickness (168). This study adjusted for the following variables; smoking; alcohol; maternal age; maternal hypertension; maternal fasting glucose; maternal height; maternal BMI; parity; gestation; sex; socioeconomic position (maternal education, housing tenure, receipt of means tested benefits); living with partner and birth weight (168).

Infant BMI

Results for variables that could influence Infant BMI are shown in Table 44. Three quantitative studies not using data from the BiB cohort (254, 263, 266), and one

qualitative study not using data from the BiB cohort (260) were identified that provided evidence of variables that might influence infant BMI. The qualitative study reported that diet and physical activity, parental BMI, cultural norms/traditions, SES and genetics were associated with infant BMI (260). Higgins *et al.* found that maternal BMI was positively associated with infant BMI in Pakistani infants (254). Variables adjusted for in associations including infant BMI were; age of the infant (254, 263, 266), survey year, mothers BMI, father's BMI, mother's employment status (254, 266), mother's social class, mother's highest educational qualification (254, 266), mother's immigration status (254, 266), mother's current smoking status, lone parent family indicator (254, 266), household income (254, 266), SES (263), infant gender (266), language spoken at home (266), bedtime on weekdays (266), and how many portions of fruit per day (266).

Table 44 Evidence for variables which could influence longer term infant anthropometrics

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)			Variables used in adjusted analysis (*or association unclear*)	Qualitative evidence
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	No association (S/NS/NP)*		
Infant waist circum-ference	Traviss *et al.* 2012 (240) (FS, QuantB)	Abdominal circumference at birth (S), maternal consumption of alcohol since birth (S), mother's BMI at 6 months post-partum, Mother's self-reported smoking after pregnancy (NS)	Mother's GHQ subscale D score in pregnancy (S)	-	-	-
	Higgins *et al.* 2012 (254) (FS, Quant)	-	-	-	Age of the infant, survey year, mothers BMI, fathers BMI mother's employment status, mother's social class, mother's highest educational qualification, mothers immigration status, mothers current smoking status, lone parent family indicator, and household income.	-
	Griffiths *et al.* 2011(267) (FS, Quant)	-	-	-	Mothers highest academic qualification, maternal socio-economic status and number of infants in household.	-
Infant skinfold thickness	West *et al.* 2013 (168) (FS, QuantB)	Birthweight (NP)	-	Generation status (NS)	Smoking; alcohol; maternal age; maternal hypertension; maternal fasting glucose; maternal height; maternal BMI; parity; gestation; sex; socioeconomic position (maternal education, housing tenure, receipt of means tested benefits); living with partner and birthweight	-
Infant BMI	Pallan *et al.* 2012 (260) (FS, Quant)	-	-	-	-	Diet and physical activity, parental BMI, cultural norms/traditions, SES and genetics

Outcome	Study	Evidence available in study to support type of association with outcome (statistical significance)			Variables used in adjusted analysis (*or association unclear*)	Qualitative evidence
		Positive (S/NS/NP)*	Negative (S/NS/NP)*	No association (S/NS/NP)*		
Infant BMI	Higgins *et al.* 2012 (254) (FS, Quant)	-	-	-	Age of the infant, survey year, mothers BMI, fathers BMI mother's employment status, mother's social class, mothers highest educational qualification, mothers immigration status, mothers current smoking status, lone parent family indicator, and household income.	-
	Saxena *et al.* 2004 (263) (FS, Quant)	-	-	-	Infant's age and socioeconomic status	-
	Zilanawala *et al.* 2015 (266) (FS, Quant)	-	-	-	Infant age, infant gender, income, education, single parenthood and mother's employment, language spoken at home migrant generation, bedtime on weekdays, portions of fruit per day	-

-No evidence identified

SR=Evidence included in systematic review, FS=Evidence identified through systematic search and not in the systematic review

Qual=Qualitative study not BiB data, QualB=Qualitative study using BiB data, Quant=Quantitative study not using BiB data, QuantB=Quantitative study using BiB data MMB= mixed methods study using BiB data.

*S=statistically significant association, NS=association not statistically significant, NP=Evidence of statistical significance not available

4.5.7 **Ethnic differences in mediating and confounding variables**

This section will give a brief overview of findings relating to ethnic differences in mediating and confounding variables, and how different mediating and confounding variables interact.

Studies suggested that South Asian[15] women were, on average shorter than White women (203, 208, 211, 212, 235, 241, 242, 274), although maternal height may be influenced by generation status (whether or not mother and father, and their grandparents had been born in the UK) (241). Evidence was unclear regarding ethnic differences in maternal age: some studies suggested South Asian women were older compared with White (168, 171, 232, 233, 235, 237, 239, 241, 243, 244, 249, 265, 283); while others suggested they were younger (201, 211, 212, 215, 216, 246, 250, 257, 258, 270, 272, 276), or that there was no difference in age (161, 203, 207, 214). Evidence suggested that maternal age in South Asian or Pakistani women could also be affected by generation status (241, 273). Evidence also found that South Asian women were more likely to be married and/or cohabiting compared with White women (201, 237, 240-243, 246, 258, 270), and that marital/cohabiting status may be affected by generation status (246). Studies showed that generally, South Asian women had a higher parity than White women (201, 203, 207, 209, 211, 212, 215, 216, 249, 250, 257, 262, 265, 268, 272, 276, 282, 283), and it was suggested that parity is also affected by generation status (241, 246).

Ethnic differences in SES were found to be dependent on the measure used. This review identified ten different measures of SES: maternal employment, maternal education, receipt of means tested benefits, housing tenure, measure of neighbourhood deprivation, financial wellbeing, paternal employment, paternal education, income quintile, and job type. Maternal employment was found to be lower in South Asian women compared with White British women (168, 239, 241, 243, 250, 258, 266, 268, 276), and maternal employment was shown to be affected by generation status (168, 241, 258). There were a higher percentage of Pakistani women in receipt of means tested benefits (241, 268, 283), although one study found that following adjustment for maternal age and parity, the association was no longer significant (241). Receipt of means tested benefits was also found to be affected by generation status (241). Generally, housing tenure was found to be higher in South

[15] Here South Asian women refers to Pakistani or South Asian women identified by the 92 studies included in framework-based synthesis familiarisation stage.

Asian women compared with White women (239, 241). Housing tenure was found to be affected by generation status (241). Measure of area of residence deprivation was also found to differ between South Asian and White women; South Asian women were found to reside in more deprived areas compared with White women (200, 201, 205, 230, 232, 240, 265). Pakistani women were found to be less likely to be struggling financially compared with White British women (243, 283). Both father's employment and education also appeared to differ between South Asian and White women; there was a higher percentage of Pakistani fathers in manual/routine employment or self-employed compared with White British fathers, who were more likely to be in non-manual or professional jobs (283). South Asian father's education also appeared to be lower compared with White father's education (250, 272). South Asian families were also more likely to be living in lower income quintiles compared with White families (250, 257, 266, 268, 272).

Smoking was found to be less common in Pakistani women compared with White women (200-202, 206, 209, 213, 216, 233, 235, 237, 239, 241, 242, 244, 283) (248, 257, 258, 262, 264, 268, 282, 283). However, smoking was affected by generation status (242) and SES (283). Alcohol consumption was also found to be lower in South Asian women (168, 200, 241, 244, 257, 262, 263).

Overall, more studies suggested that South Asian women had a higher prevalence of a family history of diabetes compared with White women (209, 210, 212, 213, 216). Studies also suggested that South Asian women had a higher prevalence of type 2 diabetes compared with White women (201, 210). South Asian women were found to have lower blood pressure compared with White women (205). South Asian women were also found to have higher levels of anaemia compared with White women (246), although these levels differed with generation status (246). Consanguinity was found to be higher in South Asian populations compared with White (200, 245, 246, 269, 271) and consanguinity was found to be affected by religion (which was shown to be more likely to be Muslim for Pakistani women)(269), maternal education (271) and generation status (246). South Asian women were also less likely to be only English speaking, and more likely to speak English and another language or another language only (268), they were also reported to be likely to be of Muslim religion (249). Pakistani families were also more likely to have a higher number of people living in their household compared with White British families (263, 265, 266).

4.5.8 **Conceptual model development**

The main conceptual model of associations between key outcomes and exposures of interest is shown in Figure 16. This has been developed using evidence from my systematic review, the IoM guidelines and this framework based synthesis.

The evidence from this framework based synthesis has also been used to develop conceptual models for each outcome of interest; including all potential confounders and mediators highlighted by the evidence. An example of these conceptual models is given in Figure 17 showing the conceptual model for GWG. Examples of conceptual models for GDM, gestational age at delivery and longer term infant anthropometrics are included in Appendix 9 (pgs.355-357).

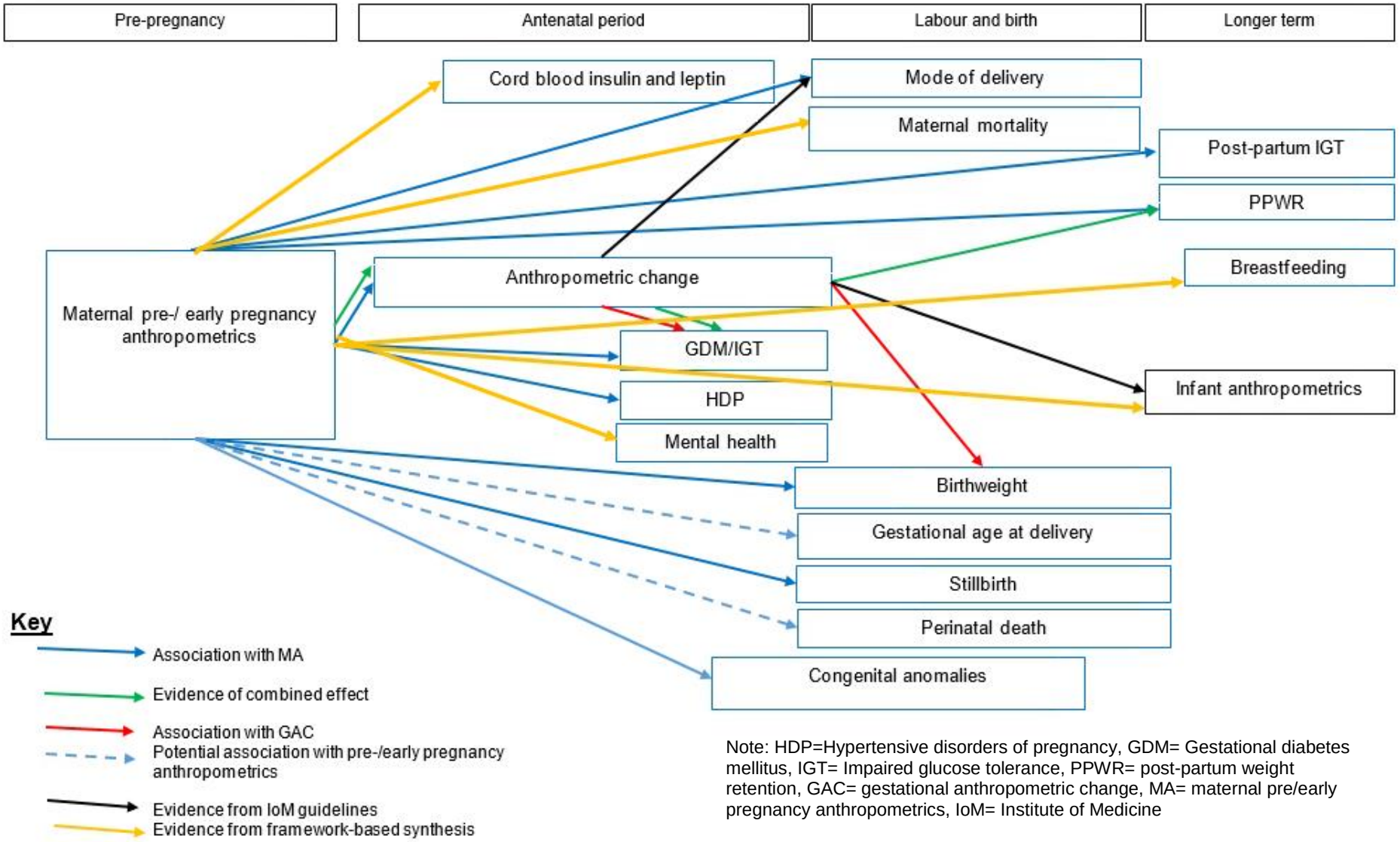


Figure 16 Conceptual model with information on associations identified from framework based synthesis added

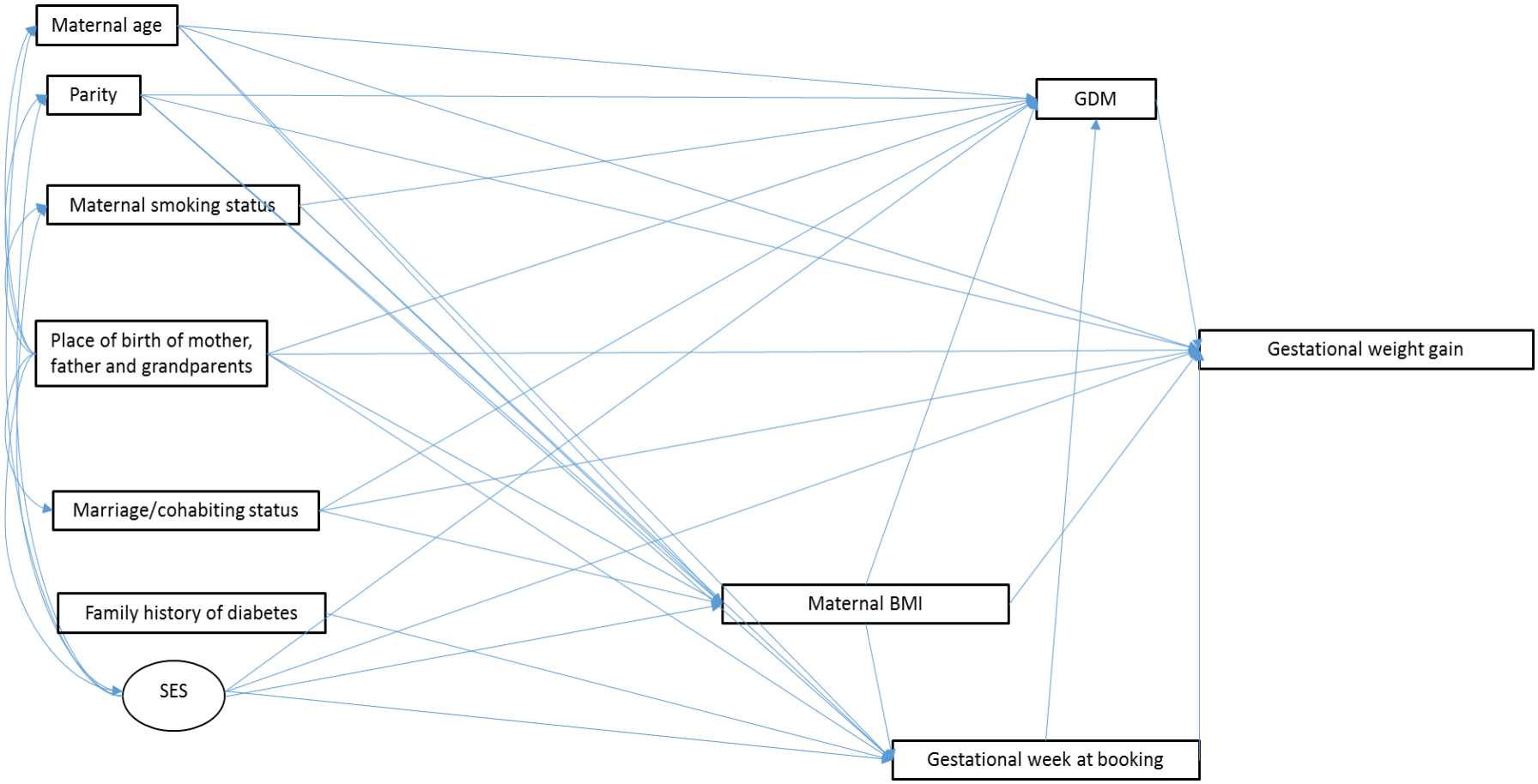


Figure 17 Conceptual model for GWG as an outcome.

Note: SES is represented as a composite variable representing variables such as IMD, employment, education, housing tenure etc.
SES= socioeconomic status; BMI= Body mass index and GDM= Gestational diabetes mellitus

4.5.9 Discussion of the strengths and limitations of the framework-based synthesis

This literature review and framework-based synthesis has integrated qualitative and quantitative literature to identify variables (i.e. confounders and mediators) that may influence the associations between maternal pre-/early pregnancy anthropometrics, gestational anthropometric change and pregnancy outcomes in Pakistani women. Results highlight that these associations are extremely complex and involve multiple different variables. In terms of conceptual model development for this cohort, the framework-based synthesis has provided me with the evidence to develop an evidence-based conceptual model, including additional pregnancy outcomes (identified where MA or GAC was included in a statistical adjustment in an association between ethnicity and pregnancy outcome of interest), confounding and mediating variables.

This systematic review was rigorous, and followed suggested guidelines for reporting mixed methods systematic reviews developed using a systematic review of mixed methods systematic reviews (224). The search strategy for this literature review and framework-based synthesis was extremely comprehensive. I worked with an information scientist to develop the search strategy. I then then used this search strategy to conduct a thorough search of 10 databases for any qualitative, quantitative, or mixed-methods studies. I also re-screened the studies identified by the search strategy for the systematic review (Chapter 3) to ensure that no relevant quantitative studies were overlooked. Supplementary searches involved searching the reference lists of all studies included and reviews that were related to the topic area, and citation searching, and had it been required, authors would have been contacted for additional information, however this was not necessary here. As with the previous systematic review in Chapter 3, despite how rigorous the review process was, grey literature was not included in the searches, this can lead to publication bias (221).

There are also limitations of this literature review and framework-based synthesis. One critique of using a framework-based approach is that it can result in forcing data into categories by applying a deductive approach to qualitative synthesis (285). However, I used data driven themes, within an a priori framework which was based on evidence from both my systematic review, and the 2009 IoM guidelines (94). This approach allowed the evidence-base to shape the final framework thus minimising the deductive

nature of the evidence-synthesis (285). This method also enabled the results of the synthesis to be expressed as a tables, these tables were then used to map the associations for each outcome in the form of conceptual models. Due to the large volume of studies identified, and the diversity in methodologies used in the included literature, an *a priori* decision was made not to quality assess the evidence included in this framework-based synthesis. While evidence would not have been included/excluded from the synthesis based on quality score, not doing a quality assessment means that I am unable to comment on the quality of the evidence included. As in Chapter 3, it may have been beneficial to take into account study quality when deciding whether or not to include an association in the conceptual model. It is possible that poor quality studies may be biased (i.e. may not truly reflect what is happening in the population under study) for example may not adjust for relevant confounders, or may only interview a specific group rather than a sample relevant of the whole population. This means that associations from biased studies may have been included in my conceptual model. However, as this step was exploratory (i.e. to develop a conceptual (hypothetical) model that I would then go on to test using data from the BiB Cohort), associations were included independent of the amount and quality of evidence. In addition, if I had quality assessed the evidence from this framework based synthesis, I would have had to use quality assessment tools relevant for each of the included study designs. The quality scores from different tools, although would give an overall idea of study quality, would not have been comparable between studies. The main issue with including poor quality evidence in terms of model development (which also applies to model development in Chapter 3) is that it may not identify an association that does actually exist for example due to a type II error (or beta error- when the results of a study suggest that there is no association between outcome and exposure, when in fact there is one (220)). (The Validation study in Chapter 5 aims to overcome this limitation).

The use of a framework-based synthesis provided me with a pragmatic way to integrate qualitative and quantitative evidence in a way that was useful to the research question. In this review, the integration of qualitative and quantitative evidence was essential as it allowed me to consider different types of associations. Quantitative literature identified statistical associations from populations of Pakistani women, and variables the

researcher or research teams thought to be confounders, and so associated with variables of interest to this review. Qualitative literature provided me with evidence of variables of interest though opinions of individual Pakistani women. One problem in research investigating particular ethnic groups, or comparing outcomes in one ethnic group in another, is ethnocentricity (286). Ethnocentricity is:

"the inherent tendency to view one's own culture as the standard against which others are judged" (286).

This is a complex issue, and one that is not easily overcome. However, by including qualitative research in this review I have been able to include some evidence of the experiences, thoughts and opinions of Pakistani women in conceptual model development, a limitation of the methods here is that I was unable to include studies in languages other than English. Another limitation here is that while the results of this framework based synthesis directly informed conceptual model development which was the aim of this review for this PhD project, the way the qualitative data was analysed was very reductive. Due to the issue of ethnocentricity, and to account for the complexity of the qualitative data it would have been interesting to also carry out a more depth synthesis of the qualitative data alone (for example a thematic analysis). Another way of reducing the influence of ethnocentricity on this research is to get input from experts who are familiar with the Pakistani population; members of the BiB research team. This has been carried out and is described in Chapter 5.

In conclusion, this review and framework-based synthesis has highlighted that the associations between MA, GAC and pregnancy outcomes in Pakistani women are complex, influenced by many confounders and mediators. Variables identified by this review have be used to further development of my conceptual model which will be used inform analysis of data from the BiB cohort (Chapter 6: Methods for analysis of data from the Born in Bradford cohort, and Chapter 7: Results from analysis of data from the Born in Bradford cohort).

Chapter 5. Validation study and discussion of conceptual model development (Phase 3)

This chapter will describe the process of, and the results from, asking members of the BiB research team to provide their expert opinion on the conceptual model developed using findings from the systematic review in Chapter 3, and the mixed methods systematic review and framework-based synthesis in Chapter 4. This chapter will provide a discussion of the strengths and limitations of this expert opinion phase, and also of using a three stage approach (systematic review, framework based synthesis, and expert opinion) to develop a conceptual model to inform analysis of data from the BiB project.

5.1 Validation study

The systematic review and framework-based synthesis stages have enabled me to develop a list of variables from the existing evidence-base to inform the conceptual model development. However, it is possible that due to the limited evidence-base relating to MA, GAC and pregnancy outcomes in Pakistani women, and the potential for type II errors leading to associations not being identified (as discussed in Chapter 4; pg.173) the evidence-base may not have highlighted all variables or associations that are relevant to this project. Further, the variables identified from international literature may not be completely relevant or comprehensive relating to the Pakistani women in the BiB cohort. Therefore, to explore the relevance of the findings of the systematic review and framework-based synthesis to the study population that will be used for the next stage of my PhD, I asked members of the BiB research team to provide their expert opinion on my findings to date.

5.2 Aim

To validate conceptual model so far and identify any relevant variables (outcomes, mediators or confounders not highlighted by phase 1 (Chapter 3) or phase 2 (Chapter 4).

5.3 Objectives

- To present the conceptual model developed from phases 1 and 2 to experts at BiB.
- To invite the experts at BiB to comment on the conceptual model and identify whether they agreed with the pregnancy outcomes that had been identified through phases 1 and 2.
- To invite the experts at BiB to comment on the conceptual model and identify whether they agreed with the confounding and mediating variables that had been identified through phases 1 and 2.
- To invite the experts at BiB to comment on the conceptual model and highlight any pregnancy outcomes that might be potentially relevant and should be included in model, but had not been highlighted by phases 1 and 2 of model development.
- To invite the experts at BiB to comment on the conceptual model and highlight any confounding or mediating variables that might be potentially relevant, but had not been highlighted by phases 1 and 2 of model development.

5.4 Methods

An email invitation was sent to members of the BiB research team who had knowledge of the cohort dataset (e.g. data managers, statisticians, those working with the dataset) and those with relevant clinical knowledge relating to pregnancy in Pakistani women in Bradford (e.g. midwives, obstetricians, gynaecologists). Potential participants were identified using the BiB website, and additional potential participants were suggested by my lead contact in the BiB team. The invitation asked if they would be able to give up an hour of their time to attend a group meeting at the BiB office in Bradford to provide feedback on the conceptual model development for this project; i.e. the findings from the systematic review and framework-based synthesis. The agenda for the meeting is in Appendix 10 (pgs.358-359).

The 1-hour meeting comprised of three stages:

1. I delivered a brief 10-minute presentation of the PhD project and the findings from Phase 1 (systematic review) and Phase 2 (framework-based synthesis) highlighting the process, key findings and development of the conceptual model to date.

2. I facilitated a discussion on the conceptual model to get feedback on the associations identified in the evidence-base between MA, GAC and pregnancy outcomes. Examples of questions to prompt discussion for this stage were: “Would you expect to see any interactions between outcomes identified?” and “Are there any other pregnancy outcomes that you would also consider?”.

3. I facilitated a discussion on the conceptual model to get feedback on the factors identified that might influence the associations between MA, GAC and the pregnancy outcomes. Examples of questions to prompt discussion for this stage were: “In your opinion, are the identified factors influencing relevant?” “Would you add any and why?” and “Would you remove any and Why?” The information that was given out at the meeting relating to this discussion is in Appendix 11 (pgs.360-364).

5.5 Results

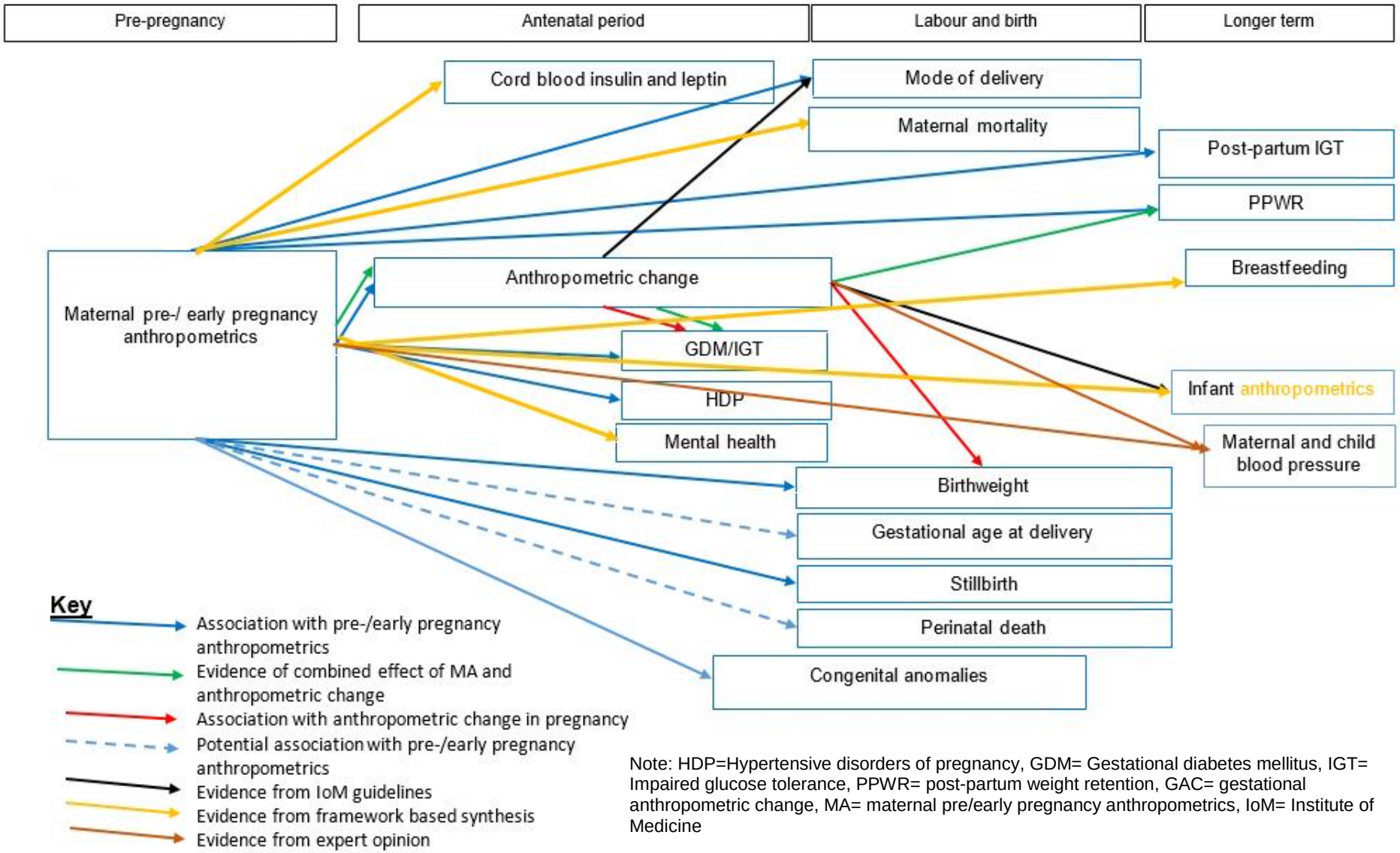
Of the seven members of the BiB research team invited, five were able to attend the meeting and provide feedback; these were a Research Midwife and Research Fellow working at BiB, two statisticians at BiB, an obstetrics and genecology clinician, and public health and clinical institute directors.

The participants of the meeting felt that the conceptual model of hypothesised associations between MA, GAC and pregnancy outcomes in Pakistani women was theoretically accurate. However, some further suggestions were made. These were that of all the outcomes identified, PPWR was of most interest to the BiB research team as it has not been explored before using the BiB data. It was also felt that it would be interesting to explore maternal and infanthood blood pressure as long-term pregnancy

outcomes in relation to MA and GAC. Finally a suggestion was made that, whether or not a mother had GDM might influence GWG as having GDM would mean antenatal intervention with dietary advice.

The participants discussed the confounding and mediating variables I had proposed from the evidence-base reviews. They felt that these data sources had identified relevant confounding and mediating variables that could potentially influence the associations between MA, GAC and pregnancy outcomes. Discussions did not identify any additional confounders or mediators to add to the conceptual model.

The final conceptual model of exposures and outcomes identified by my systematic review, framework-based synthesis and this expert opinion is shown in Figure 18.



Note: HDP=Hypertensive disorders of pregnancy, GDM= Gestational diabetes mellitus, IGT= Impaired glucose tolerance, PPWR= post-partum weight retention, GAC= gestational anthropometric change, MA= maternal pre/early pregnancy anthropometrics, IoM= Institute of Medicine

Figure 18 Conceptual model with exposures and outcomes identified by systematic review, framework based synthesis (including IoM guidelines) and expert opinion

5.6 Discussion of the strengths and limitations of the expert opinion phase

This phase of my PhD research was designed as a confirmatory step in conceptual model development. It aimed to identify any associations or variables that may not have been identified by my systematic review or framework-based synthesis due to gaps in the published literature. The strength of this approach is that it added an extra step of rigor to the model development, including the opinions from a range of experts who were familiar with the topic area and the BiB population, and also the data from the BiB cohort. One of the limitations was there could have been more people on the panel; some of those invited were unable to attend. It would also have been beneficial to include members of the BiB cohort on the panel. This would have added an extra layer to model development through patient and public involvement (PPI). However, the additional approvals required from BiB were not possible within the timeframe of this PhD project. It might also have been beneficial to record this discussion, as you might do with a focus group for qualitative research. However, detailed meeting notes were taken of all key thoughts and suggestions made by the experts on the panel and these were used to inform model development.

5.7 Discussion of conceptual model development

The final evidence-based conceptual model of associations between pregnancy outcomes and exposures; MA and GAC is shown in Figure 18, pg.179. Evidence from the systematic review identified associations between the following pregnancy outcomes: GDM, HDP, GAC, mode of delivery, birth weight, stillbirth, congenital anomalies, PPWR and post-partum IGT and MA. There were also potential associations between gestational age at delivery, perinatal mortality and MA (potential associations were those where the effect size was increased, but statistical significance was not detected (e.g. $p>0.050$ or the 95%CI included 1.00) and Asian specific BMI criteria were not applied). The systematic review also identified that GDM and birth weight were associated with GAC. There was also evidence of a combined effect of MA and GAC on GDM and PPWR. Additional associations with GAC identified from evidence in the 2009 IoM GWG guidelines were mode of delivery and infant weight. The framework-based synthesis identified further potential associations between MA and maternal death, breastfeeding and infant

anthropometrics (rather than just infant weight which was identified by the IoM guidelines).

A strength of this conceptual model development process is that it involved a rigorous three stage, evidence-based approach: 1) systematic review, 2) framework-based synthesis and 3) expert opinion. The systematic review was the most rigorous methodology, but due to the availability of evidence, it was not possible to restrict to Pakistani women only. This was addressed by the framework-based synthesis, which used an equally rigorous search strategy to identify the evidence-base to thoroughly explore all potential confounders and mediators for associations. However, due to the variation in methodologies used and lack of relevant quality assessment tools for these methodologies, I was unable to quality assess the evidence included in the framework-based synthesis. The expert opinion further explored gaps in the evidence-base and relevance of the published evidence to the Pakistani population in Bradford, which also added rigor to the conceptual model development process.

An additional benefit of the model development process was that I incorporated both quantitative and qualitative literature. This highlighted the complexity of the area of research, and the importance of utilising qualitative and mixed-methods research, particularly to identify more culturally specific mediators and confounders (e.g. religious beliefs, culture, peer support, place of birth, previous experiences and emotional reasons). Using a rigorous mixed methods approach to conceptual model development also means that I have identified variables (including exposures, outcomes, confounders and mediators) that are not available for analysis in the data from the BiB cohort. Some variables are not easily quantifiable and therefore not part of routine maternity data collection or the prospective cohort data collection. Others are absent from the cohort, including GAC (while an indicator of GWG is available (weight gain to the third trimester) and has been analysed in this PhD project, other measures of anthropometric change in pregnancy are not), maternal death, perinatal death, and childhood blood pressure. The absence of these variables of interest in the dataset is a limitation to be expected of all research using existing datasets for secondary analysis as the researcher has to work with the data available to them rather than being able to go out and collect their own data, tailored to the research question. Rather than limiting my conceptual model development to only include exposures and outcomes available in the data from the BiB project, I have taken a more exploratory approach, and included outcomes relevant to the research area

that will not only be able to guide my analysis of data from the BiB cohort, but also be able to inform future research.

Chapter 6. Methods for analysis of data from the Born in Bradford cohort

This chapter describes the methods used to test the conceptual model developed in Chapters 3-5 using the data from the BiB cohort. Firstly, I discuss the evidence-based conceptual model of all key exposures and outcomes. I then describe the final model used for SEM using GWG as an outcome. The section will then go on to describe the data analysis methods used to test the associations identified by conceptual model development. It will also then define all variables used including exposures, outcomes and confounding and mediating variables.

Not all variables identified when developing the conceptual model are available in the data from the BiB cohort. However, knowledge of these variables gained through developing an evidence-based conceptual model will inform the critical discussion of results of this analysis, including limitations and recommendations for future research.

Figure 19 shows the conceptual model highlighting exposures and outcomes that are available in the data from the BiB cohort for inclusion in the analysis. Due to the limited evidence for GWG as an exposure, all possible paths (associations) between pregnancy outcomes and MA and GWG in the model have been investigated. In Figure 19, variables that are crossed out indicate those which are not available for analysis in the BiB cohort. It has also been used where I was only able to partially investigate certain variables. I was only able to partially investigate the variables MA and GAC. Although the data from the BiB cohort contains information on different measures of MA (MUAC and tricep SFT at baseline (26-28 weeks) questionnaire), an a priori decision was made that only BMI would be investigated to ensure the project was completed within the specified timeframe. For GAC, while there was information on GWG, the data from the BiB cohort did not contain variables to enable me to investigate GAC in full (i.e. there was no information recorded on change in SFT and limb circumference measures).

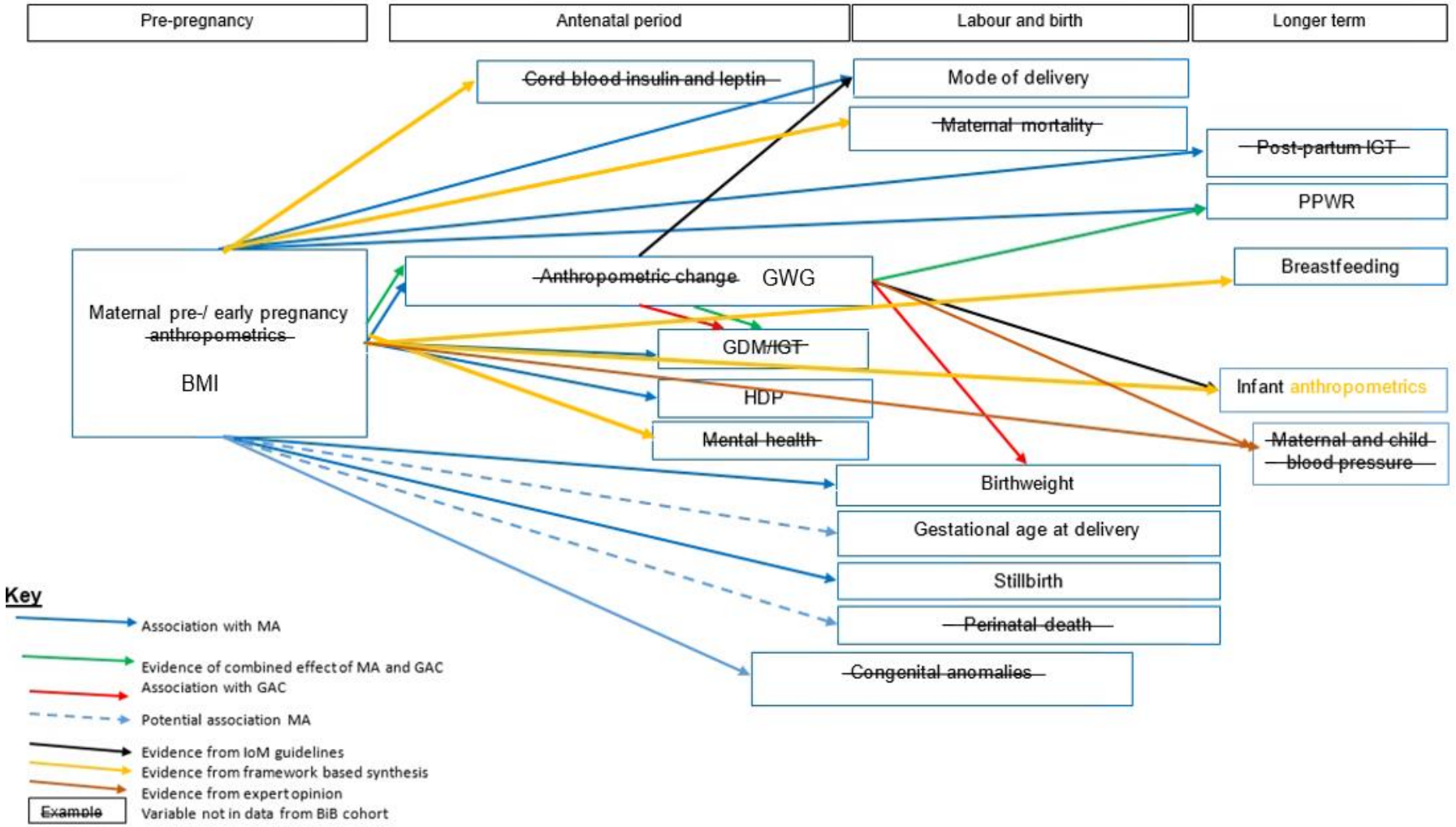


Figure 19 Conceptual model highlighting exposures and outcomes that are available in the BiB cohort for inclusion in the analysis

While conceptual models were developed from the evidence-base for all outcomes of interest shown Figure 19 (conceptual model examples shown in Appendix 9 pgs.355-357, and conceptual model for GWG shown in Chapter 4, Section 4.5.8, Figure 17, pg.171), the complexity of these models meant that SEM was not possible for all outcomes within the timeframe of this PhD research. These outcomes were instead investigated using regression analysis, and SEM was carried out for GWG as an outcome. GWG was chosen as the key outcome of interest due to the lack of evidence available for the association between GWG and MA in South Asian women (186). This chapter will describe the data analysis methods used to test all associations between MA and GAC and outcomes of interest identified through the evidence base, including the conceptual model for GWG.

6.1 Conceptual model for gestational weight gain to be tested using Born in Bradford data

In this section, the hypothesised conceptual model for GWG is described, including all individual SES variables separately (i.e. education, employment and IMD). The diagram for this model, with variables relating to SES condensed into one variable for simplicity, is shown in Figure 17 (Chapter 4, Section 4.5.8, pg.171). This model was developed based on evidence reported in Chapters 3-5[16] and is summarized in Table 45; in each column, the variables in row B are hypothesised to affect those in row A. When creating conceptual models, all possible paths between variables must be included (i.e. if one variable precedes another, it is hypothesised that the one that occurs second is affected by the one that occurs first, and a path between the two must be specified), even where there may not be an association. Paths should only be removed when there is evidence to do so from testing the conceptual model with real data. In Table 45, references have been provided where there is evidence of an association between variable in row B and variable in row A. Where there is no reference provided, this path has been drawn because there is evidence that the variable in row B is associated with another row A variable in the model, and it precedes the variable in row A. Only variables that were available to me in the data from the BiB cohort have been included in the model in Table 45.

[16] Please note that no changes to the conceptual model for GWG were made in Stage 3 (Chapter 5)

Table 45 Conceptual model for GWG as outcome; in each column, the variables in row B are hypothesised to affect those in row A

A	GWG	GDM	MUAC and tricep SFT at baseline (26-28 weeks gestation)	Gestational week of booking	Maternal BMI
B	• GDM (211) • Maternal BMI (202, 212) • MUAC and tricep SFT (202, 212) • Maternal ethnicity (202, 212) • Place of birth of the mother, father and grandparents • Language • Maternal age (211) • Smoking status • alcohol consumption • Smoking exposure • Parity (211) • Marriage and cohabitation status (275) • Gestational week of booking (211) • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal BMI (161, 171, 204-207, 212-214, 216). • MUAC and tricep SFT (161, 171, 204-207, 212-214, 216). • Maternal ethnicity (161, 171, 204-207, 212-214, 216). • Place of birth of the mother, father and grandparents (241) • Language • Maternal age (161, 204, 205, 207, 211, 214, 216, 241, 262) • Smoking status (216, 241, 262) • Alcohol consumption (262) • smoking exposure (216, 241, 262) • Parity (161, 204, 207, 211, 216, 241, 262) • Marriage and cohabitation status • Gestational week of booking (211) • History of diabetes (161, 216) • Mothers education (216, 241, 262) • Fathers education (216, 241, 262) • Mothers job (241), • Fathers job (241), • IMD (204)	• Maternal BMI • Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • Maternal age • Smoking status • Alcohol consumption • Smoking exposure • Parity (212) • Marriage and cohabitation status • Gestational week of booking • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal BMI • Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • Maternal age • Smoking status • Alcohol consumption • Smoking exposure • Parity • Marriage and cohabitation status • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal ethnicity • Place of birth of the mother, father and grandparents (168, 241) • Language • Maternal age (204, 207, 216, 232, 241), • Smoking status (216) • Alcohol consumption • Smoking exposure • Parity (204, 207, 212, 216, 241), • Marriage and cohabitation status • History of diabetes (216) • Mothers education • Fathers education • Mothers job • Fathers job • IMD (204)

A	Smoking status	Alcohol consumption	Smoking exposure	Parity	Maternal age
B	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • Maternal age • M • Alcohol consumption • Smoking exposure • Parity • Marriage and cohabitation status • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • Maternal age • smoking exposure • Parity • Marriage and cohabitation status • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • Maternal age • Parity • Marriage and cohabitation status • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • Maternal age • Marriage and cohabitation status • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • marriage and cohabitation status • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD
A	**Marriage and cohabiting status**	**IMD**	**Mothers job**	**Fathers job**	**Mothers education**
B	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job • IMD	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • History of diabetes • Mothers education • Fathers education • Mothers job • Fathers job	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • History of diabetes • Mothers education • Fathers education • Fathers job	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • History of diabetes • Mothers education • Fathers education	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • History of diabetes • Fathers education

A	Fathers education	Language	History of diabetes	Place of birth of the mother, father and grandparents	Maternal ethnicity
B	• Maternal ethnicity • Place of birth of the mother, father and grandparents • Language • History of diabetes	• Maternal ethnicity • Place of birth of the mother, father and grandparents • History of diabetes	• Maternal ethnicity • Place of birth of the mother, father and grandparents	• Maternal ethnicity	-

In each column, the variables in row B are hypothesised to affect those in row A
Note: IMD=index of multiple deprivation, SFT=skinfold thickness

6.2 Data analysis

As an essential first step to data analysis, the data were summarised (287) using frequency distributions for categorical data, and histograms and dot plots for continuous data. When continuous data were normally distributed, mean and standard deviations have been reported. Where the data were not normally distributed (skewed), median and interquartile ranges have been used.

Data analysis were restricted to Pakistani and White British women[17]. This was due to the fact Asians are the second largest ethnic group in the UK (7.5% of the population), and within the Asian population, the majority are South Asian (Indian (2.5%), Pakistani (2.0%) and Bangladeshi (0.8%)) (169, 170); and also because Pakistani women have been identified as having the highest incidence of first trimester obesity compared to White women (147). All South Asian women were not combined together in the analysis due to the high heterogeneity between the populations; for example in relation to first trimester maternal obesity (147), blood pressure (288), and risk factors for coronary heart disease (289). Combining these subgroups together may have masked the level of risk in one particular South Asian sub-population. Individual subgroup analysis of other South Asian ethnic groups was not carried out due to the small available sample size in these groups within the BiB cohort, which may have limited the reliability of the results.

Data analysis was restricted to singleton pregnancies as there are differences in risk between multiple and singleton pregnancies; for example predominantly pre-term birth (290) and low birth weight (190) which may affect the results. I have and also restricted to include one pregnancy for each woman in the data collection time period. Subsequent pregnancies in the same woman would be more similar to their previous pregnancy than pregnancies in other women in the cohort; statistically these two events are not independent. All women with a singleton pregnancy and more than one pregnancy in the cohort were identified, and only data relating to the first pregnancy in the cohort were retained for analysis (information on parity was retained).

[17] Data on ethnicity were collected by BiB and ethnicity has been self-defined by the mother.

6.2.1 Dealing with missing data

Missing data are unavoidable in epidemiological studies (291). If not dealt with correctly, missing data have the potential to incur bias due to the systematic differences between populations with and without data and undermine the validity of the results (291). The way in which missing data should be dealt with depends on how it is missing (291):

1. **"Missing completely at random":** this is where a data item is missing due to events that are independent of both observed and unobserved parameters (292) (for example; data on weight is missing due to broken scales).
2. **"Missing at random":** this occurs where missingness can be explained by differences in observed data (292) (for example; missing data on weight would be lower than recorded values if more Pakistani women refused to be weighed than White British women, since Pakistani women tend to weigh less than White British Women).
3. **"Missing not at random":** this occurs where the value of the variable that is missing is related to the reason it is missing (292) (for example; if data on weight were only recorded because it was a concern to clinician (i.e. very high or very low) and so data for women with a recommended weight are more likely to be missing. Another example could be that data on weight are missing because women were too heavy to be weighed on the scales).

When data are missing either completely at random, or at random, multiple imputation (MI) can be used (293). MI was first proposed by Rubin in 1977 (294) and is a Bayesian approach which creates several different, but plausible imputed datasets (these datasets are sampled from their predictive distribution and are based on other observed variables in the dataset) and combines the results from each of them (291). This process aims to allow for uncertainty about the missing data (291). As MI requires the modelling of the distribution of each variable with missing values based on other observed variables, it is not suitable when data are missing not at random. If MI is applied when data are missing not at random, results may be misleading due to the bias incurred (291). It is thought that this incurred bias may be as great, or greater, than that occurring in analysis which considers complete cases only (291). Therefore, where data are not missing at random, MI should not be used (291). It is likely that missing data from the BiB cohort are either "missing at random"

or “missing not at random”. Therefore, an *a priori* decision was made with guidance from a statistical expert[18] to use complete case analysis, alongside discussion of the characteristics of the populations with and without missing data in order to avoid the potential bias using MI on a dataset where data were missing not at random.

In order to explore how the missing data differs from the rest of the dataset, I first considered the exposure variables and examined the differences in demographic variables e.g. between the missing and non-missing data for each exposure. I then inspected the differences between the missing and non-missing observations for each variable using generalised linear modelling (GLM) (i.e. linear regression or logistic regression). It is expected that due to the large number of observations and variables in the dataset from the BiB cohort, a significant difference (a significant p value) would be likely to be detected. With this in mind, I have additionally examined how different the missing observations are from the non-missing observations by including the co-efficient or ORs from the regression analysis (i.e. I have considered the magnitude of the effect of being missing for each variable in turn on all other variables).

6.2.2 Exploratory analysis

To investigate the association between MA and different pregnancy outcomes (outcomes with a measurement at one time point only), a number of regression models were generated. Primarily univariate regression models (unadjusted generalised linear models (GLMs)) were carried out to estimate the unadjusted effect size of the association between each maternal ethnicity, each anthropometric exposure and outcome. Multivariable regression models (adjusted GLMs) were then generated for each exposure and pregnancy outcome, to provide an estimate of the effect size adjusting for variables that were hypothesised to be confounders of the specific association to the data analysis *a priori*. Where the outcome was a continuous variable, linear regression modelling was used, and where the outcome was binary (i.e. yes/no or 0/1), logistic regression modelling was used. Interaction terms were also then used to investigate whether or not there was a difference in the shape of the association between exposure and outcome for the two ethnic groups.

[18] Professor Steven Rushton

Model validity is a key aspect influencing the conclusions we can draw from statistical models (i.e. for valid conclusions to be drawn, models statistical models must be correctly specified and theoretically accurate). Statistical models are not direct representations of populations under study, but rather an estimation; it is only required that models represent the main features of the population without major distortion (295). Therefore, it is important to examine the correspondence between the data and the model to check for model failure. For generalised linear models, failure can occur four areas:

1. Where the probability distribution for outcome variable (i.e. normal (Gaussian) for linear regression, or binomial for logistic regression) is specified incorrectly (295). This leads to inappropriate maximum likelihood estimation parameter estimates through inappropriate use of likelihood function (295). For linear regression, it is assumed that the residuals of the association between outcome and exposure are normally distributed. The normality of the residuals was checked by plotting them on a graph; normal distribution was represented by a straight line (295). If a straight line was not observed, and the residuals were not considered to be normally distributed, a statistical transformation e.g. logarithm was applied to the y variable where y=a+bx (y=dependent variable (outcome), x=independent variable (exposure) a=y intercept and b=slope of the line) to ensure the residuals were normally distributed. Back transformations were then carried out to enable interpretation of the results e.g. antilog function (i.e. 10^y) where logarithm had been used (this was not required). For logistic regression, acceptability of model fit was checked by considering whether or not the residuals were over distributed. This was done by looking at the residual deviance (the deviance of the model with both exposure and outcome fitted; deviance is a measure of model fit for GLMs (292)) and the degrees of freedom. Ideally, the ratio of residual deviance to degrees of freedom should be 1 (i.e. no difference), although a value <2 was considered acceptable (295).
2. Where the link function, which specifies how the expected outcome value relates to the linear predictor of the exposure variable is specified incorrectly (295). The correct link functions will therefore be used, these are “identity” and “logit” for linear regression and logistic regression, respectively.

3. The occurrence of abnormal observations (i.e. outliers) may also cause the model to be incorrectly specified (295). Outliers in the dataset are scores which are different to the rest of the data and must be dealt with so as not to affect the results. If outliers are included in the dataset, they may skew the results. This is due to the fact that outliers often have a significant effect on the mean and standard deviation. Outliers can be univariate if they are extreme on a single variable, such as being more than three standard deviations from the mean (296), and were detected by inspecting frequency distributions. There are also multivariate outliers where there are extreme scores on two or more variables, or a pattern of scores is atypical. Where outliers are cases that were considered to be mistakes in coding they have been removed and recoded as "missing". If they were thought to be true values, rather than mistakes in coding, they have been retained. Decisions were made using realistic upper and lower limits.
4. Incorrect specification of the systematic part of the model (for example reliance on linear models where the association is not linear) (295). When considering BMI as an exposure it is common to observe a "J-shaped curve" between exposure and outcome (297). This occurs because risk of outcome e.g. all-cause mortality, often increases with a BMI in the underweight range, decreases slightly for women of recommended weight, and then starts to increases again when BMI reaches overweight or obese values (297). To account for this, women with an underweight BMI have been excluded from analysis where maternal BMI is considered as a continuous exposure variable.

For multivariate modelling, ensuring correct specification of the systematic part of the model (discussed above) also relates to the legitimacy of variables included. In order to decide which variables would be included in the regression models, Table 46 was used. This table was completed for all outcomes, but for the purposes of this thesis has been populated with information for GWG as an example here, another example of an outcome; gestational age at delivery, where both maternal BMI and GWG have been considered as exposures is attached as Appendix 12 (pgs.365-366). To prevent the bias caused by including mediators in regression analysis (sometimes known as overadjustment bias) (298), only confounding variables were included in adjusted regression models.

Table 46 (and those tables in Appendix 12) allowed me to consider issues of temporality with the variables in the BiB dataset. One issue was that smoking status, alcohol consumption and exposure to smoke could all be considered as confounders or mediators of the association between BMI and GWG. This is because although they are measured during pregnancy in the BiB cohort, they are likely to have crystallised (have a starting point) before pregnancy occurred. It was deemed to be unlikely that a woman who did not drink or smoke prior to pregnancy would take up drinking or smoking during pregnancy. Therefore, I have considered smoking status, alcohol consumption and exposure to smoke as confounders.

Another issue with GWG as an outcome was determining whether HDP should be included in the model. HDP such as preeclampsia usually occurs after 20 weeks of pregnancy (commonly more than 32 weeks) and in the third trimester (299). As GWG was calculated using weight measured in the third trimester, I am unable to be clear on temporality (i.e. which occurred first), and so have not included HDP in the model.

Table 46 Determining which variables are mediators, competing exposures and confounders for maternal BMI as an exposure and GWG as an outcome.

Variable	Column A: Precedes exposure **Maternal BMI**	Column B: Precedes outcome **GWG**	Column C: Follows exposure **Maternal BMI**	Mediator/ confounder/ competing exposure
Ethnicity	X	X	-	Confounder
Place of birth of mother, father and grandparents	X	X	-	Confounder
Family history of diabetes	X	X	-	Confounder
Maternal age	X	X	-	Confounder
Parity	X	X	-	Confounder
Marriage and cohabiting status	X	X	-	Confounder
SES:				
Maternal education	X	X	-	Confounder
Maternal employment	X	X	-	Confounder
Paternal education	X	X	-	Confounder
Paternal employment	X	X	-	Confounder
IMD	X	X	-	Confounder
Maternal smoking status	X	X	-	Confounder
Smoking exposure status	X	X	-	Confounder
Alcohol consumption	X	X	-	Confounder
Gestational week at booking	-	X	X	Mediator
MUAC at baseline	-	X	X	Mediator
Tricep SFT at baseline	-	X	X	Mediator
GDM	-	X	X	Mediator

Note: Those variables that are in columns A and B are confounders, and those that are in columns B and C are mediators. If any variables had been only in column B then these would have been competing exposures.

Testing for multi-collinearity in generalised linear models

Multi-collinearity occurs in a multiple regression where one or more predictor variables are highly correlated with another (300). Multi-collinearity should be avoided, as where it occurs, coefficient estimates of the regression can change erratically (300). This is because multi-collinearity exacerbates some of the pitfalls of regression analysis (300).

These include:

- The estimated regression coefficient depends on what variables are included in the model (300).
- The more predictor variables are added to the regression model, the lower the precision of the estimated regression coefficient (300).
- Conclusions that can be drawn about the null hypothesis (no effect between exposure and outcome) are limited by what variables are included in the regression model (300).
- The contribution of each predictor included in the regression model to reducing the error sum of squares[19] is dependent on the other predictor variables included in the regression model (300).

In order to test for multi-collinearity, the variance inflation factor (VIF) has been used. A VIF of >10.0 indicates serious multicollinearity (301). If identified, serious multicollinearity I planned to deal with this in one of two ways: either variable will be eliminated from the model; or variables which measure the same thing will be combined into a composite (this was not required).

6.2.3 Structural equation modelling (Path analysis where no latent variables used)

SEM was used to investigate the direct and indirect risk factors for GWG as an outcome. While the regression analysis allowed me to estimate the effect of the exposure on each outcome, adjusting for confounders it did not give me an estimate of the percentage each confounder explains of the variance in outcome, nor allow me to consider the effect of mediators. SEM allows me to investigate this, so rather than adjusting for confounders, it allowed me to consider their individual effect on the association between the MA exposure and the outcome of interest. In addition, SEM allows me to consider the contribution of mediators via analysis of indirect paths. Referring to Table 46 in this chapter (pg.195) for GWG, SEM allowed me to look at the influence of both confounders and mediators on the outcome of interest.

[19] Sum of squares is the sum of the squared difference of each observation from the overall mean, for all observations (i.e. $(observation1-mean1)^2 + (observation2-mean2)^2 + (observation3-mean3)^2 + \ldots (observationX-meanX)^2$ =Sum of squares, where X= total number of observations) (297).

Variable types in SEM and path analysis

Observed variable: These represent the data itself and can be categorical, ordinal or continuous (173).

Latent variables: In SEM, these variables correspond to factors or hypothetical constructs which are explanatory variables presumed to reflect something that it is not possible to directly observe, for example intelligence (173). Latent variables are always continuous, and the observed variables used as indirect measure of a latent variables are known as indicators (173). Where no latent variables are required; this is a path analysis.

Error or Residual terms: These are associated with either latent variables or observed variables specified as outcome variables. In the case of indicator (exposure) latent variables, the residual term represents the variance that is unexplained that the corresponding latent variable is supposed to measure (173). Given that error or residual terms must be estimated as they are not directly observable from the raw data, in SEM diagrams they are represented as latent variables (173). Model diagrams are represented by using the symbols shown in Figure 20 (174, 302).

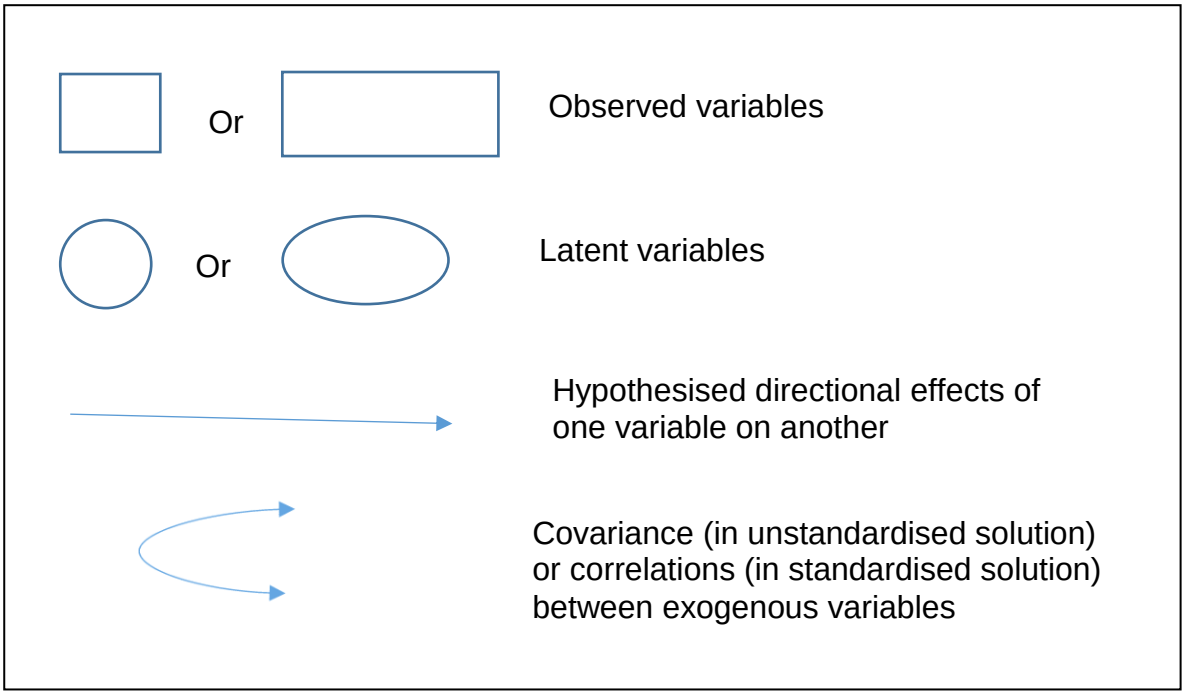


Figure 20 Symbols used to represent variables and associations between variables in SEM diagrams.
(Adapted from Kline RB. Specification. In: Principles and Practice of Structural Equation Modelling. Third ed: The Guilford Press; 2011:91-123.)

The selection of variables to be included in SEM has been guided by theoretical rather than statistical standards. This means that instead of basing the selection of variables for inclusion in the model on the results of statistical tests, as would be carried out for example, in stepwise regression, the selection of variables for SEM has been carried out by the researcher and based on existing theoretical evidence and expert opinion (303). Unlike statistically driven methods which rely on statistical computation and chance, the use of theoretical evidence to inform variable selection has provided me with the chance to think about the research problem. As it is possible for many different relationships to exist between sets of variables, the initially specified models may have poor fit to the data and so may need to be re-specified or modified (174). To improve model fit, insignificant associations (paths) will be removed from the model ($p>0.05$). Good model fit was determined using goodness of fit (GOF) indices root mean squared error of approximation (RMSEA) and comparative fit index (CFI). For RMSEA, the better the model fit, the smaller the value; a value of <0.10 was considered acceptable, and <0.06 was good. For CFI, the higher the value the better; >0.90 was considered acceptable and >0.95 was considered as good. These GOF indices were chosen over chi square statistics as

this is sensitive to sample size (it is likely that a chi square statistic will be significant, indicating poor model fit with a large sample size such as in this study) and are also sensitive to the complexity of the model (304). In initial exploratory analysis, all variables were kept in the model where there are significant paths ($p<0.050$). However, where the model is deemed too complex to interpret clearly, variables with a total effect <0.100 were removed from the model. In the first instance, exceptions to this were for key variables of interest: Ethnicity, BMI, GDM and the outcome GWG. Then the most parsimonious[20] model was identified. Reported model coefficients are standardised (i.e. units are standard deviation).

6.3 Defining variables

This section will define all variables used in the analysis; exposures, outcomes, then mediating and confounding variables (for full definitions of mediating and confounding variables please see Chapter 4, Section 4.1.1, pgs.115-116).

6.3.1 Exposure variables:

Maternal anthropometrics

In the BiB cohort, maternal BMI at booking was calculated using height measured at baseline (26-28 weeks gestation) and weight measured at first antenatal clinic visit (booking appointment, approximately 10-12 weeks gestation) using Seca 2in1 scales (Harlow Healthcare Ltd, London, UK). BMI was primarily considered as a continuous variable. A lower BMI limit was set at 11kg/m^2 as this has been found to be the lowest BMI for survival in women (305) (when excluding underweight women from analysis, this lower limit was set at 18.5kg/m^2). An upper limit of a booking BMI 80kg/m^2 was defined using both the frequency distribution in the data from the BiB cohort, and upper BMI limits used in published literature relating to maternal BMI (58, 81).

[20] The simplest model that is theoretically plausible

Maternal BMI was also categorised according to the WHO criteria; both the general population criteria (3) (shown in detail in Table 1, Chapter 1, Section 1.1.1, pg.4) for White and Pakistani women, and also the Asian-specific criteria (43) (shown in detail in Table 8, Chapter 1, Section 1.7.2, pg.30) for Pakistani women only. Further subdivision of BMI categories (i.e. consideration of maternal extreme obesity ≥50kg/m^2) was not used due to small sample size (n=11).

Gestational weight gain (also an outcome when maternal anthropometrics at booking/baseline considered as exposure)

GWG was calculated by subtracting weight in the third trimester from the weight at the booking appointment. Weight in third trimester was not part of the original cohort dataset but was retrospectively extracted from case notes for the whole BiB cohort, where women had completed the baseline questionnaire and an OGTT, and had pregnancy outcomes recorded. GWG was primarily considered as a continuous variable. Secondary analysis was also carried out with GWG as a categorical variable based on maternal booking BMI category. In order to define the upper and lower realistic limits for GWG, published literature, published guidelines and frequency distributions were considered. The IoM guidelines (94) do not provide realistic values for upper or lower limits for GWG (94). However, they do provide weight gain during pregnancy for singleton term births in the United States, 1990-2005; in 2005 around 20% of women gained >40lbs (18 kg) (94) (detail of 2009 IoM GWG guidelines given in Table 7, Chapter 1, Section 1.3.5, pg.23).

Systematic review evidence was also considered. From a systematic review of 10 studies considering GWG in women with obesity and selected maternal or new born outcomes (306), only one study provided a lower cut off for gestational weight loss (GWL) of -13.6kg (-30.0lbs) (307) and two provided an upper limit of GWG; one of 11kg (25lbs) (136) and one of 14kg (30.9lbs) (308). Only one study considered GWG above this and had an upper GWG category of ≥18.2kg (40.1lbs) (307). This study did not define the highest GWG value included (307). This systematic review only considered women with obesity, and as my project includes women with underweight who may gain more weight in pregnancy than women with obesity, it is possible that the upper limit required may be higher. In order to investigate this, evidence from women who were underweight was considered. One study found that for women who

were underweight in the very high GWG category ≥20kg (44.1lbs) mean GWG was 23.0kg (50.7lbs), and for women with obesity this was 23.7kg (52.3lbs) (135).

Using data from the BiB cohort to explore GWG distribution, the frequency distribution appeared to tail off on the right hand side above 25kg (55.1lbs) (Figure 21) which was consistent with evidence from the published literature (135) so this was used as the upper limit of GWG. The frequency distribution appeared to tail off on the left-hand side <-10kg (22.1lbs) (Figure 21) which was consistent with published literature (307) so this was used as the lower limit for GWG.

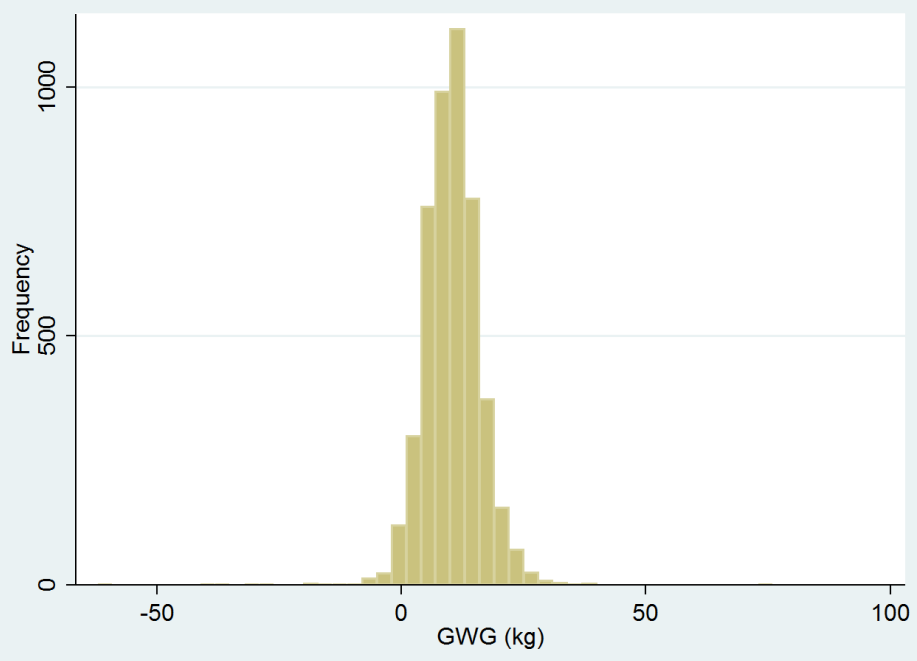


Figure 21 Histogram of all gestational weight gain

To take into account that GWG was measured at different weeks in the third trimester, analysis has also been carried out using GWG per week as a continuous variable. This was calculated by subtracting weight in the third trimester from the weight at the booking appointment, and then dividing this total by the gestational age of measurement (weeks) in the third trimester.

GWG was also categorised as low, recommended or high for each woman based on their booking BMI and using the 2009 IoM guidelines (94); as described in Table 7, Chapter 1, Section 1.3.5, pg.23.

6.3.2 Outcome variables

Details of all outcome variables that were available for the BiB cohort are given in Table 47, along with their definitions, whether they were categorical or continuous variables, and if categorical then the categories are defined.

Table 47 Outcome variables

Variable	Definition	Type	Categories
Gestational Weight Gain	Also considered as an exposure, only as an outcome when Maternal BMI an exposure	Continuous and categorical	• Low • Recommended • High
Gestational Diabetes Mellitus (GDM)	GDM was derived from the oral glucose tolerance test result and medical notes by BiB. It is defined as “Diabetes that only occurs in pregnancy, resolves during childbirth but may develop into frank diabetes in later life” (299)	Categorical	• Yes • No • Missing
Hypertensive disorders of pregnancy (HDP)	HDP was defined as “high blood pressure (hypertension) that develops due to pregnancy” (299)	Categorical	• Yes (women with mild to moderate hypertension (blood pressure record of > 140/90 on two or more occasions in the antenatal period), severe hypertension (blood pressure record of > 150/105 on two or more occasions in the antenatal period) and those who had hypertension but the severity was not classified.) • No • Missing
Child anthro-pometrics at birth	• Birth weight (g) • Child abdominal circumference at birth (cm) • Child head circumference at birth (cm) • Child mid-arm circumference at birth (cm) • Child subscapular SFT at birth (mm) • Child tricep SFT at birth (mm)	Continuous	N/A
Mode of delivery	• Caesarean section • Spontaneous delivery (reference) • Induction	Categorical	For each mode of delivery: • Yes • No • Missing

Variable	Definition	Type	Categories
Gestational age at delivery	• **Pre-term birth:** Pre-term birth has been defined as a birth occurring at <37 weeks gestation. • **Term birth (Reference):** Term birth was defined as a birth occurring ⩾37 to <42 weeks gestation. • **Post-term birth:** Post-term birth has been defined as ⩾42 weeks gestation All defined according to the 2013 ACOG committee opinion on the definition of term birth (309, 310)	Categorical	• Yes • No • Missing
Stillbirth	"The complete expulsion of a baby > 24 weeks which does not breathe, cry or show any other signs of life"(311)	Categorical	• Yes • No • Missing

ACOG= American College of Obstetricians and Gynaecologists, BiB= Born in Bradford, SFT= skinfold thickness

6.3.3 Confounding and mediating variables

Details of confounding/mediating variables[21] are given in Table 48, along with details on whether they were categorical or continuous variables, and if categorical then the categories are defined.

[21] Whether the variables are confounders of mediators will depend on the association of interest, and which variable is considered as exposure. Please note that for some outcomes, other outcome variables may also act as mediators e.g. for the association between BMI and GWG, GDM acts as a mediator.

Table 48 Confounding and mediating variables

Confounding/mediating variable	Type	Categories
Maternal age	Continuous	N/A
Gestational age at booking	Continuous	N/A
Parity	Categorical	0 (nulliparous), 1, 2, 3, ≥4
Maternal arm circumference (cm) at baseline questionnaire (26-28 weeks)	Continuous	
Maternal tricep SFT (mm) at baseline questionnaire (26-28 weeks)	Continuous	
Maternal education	Categorical	<5 GCSEs, 5 GCSEs, A Level equivalent, Higher than A level, Missing
Paternal education	Categorical	<5 GCSEs, 5 GCSEs, A Level equivalent, Higher than A level, Missing
Maternal employment	Categorical	Currently employed, Previously employed, Never employed, Missing
Paternal employment	Categorical	Employed- non-manual, Employed-manual, Self-employed, Student, Unemployed, Missing
Index of multiple deprivation	Categorical	2010 IMD quintiles were considered as a categorical variable with five categories (Note: The IMD 2010 updates the IMD 2007 and will be used in this analysis): 1 (least deprived), 2, 3, 4, 5 (most deprived)
Place of birth (generation status)	Categorical	Mother, her partner and all four of their parents UK born; Mother and her partner UK born and all four of their parents South Asian born; Mother UK born, partner and all four of their parents South Asian born; Partner UK born, mother and all four parents South Asian born; Mother, her partner and four parents all South Asian born; Missing

Confounding/mediating variable	Type	Categories
Family history of diabetes	Categorical	Yes: mother did have a history of diabetes in family no: mother did not have a history of diabetes in family Missing
Family history of high blood pressure	Categorical	Yes: mother did have a history high blood pressure in her family No: mother did not have a history high blood pressure in her family Missing
Pre-existing diabetes	Categorical	Yes: mother did have previous diabetes No: mother did not have previous diabetes Missing
Previous hypertension	Categorical	Yes: mother did have previous hypertension No: mother did previous hypertension Missing
Marital and cohabiting status	Categorical	Married and living with a partner Not married and living with a partner Not living with a partner Missing
Smoking in pregnancy	Categorical	Yes: mother smoked during pregnancy or three months before No: mother did not smoke during pregnancy or three months before Missing
Exposure to smoke in pregnancy	Categorical	Yes: mother was exposed to smoke during pregnancy No: mother was not exposed to smoke during pregnancy Missing
Alcohol consumption in pregnancy	Categorical	Yes: mother drank alcohol during pregnancy or three months before No: mother did not drink alcohol during pregnancy or three months before Missing

6.3.4 Ethical considerations

This dataset contained previously collected, fully anonymised data from the BiB and BiB 1000 cohorts. The data request was approved by the BiB executive team on the 13/12/16 and use of the BiB data for this project was covered by ethical approval from the Bradford Research Ethics committee given on the 14/08/06 (please see Appendix 13, pgs.367-370).

Ethical approval for this project was given on 5/10/15 by Newcastle University Faculty of Medical Sciences Ethics Committee (please see Appendix 14, pgs.371-372).

Chapter 7. Results from analysis of data from the Born in Bradford cohort

In this chapter, I will discuss differences between the two ethnic groups; White British and Pakistani, in terms of exposures (maternal BMI and GWG), demographic characteristics (e.g. maternal age, parity, etc.) and outcomes. Outcomes for the mother are HDP, GDM, mode of delivery (C-section and induction), breastfeeding at 6 months, and PPWR. Outcomes for the infant are outcome of birth i.e. stillbirth or livebirth, gestational age at delivery (pre-term birth <37 weeks, and post-term birth ≥42 weeks), infant anthropometrics at birth (birth weight, abdominal circumference, head circumference, mid-arm circumference, subscapular SFT and tricep SFT), and infant anthropometrics at 3 years of age (weight, abdominal circumference, subscapular SFT, tricep SFT, and thigh circumference). I will describe the associations between each outcome and exposure, first without adjusting for confounders, and then considering them using regression analysis. Following this, I will describe the association between GWG and BMI considering both confounders and mediators using SEM. Finally, I will describe the differences in missing data for BMI and GWG. This chapter addresses objectives 3-6 set out in Chapter 1, Section 1.10, pgs.34-35.

7.1 Born in Bradford population included in the analysis

There were n=11,066 women in the BiB project prior to exclusions. Following exclusions of subsequent pregnancies (n=858), and women not of either White British or Pakistani ethnicity (n=1,617; n=1,595 were of another ethnic group and n=22 had missing data on ethnicity), n=8,613 women remained. Of these women, n=4,088 were of White British ethnicity (47.46%) and n=4,525 were of Pakistani ethnicity (52.54%).

7.1.1 Ethnic differences in maternal anthropometrics

Ethnic differences in anthropometric measures are shown in Table 49.

Table 49 Ethnic differences in MA measurements

		All		White British		Pakistani		P value for ethnic difference
		n	%	n	%	n	%	
		8,613	100%	4,088	39.96	4,525	44.23	
Maternal BMI (kg/m^2)	Median (IQR)	8,076	25.10 (21.96 to 29.13)	3,815	25.43 (22.31 to 29.90)	4,261	24.78 (21.64 to 28.46)	<0.001*
Maternal BMI using WHO general population categories	Underweight (<18.5kg/m^2)	338	3.92	96	2.35	242	5.35	<0.001*
	Recommended weight (18.5 to <25.0kg/m^2) (reference[a])	3,644	42.31	1,690	41.43	1,954	43.18	0.160
	Overweight (25.0 to <30.0kg/m^2)	2,370	27.52	1,098	26.86	1,272	28.11	0.291
	Obese (≥30.0kg/m^2)	1,724	20.02	931	22.77	793	17.52	<0.001*
	Obese I (≥30.0 to <35.0 kg/m^2)	1,065	12.37	530	12.96	535	11.82	0.076
	Obese II (35 to <40.0kg/m^2)	458	5.32	270	6.60	188	4.15	<0.001*
	Obese III (≥40/m^2)	201	2.33	131	3.20	70	1.55	<0.001*
	Missing	537	6.23	273	6.68	264	5.83	0.106
Maternal BMI using Asian specific categories (43)	Underweight (<18.5kg/m^2)	338	3.92	96	2.35	242	5.35	<0.001*
	Recommended weight (18.5 to <23.0kg/m^2) (reference[a])	2,986	34.67	1,690	41.43	1,296	28.64	<0.001*
	Overweight (23.0 to <27.5kg/m^2)	2,511	29.15	1,098	26.86	1,413	31.23	<0.001*
	Obese (≥27.5kg/m^2)	2,241	26.02	931	22.77	1,310	28.95	<0.001*
	Obese I (27.5 to <32.5kg/m^2)	867	10.07	530	12.96	867	19.16	<0.001*
	Obese II (32.5 to <37.5kg/m^2)	309	3.59	270	6.60	309	6.83	0.762
	Obese III (≥37.5/m^2)	134	1.56	131	3.20	134	2.96	0.467
	Missing	537	6.23	273	6.68	264	5.83	0.106

		All		White British		Pakistani		P value for ethnic difference
		n	%	n	%	n	%	
		8,613	100%	4,088	39.96	4,525	44.23	
Maternal height (cm)	Mean (SD)	8,441	161.81 (6.35)	4,029	164.11 (6.20)	4,412	159.71 (5.73)	<0.001*
Maternal arm circumference at 26-28 week questionnaire (cm)	Mean (SD)	3,332	29.91 (4.50)	2,348	30.47 (4.57)	984	28.58 (4.02)	<0.001*
Maternal tricep skinfold thickness at 26-28 week questionnaire (mm)	Mean (SD)	3,270	25.33 (7.23)	2,320	25.72 (7.26)	950	24.36 (7.08)	<0.001*
Maternal weight at booking (weeks gestation) (kg)	Median (IQR)	8,240	65.00 (57.00 to 76.00)	3,874	68.70 (60.00 to 82.00)	4,366	63.00 (55.00 to 73.00)	<0.001*
Maternal weight at 26-28 week questionnaire (weeks gestation) (kg)	Median (IQR)	8,314	71.80 (63.30 to 82.40)	3,970	74.88 (65.50 to 87.40)	4,344	69.30 (61.28 to 78.80)	<0.001*

*Indicates statistical significance P<0.05 calculated using Pearson's chi squared for categorical data, Wicoxon Rank Sum test for skewed continuous data and t-test for normally distributed continuous data

[a] Indicates the reference groups used for p value calculation using Pearson's chi squared test; all other categories in variable are compared to this reference category. To calculate the p value for the reference categories they have been compared with all other possible outcomes in that variable except missing i.e. reference compared with non-reference in each ethnic group.

[b] The p value for the Missing category was calculated by comparing the number of missing with the number of non-missing cases in each ethnic group.

Mean maternal height was 161.51cm (SD 6.35cm). The mean height was significantly lower in Pakistani women than it was in White British women (159.71cm SD 5.73cm and 164.11cm SD 6.20cm, respectively p<0.001). Median maternal weight at booking was 65.00kg (interquartile range (IQR) 57.00kg to 76.00kg); this was significantly lower in Pakistani women (Median: 63.00kg IQR 55.00kg to 73.00kg) compared with White British women (Median: 68.70kg IQR 60.00kg to 82.00kg, p<0.001). Maternal weight was measured again at baseline (26-28 weeks gestation); the median value had increased from weight at booking to 71.80kg (IQR 63.30kg to 82.40kg), and was still significantly lower in Pakistani women (median: 69.30kg IQR 61.28kg to 78.80kg) compared with White British women (median: 74.88kg IQR 65.50kg to 87.40kg, p<0.001). In addition to maternal weight and height, two other anthropometric measures were recorded at baseline (26-28 weeks gestation): maternal MUAC and tricep SFT. The mean MUAC was 29.91cm (SD 4.50); this was significantly lower in Pakistani women compared with White British women (28.58cm SD 4.02 and 30.47cm SD 4.57, respectively p<0.001). The mean tricep SFT was 25.33mm (SD 7.23); this was also significantly lower in Pakistani women compared with White British women (mean 24.36mm SD 7.08 and 25.72mm SD 7.26 respectively p<0.001).

Ethnic differences in BMI when using the general population BMI criteria[22] for White British and Pakistani women

When using the WHO BMI categories for the general population, 42.31% of women had a recommended BMI. The percentage of women with recommended BMI was not significantly different for the two ethnic groups; 43.18% in Pakistani women and 41.43% in White British women (p=0.160). There were 3.92% of all included women who had an underweight BMI; this was significantly higher in Pakistani women (5.35%) compared with White British women (2.35%; p<0.001). Percentages of women with a BMI in the overweight range did not differ significantly by ethnicity; 27.52% for the whole population had a BMI in the overweight range, this was 28.11% in Pakistani women, and 26.86% in White British women (p=0.261). Percentages of

[22]Underweight BMI <18.5kg/m^2; recommended BMI ≥18.5 to <25kg/m^2; overweight BMI 25.0 to <30.0kg/m^2; obese BMI ≥30kg/m^2; Obese I BMI ≥30.0 to <35.0kg/m^2; Obese II BMI ≥35 to <40.0kg/m^2; obese III BMI ≥40/m^2

those with obesity differed significantly by ethnicity; 20.02% of all women had obesity; 17.52% in Pakistani women and 22.77% in White British women (p<0.001). Of those women who had a BMI in the obese range, 12.37% had class I obesity this was not significantly different between the two ethnic groups (11.82% in Pakistani women and 12.96% in White British women, p=0.076). There were 5.32% women with class II obesity; this was significantly lower for Pakistani women at 4.15% compared with White British women at 6.60% (p<0.001). Finally, 2.33% of women had class III obesity this was also significantly lower for Pakistani women at 1.55% compared with White British women at 3.20% (p<0.001).

Effect of applying Asian specific BMI criteria[23] in the Pakistani population

When applying the WHO BMI criteria for Asian populations to women of Pakistani ethnicity, there was no change to the underweight category as the cut offs are the same for both general population, and Asian specific BMI cut offs. The percentage of Pakistani women with a recommended BMI decreased from 43.18% when using general population BMI criteria to 28.64% when using BMI criteria specific to the Asian population. The percentage of Pakistani women with a BMI in the overweight range increased from 28.11% to 31.23%. The percentage of Pakistani women with a BMI in the obese range increased from 17.52% to 28.95%: class I obesity increased from 11.82% to 19.16%; class II obesity increased from 4.15% to 6.83% and class III obesity increased from 1.55% to 2.96%.

Ethnic differences in BMI when using the general population BMI criteria for White British population, and the Asian specific BMI criteria for Pakistani women

I also compared the percentages of women with a BMI in each BMI category using general population BMI criteria for White British women, and BMI criteria specific to the Asian population for Pakistani women. There were a significantly lower percentage of Pakistani women with a BMI in the recommended range compared with White British women when using the BMI criteria for Asian population (28.64% in

[23] Underweight BMI <18.5kg/m^2; Recommended weight BMI 18.5 to <23.0kg/m^2; Overweight BMI 23.0 to <27.5kg/m^2; Obese ≥27.5kg/m^2; Obese I BMI 27.5 to <32.5kg/m^2; Obese II BMI 32.5 to <37.5kg/m^2; Obese III BMI ≥37.5kg/m^2

Pakistani, 41.43% in White British; p<0.001). When using the BMI criteria for the general population, there had been no significant difference between the percentages of women with recommended BMI between the two ethnic groups (p=0.160). There was a significantly higher percentage of Pakistani women with an overweight BMI compared with White British women (31.23% in Pakistani women and 26.86% in White British women; p<0.001). When using BMI for the general population, the percentage of Pakistani women with an overweight BMI had been lower, but did not reach statistical significance (p=0.291). There was also a significantly higher percentage of Pakistani women with an obese BMI compared with White British women (28.95% in Pakistani women and 22.77% in White British women; p<0.001); when using BMI for the general population, the percentage of Pakistani women with an obese BMI had been significantly lower (p<0.001).

When considering the subgroups of obesity; there were a significantly higher percentage of Pakistani women with a BMI in the obese class I range compared with White British women (19.16% in Pakistani women and 12.96% in White British women; p<0.001). When using BMI for the general population, the percentage of Pakistani women with a BMI in the obese class I range had been lower, but this difference did not reach statistical significance (p=0.076). There were also now higher percentages of Pakistani women with class II obesity (6.83% compared to 4.15% in White British women, p=0.762) and class III obesity (2.96% compared to 1.55 in White British women, p=0.467). Although this was not statistically significantly higher for Pakistani women, when using the BMI criteria for the general population for both ethnic groups, the percentage in Pakistani women had been significantly lower for both obesity classes (p<0.001 for both).

7.1.2 Ethnic differences in gestational weight gain

Ethnic differences in GWG are shown in Table 50.

Table 50 Maternal GWG excluding missing data

		All		White British		Pakistani		P value for ethnic difference
		n	%	n	%	n	%	
Early pregnancy weight change (kg) (from booking to baseline questionnaire)	Mean (SD)	7,932	5.94 (3.61)	3,748	5.84 (3.67)	4,184	6.03 (3.56)	0.018*
GWG (kg) (from booking to weight in the third trimester)	Mean (SD)	4,330	10.00 (5.14)	1,721	10.20 (5.27)	2,609	9.87 (5.05)	0.039*
Date of weight measured in third trimester	Mean (SD)	4,472	36.01 (1.94)	1,792	36.14 (2.03)	2,680	36.04 (1.87)	0.109
GWG according to IoM categories (WHO BMI criteria for general population used to estimate GWG level (low/recommended/high) for both Ethnic groups)								
Women with underweight BMI (<18.5kg/m^2)	Low <12.5kg	131	64.22	25	53.19	106	67.52	0.074
	Recommended 12.5-18kg (reference[a])	59	28.92	16	34.04	43	27.39	0.378
	High >18kg	14	6.86	7	12.77	8	5.10	0.078
Women with recommended BMI (18.5 to <25.0kg/m^2)	Low <11.5kg	1,045	53.67	371	50.75	674	55.43	0.045*
	Recommended 11.5-16kg (reference[a])	655	33.64	267	36.53	388	31.91	0.037*
	High >16kg	247	12.69	93	12.72	154	12.66	0.970
Women with overweight BMI (25.0 to <30.0kg/m^2)	Low <7.5kg	428	34.60	147	29.70	281	37.87	0.003*
	Recommended 7.5-11.5 (reference[a])	404	32.66	153	30.91	251	33.83	0.284
	High >11.5kg	405	32.74	195	39.39	210	28.30	<0.001
Women with obese BMI (≥30/m^2)	Low <5kg	314	36.05	158	37.09	156	35.06	0.532
	Recommended 5-9kg (reference[a])	266	30.54	112	26.29	154	34.61	0.008*
	High >9kg	291	33.41	156	36.62	135	30.34	0.050
GWG categories for BMI	Low	1,787	43.44	676	40.53	1,111	45.42	0.002*
	Recommended (reference[a])	1,384	33.64	548	32.85	836	34.18	0.377
	High	943	22.92	444	26.62	499	20.40	<0.001*

		All		White British		Pakistani		P value for ethnic difference
		n	%	n	%	n	%	
GWG according to IoM categories (WHO BMI criteria for Asian population used for Pakistani women, and WHO BMI criteria for the general population used for White British women to estimate GWG level (low/recommended/high)								
Women with underweight BMI (<18.5kg/m^2)	Low <12.5kg	131	64.22	25	53.19	106	67.52	0.074
	Recommended 12.5-18kg (reference[a])	59	28.92	16	34.04	43	27.39	0.378
	High >18kg	14	6.86	7	12.77	8	5.10	0.078
Women with recommended BMI (White British: 18.5 to <25.0kg/m^2) (Pakistani: 18.5 to <23.0kg/m^2)	Low <11.5kg	778	51.39	371	50.75	407	51.98	0.633
	Recommended 11.5-16kg (reference[a])	534	35.27	267	36.53	267	34.10	0.324
	High >16kg	202	13.34	93	12.72	109	13.92	0.493
Women with overweight BMI (White British: 25.0 to <30.0kg/m^2) (Pakistani: 23.0 to <27.5kg/m^2)	Low <7.5kg	421	30.93	147	29.70	274	31.64	0.456
	Recommended 7.5-11.5kg (reference[a])	448	32.92	153	30.91	295	34.06	0.234
	High >11.5kg	492	36.15	195	39.39	297	34.30	0.060
Women with obese BMI (White British: ≥30/m^2) (Pakistani: ≥27.5kg/m^2)	Low <5kg	393	33.31	158	37.09	235	31.17	0.038*
	Recommended 5-9kg (reference[a])	367	31.10	112	26.29	255	33.82	0.007*
	High >9kg	420	35.59	156	36.62	264	35.01	0.580
GWG categories for BMI	Low	1,592	38.70	676	40.53	916	37.45	0.384
	Recommended[a]	1,408	34.22	548	32.85	860	35.16	0.363
	High	1,114	27.08	444	26.62	670	27.39	0.999

*Indicates statistical significance P<0.05 calculated using Pearson's chi squared for categorical data, Wicoxon Rank Sum test for skewed continuous data and t-test for normally distributed continuous data

[a] Indicates the reference groups used for p value calculation using parsons chi squared test; all other categories in variable are compared to this reference category. To calculate the p value for the reference categories they have been compared with all other possible outcomes in that variable except missing i.e. reference compared with non-reference in each ethnic group.

[b] The p value for the Missing category was calculated by comparing the number of missing with the number of non-missing cases in each ethnic group.

[C]GWG is weight change from booking to weight in the third trimester

GWG was calculated based on maternal weight measurements at three time points; booking (approximately 10-12 weeks gestation), baseline questionnaire (26-28 weeks gestation) and in the third trimester for a subsample of women. On average, the early GWG between booking and 26-28 weeks was 5.9kg (SD 3.61kg). Mean early weight change was significantly higher in Pakistani women 6.03kg (SD 3.56kg), compared to White British 5.84kg (SD 3.67kg) (p=0.018). Mean GWG (between booking and the third trimester) was 10.00kg (SD 5.14kg); this was significantly lower in the Pakistani women 9.87kg (SD 5.05kg) compared with White British women 10.20kg (SD 5.27kg) (p=0.039).

Due to the large proportion of missing data for GWG (52.23% in whole population; 59.20% in White British and 45.94% Pakistani women), and the effect this missing data has on the percentages in each GWG group when included in descriptive analysis, the proportions of GWG will be discussed excluding missing data to avoid confusion. A table reporting the missing data is in Appendix 15 (pgs.373-374). For more information on missing data for GWG, and how it relates to demographic variables, please see Section 7.3, pgs.277-285 in this chapter.

Comparing ethnic differences in overall gestational weight gain

Low GWG

When using the general population BMI criteria to calculate GWG using the 2009 IoM recommendations, 43.44% of women had low GWG for their BMI category. The proportion with low GWG was significantly higher in Pakistani women compared with White British women (45.42%, 40.53% respectively, p=0.002). When the Asian specific BMI cut offs were applied for Pakistani women, the proportion with low GWG for BMI fell from 45.42% to 37.45%, and the ethnic difference was no longer significant (p=0.384).

Recommended GWG

There were 33.64% of women who had recommended GWG for their BMI category. There was no significant difference in the proportion of women with recommended GWG between the two ethnic groups (32.85% in White British women and 34.18% in Pakistani women, p=0.377). When the Asian specific BMI cut offs were applied for

the Pakistani women, the proportion with recommended GWG for their BMI rose slightly from 34.18% to 35.16% and the ethnic difference remained non-significant (p=0.363).

High GWG

There were 22.92% of women who had high GWG for their BMI category. This was significantly lower in Pakistani women compared with White British women (20.40% in Pakistani women and 26.62% in White British women, p<0.001). However, when the Asian specific BMI cut offs were applied for the Pakistani women, the proportion of women with a high level of GWG for their BMI rose to from 20.42% to 27.39%; higher than that in White British women, although there was no significant difference (p=0.999).

Comparing ethnic differences in gestational weight gain specific to BMI group

Underweight

When considering only women with an underweight BMI, 64.22% of the population had low GWG (<12kg) for their BMI. This was higher in Pakistani women (67.52%) compared with White British women (53.19%), although the difference did not reach significance (p=0.074). 28.92% of the population with an underweight BMI had recommended GWG (12.5-18kg). This was lower in Pakistani women (27.39%) compared with White British women (34.04%), although the difference was not significant (p=0.378). 6.86% of women with an underweight BMI had high GWG (>18kg). This was lower in Pakistani women (5.10%) compared with White British women (12.77%), although the difference did not reach significance (p=0.078).

Recommended weight

When the general population BMI criteria were used to calculate GWG, 53.67% of women with a recommended BMI had low GWG; this was significantly higher in Pakistani women compared with White British women (55.43% and 50.75% respectively, p=0.045). However, when the Asian specific BMI criteria were applied for the Pakistani population, the difference between the two ethnic groups was no longer significant (p=0.633). Using general population BMI criteria, Pakistani women

with a recommended BMI were significantly less likely to gain weight in the recommended range compared with White women. However, the difference was no longer significant when applying the Asian BMI criteria (p=0.324). Using general population BMI criteria for recommended BMI, there was no difference between Pakistani and White British women and high GWG; the proportion of Pakistani women with high GWG increased when applying Asian BMI criteria but there was no significant difference (p=0.493).

Overweight

When the general population criteria were used to calculate GWG, 34.60% of women with an overweight BMI had low GWG. This was significantly higher in Pakistani women compared with White British women (37.87% and 29.70% respectively, p=0.003). However, when the Asian specific BMI criteria were applied for the Pakistani population, the difference between the two ethnic groups was no longer significant (p=0.456). Using the general population BMI criteria, there was no significant ethnic difference in those gaining weight in the recommended range (p=0.284). This remained true when applying the Asian specific BMI criteria (p=0.234). Using general population BMI criteria for recommended BMI, Pakistani women with an overweight BMI were significantly less likely to gain high GWG compared with White British women (p<0.001); the proportion of Pakistani women with high GWG increased when applying Asian BMI criteria but there was no significant difference (p=0.060).

Obese

When the general population criteria were used to calculate GWG and only women with a BMI in the obese range were considered, 36.05% of women with an obese BMI had low GWG. This was not significantly different between the two ethnic groups (p=0.532). However, when the Asian specific BMI criteria were applied for the Pakistani population, the percentage with low GWG fell, and there was now a significant difference between the two ethnic groups (p=0.038). When the general population criteria were used to calculate GWG, 30.54% of women with an obese BMI had recommended GWG; this was significantly higher in Pakistani women

compared with White British women (p=0.008). This remained the same when applying the Asian specific BMI criteria were applied for the Pakistani population (p=0.038). When the general population criteria were used to calculate GWG, 33.41% of women with an obese BMI had high GWG. This was lower in Pakistani women compared with White British Women, although was not significant (p=0.050). When the Asian specific BMI criteria were applied for the Pakistani population the difference between the two ethnic groups remained insignificant (p=0.580).

7.1.3 Ethnic differences in demographic characteristics at baseline questionnaire

For detailed information on demographic characteristics for the two ethnic groups, and estimated effect sizes for the difference, please see Table 51. On average, compared with White British women, Pakistani women were older, had a higher parity and booked later in pregnancy. They were also more likely to live in more deprived areas, to have never been employed, although have a higher level of education. Pakistani fathers were more likely to have a manual job, or be self-employed, and had a higher level of education. Pakistani parents were more likely to be married and living with a partner. Mothers were less likely to smoke, be exposed to smoke, or drink alcohol during pregnancy. They were also less likely to have been diagnosed hypertension prior to pregnancy. They were more likely to have had the questionnaire administered in a language other than English (Mirpuri/Punjabi/Urdu). The place of birth of the mother, father and grandparents was also considered, for the Pakistani population, it was most likely for both parents and all four grandparents to be born in South Asia.

Table 51 Demographic characteristics at baseline questionnaire (26-28 weeks)

		BiB							
		All		White British		Pakistani		Effect size for outcome in Pakistani women compared with White British women (95% CI)	**P value for ethnic difference**
		n	%	n	%	n	%		
Maternal age (years)	Mean (SD)	8,595	27.17 (5.67)	4,079	26.59 (6.09)	4,516	27.69 (5.21)	1.10 (0.86 to 1.33)	<0.001*
Parity	0 (reference[a])	3,543	41.14	2,019	49.39	1,524	33.68	1 (ref)	
	1	2,150	24.96	1,114	27.25	1,036	22.90	0.79 (0.72 to 0.88)	<0.001*
	2	1,325	15.38	476	11.64	849	18.76	1.77 (1.57 to 2.00)	<0.001*
	3	696	8.08	166	4.06	530	11.71	3.16 (2.64 to 3.78)	<0.001*
	≥4	446	5.18	104	2.54	342	7.56	3.15 (2.15 to 3.94)	<0.001*
	Missing[b]	453	5.28	209	5.11	244	5.39	1.06 (0.88 to 1.28)	0.561
Gestational age at booking[c]	Mean (SD)	7,914	12.49 (3.07)	3,759	12.26 (2.87)	4,155	12.70 (3.23)	0.45 (0.31 to 0.58)	<0.001*
IMD 2010	1 (Most deprived) (reference[a])	5,688	66.04	2,085	51.00	3,603	79.62	1 (ref)	
	2	1,521	17.66	885	21.65	636	14.06	0.42 (0.37 to 0.47)	<0.001*
	3	976	11.33	726	17.76	250	5.52	0.20 (0.17 to 0.23)	<0.001*
	4	271	3.15	247	6.04	24	0.53	0.06 (0.04 to 0.09)	<0.001*
	5 (Least deprived)	154	1.79	143	3.50	11	0.24	0.05 (0.02 to 0.08)	<0.001*
	Missing[b]	3	0.03	2	0.05	1	0.02	0.45 (0.04 to 4.98)	0.516
Father's Job	Employed, non-manual (reference[a])	3,265	37.91	1,934	47.31	1,331	29.41	1 (ref)	
	Employed, manual	2,837	32.94	1,063	26.00	1,774	39.20	2.42 (2.19 to 2.69)	<0.001*
	Self-employed	1,256	14.58	396	9.69	860	19.01	3.26 (2.75 to 3.62)	<0.001*
	Student	110	1.28	55	1.35	55	1.22	1.45 (0.99 to 2.12)	0.054
	Unemployed	664	7.71	362	8.86	302	6.67	1.21 (1.02 to 1.43)	0.025
	Missing[b]	481	5.58	278	6.80	203	4.49	0.64 (0.53 to 0.78)	<0.001*

		BiB							
		All		White British		Pakistani		Effect size for outcome in Pakistani women compared with White British women (95% CI)	P value for ethnic difference
		n	%	n	%	n	%		
Mother's Job	Currently employed (reference[a])	3,718	43.17	2,648	64.77	1,070	23.65	1 (ref)	
	Previously employed	2,461	28.57	1,087	26.59	1,374	30.36	3.13 (2.81 to 3.48)	<0.001*
	Never employed	2,422	28.12	351	8.59	2,071	45.77	14.60 (12.78 to 16.69)	<0.001*
	Missing[b]	12	0.14	2	0.05	10	0.22	4.52 (1.00 to 20.66)	0.051
Father's highest educational qualification	<5 GCSE equivalent	2,177	25.28	1,056	25.83	1,121	24.77	0.80 (0.72 to 0.89)	<0.001*
	5 GCSE equivalent (reference[a])	1,398	16.23	714	17.47	684	15.12	1 (ref)	
	A-level equivalent	894	10.38	487	11.91	407	8.99	0.79 (0.67 to 0.92)	0.003*
	Higher than A-level equivalent	1,926	22.36	613	15.00	1,313	29.02	2.02 (1.78 to 2.29)	<0.001*
	Missing[b]	2,218	25.57	1,218	29.79	1,000	22.10	0.67 (0.61 to 0.74)	<0.001*
Mother's highest educational qualification	<5 GCSE equivalent	1,948	23.03	813	19.89	1,171	25.88	0.70 (0.62 to 0.78)	<0.001*
	5 GCSE equivalent (reference[a])	2,810	32.63	1,403	34.32	1,407	31.09	1 (ref)	
	A-level equivalent	1,255	14.57	695	17.00	560	12.38	0.56 (0.48 to 0.64)	<0.001*
	Higher than A-level equivalent	1,947	22.61	777	19.01	1,170	25.86	1.05 (0.92 to 1.19)	0.494
	Missing[b]	617	7.16	400	9.78	217	4.80	0.46 (0.39 to 0.55)	<0.001*
Marital and cohabitation status	Married and living with partner (reference[a])	5,548	63.37	1,270	31.07	4,188	92.55	1 (ref)	
	Not married and living with partner	1,646	19.11	1,624	39.73	22	0.49	0.00 (0.00 to 0.01)	<0.001*
	Not living with partner	1,491	17.31	1,186	29.01	305	6.74	0.08 (0.07 to 0.09)	<0.001*
	Missing[b]	18	0.21	8	0.20	10	0.22	1.12 (0.45 to 2.86)	0.797

		BiB							
		All		White British		Pakistani		Effect size for outcome in Pakistani women compared with White British women (95% CI)	P value for ethnic difference
		n	%	n	%	n	%		
Mother drank alcohol during pregnancy	No (reference[a])	5,782	67.13	1,285	31.43	4,497	99.38	1 (ref)	
	Yes	2,811	32.64	2,796	68.40	15	0.33	0.00 (0.00 to 0.00)	<0.001*
	Missing[b]	20	0.23	7	0.17	13	0.29	1.68 (0.67 to 4.21)	0.269
Mother smoked during pregnancy	No (reference[a])	7,054	81.90	2,699	66.02	4,355	96.24	1 (ref)	
	Yes	1,545	17.94	1,386	33.90	159	3.51	0.07 (0.06 to 0.08)	<0.001*
	Missing[b]	14	0.16	3	0.07	11	0.24	3.32 (0.93 to 11.90)	0.066
Mother exposed to smoke during pregnancy	No (reference[a])	5,683	65.98	2,304	56.36	3,378	74.67	1 (ref)	
	Yes	2,881	33.45	1,769	43.27	1,112	24.57	0.43 (0.39 to 0.47)	<0.001*
	Missing[b]	49	0.57	15	0.37	34	0.75	2.05 (1.12 to 3.78)	0.020*
Diabetes prior to pregnancy (Type I or II)	No (reference[a])	8,118	94.26	3,840	93.93	4,278	94.54	1 (ref)	
	Yes	27	0.31	15	0.37	12	0.27	0.72 (0.34 to 1.54)	0.393
	Missing[b]	468	5.43	233	5.70	235	5.19	0.91 (0.75 to 1.09)	0.301
Pre-existing hypertension	No (reference[a])	8,056	93.53	3,804	93.05	4,252	93.97	1.63 (1.04 to 2.54)	0.032
	Yes	81	0.94	48	1.17	33	0.73	0.62 (0.39 to 0.96)	0.032
	Missing[b]	476	5.53	236	5.77	240	5.30	0.91 (0.76 to 1.10)	0.342
Language used to administer questionnaire	English (reference[a])	6,910	80.23	4,077	99.73	2,833	62.61	1 (ref)	
	Mirpuri/Punjabi/Urdu	1,673	19.42	2	0.05	1,671	36.93	1202.37 (300.21 to 4815.60)	<0.001*
	Missing[b]	30	0.35	9	0.22	21	0.46	2.11 (0.97 to 4.61)	0.061

		BiB						Effect size for outcome in Pakistani women compared with White British women (95% CI)	P value for ethnic difference
		All		White British		Pakistani			
		n	%	n	%	n	%		
Place of birth of mother, father and grandparents	All born in UK- White British English (reference)	4,088	49.43	4,088	100	0	-	-	-
	Both parents and all four grandparents South born in Pakistan	1,409	31.14	-	-	1,409	31.14	-	-
	Mother UK born, father and all four grandparents born in Pakistan	1,205	26.63	-	-	1,205	26.63	-	-
	Father UK born, mother and all four grandparents born in Pakistan	1,078	23.82	-	-	1,078	23.82	-	-
	Both parents UK born and all four grandparents born in Pakistan	491	10.85	-	-	491	10.85	-	-
	Missing[b]	342	7.56	-	-	342	7.56	-	-

*Indicated statistical significance p<0.05

[a] Indicates the reference groups used for univariate regression for effect size and p value calculation. All other categories in variable are compared to this reference category.

[b] The p value for the missing category was calculated by comparing the number of missing with the number of non-missing cases in each ethnic group.

[C]Gestational age at booking is measured in weeks

7.1.4 Ethnic differences in pregnancy outcomes

Ethnic differences in pregnancy outcomes are shown in Table 52 and Table 53. Nine outcomes were considered in total. Five were maternal outcomes: HDP, GDM, mode of delivery, breastfeeding, and PPWR shown in Table 52. Four were infant pregnancy outcomes: outcome of birth, gestational age at delivery, infant anthropometric measures at birth and infant anthropometrics at three years of age, shown in Table 53.

Maternal pregnancy outcomes

Unadjusted analyses identified that Pakistani women were significantly less likely to have hypertension in pregnancy or a C-section compared with White British women and significantly more likely to have GDM compared with White British women. Although the odds of induction were slightly lower in Pakistani women compared with White British women, there was no significant difference. PPWR (kg) at 3 years, and odds of breastfeeding were also significantly higher for Pakistani women (Table 52).

Infant pregnancy outcomes

Unadjusted analyses identified that Infants of Pakistani women had significantly lower odds of post-term birth >42 weeks compared with Infants of White British women and were significantly smaller for every measurement taken. On average they were lighter at birth by -220.04g compared with Infants of White British women, had significantly smaller abdominal circumferences and smaller head circumferences compared with Infants of White British women. Although Infants of Pakistani women had higher odds of being stillborn and lower odds of pre-term birth <37 weeks compared with Infants of White British women, there was no significant difference between the two ethnic groups. At 3 years of age, infant abdominal circumference, tricep SFT and thigh circumferences were significantly lower for Infants of Pakistani women compared with Infants of White British women. There were no significant ethnic differences for infant weight or subscapular SFT (although subscapular SFT was lower for Pakistani infants compared with White British infants; Table 53).

Table 52 Maternal pregnancy outcomes

		BiB							
		All		White British		Pakistani		Unadjusted odds ratio for outcome in Pakistani women compared with White British women (95% CI)	P value for ethnic difference
		n	%	n	%	n	%		
		8,613	100%	4,088	39.96	4,525	44.23		
Hyper-tension	No [a]	7,667	89.02	3,595	87.94	4,075	89.99	1 (ref)	-
	Yes	469	5.45	257	6.29	212	4.69	0.73 (0.60 to 0.88)	0.001*
	Missing [b]	477	5.54	236	5.77	241	5.33	0.92 (0.76 to 1.10)	0.365
GDM	No [a]	7,799	90.55	3,811	93.22	3,988	88.13	1 (ref)	-
	Yes	679	7.88	195	4.77	484	10.70	2.37 (2.00 to 2.81)	<0.001*
	Missing [b]	135	1.57	82	2.01	53	1.17	0.58 (0.41 to 0.82)	0.002*
Mode of delivery	Spontaneous delivery [a]	5,920	68.73	2,744	67.12	3,176	70.19	1 (ref)	-
	C-section	807	9.37	414	10.13	393	8.69	0.82 (0.71 to 0.95)	0.008*
	Induction	1,761	20.45	855	20.91	906	20.02	0.92 (0.82 to 1.02)	0.104
	Missing [b]	125	1.45	75	1.83	50	1.10	0.60 (0.42 to 0.86)	0.005*
Any breastfeeding at 6 months	No [a]	250	2.90	141	3.45	109	2.41	1 (ref)	-
	Yes	792	9.20	308	7.53	484	10.70	2.03 (1.52 to 2.71)	<0.001*
	Missing	7571	87.90	3,639	89.02	3,932	86.90	0.82 (0.73 to 0.93)	0.003
PPWR at 3 years (kg)	Mean (SD)	781	3.76 (6.98)	311	2.00 (7.60)	470	4.93 (6.28)	2.93 (1.94 to 3.91)	<0.001*

* p<0.05 indicated statistical significance of the univariate regression (linear or logistic) analysis comparing outcome in Pakistani women with White British women

[a] Indicates the reference groups used for univariate logistic regression for odds ratio, 95% CI and p value calculation. All other categories in variable are compared to this reference category, [b] Indicates the missing category is compared to all non-missing data (i.e. the odds of being missing compared with not being missing)

Table 53 Pregnancy outcomes for infant

		BiB							
		All		White British		Pakistani		Unadjusted effect size for outcome in Pakistani women compared with White British women (95% CI)	P value for ethnic difference
		n	%	n	%	n	%		
		8,613	100%	4,088	39.96	4,525	44.23		
Outcome of birth	Livebirth [a]	8,444	98.04	3,998	97.80	4,446	98.25	1 (ref)	-
	Stillbirth	49	0.57	17	0.42	32	0.71	1.69 (0.94 to 3.05)	0.080
	Missing [b]	120	1.39	73	1.79	47	1.04	0.58 (0.40 to 0.84)	0.004*
Gestational age at delivery (Weeks)	Pre term birth (<37 weeks)	566	6.57	283	6.92	283	6.25	0.89 (0.75 to 1.05)	0.165
	Term birth (37-42 weeks)[a]	7,867	91.34	3,696	90.41	4,171	92.18	1 (ref)	-
	Post-term birth (≥42 weeks)	60	0.70	36	0.88	24	0.53	0.59 (0.35 to 0.99)	0.047*
	Missing [b]	120	1.39	73	1.79	47	1.04	0.58 (0.40 to 0.84)	0.004*
Anthropometric measures at birth									
Birth weight (g)	Mean (SD)	8,492	3234.87 (559.78)	4,014	3350.90 (565.06)	4,478	3130.86 (534.06)	-220.04 (-243.42 to -196.65)	<0.001*
Infant abdominal circumference at birth (cm)	Mean (SD)	7,378	31.30 (2.59)	3,481	32.00 (2.48)	3,897	30.69 (2.53)	-1.31 (-1.42 to -1.19)	<0.001*
Infant head circumference at birth (cm)	Mean (SD)	7,762	34.28 (1.59)	3,763	34.54 (1.59)	4,089	34.04 (1.56)	-0.49 (-0.56 to -0.42)	<0.001*
Infant mid-arm circumference at birth (cm)	Mean (SD)	7,363	10.69 (1.07)	3,483	10.84 (1.07)	3,880	10.56 (1.05)	-0.29 (-0.34 to -24)	<0.001*
Infant subscapular SFT at birth (mm)	Mean (SD)	5,778	4.73 (1.09)	2,600	4.83 (1.09)	3,178	4.65 (1.09)	-0.17 (-0.23 to -0.11)	<0.001*
Infant tricep SFT (mm)	Mean (SD)	5,800	5.10 (1.09)	2,610	5.19 (1.10)	3,190	5.03 (1.06)	-1.68 (-0.22 to 0.11)	<0.001*

		BiB All		BiB White British		BiB Pakistani		Unadjusted effect size for outcome in Pakistani women compared with White British women (95% CI)	P value for ethnic difference
		n	%	n	%	n	%		
		8,613	100%	4,088	39.96	4,525	44.23		
Anthropometric measures at 3 years									
Weight (kg)	Mean (SD)	887	14.86 (2.04)	389	14.40 (1.92)	498	14.87 (2.13)	0.03 (-0.24 to 0.30)	0.825
Abdominal circumference (cm)	Mean (SD)	732	50.35 (3.75)	328	50.70 (3.47)	404	50.10 (3.93)	-0.64 (-1.18 to -0.09)	0.022*
Tricep SFT (mm)	Mean (SD)	585	10.65 (2.77)	268	11.27 (2.66)	317	10.12 (2.76)	-1.15 (-1.60 to -0.71)	<0.001*
Subscapular SFT (mm)	Mean (SD)	495	6.49 (1.94)	266	6.60 (1.90)	269	6.40 (1.97)	-0.20 (-0.55 to 0.14)	0.243
Thigh circumference (cm)	Mean (SD)	477	13.19 (4.00)	215	14.03 (3.73)	262	12.50 (4.08)	-1.53 (-2.24 to -0.82)	<0.001*
Weight (kg)	Mean (SD)	887	14.86 (2.04)	389	14.40 (1.92)	498	14.87 (2.13)	0.03 (-0.24 to 0.30)	0.825

*Indicated statistical significance p<0.05

[a] Indicates the reference groups used for univariate logistic regression for odds ratio, 95% CI and p value calculation. All other categories in variable are compared to this reference category

[b] The missing category is compared to all non-missing data (i.e. the odds of being missing compared with not being missing)

7.1.5 Exploring the association between maternal body mass index, gestational weight gain and antenatal pregnancy outcomes in Pakistani and White women

Table 54 shows results for maternal BMI as the exposure, and Table 55 shows results for early GWG as the exposure (weight at booking to weight at baseline questionnaire)

Table 54 Maternal BMI (≥18.5kg/m^2) as exposure for antenatal outcomes

Pregnancy outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted
GWG (kg)	-0.30 (-0.32 to -0.27)*	-0.26 (-0.30 to -0.22)*	-0.29 (-0.33 to -0.25)*	-0.27 (-0.32 to -0.21)*	-0.31 (-0.36 to -0.27)*	-0.24 (-0.30 to -0.19)*	0.497	0.517
GDM	1.07 (1.05 to 1.08)*	1.07 (1.05 to 1.09)*	1.05 (1.03 to 1.08)*	1.03 (1.00 to 1.07)*	1.09 (1.07 to 1.11)*	1.08 (1.06 to 1.11)*	<0.001*	0.045*
Pregnancy induced hypertension	1.10 (1.09 to 1.13)*	1.12 (1.09 to 1.14)*	1.11 (1.09 to 1.29)*	1.12 (1.09 to 1.15)*	1.09 (1.07 to 1.12)*	1.11 (1.08 to 1.15)*	0.517	0.492

*Significant association (p<0.05)

[&]Adjusted for maternal age, parity, place of birth of mother, father and their parents, gestational age at booking, smoking, family history of diabetes, previous diabetes, alcohol consumption environmental tobacco smoke, Index of Multiple Deprivation, parental education and employment (note fathers education omitted due to collinearity)

[A]P value for interaction between Ethnicity and BMI on outcome (shows whether or not there is a significant difference in Pakistani women compared with White British women in the shape of association between maternal BMI and outcome)

The number of participants in the analysis for whole cohort for each outcome, unadjusted then adjusted, respectively, were n=4,259 and n=2,471 for GWG; n=8,070 and n=4,459 for GDM and n=7,819 and n=4,451 for pregnancy induced hypertensionThe number of participants in the analysis for White British women for each outcome, unadjusted then adjusted, respectively, were n=1,699 and n=942 for GWG; n=3,812 and n=2,048 for GDM and n=3,703 and n=2,044 for pregnancy induced hypertension.

The number of participants in the analysis for Pakistani women for each outcome, unadjusted then adjusted, respectively, were n=2,560 and n=1,529 for GWG; n=4,258 and n=2,341 for GDM and n=4,116 and n=2,390 for pregnancy induced hypertension

Table 55 Early GWG as exposure for antenatal outcomes

Pregnancy outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted[&]
GDM	0.98 (0.96 to >1.00)	1.02 (0.99 to 1.06)	0.97 (0.93 to 1.01)	1.00 (0.94 to 1.06)	0.98 (0.95 to 1.01)	1.03 (0.98 to 1.07)	0.727	0.922
Pregnancy induced hypertension	1.00 (0.97 to 1.02)	1.03 (<1.00 to 1.07)	1.00 (0.96 to 1.03)	1.05 (<1.00 to 1.10)	1.00 (0.96 to 1.02)	1.02 (0.96 to 1.08)	0.829	0.965

*Significant association (p<0.05)

[&]Adjusted for maternal BMI, maternal age, parity, place of birth of mother, father and their parents, gestational age at booking, smoking, family history of diabetes, previous diabetes, alcohol consumption environmental tobacco smoke, Index of Multiple Deprivation, parental education and employment (note fathers education omitted due to collinearity)

[A]P value for interaction between Ethnicity and BMI on outcome (shows whether or not there is a significant difference in Pakistani women compared with White British women in the shape of association between early GWG and outcome)

The number of participants in the analysis for whole cohort for each outcome, unadjusted then adjusted, respectively, were n=7,926 and n=4,385 for GDM and n=7,678 and n=4,377 for pregnancy induced hypertension

The number of participants in the analysis for White British women for each outcome, unadjusted then adjusted, respectively, were n= 3,745 and n=2,019 for GDM and n= 3,637and n=2,015 for pregnancy induced hypertension.

The number of participants in the analysis for Pakistani women for each outcome, unadjusted then adjusted, respectively, were n=4,181 and n=2,356 for GDM and n=4,041 and n=2,345 for pregnancy induced hypertension

Gestational weight gain (as an outcome)

BMI

As maternal BMI increased, GWG decreased significantly for both Pakistani and White British women in both adjusted and unadjusted models. Although there was no change in the significance of the results following adjustment, there was a decrease in GWG for both ethnic groups. This was more pronounced in Pakistani women compared with White British women. Prior to adjustment, the effect size was larger for Pakistani women compared with White British women (-0.31kg (95%CI -0.36 to -0.27) and -0.29 (95%CI 0.33 to -0.25), respectively) this meant that on average, for each 1kg/m^2 increase in maternal BMI, overall GWG decreased by 0.31kg for Pakistani women, and by 0.29kg for White British women Following adjustment, this changed so that the effect size was smaller for Pakistani women compared with White British women (-0.24kg (95%CI -0.30 to -0.19) and -0.27kg (95%CI -0.32 to -0.21), respectively; Table 54). When considering the interaction between ethnicity and BMI on GWG, there was no significant difference in the shape of the association between BMI and GWG between the two ethnic groups in either the unadjusted or adjusted model (p=0.497 and p=0.517 respectively; Table 54).

Gestational diabetes mellitus

BMI

As maternal BMI increased, the odds of GDM increased significantly for both ethnic groups, and were higher for Pakistani women (Pakistani OR 1.09 (95%CI 1.07 to 1.11) and White British OR 1.05 (95%CI 1.03 to 1.08); Table 54). Following adjustment, AORs in both ethnic groups decreased slightly but remained significantly increased and there was very little change to the effect size estimates; the effect size was still greater for Pakistani women (Pakistani AOR 1.08 (95%CI 1.06 to 1.11) and White British AOR 1.03 (95%CI 1.00 to 1.07)). There was a significant interaction between maternal BMI and ethnicity on GDM in both the unadjusted and adjusted models (p<0.001 for unadjusted model, and 0.045 for adjusted model; Table 54). This means that there was a significant difference in the shape of the association between maternal BMI and GDM in Pakistani women compared with White British women. It can be observed that not only do Pakistani women have higher odds of GDM at each BMI point, but the odds of GDM also increase at a much faster rate

with increasing maternal BMI. The graph for the unadjusted regression model with ethnicity fitted as an interaction term is depicted in Figure 22, and the graph for the adjusted regression model using a lowess curve is shown in Figure 23.

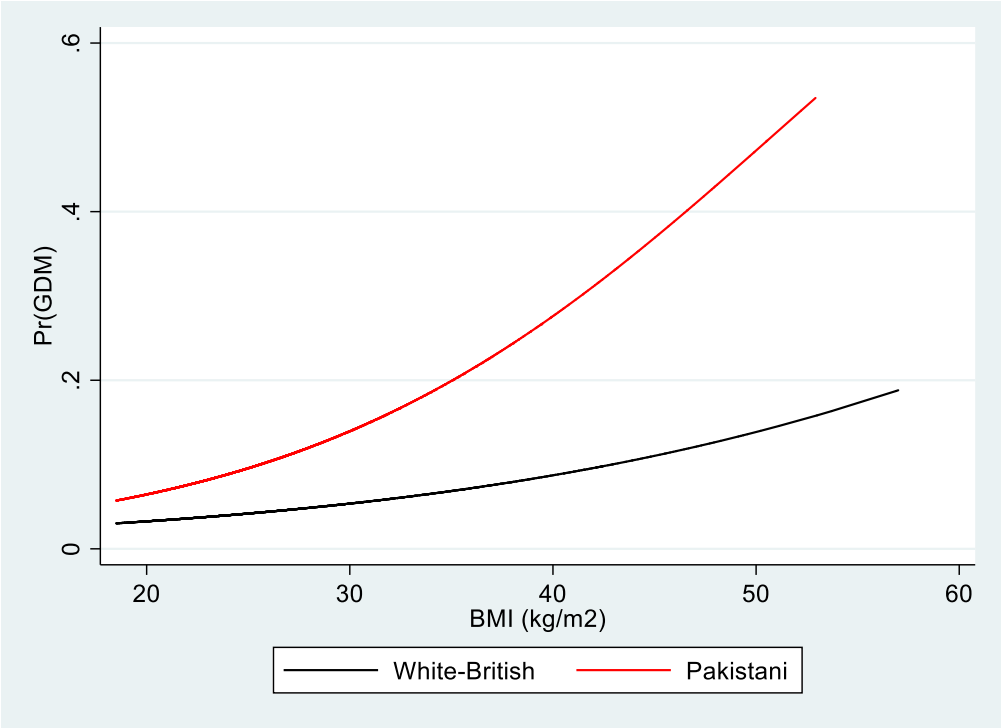


Figure 22 Graph for the unadjusted logistic regression model between BMI and GDM in pregnancy with ethnicity fitted as an interaction term
Note: Pr(GDM) gives an indication of probability of GDM; the higher Pr(GDM), the more likely the outcome of GDM is.

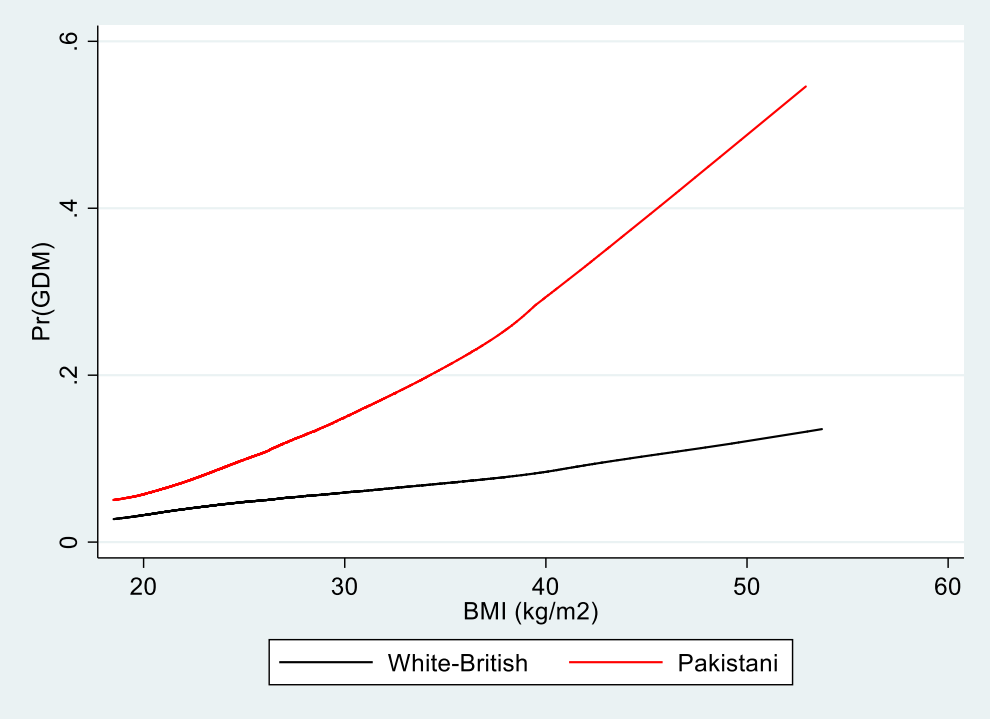


Figure 23 Two-way lowess smoother plot for the adjusted regression model between BMI and GDM with ethnicity fitted as an interaction term
Note: Pr(GDM) gives an indication of probability of GDM; the higher Pr(GDM), the more likely the outcome of GDM is.

Early GWG

Early GWG was not significantly associated with GDM in either ethnic group, and there were very little difference in effect sizes between the two groups (OR 0.98 (95%CI 0.95 to 1.01) for Pakistani women and OR 0.97 (95%CI 0.93 to 1.01)). Following adjustment, odds increased slightly for both ethnic groups but remained non-significant, and effect sizes remained similar for the two ethnic groups (AOR 1.03 (95%CI 0.98 to 1.07) for Pakistani women and AOR 1.00 (95%CI 0.94 to 1.06) for White British women). For both unadjusted and adjusted results, although not significant, the effect size was very slightly greater for Pakistani women, but the difference in odds was very small. When considering the interaction between ethnicity and early GWG on GDM, there was no significant difference between the shape of the association between GWG on GDM in the two ethnic groups in either the unadjusted or adjusted model (p=0.727 and p=0.922, respectively; Table 55).

Pregnancy induced hypertension

BMI

With an increase in maternal BMI, odds of pregnancy induced hypertension increased significantly for both ethnic groups (OR 1.09 (95%CI 1.07 to 1.12) for Pakistani women and OR 1.11 (95%CI 1.09 to 1.29) for White British women). Although these odds increased slightly following adjustment (AOR 1.11 (95%CI 1.0 to 1.15) for Pakistani women and OR 1.12 (95%CI 1.09 to 1.15) for White British women), the significance and direction of the associations remained the same. Overall, in both unadjusted and adjusted analysis, odds of pregnancy induced hypertension associated with a 1kg/m^2 increase in maternal BMI were very slightly lower for Pakistani women than White British women, but the difference in odds was very small. When considering the interaction between ethnicity and BMI on pregnancy induced hypertension, there was no significant difference between the shape of the association between BMI and pregnancy induced hypertension in the two ethnic groups in either the unadjusted or adjusted model (p=0.517 and p=0.492, respectively; Table 54).

Early GWG

Early GWG was not significantly associated with pregnancy induced hypertension in either ethnic group in either the unadjusted (OR 1.00 (95%CI 0.96 to 1.02) for Pakistani women and OR 1.00 (95%CI 0.96 to 1.03) for White British women) or adjusted models (AOR 1.02 (95%CI 0.96 to 1.08) for Pakistani women and AOR 1.05 (95%CI <1.00 to 1.10) for White British women). Overall, the effect size was slightly smaller for Pakistani women meaning that the odds of hypertensive disorders of pregnancy associated with a 1kg increase in early GWG were lower for Pakistani than for White British women. However, when considering the interaction between ethnicity and early GWG on pregnancy induced hypertension, there was no significant difference between the shape of the association between GWG on GDM in the two ethnic groups in either the unadjusted or adjusted model (p=0.829 and p=0.965, respectively; Table 55).

7.1.6 Exploring the association between maternal body mass index, gestational weight gain and pregnancy outcomes for mother and infant in Pakistani and White women: Maternal outcomes

Table 56 shows results for maternal BMI as the exposure, and Table 57 shows results for GWG as the exposure.

Table 56 Maternal BMI (≥18.5kg/m^2) as exposure for pregnancy outcomes for mother and infant in Pakistani and White women: Maternal outcomes

Pregnancy outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted
Mode of delivery								
C-section	1.09 (1.07 to 1.10)*	1.06 (1.04 to 1.09)*	1.09 (1.07 to 1.11)*	1.08 (1.05 to 1.11)*	1.08 (1.06 to 1.10)*	1.05 (1.01 to 1.08)*	0.101	0.160
Induction	1.06 (1.05 to 1.07)*	1.08 (1.06 to 1.09)*	1.07 (1.05 to 1.08)*	1.08 (1.05 to 1.10)*	1.06 (1.04 to 1.07)*	1.07 (1.05 to 1.09)*	0.336	0.453
Any breastfeeding at 6 months	0.98 (0.95 to 1.00)	0.97 (0.94 to 1.01)	0.99 (0.95 to 1.02)	0.98 (0.92 to 1.04)	0.98 (0.95 to 1.02)	0.96 (0.91 to 1.02)	0.783	0.808
Post-partum weight retention at 3 years (kg)	-0.17 (-0.27 to -0.08)*	-0.19 (-0.32 to -0.07)*	-0.07 (-0.23 to 0.08)	-0.13 (-0.34 to 0.07)	-0.21 (-0.34 to -0.09)*	-0.23 (-0.40 to -0.05)*	0.155	0.451

*Significant association ($p<0.05$)

[&]Adjusted for maternal age, parity, place of birth of mother, father and their parents, gestational age at booking, smoking, alcohol consumption, exposure to smoke, family history of diabetes, previous diabetes, and the following measures of SES: IMD quintile 2010, mother's and father's education and mothers and father's employment.

[A]P value for interaction between Ethnicity and BMI on outcome (shows whether or not there is a significant difference in Pakistani women compared with White British women in the shape of association between BMI and outcome).The number of participants in the analysis for whole cohort for each outcome, unadjusted then adjusted, respectively, were n=6,394 and n=3,501 for C-Section; n=7,311 and n=4,055 for induction; n=1,011 and n=576 for any breastfeeding at 6 months and n=774 and n=464 for post-partum weight retention

The number of participants in the analysis for White British women for each outcome, unadjusted then adjusted, respectively, were n=2,996 and n=1,575 for C-Section; n=3,425 and n= 1,853 for induction; n=431 and n=235 for any breastfeeding at 6 months and n=309 and n=173 for post-partum weight retention

The number of participants in the analysis for Pakistani women for each outcome, unadjusted then adjusted, respectively, were n=3,398 and n=1,897 for C-Section; n=3,886 and n=2,198 for induction; n=580 and n=329 for any breastfeeding at 6 months and n=465 and n=291 for post-partum weight retention

Table 57 Maternal GWG as exposure for pregnancy outcomes for mother and infant in Pakistani and White women: Maternal outcomes

Outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted
Mode of delivery								
C-section	1.00 (0.98 to 1.02)	1.05 (1.01 to 1.08)*	0.99 (0.96 to 1.03)	1.06 (1.00 to 1.12)*	1.01 (0.98 to 1.04)	1.04 (0.99 to 1.09)	0.496	0.677
Induction	1.02 (<1.00 to 1.03)	1.03 (1.01 to 1.05)*	1.00 (0.98 to 1.03)	1.04 (>1.00 to 1.08)*	1.02 (1.00 to 1.04)*	1.03 (<1.00 to 1.06)	0.186	0.925
Any breastfeeding at 6 months	0.96 (0.94 to 0.99)*	0.95 (0.91 to 0.99)*	0.97 (0.94 to 1.01)	0.96 (0.90 to 1.02)	0.96 (0.92 to 0.99)*	0.93 (0.87 to 0.99)*	0.596	0.626
Post-partum weight retention at 3 years (kg)	0.27 (0.13 to 0.40)*	0.27 (0.09 to 0.45)	0.22 (-0.07 to 0.52)	0.40 (-0.11 to 0.91)	0.30 (0.16 to 0.44)*	0.25 (0.04 to 0.46)*	0.606	0.715

*Significant association (p<0.05)

[A] P value for interaction between Ethnicity and BMI on outcome (shows whether or not there is a significant difference in Pakistani women compared with White British women in the shape of association between early GWG and outcome).

[B] Adjustments made for maternal BMI, maternal age, parity, smoking, place of birth of mother, father and their parents, alcohol consumption, exposure to tobacco smoke, marital and cohabiting status, gestational age at booking, history of diabetes, IMD, mothers education, mothers job, fathers education and fathers job

The number of participants in the analysis for whole cohort for each outcome, unadjusted then adjusted, respectively, were n=3,542 and n=1,984 for C-Section; n=3,995 and n=2,284 for induction; n=551 and n=337 for any breastfeeding at 6 months and n=430 and n=271 for post-partum weight retention

The number of participants in the analysis for White British women for each outcome, unadjusted then adjusted, respectively, were n=1,392 and n=747 for C-Section; n=1,562 and n= 859 for induction; n=185 and n=103 for any breastfeeding at 6 months and n=131 and n=78 for post-partum weight retention

The number of participants in the analysis for Pakistani women for each outcome, unadjusted then adjusted, respectively, were n=2,132 and n=1,183 for C-Section; n=2,433 and n=1,418 for induction; n=366 and n=220 for any breastfeeding at 6 months and n=299 and n=193 for post-partum weight retention

Mode of delivery

C-section

BMI

In the unadjusted models, odds of C-section increased significantly with increasing BMI for both ethnic groups. The increase was smaller in Pakistani women compared with White British women (OR 1.08 (95%CI 1.06 to 1.10) for Pakistani women and OR 1.09 (95%CI 1.07 to 1.11) for White British women; Table 56). Following adjustment, the odds decreased for both ethnic groups although the direction and significance of the association remained the same; Pakistani women still had lower odds C-section compared with White British women (AOR 1.05 (95%CI 1.01 to 1.08) for Pakistani women and AOR 1.08 (95%CI 1.05 to 1.11) for White British women). When considering the interaction between ethnicity and BMI on C-section, there was no significant difference between the shape of the association between BMI and C-section in the two ethnic groups in either the unadjusted model or adjusted model (p=0.549 and 0.160; Table 56).

GWG

GWG was not associated with C-section in unadjusted models for either ethnic group but the estimated effect sizes were slightly higher for Pakistani women compared with White British women (OR 1.01 (95%CI 0.98 to 1.14) for Pakistani women and OR 0.99 (95%CI 0.98 to 1.03) for White British women; Table 57).Following adjustment, AORs increased for both ethnic groups but were now lower for Pakistani women compared with White British women (AOR 1.04 (95%CI 0.99 to 1.09) for Pakistani women and AOR 1.06 (95%CI 1.00 to 1.12) for White British women). When considering the interaction between ethnicity and GWG on C-section, there was no significant difference between the shape of the association between GWG on C-section in the two ethnic groups in either the unadjusted or adjusted model (p=0.496 and p=0.677, respectively; Table 57).

Induction

BMI

In the unadjusted models, odds of induction increased significantly with increasing BMI for both ethnic groups in both unadjusted (OR 1.06 (95%CI 1.04 to 1.07) for Pakistani women and OR 1.07 (95%CI 1.05 to 1.08) for White British women; Table 56) and adjusted models (AOR 1.05 (95%CI 1.01 to 1.08) for Pakistani women and AOR 1.08 (95%CI 1.05 to 1.10) for White British women; Table 56), the increase in odds of induction associated with a 1kg/m^2 increase in maternal BMI was smaller in Pakistani women compared with White British women. When considering the interaction between ethnicity and BMI on induction, there was no significant difference between the shape of the association between BMI and induction in the two ethnic groups in either the unadjusted or adjusted model (p=0.336 and p=0.435, respectively; Table 56).

GWG

Odds of induction associated with a 1kg increase in GWG were higher for Pakistani women compared with White British women in unadjusted models (OR 1.02 (95%CI 1.00 to 1.04) for Pakistani women and OR 1.00 (95%CI 0.98 to 1.03) for White British women; Table 57). . Following adjustment, although ORs increased for both ethnic groups, Pakistani women now had lower odds of induction associated with a 1kg increase in GWG compared with White British women (AOR 1.03 (95%CI <1.00 to 1.06) for Pakistani women and AOR 1.04 (95%CI <1.00 to 1.08) for White British women; Table 57). When considering the interaction between ethnicity and GWG on induction, there was no significant difference between the shape of the association between GWG on induction in the two ethnic groups in either the unadjusted or adjusted model (p=0.186 and p=0.925, respectively; Table 57).

Breastfeeding at 6 months

BMI

There was a general trend of decreased odds of breastfeeding at 6 months with increasing maternal BMI. However, this was not significant for either ethnic group either prior to, or following adjustment. Unadjusted odds of breastfeeding at 6 months

were not significantly associated with a 1kg/m^2 increase in maternal BMI for either ethnic group (OR 0.98 (95%CI 0.98 to 1.02) for Pakistani women and OR 0.99 (95%CI 0.95 to 1.02) for White British women; Table 56). Following adjustment for confounders, odds decreased slightly for both ethnic groups but the results remained insignificant (AOR 0.96 (95%CI 0.91 to 1.02) for Pakistani women and OR 0.98 (95%CI 0.92 to 1.04) for White British women; Table 56). When considering the interaction between ethnicity and BMI on breastfeeding at 6 months, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.783 and p=0.808, respectively; Table 56).

GWG

There was a general trend of decreased odds of breastfeeding at 6 months with increasing maternal GWG for both ethnic groups. However, the effect was more pronounced for Pakistani women. Breastfeeding at 6 months was significantly negatively associated with GWG for Pakistani women in both unadjusted and adjusted models (OR 0.96 (95%CI 0.92 to 0.99) and AOR 0.93 (95%CI 0.87 to 0.99); Table 57, while the direction of the effect was the same for White British women, there was no significant association (OR 0.97 (95%CI 0.94 to 1.01) and AOR 0.96 (95%CI 0.90 to 1.02); Table 57). When considering the interaction between ethnicity and GWG on breastfeeding at 6 months, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.596 and p=0.626, respectively; Table 57).

Post-partum weight retention at 3 years

BMI

For both ethnic groups, increasing maternal BMI was associated with lower PPWR, although the estimated effect size was larger (i.e. lower PPWR), and only reaches significance for Pakistani women. In unadjusted analysis, PPWR at 3 years was significantly negatively associated with increasing maternal BMI for Pakistani women but not White British women (-0.21kg (95%CI -0.34 to -0.09) for Pakistani women and -0.07kg (95%CI -0.23 to 0.08) for White British women; Table 56). Following

adjustment, although effect sizes increased, this remained true (i.e. lower PPWR associated with increasing maternal BMI than in unadjusted analysis; -0.23kg (95%CI -0.40 to -0.05) for Pakistani women and -0.13kg (95%CI -0.34 to 0.07) for White British women; Table 56). When considering the interaction between ethnicity and BMI on PPWR at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.155 and p=0.051, respectively; Table 56).

GWG

For both ethnic groups, estimated effect sizes showed that there was a general trend of increasing PPWR with increasing GWG. In unadjusted analysis, the positive association between PPWR at 3 years and GWG reached significance for Pakistani women but not for White British women (0.30kg (95%CI 0.16 to 0.44) for Pakistani women and 0.22kg (95%CI -0.07 to 0.52) for White British women; Table 57). Following adjustment, the strength of the association[24] decreased for Pakistani women and there was now less PPWR associated with a 1kg increase in GWG, but it remained significant (0.25kg (95%CI 0.04 to 0.46); Table 57). In white British women, the strength increased (i.e. there was now more PPWR associated with a 1kg increase in GWG) but still did not reach significance (0.40kg (95%CI -0.11 to 0.92); Table 57). When considering the interaction between ethnicity and GWG on PPWR at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.606 and p=0.715, respectively; Table 57).

[24] The strength of the association refers to the effect size, giving an indication of the magnitude of the association, i.e. the larger the effect size the stronger the association between outcome and exposure. An increased strength implies that there is a larger increase or decrease in outcome with increasing exposure. Please note that the strength of the association does not refer to direction of effect.

7.1.7 Exploring the association between maternal body mass index, gestational weight gain and pregnancy outcomes for mother and infant in Pakistani and White women: Infant outcomes

Results for maternal BMI as exposure are shown in Table 58 and results for GWG as an exposure are shown in Table 59.

Table 58 Maternal BMI (≥18.5kg/m^2) as exposure for pregnancy outcomes for mother and infant in Pakistani and White women: infant outcomes

Outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted[&] coefficient or odds ratio (95%CI)	Un-adjusted	Ad-justed
Stillbirth^	1.00 (0.95 to 1.06)	1.00 (0.92 to 1.09)	1.02 (0.94 to 1.10)	1.04 (0.89 to 1.22)	1.00 (0.93 to 1.07)	0.94 (0.83 to 1.07)	0.754	0.193
Gestational age at delivery^								
Pre-term (<37 weeks gestation)	1.00 (0.98 to 1.01)	1.01 (0.98 to 1.03)	0.98 (0.96 to 1.01)	0.99 (0.96 to 1.02)	1.01 (0.99 to 1.04)	1.03 (1.00 to 1.08)*	0.061	0.049*
Post-term (≥42 weeks gestation)	1.02 (0.97 to 1.07)	1.02 (0.96 to 1.09)	1.03 (0.97 to1.08)	1.04 (0.96 to 1.12)	0.99 (0.91 to 1.08)	1.00 (0.88 to 1.14)	0.509	0.891
Infant anthropometrics at birth								
Birth weight (g^)	17.59 (15.39 to 19.79)*	15.43 (12.37 to 18.49)*	16.00 (12.92 to 18.98)*	16.67 (12.46 to 20.87)*	16.46 (13.33 to 19.58)*	13.77 (9.24 to 18.30)*	0.820	0.693
Infant abdominal circumference at birth (cm)^	0.06 (0.05 to 0.07)*	0.04 (0.02 to 0.05)*	0.05 (0.03 to 0.06)*	0.05 (0.03 to 0.07)*	0.04 (0.03 to 0.06)*	0.02 (-0.01 to 0.04)	0.650	0.188
Infant head circumference at birth (cm)^	0.04 (0.03 to 0.05)*	0.03 (0.02 to 0.04)*	0.04 (0.03 to 0.05)*	0.04 (0.03 to 0.05)*	0.03 (0.02 to 0.04)*	0.03 (0.01 to 0.04)*	0.257	0.444
Infant mid-arm circumference at birth (cm)^	0.03 (0.02 to 0.03)*	0.02 (0.02 to 0.03)*	0.02 (0.02 to 0.03)*	0.03 (0.02 to 0.03)*	0.02 (0.02 to 0.03)*	0.02 (0.01 to 0.03)*	0.643	0.614
Infant subscapular SFT at birth (mm)^	0.03 (0.03 to 0.04)*	0.03 (0.02 to 0.03)*	0.03 (0.02 to 0.03)*	0.03 (0.02 to 0.04)*	0.04 (0.03 to 0.05)*	0.03 (0.01 to 0.04)*	0.070	0.712
Infant tricep SFT at birth (mm)^	0.03 (0.03 to 0.04)*	0.02 (0.02 to 0.03)*	0.02 (0.02 to 0.03)*	0.03 (0.01 to 0.04)*	0.03 (0.03 to 0.04)*	0.03 (0.01 to 0.04)*	0.137	0.363

Outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Un-adjusted	Ad-justed
Anthropometric measures of infant at 3 years								
Weight (kg)	0.06 (0.03 to 0.09)*	0.08 (0.04 to 0.11)*	0.06 (0.02 to 0.10)*	0.09 (0.04 to 0.14)*	0.06 (0.02 to 0.10)*	0.08 (0.03 to 0.13)*	0.970	0.549
Abdominal circumference (cm)	0.10 (0.04 to 0.15)*	0.14 (0.07 to 0.21)*	0.09 (0.03 to 0.16)*	0.12 (0.02 to 0.22)*	0.09 (0.01 to 0.17)*	0.16 (0.06 to 0.27)*	0.900	0.878
Tricep SFT (mm)	0.04 (0.01 to 0.09)*	0.05 (-0.01 to 0.11)	0.02 (-0.04 to 0.08)	0.02 (-0.07 to 0.12)	0.05 (-0.02 to 0.11)	0.07 (-0.01 to 0.15)	0.493	0.629
Subscapular SFT (mm)	0.02 (-0.01 to 0.05)	0.02 (-0.03 to 0.06)	0.01 (-0.04 to 0.05)	-0.01 (-0.07 to 0.06)	0.04 (-0.01 to 0.09)	0.03 (-0.04 to 0.10)	0.259	0.648
Thigh circumference (cm)	0.12 (0.05 to 0.19)*	0.09 (0.01 to 0.17)*	0.02 (-0.07 to 0.12)	-0.01 (-0.11 to 0.09)	0.20 (0.09 to 0.30)*	0.19 (0.06 to 0.33)*	0.010*	0.031*

*Significant association (p<0.05); [&]Adjusted for maternal age, parity, place of birth of mother, father and their parents, gestational age at booking, smoking, alcohol consumption, exposure to smoke, family history of diabetes, previous diabetes, and the following measures of SES: IMD quintile 2010, mother's and father's education and mothers and father's employment.; [A]P value for interaction between Ethnicity and BMI on outcome (shows whether there is a significant difference in Pakistani women compared with White British women in the shape of association between BMI and outcome). ^Insufficient numbers to run adjusted models

The number of participants in the analysis for whole cohort for each outcome, unadjusted then adjusted, respectively, were n=8,076 and n=2,945 for stillbirth; n= 8,021 and n=4,428 for pre-term birth; n=7,547 and n=4,179 for post-term birth; n=8,075 and n=4,458 for birth weight; n=7,048 and n=1,487 for abdominal circumference at birth; n=7,412 and n=4,125 for head circumference at birth; n=7,033 and n=3,915 for mid upper arm circumference at birth; n=5,541 and n=3,093 subscapular skinfold thickness at birth; n=5,563 and n=3,110 for tricep skinfold thickness at birth; n=851 and n=500 for weight at 3 years; n=700 and n=420 for abdominal circumference at 3 years; n=474 and n=284 subscapular skinfold thickness at 3 years and n=457; n=273 for tricep skinfold thickness at 3 years and n=457 and n=273 for thigh circumference at 3 years.

The number of participants in the analysis for White British women for each outcome, unadjusted then adjusted, respectively, were n=3,815 and n=657 for stillbirth; n=3,781 and n=2,029 for pre-term birth; n=3,556 and n=1,432 for post-term birth; n=3,814 and n=2,047 for birth weight; n=3,320 and n=1,038 abdominal circumference at birth; n=3,501 and n=1,892 infant head circumference at birth; n=3,322 and n=1,809 for mid upper arm circumference at birth; n=2,484 and n=1,343 subscapular skinfold thickness at birth; n=2,494 and n=1,351 for tricep skinfold thickness at birth; n=369 and n=203 for weight at 3 years; n=312 and n=176 for abdominal circumference at 3 years; n=255 and n=146 for tricep skinfold thickness at 3 years; n=215 and n=125 subscapular skinfold thickness at 3 years and n=204 and n=116 for thigh circumference at 3 years.

The number of participants in the analysis for Pakistani women for each outcome, unadjusted then adjusted, respectively, were n=4,261 and n=1,486 for stillbirth; n=4,240 and n=2,382 for pre-term birth; n=3,991 and n=1,785 for post-term birth; n=4,261 and n=2,411 for birth weight; n=829 and n=449 abdominal circumference at birth; n=3,911 and n=2,233 infant head circumference at birth; n=3,711 and n=2,104 for mid upper arm circumference at birth; n=3,057 and n=1,750 subscapular skinfold thickness at birth; n=3,069 and n=1,759 for tricep skinfold thickness at birth; n=482 and n=297 for weight at 3 years; n=388 and n=244 for abdominal circumference at 3 years; and n=304 and n=189 for tricep skinfold thickness at 3 years ; n=225 and n=159 subscapular skinfold thickness at 3 years and n=253 and n=157 for thigh circumference at 3 years.

Table 59 Maternal GWG as exposure for pregnancy outcomes for mother and infant in Pakistani and White women: infant outcomes

Outcome	Whole cohort		White British		Pakistani		[A]P value for interaction	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted
Stillbirth^	1.00 (0.91 to 1.10)	1.04 (0.87 to 1.24)	0.99 (0.80 to 1.23)	-	1.00 (0.90 to 1.12)	-	0.932	-
Gestational age at delivery								
Pre-term (<37 weeks gestation)	0.95 (0.91 to 0.98)*	0.93 (0.87 to 0.99)*	0.93 (0.87 to 0.99)*	0.87 (0.75 to 1.00)	0.96 (0.91 to 1.01)	0.94 (0.87 to 1.02)	0.415	0.469
Post-term (≥42 weeks gestation	0.98 (0.92 to 1.04)	1.00 (0.90 to 1.10)	1.01 (0.93 to 1.09)	1.09 (0.92 to 1.30)	0.94 (0.86 to 1.02)	0.95 (0.82 to 1.10)	0.244	0.138
Infant anthropometrics at birth								
Birth weight (g)	13.54 (10.76 to 16.32)*	23.47 (19.70 to 27.23)*	15.10 (10.85 to 19.36)*	24.14 (18.67 to 30.21)*	11.24 (7.74 to 14.74)*	22.92 (18.07 to 27.78)*	0.167	0.554
Infant abdominal circumference at birth (cm)	0.03 (0.01 to 0.04)*	0.06 (0.03 to 0.08)*	0.02 (0.01 to 0.05)*	0.06 (0.03 to 0.09)*	0.02 (<0.00 to 0.04)	0.06 (0.03 to 0.08)*	0.560	0.911
Infant head circumference at birth (cm)	0.03 (0.02 to 0.04)*	0.05 (0.03 to 0.06)*	0.03 (0.02 to 0.04)*	0.05 (0.03 to 0.07)*	0.03 (0.02 to 0.04)*	0.05 (0.03 to 0.06)*	0.662	0.872
Infant mid- arm circumference at birth (cm)	0.02 (0.01 to 0.02)*	0.04 (0.03 to 0.04)*	0.02 (0.01 to 0.03)*	0.04 (0.02 to 0.05)*	0.01 (0.01 to 0.02)*	0.03 (0.02 to 0.05)*	0.790	0.815
Infant subscapular SFT at birth (mm)	0.02 (0.01 to 0.02)*	0.03 (0.02 to 0.04)*	0.02 (0.01 to 0.03)*	0.03 (0.02 to 0.05)*	0.01 (0.01 to 0.02)*	0.03 (0.01 to 0.04)*	0.127	0.310
Infant tricep SFT at birth (mm)	0.02 (0.01 to 0.02)*	0.03 (0.02 to 0.04)*	0.03 (0.01 to 0.04)*	0.04 (0.02 to 0.06)*	0.01 (<-0.00 to 0.02)	0.03 (0.02 to 0.04)*	0.028*	0.116

Outcome	Whole cohort		White British		Pakistani		[A]P value for interaction	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted
Anthropometric measures of infant at 3 years								
Weight (kg)	0.03 (-0.01 to 0.07)	0.06 (0.01 to 0.11)*	-0.01 (-0.06 to 0.05)	0.01 (-0.08 to 0.12)	0.05 (-0.00 to 0.10)	0.06 (>0.00 to 0.13) (p=0.050)	0.185	0.809
Abdominal circumference (cm)	0.02 (-0.05 to 0.10)	0.06 (-0.05 to 0.16)	-0.03 (-0.15 to 0.09)	0.08 (-0.12 to 0.29)	0.04 (-0.05 to 0.15)	0.07 (-0.08 to 0.21)	0.359	0.387
Tricep SFT (mm)	0.03 (-0.03 to 0.10)	0.06 (-0.03 to 0.15)	0.02 (-0.10 to 0.13)	0.04 (-0.26 to 0.34)	0.04 (-0.04 to 0.12)	0.09 (-0.01 to 0.18)	0.708	0.831
Subscapular SFT (mm)	0.02 (-0.03 to 0.06)	0.05 (-0.02 to 0.12)	0.01 (-0.06 to 0.08)	0.06 (-0.17 to 0.28)	0.02 (-0.04 to 0.08)	0.05 (-0.04 to 0.14)	0.854	0.894
Thigh circumference (cm)	-0.04 (-0.13 to 0.05)	0.04 (-0.10 to 0.18)	0.01 (-0.13 to 0.16)	0.12 (-0.16 to 0.40)	-0.08 (-0.20 to 0.05)	0.04 (-0.15 to 0.24)	0.369	0.113

[A]P value for interaction between Ethnicity and GWG on outcome (shows whether there is a significant difference in Pakistani women compared with White British women in the shape of association between GWG and outcome).

Adjustments made for maternal BMI, age, parity, smoking, generation, alcohol consumption, exposure to tobacco smoke, marital and cohabiting status, gestational age at booking, history of diabetes, mothers education, mothers job, fathers education and fathers job

*significant p<0.05; ^Insufficient numbers to run adjusted models

The number of participants in the analysis for whole cohort for each outcome, unadjusted then adjusted, respectively, were n=4,330 and n=569 for stillbirth; n=4,289 and n=2,314 for pre-term birth; n=4,238 and n=1,733 for post-term birth; n=4,330 and n=2,471 for birth weight; n=3,837and n=2,207 for abdominal circumference at birth; n=4,002 and n=2,301 for head circumference at birth; n=3,833 and n=2,205 for mid upper arm circumference at birth; n=3,084 and n=1,784 subscapular skinfold thickness at birth; n=3,092 and n=1,790 for tricep skinfold thickness at birth; n=460 and n=284 for weight at 3 years; n=380 and n=238 for abdominal circumference at 3 years; n=255 and n=157 subscapular skinfold thickness at 3 years and n=299; n=186 for tricep skinfold thickness at 3 years and n=247 and n=156 for thigh circumference at 3 years.

The number of participants in the analysis for White British women for each outcome, unadjusted then adjusted, respectively, were n=1,721 (numbers insufficient for adjusted analysis) for stillbirth; n=1,700 and n=784 for pre-term birth; n=1,690 and n=260 for post-term birth; n=1,721 and n=942 for birth weight; n=1,513 and n=839 abdominal circumference at birth; n=1,586 and n=872 infant head circumference at birth; n=1,518 and n=843 for mid upper arm circumference at birth; n=1,137 and n=637 subscapular skinfold thickness at birth; n=1,141 and n=640 for tricep skinfold thickness at birth; n=154 and n=91 for weight at 3 years; n=129 and n=76 for abdominal circumference at 3 years; n=108 and n=62 for tricep skinfold thickness at 3 years; n=91 and n=54 subscapular skinfold thickness at 3 years and n=84 and n=52 for thigh circumference at 3 years.

The number of participants in the analysis for Pakistani women for each outcome, unadjusted then adjusted, respectively, were n=569 (numbers insufficient for adjusted analysis) for stillbirth n=2,589 and n=1,266 for pre-term birth; n=2,548 and n=1,183 for post-term birth; n=2,609 and n=1,529 for birth weight; n=2,324and n=1,368 abdominal circumference at birth; n=2,416 and n=1,429 infant head circumference at birth; n=2,315 and n=1,362 for mid upper arm circumference at birth; n=1,947 and n=1,147 subscapular skinfold thickness at birth; n=1,951 and n=1,150 for tricep skinfold thickness at birth; n=306 and n=193for weight at 3 years; n=251 and n=162 for abdominal circumference at 3 years; and n=199 and n=124 for tricep skinfold thickness at 3 years; n=164 and n=103 subscapular skinfold thickness at 3 years and n=163 and n=104 for thigh circumference at 3 years

Stillbirth

BMI

There was no significant association between maternal BMI and stillbirth in either ethnic group, although the odds were lower for Pakistani women compared with White British women in both unadjusted (OR 1.00 (95%CI 0.93 to 1.07) and OR 1.02 (95%CI 0.96 to 1.10), respectively) and adjusted models (AOR 0.94 (95%CI 0.83 to 1.07) and AOR 1.04 (95%CI 0.89 to 1.22), respectively). When considering the interaction between ethnicity and BMI on stillbirth, there was no significant difference between the shape of the association between BMI and stillbirth in the two ethnic groups in either the unadjusted or adjusted model (p=0.754 and p=0.193 respectively; Table 58).

GWG

There were only sufficient numbers to run unadjusted analysis for GWG as an exposure for stillbirth in the two ethnic groups. Results showed no significant association between GWG and stillbirth in either ethnic group, although the effect size was slightly higher for Pakistani women, the upper limit of the 95%CI was higher for White British women (OR 1.00 (95%CI 0.87 to 1.02) and OR 0.98 (95%CI 0.96 to 1.01), respectively). When considering the interaction between ethnicity and GWG on stillbirth there was no significant difference between the shape of the association between GWG on stillbirth in the two ethnic groups (p=0.932; Table 59). These results should be interpreted with caution due to the small sample size for this analysis.

Gestational age at delivery

Pre-term birth (<37 weeks)

BMI

In the unadjusted models, odds of pre-term birth (<37 weeks) were not significantly associated with BMI in either ethnic group, although the odds were higher for Pakistani women compared with White British women (OR 1.01 (95%CI 0.99 to 1.04) and OR 0.98 (95%CI 0.96 to 1.01), respectively). Following adjustment, the direction of the association remained the same in each ethnic group, and although odds

increased slightly, the association only reached significance for infants of Pakistani women (AOR 1.03 (95%CI 1.00 to 1.08) and AOR 0.99 (95%CI 0.96 to 1.02), respectively). There was no significance ethnic difference in the shape of the association between BMI and pre-term birth for the unadjusted model (p=0.061; Table 58). However, considering the interaction between ethnicity and BMI on induction, there was a significant difference in the shape of the association between BMI and induction in the two ethnic groups in the adjusted model with odds of pre-term birth increasing for infants born to Pakistani women, and decreasing with increasing BMI in infants born to White British women (p=0.049; Table 58). The graph for the adjusted regression model with ethnicity fitted as an interaction term is depicted in Figure 24. For Pakistani women, as BMI increases the adjusted odds of pre-term birth increase, while for White British women adjusted odds of pre-term birth appear to decrease with increasing BMI.

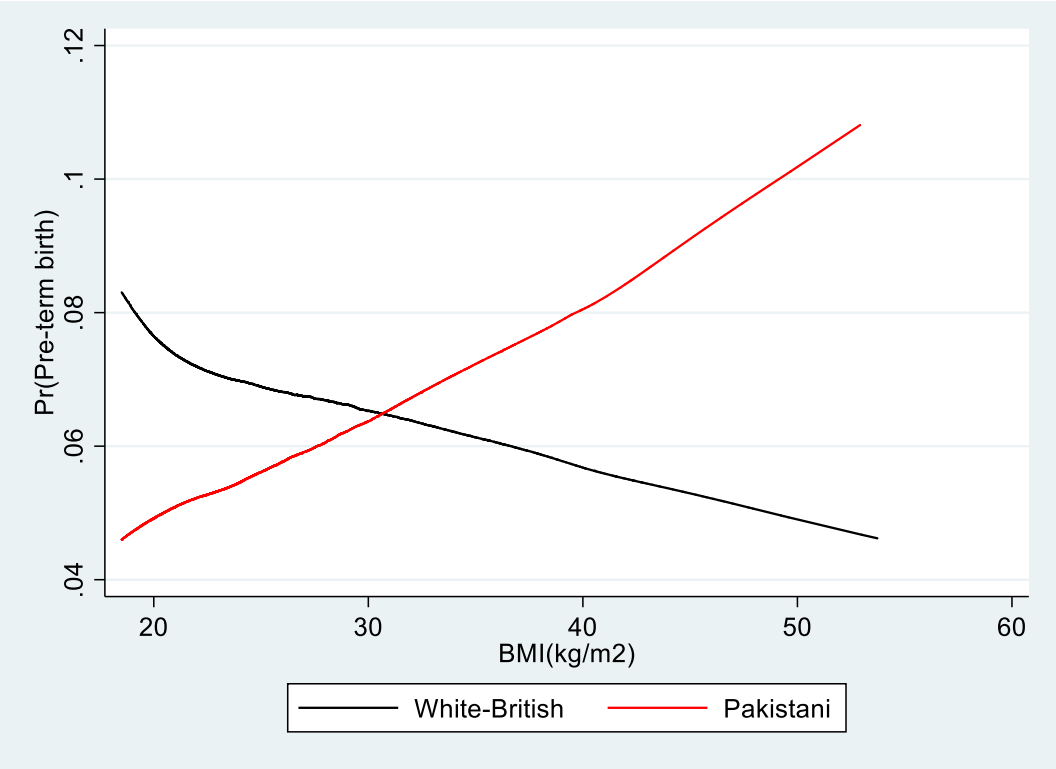


Figure 24 Two-way lowess smoother plot for the adjusted regression model between pre-term birth (<37 weeks) and BMI with ethnicity fitted as an interaction term
Note: Pr(Pre-term birth) gives an indication of probability of pre-term birth; the higher Pr(Pre-term birth), the more likely the outcome of pre-term birth is.

GWG

GWG was negatively associated with the odds of pre-term birth in unadjusted models for both ethnic groups; odds were slightly higher for infants born to Pakistani women compared with infants born to White British women (for whom odds of pre-term birth were significantly decreased with increasing GWG; OR 0.96 (95% 0.91 to 1.01) for infants born to Pakistani women and OR 0.93 (95%CI 0.87 to 0.99) for infants born to White British women).. Following adjustment, odds of pre-term birth decreased for both ethnic groups, remaining slightly higher for infants born to Pakistani women compared with infants born to White British women (AOR 0.94 (95%CI 0.87 to 1.02) for infants born to Pakistani women and AOR 0.87 (95%CI 0.75 to 1.00) for infants born to White British women) . When considering the interaction between ethnicity and GWG on pre-term birth, there was no significant difference between the shape of the association between GWG on pre-term birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.415 and p=0.469, respectively; Table 59).

Post-term birth (>42 weeks gestation)

BMI

Unadjusted odds of post-term birth (>42 weeks) were not significant for either ethnic group with a 1kg/m^2 increase in maternal BMI. However, odds were lower for infants of Pakistani women compared with infants of White British women (OR 0.99 (95%CI 0.91 to 1.08) for infants born to Pakistani women and OR 1.03 (95%CI 0.97 to 1.08) for infants born to White British women). Following adjustment, odds increased slightly but the results for both ethnic groups remained insignificant, staying lower for infants born to Pakistani women compared with infants born to White British women (AOR 1.00 (95%CI 0.88 to 1.14) and AOR 1.04 (95%CI 0.96 to 1.12); respectively). When considering the interaction between ethnicity and BMI on post-term birth, there was no significant difference between the shape of the association between BMI and post-term birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.509 and p=0.891, respectively; Table 58).

GWG

GWG was not significantly associated with post-term birth in either ethnic group. Despite this, odds were lower in infants of Pakistani women compared with infants of White British women (OR 0.94 (95%CI 0.86 to 1.02) and OR 1.01 (95%CI 0.93 to 1.09); respectively). Following adjustment, odds increased for both ethnic groups, but remained lower in infants of Pakistani women compared with infants of White British women (AOR 0.95 (0.82 to 1.10) and AOR 1.09 (0.92 to 1.30), respectively). When considering the interaction between ethnicity and GWG on post-term birth, there was no significant difference between the shape of the association between GWG on post-term birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.244 and p=0.138, respectively; Table 59).

Infant anthropometrics at birth

Birth weight

BMI

Birth weight significantly increased with increasing BMI in both ethnic groups. In the unadjusted models, infants of Pakistani women a higher increase in birthweight associated with a 1kg/m^2 increase in maternal BMI compared with infants of White British women (16.46g (95%CI 13.33 to 19.58) and 16.00g (95%CI 12.92 to 18.98), respectively). Following adjustment, although the association was still significant, the association reduced for infants of Pakistani women, whereas the effect size estimate increased slightly for infants of White British women so that the overall effect was smaller for infants of Pakistani women compared with infants of White British women (13.77g (95%CI 9.24 to 18.30) and 16.67g (95%CI 12.46 to 20.87), respectively). When considering the interaction between ethnicity and BMI on birth weight, there was no significant difference between the shape of the association between BMI and birth weight in the two ethnic groups in either the unadjusted or adjusted models (P=0.820 and p=0.693, respectively; Table 58).

GWG

GWG was significantly positively associated with birth weight in both ethnic groups. Infants of Pakistani women had lower birth weight associated with a 1kg increase in GWG compared with infants of White British women (11.24g (95%CI 7.74 to 14.74)

and 15.10g (95%CI 10.85 to 19.36), respectively). Following adjustment, the strength of the association increased for both ethnic groups (i.e. there was now a larger increase in birth weight associated with a 1kg increase in GWG); although it was still a lower association in infants of Pakistani women compared with infants of White British women (22.92g (95%CI 18.07 to 27.78) and 24.14 (95%CI 18.67 to 30.21), respectively). When considering the interaction between ethnicity and GWG on birth weight, there was no significant difference between the shape of the association between GWG on birth weight in the two ethnic groups in either the unadjusted or adjusted model (p=0.167 and p=0.554, respectively; Table 59).

Infant abdominal circumference at birth

BMI

Unadjusted results showed that as maternal BMI increased, infant abdominal circumference at birth significantly increased for both ethnic groups, although the effect size for both was small (0.04cm (95%CI 0.03 to 0.06) for infants of Pakistani women and 0.05cm (95%CI 0.03 to 0.06) for infants of White British women). However, following adjustment, the association between maternal BMI and infant abdominal circumference in infants of Pakistani was lower, and no longer significant, while in infants of White British women, the association remained the same (0.02cm (95%CI -0.01 to 0.04) and 0.05cm (95%CI 0.03 to 0.07); respectively). When considering the interaction between ethnicity and BMI on infant abdominal circumference at birth, there was no significant difference between the shape of the association between BMI and infant abdominal circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.650 and 0.188, respectively; Table 58).

GWG

GWG was positively associated with infant abdominal circumference at birth in both ethnic groups. However, although the effect sizes were similar, in the unadjusted models this only reached significance for infants of White British women (0.02cm (95%CI <0.01 to 0.04) for infants of Pakistani women and 0.02cm (95%CI 0.01 to 0.05) for infants of White British women). Following adjustment, the direction of the

association remained the same, but the strength increased (there was now a larger increase in abdominal circumference associated with a 1kg increase in GWG) and now reached significance for both ethnic groups, and the effect size was very similar for each, but the upper limit for the 95%CI was slightly higher for infants of White British women (0.06cm (95%CI 0.03 to 0.09)) than for infants of Pakistani women (0.06cm (95%CI 0.03 to 0.08)). When considering the interaction between ethnicity and GWG on infant abdominal circumference at birth, there was no significant difference between the shape of the association between GWG on infant abdominal circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.560 and p=0.911, respectively; Table 59)

Infant head circumference at birth (cm)

BMI

In both the unadjusted and adjusted models, infant head circumference increased significantly with increasing maternal BMI for both ethnic groups, although the effect size was slightly smaller in infants born to Pakistani women (unadjusted 0.03cm (95%CI 0.02 to 0.04) and adjusted 0.03cm (95%CI 0.01 to 0.04)) compared with infants born to White British women (unadjusted and adjusted 0.04cm (95%CI 0.03 to 0.05)).When considering the interaction between ethnicity and BMI on infant head circumference at birth, there was no significant difference between the shape of the association between BMI and infant head circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.257 and 0.444, respectively; Table 58).

GWG

GWG was significantly positively associated with infant head circumference at birth in both the unadjusted and adjusted models for both ethnic groups. In the unadjusted models there was no difference between the two ethnic groups (0.03cm (95%CI 0.02 to 0.04) for both). Following adjustment, the association strengthened in both ethnic groups, and although both had the same coefficient, the confidence interval was slightly wider for infants of Pakistani women compared with White British (0.05cm (95%CI 0.03 to 0.06) for infants of Pakistani women and 0.05cm (95%CI 0.03 to

0.07) for infants of White British women). When considering the interaction between ethnicity and GWG on infant head circumference at birth, there was no significant difference between the shape of the association between GWG on infant head circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.662 and p=0.872, respectively; Table 59).

Infant mid-arm circumference at birth (cm)

BMI

In the unadjusted models, infant mid-arm circumference at birth increased significantly with increasing maternal BMI. This was true for both ethnic groups, and the effect size was the same for each (0.02cm increase in infant mid arm circumference per 1kg/m^2 increase in maternal BMI (95% 0.02 to 0.03). The direction and significance of the association did not alter for either ethnic groups following adjustment, although the effect size was now smaller for infants of Pakistani women compared with infants of White British women (0.02cm (95%CI 0.01 to 0.02) and 0.03cm (95%CI 0.02 to 0.03), respectively). When considering the interaction between ethnicity and BMI on infant head circumference at birth, there was no significant difference between the shape of the association between BMI and infant head circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.643 and p=0.614 respectively; Table 58).

GWG

GWG was significantly positively associated with infant mid-arm circumference at birth in both the unadjusted and adjusted models for both ethnic groups. In the unadjusted models, there was a slightly weaker association for infants of Pakistani women compared with infants of White British women (0.01cm per 1kg increase in GWG (95%CI 0.01 to 0.02) and 0.02cm (95%CI 0.01 to 0.03), respectively). Following adjustment, the association strengthened in both ethnic groups, but remained weaker for infants of Pakistani women compared with infants of White British women (0.03cm (95%CI 0.02 to 0.05) and 0.04cm (95%CI 0.02 to 0.05), respectively) meaning that there was less mid arm circumference associated with a 1kg increase in GWG for infants of Pakistani women compared with infants of White

British women). When considering the interaction between ethnicity and GWG on infant mid-arm circumference at birth, there was no significant difference between the shape of the association between GWG on infant mid-arm circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.790 and p=0.815, respectively; Table 59).

Infant subscapular SFT at birth

BMI

In unadjusted analysis, with increasing maternal BMI, infant SFT at birth significantly increased for both ethnic groups, and was slightly higher for infants of Pakistani women compared with infants of White British women, although the effect size was very small for both ethnic groups (0.04mm (95%CI 0.03 to 0.05) and 0.03mm (95%CI 0.02 to 0.03), respectively). This remained the same following adjustment for infants of Pakistani women, and decreased slightly in infants of White British women (0.03mm (95%CI 0.02 to 0.04) and 0.03mm (0.01 to 0.04), respectively. When considering the interaction between ethnicity and BMI on infant subscapular SFT at birth, there was no significant difference between the shape of the association between BMI and infant head circumference at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.070 and p=0.712 respectively; Table 58).

GWG

GWG was positively associated with infant subscapular SFT at birth in both ethnic groups.. Despite this, the effect size for both ethnic groups was very small (0.01mm (95%CI 0.01 to 0.02) for infants of Pakistani women and 0.02mm (95%CI 0.01 to 0.03) for infants of White British women). Following adjustment, the direction of the association remained the same, but the effect sizes increased slightly (meaning that there was a larger increase in infant subscapular SFT associated with a 1kg increase in GWG, but the effect sizes were still very small) for both infants of Pakistani women and for infants of White British women (0.03mm (95%CI 0.01 to 0.04) for infants of Pakistani women and 0.03 (95%CI 0.02 to 0.05) for infants of White British women). . When considering the interaction between ethnicity and GWG on subscapular SFT at birth, there was no significant difference between the shape of the association

between GWG on infant subscapular SFT at birth in the two ethnic groups in either the unadjusted or adjusted model (p=0.127 and p=0.310, respectively; Table 59).

Infant tricep SFT at birth

BMI

Infant tricep SFT increased significantly with increasing maternal BMI, this was true for both ethnic groups although was slightly higher for infants of Pakistani women compared with infants of White British women prior to adjustment; despite this, the effect sizes were small for both ethnic groups (0.03mm (95%CI 0.03 to 0.04) for infants of Pakistani women and 0.02mm (95%CI 0.02 to 0.03) for infants of White British women). Following adjustment, these values increased slightly for infants of White British women and the effect size was now the same for both ethnic groups (0.03mm increase in infant tricep SFT at birth per 1kg GWG (95%CI 0.01 to 0.04)). Again, although significantly increased, it is worth noting that the effect sizes were small. When considering the interaction between ethnicity and BMI on infant tricep SFT, there was no significant difference between the shape of the association between BMI and infant tricep SFT in the two ethnic groups in either the unadjusted or adjusted model (p=0.137 and p=0.363, respectively; Table 58).

GWG

GWG was positively associated with infant tricep SFT at birth in both ethnic groups. However, in the unadjusted models this only reached significance for infants of White British women, and the effect sizes were small (0.01mm (<0.00 to 0.02) for infants of Pakistani women and 0.03mm (95%CI 0.01 to 0.04) for infants of White British women). Following adjustment, the direction of the association remained the same, but the strength increased (meaning there was now a larger increase in infant tricep SFT associated with a 1kg increase in GWG) and now reached significance for both infants of Pakistani women, and for infants of White British women, although again, the effect sizes remained small (0.03mm (95%CI 0.02 to 0.04) for infants of Pakistani women and 0.04mm (95%CI 0.02 to 0.06) for infants of White British women). When considering the interaction between ethnicity and GWG on subscapular SFT at birth, there was a significant difference between the shape of the association between

GWG on infant subscapular SFT at birth in the two ethnic groups in the unadjusted model (p=0.028; Table 59). However, following adjustment this difference was no longer significant (p=0.116; Table 59).

Infant anthropometrics at 3 years of age

Infant weight at 3 years

BMI

In unadjusted analysis, infant weight at 3 years was significantly positively associated with maternal BMI at booking for both ethnic groups, although the effect size was small; for both ethnic groups, a 1kg/m^2 increase in maternal BMI was associated with 0.06kg increase in infant weight at three years (95%CI 0.02 to 0.10). Following adjustment, the effect size increased for both ethnic groups and was now slightly weaker for infants of Pakistani women (i.e. had a smaller amount of weight at 3 years associated with a 1kg/m^2 increase in maternal BMI) compared with infants of White British women, and effect sizes were still relatively small (0.08kg (95%CI 0.03 to 0.13) for Pakistani women and 0.09kg (95%CI 0.04 to 0.14) for White British women). When considering the interaction between ethnicity and BMI on infant weight at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.970 and p=0.549, respectively; Table 58).

GWG

In unadjusted analysis, although neither association was significant and the effect sizes were small, infants of Pakistani women had an increase in weight for 1kg GWG (0.05kg (95%CI -0.00 to 0.10) compared with infants of White British women, who had a slight decrease in weight at 3 years of age (-0.01kg (95%CI -0.06 to 0.05). In adjusted analysis, the association increased slightly for both ethnic groups, and remained higher in infants of Pakistani women compared with infants of White British women, (0.06kg (95%CI >0.00 to 0.13) for infants of Pakistani women and 0.01kg (95%CI -0.08 to 0.12) for infants of White British women. When considering the interaction between ethnicity and GWG on infant weight at 3 years, there was no

significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.185 and p=0.809, respectively; Table 59).

Infant abdominal circumference at 3 years

BMI

In unadjusted analysis, infant abdominal circumference at 3 years was significantly associated with maternal BMI at booking, and the effect size was the same in infants of both ethnic groups (0.09cm (95%CI 0.01 to 0.17) for infants of Pakistani women and 0.09cm (95%CI 0.03 to 0.16) for infants of White British women). The direction of the association remained the same following adjustment, although the coefficient increased for both ethnic groups and the effect size was now greater for infants of Pakistani women compared with infants of White British women (0.16cm (95%CI 0.06 to 0.27) for infants of Pakistani women and 0.12cm (95%CI 0.02 to 0.22) for infants of White British women). When considering the interaction between ethnicity and BMI on infant abdominal circumference at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.900 and p=0.878, respectively; Table 58).

GWG

There was no significant association between infant abdominal circumference at 3 years and GWG for either ethnic group in either unadjusted or adjusted analysis. Despite this, in unadjusted analysis, the direction of the association was positive for infants of Pakistani women and negative for infants of White British women (0.04cm (95%CI -0.05 to 0.15) for infants of Pakistani women and -0.03 (95%CI -0.15 to 0.09) for infants of White British women). Following adjustment, the effect size increased for both ethnic groups, meaning that it was now positive for infants of White British women, although still not significant. The overall effect size was also now lower for infants of Pakistani women, but only very slightly (0.07cm (95%CI -0.08 to 0.21) for infants of Pakistani women and 0.08 (-0.12 to 0.29) and for infants of White British women). When considering the interaction between ethnicity and GWG on infant abdominal circumference at 3 years, there was no significant difference between the

shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.359 and p=0.387, respectively; Table 59).

Infant tricep SFT at 3 years

BMI

There was no significant association between infant tricep SFT at 3 years and maternal BMI at booking for either ethnic group in either unadjusted or adjusted analysis. However, the effect size was greater for infants of Pakistani women compared with infants of White British women in both unadjusted (0.05mm (95%CI -0.02 to 0.11) and 0.02mm (95%CI -0.04 to 0.08), respectively) and adjusted (0.07mm (95%CI -0.01 to 0.15) and 0.02 (95%CO -0.07 to 0.12), respectively), although the effect size was small. When considering the interaction between ethnicity and BMI on infant tricep SFT at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.493 and p=0.629, respectively; Table 58).

GWG

There was no significant association between infant tricep SFT at 3 years and GWG for either ethnic group in either unadjusted or adjusted analysis. In unadjusted analysis, the effect size was larger for infants of Pakistani women compared with infants of White British women (0.04mm (95%CI -0.04 to 0.12) and 0.02mm (95%CI -0.10 to 0.13), respectively). Following adjustment, although the effect size increased for both ethnic groups, it was still larger for infants of Pakistani women compared with White British infants (0.09mm (95%CI -0.01 to 0.18) and 0.04 (95%CI -0.26 to 0.34), respectively. When considering the interaction between ethnicity and GWG on infant tricep SFT at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.708 and p=0.813, respectively; Table 59).

Infant subscapular SFT at 3 years

BMI

There was no significant association between infant subscapular SFT at 3 years and maternal BMI at booking for either ethnic group in either unadjusted or adjusted analysis. However, the effect size was greater for infants of Pakistani women compared with infants of White British women in both unadjusted (0.04mm (95%CI -0.01 to 0.09) and 0.01mm (95%CI -0.04 to 0.05), respectively) and adjusted analysis (0.03 (95%CI -0.04 to 0.10) and -0.01 (95%CI -0.07 to 0.06), respectively). Following adjustment, the association for White British women was now negative but the effect size was very small and results did not reach significant. When considering the interaction between ethnicity and BMI on infant subscapular SFT at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.259 and p=0.648, respectively; Table 58).

GWG

There was no significant association between infant subscapular SFT at 3 years and GWG for either ethnic group in either unadjusted or adjusted analysis. In unadjusted analysis, the association was stronger for infants of Pakistani women compared with White British (0.02mm (95%CI -0.04 to 0.08) and 0.01mm (95%CI -0.06 to 0.08), respectively). Following adjustment, the association strengthened for both ethnic groups, and was now slightly weaker for infants of Pakistani women compared with infants of White British women (0.05mm (95%CI -0.04 to 0.14) and 0.6mm (95%CI -0.17 to 0.28), respectively). When considering the interaction between ethnicity and GWG on infant subscapular SFT at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.854 and p=0.894, respectively; Table 59).

Infant thigh circumference at 3 years

BMI

In both unadjusted and adjusted analysis, infant thigh circumference was significantly positively associated with maternal BMI at booking for infants of Pakistani women,

but not for infants of White British women. In unadjusted analysis the effect size was greater for infants of Pakistani women compared with infants of White British women (0.20cm (95%CI 0.09 to 0.30) and 0.02cm (95%CI -0.07 to 0.12), respectively). This remained true following adjustment (0.19cm (95%CI 0.06 to 0.33) for infants of Pakistani women and -0.01cm (95%CI -0.11 to 0.09) for infants of White British women). There was a significant interaction between maternal BMI and ethnicity on infant thigh circumference at 3 years in both the unadjusted and adjusted models (p=0.010 for unadjusted model, and 0.031 for adjusted model; Table 58). This means that there was a significant difference in the shape of the association between maternal BMI and infant thigh circumference in infants of Pakistani women compared with infants of White British women. The graph for the unadjusted regression model with ethnicity fitted as an interaction term is depicted in Figure 25, and the graph for the adjusted regression model using a lowess curve is shown in Figure 26.

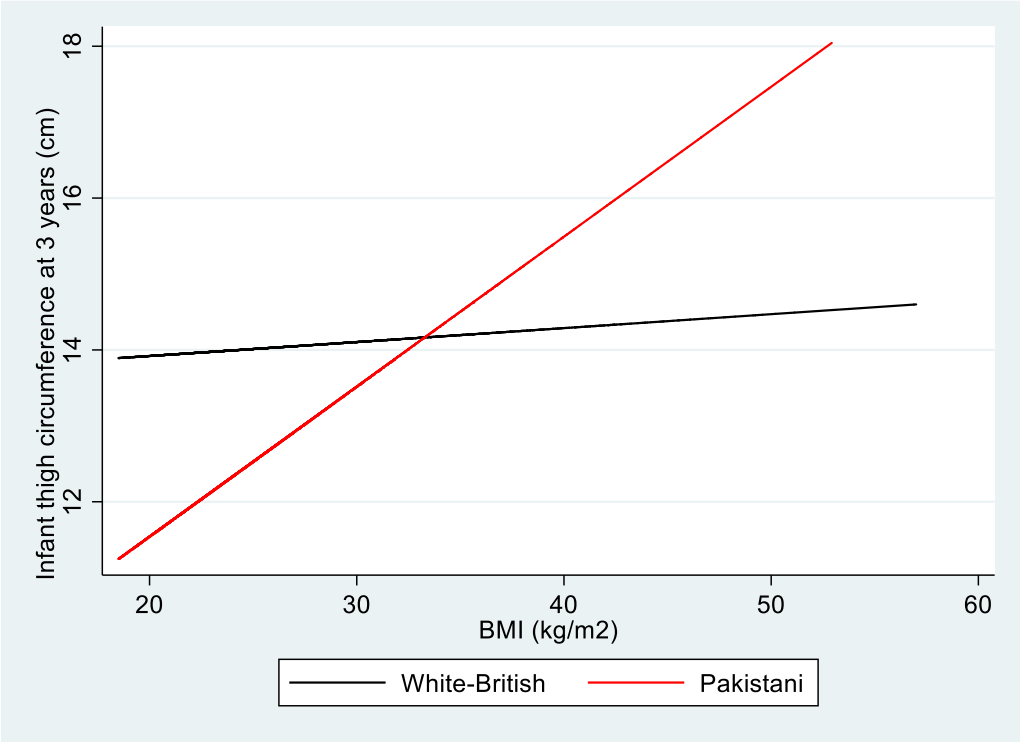


Figure 25 Graph for the unadjusted regression model between infant thigh circumference at 3 years and BMI with ethnicity fitted as an interaction term

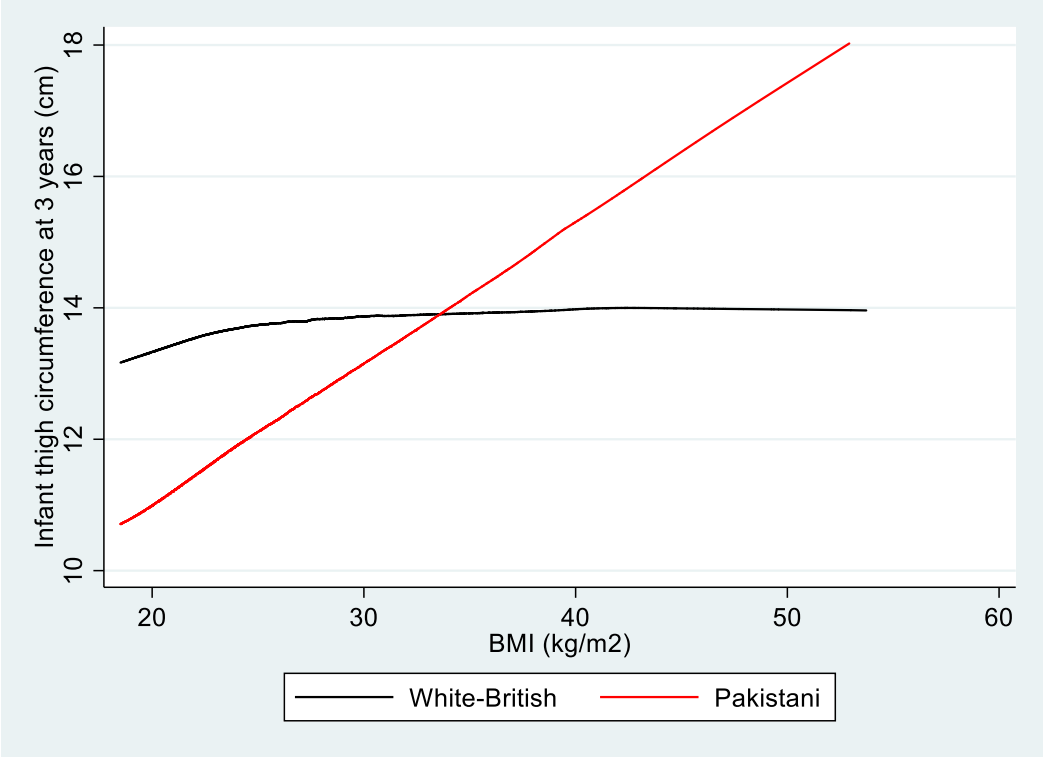


Figure 26 Two-way lowess smoother plot of the adjusted regression model between infant thigh circumference at 3 years and BMI with ethnicity fitted as an interaction term

GWG

There was no significant association between infant thigh circumference at 3 years and GWG for either ethnic group in either unadjusted or adjusted analysis. In unadjusted analysis, the association was negative for infants of Pakistani women and positive for infants of White British women (-0.08cm (95%CI -0.20 to 0.05) and 0.01 (95%CI -0.13 to 0.16), respectively). Following adjustment, the association was now positive for both ethnic groups, although was weaker for infants of Pakistani women compared with infants of White British women (0.04cm (95%CI -0.15 to 0.24) and 0.12cm (95%CI -0.16 to 0.40), respectively). When considering the interaction between ethnicity and GWG on infant thigh circumference at 3 years, there was no significant difference between the shape of the association in the two ethnic groups in either the unadjusted or adjusted model (p=0.369 and p=0.113, respectively; Table 59).

7.1.8 Gestational weight gain per week

When divided by the number of weeks gestation, there were very few changes to the direction, and significance of the associations overall (although the actual effect sizes were altered by using GWG per week rather than overall GWG; tables of results for maternal and infant outcomes are attached in Appendix 16, pgs.375-377). Please note that some of the confidence intervals were very wide in analysis using GWG per week as an exposure and so results should be interpreted with caution.

When using GWG per week, there were now significant interactions between ethnicity and GWG per week on pre-term birth, in both unadjusted (p=0.030) and adjusted models (p=0.008). Results showed that in adjusted models infants born to Pakistani women had higher odds of pre-term birth compared with infants born to White British women with increasing GWG per week (AOR 2.44 (95%CI 0.25 to 24.00), and AOR 0.10 (95%CI <0.01 to 0.24), respectively). There were also changes to the results for infant tricep SFT at birth, and at three years. In the analysis of overall GWG, the only significant interaction had been for infant tricep SFT at birth in the unadjusted analysis. Using GWG per week, significant interactions were identified in both the unadjusted (p=0.022) and adjusted models (p=0.016). In addition, there had been no significant interactions between ethnicity and GWG on infant thigh SFT at three years. However, when GWG per week was used, there was a significant interaction for infant thigh SFT in the adjusted model (p=0.030).

7.1.9 Gestational weight gain categorised according to maternal body mass index; comparing use of general population body mass index criteria with Asian specific body mass index criteria

GWG was also considered as a categorical exposure, based on maternal BMI group using both the general population BMI cut offs, and the Asian specific BMI cut offs, results are shown in Tables 60 and 61; Table 60 for maternal outcomes, and Table 61 for infant outcomes.

Table 60 GWG categorised according to BMI using general population, and Asian specific criteria (Categorical): maternal outcomes

GWG		Effect size of outcome (95%CI)						P value for interaction between Ethnicity and BMI on outcome			
		White British		Pakistani		Pakistani (GWG calculated using Asian specific BMI)		General population		Asian specific	
		UA	A	UA	A	UA	A	UA	A	UA	A
Mode of delivery											
C-section	L	0.69 (0.48 to 0.98)*	0.73 (0.43 to 1.24)	0.93 (0.68 to 1.28)	0.93 (0.60 to 1.43)	0.65 (0.47 to 0.91)*	0.61 (0.38 to 0.96)*	ns	ns	ns	ns
	H	1.56 (1.09 to 2.23)*	1.73 (1.02 to 2.94)*	1.41 (0.97 to 2.04)	1.71 (1.03 to 2.82)*	1.24 (0.88 to 1.75)	1.31 (0.82 to 2.10)	ns	ns	ns	ns
Induction	L	0.73 (0.56 to 0.94)*	0.68 (0.48 to 0.98)	0.71 (0.58 to 0.87)*	0.73 (0.55 to 0.96)*	0.67 (0.54 to 0.83)*	0.72 (0.54 to 0.95)*	ns	ns	ns	ns
	H	1.46 (1.12 to 1.91)*	1.72 (1.19 to 2.48)*	1.55 (1.22 to 1.97)*	1.75 (1.28 to 2.40)*	1.49 (1.20 to 1.85)*	1.50 (1.12 to 2.00)*	ns	ns	ns	ns
Breastfeeding at 6 months	L	0.96 (0.51 to 1.82)	1.93 (0.49 to 7.69)	0.97 (0.57 to 1.65)	1.55 (0.69 to 3.49)	0.86 (0.51 to 1.45)	1.21 (0.55 to 2.68)	ns	ns	ns	ns
	H	0.97 (0.48 to 1.96)	0.45 (0.10 to 2.07)	0.94 (0.48 to 1.81)	0.70 (0.27 to 1.81)	1.33 (0.71 to 2.49)	0.92 (0.39 to 2.91)	ns	ns	ns	ns
3 year PPWR (kg)	L	-0.36 (-3.35 to 2.69)	-2.70 (-6.79 to 1.39)	-1.80 (-3.25 to -0.36)*	-2.25 (-4.31 to -0.20)*	-2.02 (-3.46 to -0.57)*	-2.72 (-4.72 to -0.72)*	ns	ns	ns	ns
	H	1.97 (-1.35 to 5.29)	1.90 (-3.17 to 6.97)	1.42 (-0.48 to 3.33)	1.01 (-1.54 to 3.56)	1.36 (-0.29 to 3.02)	1.38 (-0.87 to 6.64)	ns	ns	ns	ns

[A]P value for interaction between Ethnicity and BMI on outcome (shows whether there is a significant difference in Pakistani women compared with White British women in the shape of association between early GWG and outcome). UA= unadjusted, A= adjusted, L=low, H=high, ns=non-significant

Table 61 GWG categorised according to BMI using general population, and Asian specific criteria (Categorical): infant outcomes

Outcome	GWG	Effect size of outcome (95%CI)						P value for interaction between Ethnicity and BMI on outcome			
		White British		Pakistani		Pakistani (GWG calculated using Asian specific BMI)		General population		Asian specific	
		UA	A[&]	UA	A[&]	UA	A[&]	UA	A[&]	UA	A[&]
Stillbirth	L	0.73 (0.07 to 8.10)	-	1.03 (0.35 to 3.07)	-	1.29 (0.43 to 3.85)	-	ns	-	ns	-
	H	-	-	1.17 (0.32 to 4.27)	-	0.83 (0.23 to 3.03)	-	-		-	
Gestational age at delivery											
Pre-term (<37 weeks gestation)	L	1.48 (0.68 to 3.21)	1.45 (0.38 to 5.48)	1.66 (0.99 to 2.80)	1.46 (0.71 to 3.03)	1.93 (1.16 to 3.22)*	1.93 (0.95 to 3.91)	ns	ns	ns	ns
	H	0.23 (0.05 to 0.97)*	0.53 (0.10 to 2.74)	0.99 (0.52 to 1.88)	0.74 (0.29 to 1.88)	0.98 (0.55 to 1.74)	0.81 (0.36 to 1.82)	ns	ns	ns	ns
Post-term (≥42 weeks gestation)	L	0.98 (0.40 to 2.42)	1.14 (0.18 to 7.32)	1.92 (0.74 to 4.97)	1.25 (0.31 to 5.00)	1.53 (0.61 to 3.88)	1.80 (0.46 7.05)	ns	ns	ns	ns
	H	1.47 (0.58 to 3.71)	2.14 (0.37 to 12.28)	0.23 (0.03 to 1.72)	0.28 (0.03 to 2.65)	0.16 (0.02 to 1.22)	0.20 (0.02 to 1.84)	ns	ns	ns	ns
Infant anthropometrics at birth											
Birth weight (g)	L	-189.65 (-235.32 to -143.98)*	-171.82 (-234.32 to -109.32)*	-165.73 (-201.90 to -129.54)*	-173.31 (-220.56 to -126.05)*	-193.81 (-229.65 to -157.98)*	-195.70 (-243.05 to -148.35)*	ns	ns	ns	ns
	H	244.26 (193.88 to 294.64)*	230.72 (164.04 to 297.41)*	185.96 (141.12 to 230.79)*	192.94 (134.96 to 250.93)*	185.00 (145.01 to 225.00)*	179.05 (127.38 to 230.71)*	ns	ns	**s**	ns
Infant abdominal circumference at birth (cm)	L	-0.45 (-0.69 to -0.21)*	-0.42 (-0.77 to -0.07)*	-0.38 (-0.58 to -0.17)*	-0.44 (-0.71 to -0.17)*	-0.50 (-0.70 to -0.29)*	-0.56 (-0.82 to -0.29)*	ns	ns	ns	ns
	H	0.56 (0.29 to 0.83)*	0.60 (0.23 to 0.97)*	0.27 (0.02 to 0.53)*	0.27 (-0.07 to 0.60)	0.40 (0.17 to 0.62)*	0.35 (0.05 to 0.64)*	ns	ns	ns	ns

Outcome	GWG	Effect size of outcome (95%CI)						P value for interaction between Ethnicity and BMI on outcome			
		White British		Pakistani		Pakistani (GWG calculated using Asian specific BMI)		General population		Asian specific	
		UA	A[&]	UA	A[&]	UA	A[&]	UA	A[&]	UA	A[&]
Infant head circumference at birth (cm)	L	-0.45 (-0.59 to 0.31)*	-0.39 (-0.58 to -0.19)*	-0.34 (-0.45 to -0.23)*	-0.33 (-0.48 to -0.19)*	-0.41 (-0.52 to -0.29)*	-0.42 (-0.56 to -0.27)*	ns	ns	ns	ns
	H	0.57 (0.41 to 0.72)*	0.44 (0.23 to 0.65)*	0.43 (0.29 to 0.57)*	0.41 (0.23 to 0.59)*	0.44 (0.32 to 0.57)*	0.42 (0.26 to 0.58)*	ns	ns	ns	ns
Infant mid- arm circumference at birth (cm)	L	-0.23 (-0.33 to -0.13)*	-0.27 (-0.42 to -0.13)*	-0.19 (-0.28 to -0.11)*	-0.25 (-0.36 to -0.14)*	-0.26 (-0.34 to -0.17)*	-0.31 (-0.47 to -0.20)*	ns	ns	ns	ns
	H	0.23 (0.12 to 0.35)*	0.28 (0.12 to 0.43)*	0.27 (0.16 to 0.37)*	0.31 (0.17 to 0.44)*	0.26 (0.17 to 0.35)*	0.29 (0.17 to 0.41)*	ns	ns	ns	ns
Infant sub-scapular SFT at birth (mm)	L	-0.34 (-0.47 to -0.21)*	-0.26 -0.46 to -0.09)*	-0.20 (-0.29 to -0.07)*	-0.17 (-0.30 to -0.05)*	-0.25 (-0.34 to -0.15)*	-0.19 (-0.32 to -0.07)*	ns	ns	ns	ns
	H	0.33 (0.19 to 0.48)*	(0.29 0.09 to 0.49)*	0.26 (0.14 to 0.38)*	0.25 (0.10 to 0.41)*	0.27 (0.16 to 0.38)*	0.25 (0.11 to 0.39)	ns	ns	ns	ns
Infant tricep SFT at birth (mm)	L	-0.35 (-0.48 to -0.21)*	-0.29 (-0.47 to -0.09)*	-0.19 (-0.28 to -0.09)*	-0.20 (-0.33 to -0.08)*	-0.20 (-0.30 to -0.11)*	-0.21 (-0.33 to -0.09)*	ns	ns	**s**	ns
	H	0.39 (0.25 to 0.54)*	0.35 (0.15 to 0.56)*	0.18 (0.06 to 0.30)*	0.19 (0.04 to 0.35)*	0.21 (0.11 to 0.31)*	0.20 (0.07 to 0.33)*	**s**	ns	**s**	ns
Anthropometric measures of infant at 3 years											
Infant weight at 3 years (kg)	L	0.02 (-0.56 to 0.60)	-0.27 (-1.06 to 0.52)	-0.70 (-1.21 to -0.19)*	-0.76 (-1.41 to -1.12)*	-0.68 (-1.18 to -0.17)*	-0.71 (-1.13 to -0.08)*	ns	ns	ns	ns
	H	-0.04 (-0.69 to 0.61)	-0.12 (-1.06 to 0.80)	0.79 (0.13 to 1.46)*	0.33 (-0.48 to 1.14)	0.81 (0.22 to 1.39)*	0.54 (-0.17 to 1.25)	ns	ns	ns	ns
Infant abdominal circumference at 3 years (cm)	L	-0.06 (-1.25 to 1.13)	-0.97 (-2.75 to 0.81)	-0.97 (-2.01 to 0.07)	-0.67 (-2.11 to 0.77)	-0.63 (-1.66 to 0.40)	-0.23 (-1.60 to 1.14)	ns	ns	ns	ns
	H	-0.05 (-1.37 to 1.27)	-0.81 (-2.96 to 1.34)	1.12 (-0.29 to 2.53)	0.14 (-1.63 to 1.92)	0.74 -0.45 to 1.95)	0.02 (-1.55 to 1.58)	ns	ns	ns	ns

Outcome	GWG	Effect size of outcome (95%CI)						P value for interaction between Ethnicity and BMI on outcome			
		White British		Pakistani		Pakistani (GWG calculated using Asian specific BMI)		General population		Asian specific	
		UA	A[&]	UA	A[&]	UA	A[&]	UA	A[&]	UA	A[&]
Infant tricep SFT at 3 years (mm)	L	**-0.31 (-1.56 to 0.93)**	**0.55 (-2.02 to 3.13)**	**-0.80 (-1.60 to -0.01)***	**-1.19 (-2.15 to-0.22)***	**-0.83 (-1.60 to -0.05)***	**-0.92 (-1.83 to -0.01)***	**ns**	**ns**	**ns**	**ns**
	H	-0.10 (-1.50 to 1.30)	0.58 (-3.12 to 4.28)	1.01 (-0.63 to 2.10)	0.03 (-1.17 to 1.24)	0.51 (-0.39 to 1.41)	0.03 (-1.04 to 1.10)	ns	ns	ns	ns
Infant subscapular SFT at 3 years (mm)	L	-0.37 (-1.15 to 0.41)	0.25 (-1.27 to 1.76)	-0.26 (-0.90 to 0.39)	-0.48 (-1.28 to 0.32)	-0.15 (-0.78 to 0.49)	-0.49 (-1.23 to 0.25)	ns	ns	ns	ns
	H	0.16 (-0.75 to 1.07)	0.59 (-1.80 to 2.99)	0.57 (-0.36 to 1.50)	-0.91 (-1.15 to 0.97)	0.15 (-0.62 to 0.92)	-0.23 (-1.15 to 0.69)	ns	ns	ns	ns
Infant thigh circumference at 3 years (mm)	L	0.23 (-1.38 to 1.83)	0.33 (-2.10 to 2.76)	-0.29 (-1.57 to 0.99)	-0.81 (-2.62 to 0.99)	-0.42 (-1.68 to 0.84)	-0.56 (-2.24 to 1.13)	ns	ns	ns	ns
	H	-0.19 (-1.94 to 1.57)	1.23 (-2.73 to 5.21)	0.24 (-1.53 to 2.03)	-0.13 (-2.32 to 2.05)	-0.38 (-1.85 to 1.11)	-1.17 (-3.14 to 0.81)	ns	ns	ns	ns

[A]P value for interaction between Ethnicity and BMI on outcome (shows whether there is a significant difference in Pakistani women compared with White British women in the shape of association between early GWG and outcome). UA=unadjusted, A=adjusted, L=low, H=high, ns=non-significant, **s**=significant.
[&]Adjustments made for age, parity, smoking, generation, alcohol consumption, exposure to tobacco smoke, marital and cohabiting status, gestational age at booking, history of diabetes, mother's education, mother's job, father's education and father's job

Significant associations within the ethnic groups were identified for some pregnancy outcomes; for the mother these were; C-section, induction and PPWR, and for the infant these were anthropometric measures at birth (birth weight, abdominal circumference, MUAC and tricep SFT), and infant anthropometrics at three years of age (weight and tricep SFT). Despite the significant associations within the ethnic groups, there were no significant interactions between ethnicity and GWG on any of the outcomes following adjustment. Although application of the Asian specific BMI criteria to calculate level of GWG altered the strength of the association with the pregnancy outcomes of interest, there were still no significant interactions between ethnicity and GWG on pregnancy outcomes following adjustment. This suggests that there is no significant ethnic difference in the shape of the association between each pregnancy outcome and GWG according to maternal BMI category, independent of whether BMI criteria for the general population or the Asian population are used. When interpreting the results in Tables 60 and 61, caution should be applied where the sample size is small. Sample size effects this analysis more because GWG is categorised; it is a particular issue for binary outcomes, or where the analysis uses a subsample of the BiB cohort (BIB1000, at a later stage of follow up and therefore is subject to loss to follow up), particularly for adjusted analysis. The effect of a smaller sample size is reflected in the width of the 95%CI estimates.

7.2 Structural equation modelling for gestational weight gain

This section will present the results from SEM analysis investigating indirect and direct predictors of GWG using data from the BiB cohort. Figure 27 illustrates path analysis (SEM without the use of latent variables) for GWG as an outcome, following removal of insignificant paths ($p>0.05$), and variables with a standardized total effect β coefficient on GWG <0.100 for clarity. Removal of variables from the model was irrespective of direction of effect, but for this model, excluded key variables of interest ethnicity and GDM, which were retained. The sample size for this analysis was n=1,312. In Figure 27, significant effects are included and represented by arrows. These arrows are labelled with β coefficients, which give an indication of effect size and direction (+ is a positive association i.e. outcome increases with one unit increase of explanatory variables, - is a negative association i.e. outcome decreases with a one unit increase in explanatory variable). The direction of the arrows

represents direction of hypothesised causal flow; solid arrows indicate direct effects (i.e. exposure → outcome) and dashed arrows indicate indirect effects (i.e. exposure→ mediator → outcome). In Figure 27, numbers in brackets within the boxes show the variance unexplained by the model for each variable. A full breakdown of direct, indirect and total effects for the model depicted in Figure 27 is given in Table 62.

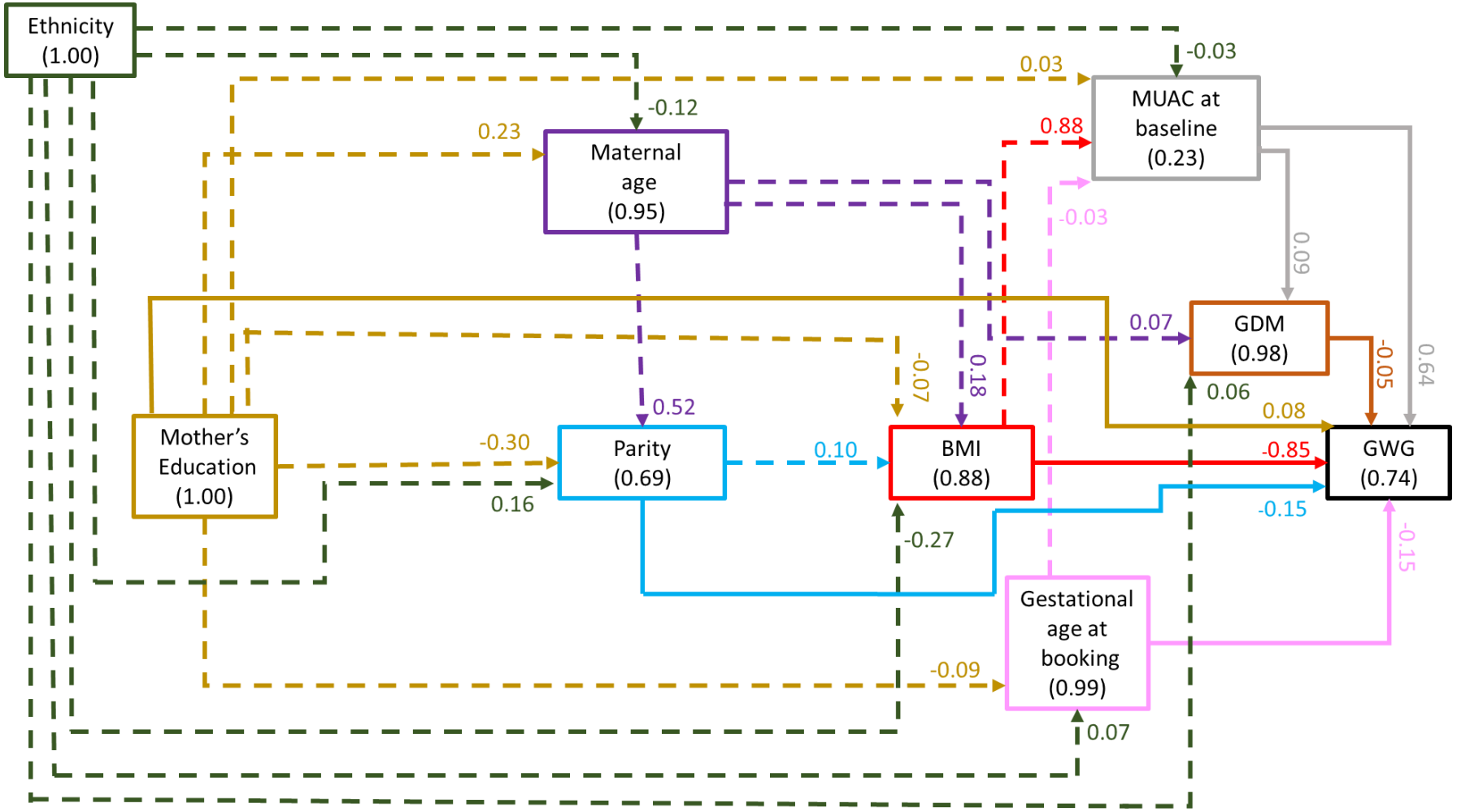


Figure 27 Path analysis for GWG including ethnicity and GDM.

The individual value on a line represents the direct effects of a unit change in the exposure, i.e. the driving explanatory variable, on the change in the outcome variable, at the end of the arrow. Solid arrows indicate standardized direct effects (i.e. exposure→ outcome) and dashed arrows indicate standardized indirect effects (i.e. exposure→ mediator (where the mediator then has a direct effect on the outcome). The range of values is between −1 and +1, where 1 (−1) means a 1:1 impact of the driver on the outcome. Figures in parentheses within the boxes represent extent of residual variation left unexplained by model in each variable. Units are standard deviation. Error-terms omitted from the model for simplicity.

Table 62 Full breakdown of direct, indirect and total effects for the model in Figure 27

	Driving explanatory variable	Direct effect		Indirect effect		Total effect	
		Standardized[a]	Unstandardized	Standardized[a]	Unstandardized	Standardized[a]	Unstandardized
BMI	**Parity**	0.10 (0.04 to 0.24)*	0.52 (0.20 to 0.85)*	-	-	0.10 (0.04 to 0.24)*	0.52 (0.20 to 0.85)*
	Maternal age	0.18 (0.12 to 0.16)*	0.19 (0.12 to 0.25)*	0.05 (0.01 to 0.08)*	0.05 (0.02 to 0.09)*	0.23 (0.18 to 0.28)*	0.24 (0.19 to 0.29)*
	Mother's education	-0.07 (-0.12 to -0.01)*	-0.35 (-0.64 to 0.06)*	0.02 (-0.01 to 0.05)*	0.13 (-0.01 to 0.26)	-0.04 (-0.11 to <0.01)	-0.22 (-0.49 to 0.05)
	Ethnicity	-0.27 (-0.32 to -0.22)*	-3.11 (-3.72 to -2.51)*	0.02 (0.01 to 0.03)*	0.18 (0.06 to 0.39)	-0.25 (-0.31 to -0.19)*	-2.93 (-3.5 to -2.34)*
GWG	**BMI**	-0.84 (-0.94 to -0.75)*	-0.75 (-0.84 to -0.66)*	0.56 (0.44 to 0.62)*	0.50 (0.42 to 0.58)	-0.28 (-0.33 to -0.23)*	-0.25 (-0.29 to -0.21)*
	GDM	-0.05 (-0.10 to -0.01)*	-1.62 (-3.15 to -0.10)*	-	-	-0.05 (-0.10 to -0.01)*	-1.63 (-3.15 to -0.10)*
	MUAC	0.64 (0.55 to 0.74)*	0.72 (0.61 to 0.83)*	-0.01 (-0.01 to >0.01)	-0.01 (-0.01 to >0.01)	0.64 (0.51 to 0.71)*	0.71 (0.60 to 0.82)*
	Parity	-0.15 (-0.22 to -0.11)*	-0.72 (-0.94 to -0.49)*	-0.03 (-0.05 to -0.01)*	-0.13 (-0.22 to -0.05)	-0.18 (-0.22 to -0.12)*	-0.85 (-1.09 to -0.61)*
	Gestational age at booking	-0.15 (-0.20 to -0.10)*	-0.24 (-0.32 to -0.16)*	-0.02 (-0.04 to -0.01)*	-0.04 (-0.06 to -0.01)	-0.17 (-0.21 to -0.10)*	-0.28 (-0.36 to -0.20)*
	Maternal age	-	-	-0.15 (-0.17 to -0.11)*	-0.14 (-0.16 to -0.11)	-0.15 (-0.17 to -0.11)*	-0.14 (-0.16 to -0.11)*
	Mothers education	0.08 (0.03 to 0.13)*	0.38 (0.16 to 0.60)*	0.07 (0.04 to 0.10)*	0.34 (0.21 to 0.47)	0.16 (0.10 to 0.23)*	0.72 (0.48 to 0.97)*
	Ethnicity	-	-	0.01 (-0.02 to 0.04)	0.12 (-0.19 to 0.43)	0.01 (-0.02 to 0.04)	0.12 (-0.19 o 0.43)
GDM	**BMI**	-	-	0.08 (0.04 to 0.14)*	<0.01 (<0.01 to 0.01)	0.08 (0.04 to 0.14)*	<0.01 (<0.01 to 0.01)*
	MUAC	0.09 (0.04 to 0.15)*	<0.01 (<0.01 to <0.001)*	-	-	0.09 (0.04 to 0.15)*	<0.01 (<0.01 to 0.01)*
	Parity	-	-	0.01 (<0.01 to 0.02)*	<0.01 (<0.01 to <0.01)*	0.01 (<0.01 to 0.02)*	<0.01 (<0.01 to <0.01)*
	Gestational age at booking	-	-	<-0.01 (-0.01 to <0.01)	<-0.01 (-0.01 to <0.01)	>-0.01 (>-0.01 to 0.02)	>-0.01 (>-0.01 to <0.01)
	Maternal age	0.06 (<0.01 to 0.11)*	<0.01 (<0.01 to <0.01)*	0.02 (0.01 to 0.03)*	<0.01 (<0.01 to <0.01)*	0.07 (<0.01 to <0.01)*	<0.01 (<0.01 to <0.01)*
	Mothers education	-	-	0.01 (-0.01 to 0.02)	<0.01 (>-0.01 to <0.01)	0.01 (-0.01 to 0.02)	<0.01 (>-0.01 to <0.01)
	Ethnicity	0.08 (0.07 to 0.14)*	0.03 (0.01 to 0.04)*	-0.02 (-0.04 to -0.01)*	-0.01 (-0.01 to >-0.01)*	0.06 (<0.01 to 0.11)*	0.02 (<0.01 to 0.04)*

	Driving explanatory variable	Direct effect		Indirect effect		Total effect	
		Standardized[a]	Unstandardized	Standardized[a]	Unstandardized	Standardized[a]	Unstandardized
MUAC	**BMI**	0.88 (0.86 to 0.89)*	0.70 (0.68 to 0.72)*	-	-	0.88 (0.86 to 0.89) *	0.70 (0.68 to 0.72)*
	Parity	-	-	0.09 (0.02 to 0.13)*	0.37 (0.14 to 0.59)*	0.09 (0.02 to 0.13) *	0.37 (0.14 to 0.59)*
	Gestational age at booking	-0.03 (-0.06 to -0.01)*	-0.05 (-0.09 to -0.01)*	-	-	-0.03 (-0.06 to >-0.01) *	-0.05 (-0.09 to -0.01)*
	Maternal age	-	-	0.20 (0.15 to 0.25)*	0.17 (0.13 to 0.21)*	0.20 (0.15 to 0.25)*	0.17 (0.13 to 0.21)*
	Mothers education	0.03 (0.01 to 0.06)*	0.13 (0.03 to 0.24)*	-0.03 (-0.09 to 0.01)	-0.14 (-0.34 to 0.05)	>-0.01 (-0.05 to >-0.01)*	-0.01 (-0.23 to 0.21)*
	Ethnicity	-0.03 (-0.06 to -0.01)*	-0.30 (-0.55 to -0.06)*	-0.22 (-0.27 to -0.18)*	-2.08 (-2.50 to -1.65)*	-0.25 (-0.31 to -0.20)*	-2.38 (-0.29 to -1.89)*
Parity	**Maternal age**	0.52 (0.48 to 0.56)*	0.10 (0.09 to 0.11)*	-	-	0.52 (0.48 to 0.56)*	0.10 (0.09 to 0.11)*
	Mothers education	-0.30 (-0.34 to -0.26)*	-0.29 (-0.34 to -0.25)*	0.12 (0.08 to 0.14)*	0.12 (0.09 to 0.15)*	-0.18 (-0.45 to -0.56)*	-0.18 (-0.23 to -0.21)*
	Ethnicity	0.16 (0.11 to 0.20)*	0.34 (0.24 to 0.43)*	-	-	0.16 (0.11 to 0.20)*	0.34 (0.24 to 0.43)*
Gestational age at booking	**Mothers education**	-0.09 (-0.14 to -0.03)*	-0.25 (-0.40 to -0.10)*	-	-	-0.09 (-0.14 to -0.03)*	-0.25 (-0.40 to -0.10)*
	Ethnicity	0.07 (0.02 to 0.12)*	0.44 (0.10 to 0.77)*	-	-	0.07 (0.02 to 0.12)*	0.44 (0.10 to 0.77)*
Maternal age	**Mothers education**	0.23 (0.18 to 0.28)*	1.16 (0.90 to 1.43)*	-	-	0.23 (0.18 to 0.28)*	1.16 (0.90 to 1.43)*

* p value <0.05

[a] Units for standardized results are standard deviation

Note: Direct effects indicate paths between exposure and outcome, i.e. not taking into account mediators. Indirect effects indicate the paths between exposure and mediator where the mediator then has a direct effect on the outcome. Total effects are the sum of the direct and indirect effects.

The model fit for the SEM in Figure 28 was good; RMSEA <0.001; 95%CI 0.000 to 0.022, CFI of 0.998. The variance in GWG explained by the variables included in this path model is 26% (R^2=0.257).

Below, total, direct and indirect effects shown in Table 62 for the model Figure 27 are discussed. Standardized effects are presented in units of standard deviation (SD); this allows a direct comparison of the effect sizes of each driving explanatory variable on GWG as the units are the same. Unstandardized effect sizes cannot be compared between variables, but do give an indication of the actual effect size between each explanatory variable on GWG (i.e. the kg change in GWG per one unit change in explanatory variable e.g.1kg/m^2 BMI or 1cm of MUAC).

Total effects are the sum of the indirect and direct effects of driving explanatory variables on the outcome. Significant total effects of driving explanatory variables on GWG, in descending order of standardized effect size (independent to the direction of effect), were; MUAC, BMI, parity, gestational age at booking, mothers education, maternal age and GDM. Results showed that ethnicity did not significantly predict GWG; ethnicity had a standardized total effect of 0.01SD (95%CI -0.02 to 0.04) and unstandardized effect of 0.12kg (95%CI -0.19 to 0.43; p=0.438). This suggests that in this model, Pakistani women gained, on average 0.12kg more than White British women did, but that this difference was not significant.

MUAC at baseline has the largest standardized total effect on GWG (β 0.64 (, P<0.001; Table 62). This suggested that with a 1SD increase in MUAC, GWG increased by 0.64SD or, as indicated by unstandardized effects; a 1cm increase in MUAC, leads to a 0.71kg increase in GWG (Table 62). The next largest predictor of GWG was maternal BMI; a 1SD increase in maternal BMI lead to a 0.28SD decrease in GWG (95%CI -0.33 to -0.23; p<0.001), or as indicated by unstandardized effects; a 1kg/m^2 increase in maternal BMI led to a 0.25kg decrease in GWG (95%CI -0.29 to -0.21) . Parity was the next; with a 1SD increase in parity, GWG decreased by 0.18SD (95%CI -0.22 to -0.12; p<0.001), or as indicated by unstandardized effects; an increase in parity of one led to a 0.85kg decrease in GWG (95%CI -1.09 to -0.61). Gestational age at booking had the next largest effect size; a 1SD increase in gestational age at booking let to a 0.17SD increase in GWG (95%CI -0.21 to -0.10; p<0.001), or a 1 day increase in gestational age a booking led to a 0.28kg decrease in GWG (95%CI -0.36 to -0.20). Mothers education was next; a 1SD increase in

mothers education led to a 0.16SD increase in GWG (95%CI 0.10 to 0.23), or a one unit increase in maternal education (i.e. <5 GCSEs, ≥5GCSEs, A level equivalent, higher education) led to, on average, a 0.72kg (95%CI 0.48 to 0.97) increase in GWG (so as maternal education increased, so did GWG). Maternal age also had a significant total effect on GWG; a 1SD increase in maternal age led to a 0.15SD decrease in GWG (95%CI -0.17 to -0.11; p<0.001), or a one year increase in maternal age led to a 0.14kg (95%CI -0.16 to -0.11) decrease in GWG according to unstandardized total effects (Table 62). Finally, GDM also had a significant total effect on GWG; a 1SD increase in GDM led to a 0.05SD decrease in GWG (95%CI -0.10 to -0.01; p=0.037), or as shown by unstandardized total effects for GDM; women with GDM had on average, a 1.63kg (95%CI -3.15 to -0.10) decrease in GWG compared with women without GDM (Table 62).

Variables that had a direct effect on GWG in descending order of standardized effect size (independent to direction of effect) were: BMI, MUAC, parity, gestational age at booking, mother's education and GDM. This means that these variables have a significant effect on GWG that was not mediated by any other variables in the model. A one SD increase in maternal BMI led to a 0.84 SD decrease in GWG (95%CI -0.94 to -0.75); or as shown by the indirect effects in Table 62, a 1kg/m^2 increase in BMI led to on average, a 0.75kg decrease in GWG (95%CI -0.84 to -0.66). A one SD increase in MUAC led to a 0.64 SD increase in GWG (95%CI (0.55 to 0.74); or as shown in Table 62, a 1cm increase in MUAC led to, on average, a 0.72kg increase in GWG (95%CI 0.61 to 0.83). A one SD increase in parity led to a 0.15 SD decrease in GWG (95%CI -0.22 to -0.11; p<0.001); or as shown by unstandardized direct effects in Table 62, an increase in parity of one led to, on average, a 0.72kg decrease in GWG (95%CI (-0.94 to -0.49). A one SD increase in gestational age at booking led to a 0.15 SD decrease in GWG (95%CI -0.20 to -0.10; p<0.001); or as shown by unstandardized direct effects in Table 62, a one day increase in gestational age at booking led to, on average, a 0.24kg decrease in GWG (95%CI -0.32 to -0.16). A one SD increase in mothers education led to a 0.08 SD increase in GWG (95%CI 0.03 to 0.13; p<0.001); or as shown by unstandardized direct effects in Table 62, a one unit increase in mothers education led to, on average, a 0.38kg increase in GWG (95%CI 0.16 to 0.60) . GDM also had a significant direct effect on GWG; a one SD increase in GDM led to a 0.05 SD decrease in GWG (95%CI -0.10 to -0.01; p=0.037); or as shown by unstandardized direct effects in Table 62, mothers with GDM had, on

average, a 1.62kg decrease in GWG, although the 95% confidence intervals were wide, and ranged from a decrease of 3.1kg to a decrease of only 0.10kg (95%CI -3.15 to -0.10). Neither maternal age nor ethnicity had direct effects on GWG.

Some driving explanatory variables also had indirect effects on GDM, i.e. they were associated with another explanatory variable (a mediator), which then, in turn was associated with GWG. The variables with significant indirect effects in order of effect size (independent of direction of effect) were; BMI (standardized: 0.56 (95%CI 0.44 to 0.62), unstandardized: 0.50kg (95%CI 0.42 to 0.58)), maternal age (standardized: -0.15 (95%CI -0.17 to -0.11), unstandardized: -0.14kg (95%CI -0.16 to -0.11)), mothers education (standardized: 0.07 (95%CI 0.04 to 0.10), unstandardized: 0.34kg (95%CI 0.21 to 0.47)), parity (standardized: -0.03 (95%CI -0.05 to -0.01), unstandardized: -0.13kg (-0.22 to -0.05)) and gestational age at booking; although the effect size for gestational age at booking was very small (standardized: -0.02 (95%CI -0.04 to -0.01), unstandardized: -0.04kg (95%CI -0.06 to -0.01); Table 62). MUAC and ethnicity also had indirect effects on GWG, but these were not significant and effect sizes were very small (Table 62).

Figure 29 shows the most parsimonious model. Results show that ethnicity can be removed from the model while retaining good model fit (RMSEA=<0.001; 95%CI 0.000 to 0.026, CFI of 0.999). The variance in GWG explained by the variables included in this path model is still 26% (R^2=0.257). This indicated that in this population, ethnicity is not a significant predictor of GWG.

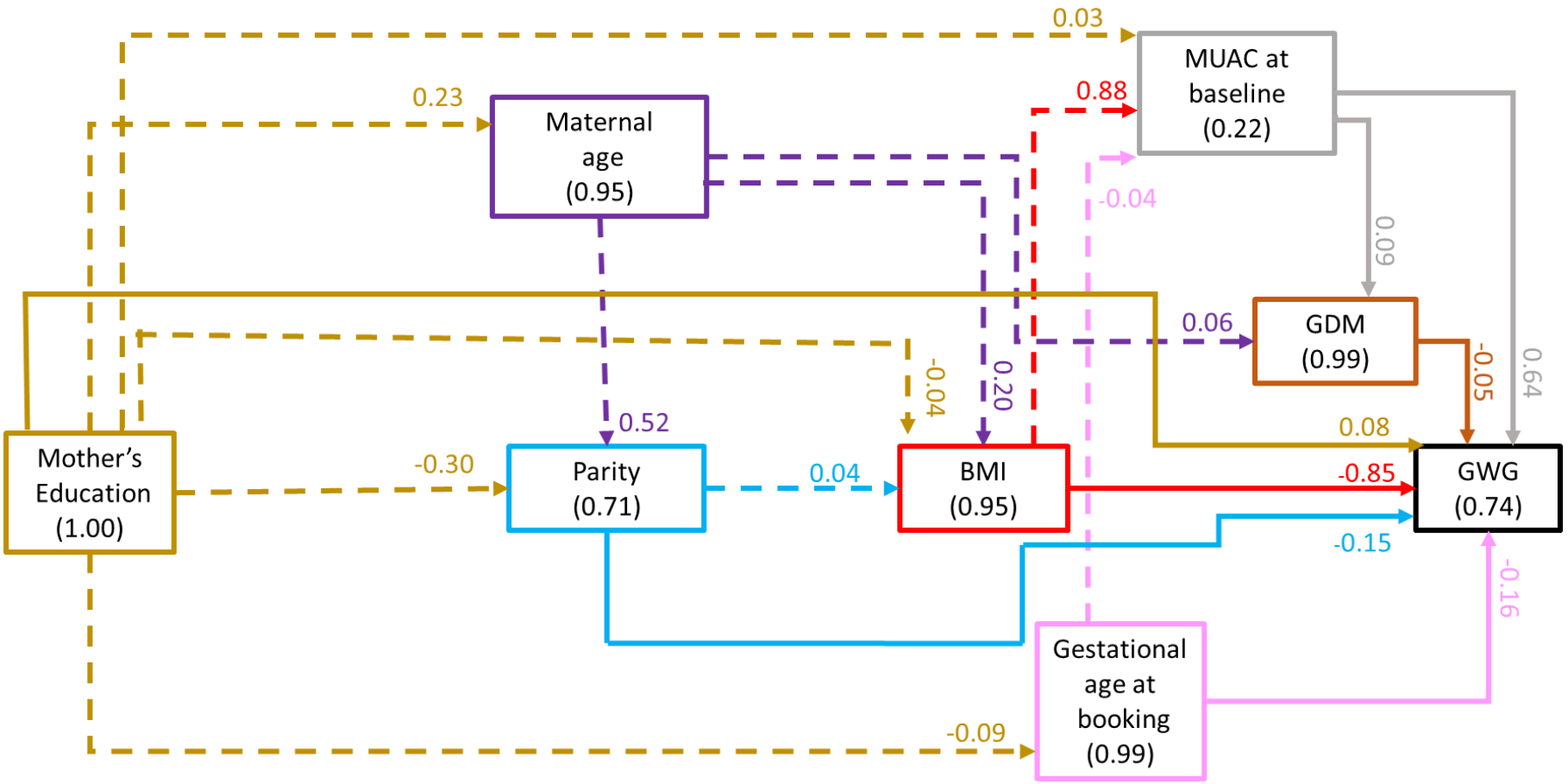


Figure 28 Path analysis for GWG; the most parsimonious model

The individual value on a line represents the direct effects of a unit change in the exposure, i.e. the driving explanatory variable, on the change in the outcome variable, at the end of the arrow. Solid arrows indicate standardized direct effects (i.e. exposure-> outcome) and dashed arrows indicate standardized indirect effects (i.e. exposure-> mediator (where the mediator then has a direct effect on the outcome)). The range of values is between −1 and +1, where 1 (−1) means a 1:1 impact of the driver on the outcome. Figures in parentheses within the boxes represent extent of residual variation left unexplained by model in each variable. Units are standard deviation. Error-terms omitted from the model for simplicity.

7.3 Exploring missing data

For each of the exposure variables (maternal BMI and GWG) it is important to consider whether and how women with missing data for the exposure vary from women with data for the exposure. This section will explore the differences between the two groups (missing and non-missing) for each of the exposures. Table 63 shows results for missing BMI and Table 64 shows results for missing GWG. R squared value gives the variation in variable of interest that is explained by whether or not BMI or GWG is missing (multiply by 100 to give the percentage variance explained).

Table 63 Comparing those with complete data for BMI (n=8,076) with those with missing BMI data (n=537)

Variable	Category	Odds ratio or coefficient (95% CI)[$]	R squared[£]	P value[$]
Ethnicity	White British (reference[a])	-	-	-
	Pakistani	0.87 (0.73 to 1.03)	<0.001	0.106
Maternal age (years)		0.06 (-0.43 to 0.56)	<0.001	<0.001*
Maternal height at booking (cm)		1.37 (0.71 to 2.03)	0.002	<0.001*
Maternal weight at booking (kg)^		-0.01 (-0.05 to 0.03)	<0.001	0.543
Gestational age at booking		0.03 (<0.01 to 0.05)	0.001	0.033*
Maternal weight at 26-28 week questionnaire (kg)^		-0.01 (-0.03 to 0.02)	<0.001	0.519
Maternal mid upper arm circumference at 26-28 week questionnaire (cm) ^		<-0.01 (-0.03 to 0.02)	<0.001	0.721
Maternal tricep skinfold thickness at booking (cm)		-0.73 (-1.76 to 0.30)	0.001	0.222
Parity	0 (reference[a])	-	-	-
	1	1.03 (0.75 to 1.29)	<0.001	0.804
	2	0.99 (0.75 to 1.30)	<0.001	0.930
	3	1.28 (0.92 to 1.78)	<0.001	0.151
	≥4	0.96 (0.61 to 1.51)	<0.001	0.864
Place of birth of mother, father and grandparents	All born in UK- White British English (reference[a])	-	-	-
	Both parents and all four grandparents South born in Pakistan	0.77 (0.58 to 1.03)	0.001	0.066
	Mother UK born, father and all four grandparents born in Pakistan	1.14 (0.90 to 1.14)	0.001	0.277
	Father UK born, mother and all four grandparents born in Pakistan	0.70 (0.53 to 0.93)	0.001	0.010*
	Both parents UK born, all four grandparents born in Pakistan	1.02 (0.85 to 1.71)	<0.001	0.313
Previous diabetes	No (reference[a])	-	-	-
	Yes	8.85 (3.71 to 21.07)	0.03	<0.001*
Previous hypertension	No (reference[a])			
	Yes	1.63 (0.65 to 4.06)	0.001	0.324
Family history of diabetes	No (reference)			
	Yes	0.84 (0.67 to 1.05)	<0.001	0.188
Family history of high blood pressure	No (reference)			
	Yes	1.06 (0.85 to 1.31)	<0.001	0.811

Variable	Category	Odds ratio or coefficient (95% CI)[$]	R squared[£]	P value[$]
Marital and cohabiting status	Married and cohabiting (reference[a])			
	Not married and cohabiting	1.07 (0.85 to 1.35)	<0.001	0.551
	Not cohabiting	1.27 (1.00 to 1.57)	0.001	0.053
Language	English (reference[a])			
	Mirpuri/Punjabi/Urdu	0.90 (0.72 to 1.13)	<0.001	0.345
Fathers Job	Employed, non-manual (reference[a])	-	-	-
	Employed, manual	0.85 (0.69 to 1.06)	<0.001	0.141
	Self-employed	1.07 (0.82 to 1.39)	<0.001	0.616
	Student	0.71 (0.29 to 1.76)	0.001	0.439
	Unemployed	0.96 (0.68 to 1.36)	<0.001	0.803
Mothers Job	Currently employed (reference[a])	-	-	-
	Previously employed	1.14 (0.93 to 1.41)	<0.001	0.204
	Never employed	1.04 (0.84 to 1.29)	<0.001	0.689
Fathers education	5 GCSEs (reference[a])	-	-	-
	<5 GCSEs	0.88 (0.66 to 1.18)	<0.001	0.401
	A level equivalent	1.07 (0.78 to 1.47)	<0.001	0.694
	Higher education	1.09 (0.84 to 1.39)	<0.001	0.525
Mothers education	5 GCSEs (reference[a])	-	-	-
	<5 GCSEs	0.85 (0.68 to 1.08)	<0.001	0.185
	A level equivalent	0.89 (0.67 to 1.19)	<0.001	0.419
	Higher education	0.89 (0.69 to 1.14)	<0.001	0.344
Alcohol consumption in pregnancy or 3 months before	No (reference[a])	-	-	-
	Yes	1.10 (0.92 to 1.32)	<0.001	0.313
Smoking Exposure in pregnancy or 3 months before	No (reference[a])	-	-	-
	Yes	0.92 (0.76 to 1.12)	<0.001	0.358
Smoking in pregnancy or 3 months before	No (reference[a])	-	-	-
	Yes	1.22 (0.98 to 1.52)	<0.001	0.077
Gestational age at delivery	Term birth (37-41 weeks) (reference[a])	-	-	-
	Pre-term birth (<37 weeks)	1.40 (0.99 to 1.98)	0.001	0.071
	Post-term birth (>42 weeks)	1.82 (0.72 to 4.56)	0.002	0.241
GWG (kg)		0.22 (-0.98 to 1.42)	<0.001	0.717

Variable	Category		Odds ratio or coefficient (95% CI)[$]	R squared[£]	P value[$]
Mode of delivery	Spontaneous delivery (reference[a])		-	-	-
	C-section		1.20 (0.89 to 1.61)	<0.001	0.233
	Induction		1.04 (0.83 to 1.30)	<0.001	0.916
GDM	No (reference[a])		-	-	-
	Yes		1.34 (0.96 to 1.86)	<0.001	0.093
Hypertension in pregnancy	No (reference[a])		-	-	-
	Yes		1.04 (0.65 to 1.68)	<0.001	0.859
Birthweight (g)		-	-17.47 (-72.57 to 37.62)	<0.001	0.534
Infant abdominal circumference at birth (cm)		-	-0.23 (-0.52 to 0.05)	<0.001	0.109
Infant head circumference at birth (cm)		-	-0.04 (-0.21 to 0.13)	<0.001	0.616
Infant mid upper arm circumference at birth (cm)		-	-0.10 (-0.22 to 0.02)	<0.001	0.099
Infant subscapular skinfold thickness at birth (cm)^		-	-0.02 (-0.04 to 0.02)	<0.001	0.350
Infant tricep skinfold thickness at birth (cm)^		-	<0.01 (-0.02 to 0.03)	<0.001	0.836
Outcome of Birth	Livebirth (reference)		-	-	-
	Stillbirth		1.27	<0.001	0.704

[£]R squared is the deviance explained calculated by "1-(residual deviance/null deviance is the variance in variable which is explained by whether or not BMI is missing)

[&]Odds ratios provided for categorical variables where logistic regression was used, B coefficients provided for continuous variables where linear regression was used

[$]A p value less than 0.05 is considered statistically significant

*indicates a statistically significant p value

^Indicates a model where residuals were not normally distributed and needed to be transformed. Results shown are a back transformation of the regression output.

[a] Indicates the reference groups used in logistic regression for odds ratio, 95% CI and p value calculation. All other categories in variable are compared to this reference category

Note: All ratios for residual deviance to degrees of freedom in logistic regression models (categorical outcomes) were <2 (data not displayed). Therefore, the distribution of residuals was considered acceptable, and no transformations were required.

Table 64 Comparing those with complete data for GWG (n=4,362) with those with missing GWG data (n=4,246)

Variable	Category	Odds ratio or coefficient (95% CI)[$]	R squared[£]	P value[$]
Ethnicity	White British (reference[a])	-	-	-
	Pakistani	0.53 (0.49 to 0.58)	0.018	<0.001*
Maternal BMI (kg/m^2)	-	0.01 (0.00 to 0.02)	0.001	<0.001*
Maternal age (years)	-	0.44 (0.20 to 0.68)	0.002	<0.001*
Maternal height at booking (cm)	-	0.51 (0.24 to 0.78)	0.002	0.001*
Maternal weight at booking (kg)^	-	0.02 (0.01 to 0.03)	0.002	<0.001*
Gestational age at booking	-	<0.01 (<-0.01 to 0.02)	<0.001	0.160
Maternal weight at 26-28 week questionnaire (kg)^	-	0.02 (0.01 to 0.02)	0.001	0.001
Maternal mid upper arm circumference at 26-28 week questionnaire (cm) ^	-	0.001 (<-0.01 to 0.02)	0.001	0.118
Maternal tricep skinfold thickness at booking (cm)	-	0.04 (-0.45 to 0.53)	<0.001	0.865
Parity	0 (reference[a])	-	-	-
	1	0.99 (0.90 to 1.09)	<0.001	0.861
	2	0.93 (0.83 to 1.04)	<0.001	0.244
	3	1.09 (0.94 to 1.28)	<0.001	0.237
	≥4	1.11 (0.92 to 1.34)	<0.001	0.280
Place of birth of mother, father and grandparents	All born in UK- White British English (reference[a])	-	-	-
	Both parents and all four grandparents born in Pakistan	0.59 (0.52 to 0.68)	0.010	<0.001*
	Mother UK born, father and all four grandparents born in Pakistan	0.78 (0.69 to 0.87)	0.002	<0.001*
	Father UK born, mother and all four grandparents born in Pakistan	0.68 (0.60 to 0.77)	0.006	<0.001*
	Both parents UK born, all four grandparents born in Pakistan	0.78 (0.65 to 0.94)	0.002	0.007*
Previous diabetes	No (reference[a])	-	-	-
	Yes	27.91 (3.78 to 205.78)	0.086	<0.001*
Previous hypertension	No (reference[a])	-	-	-
	Yes	2.41 (1.50 to 3.87)	0.016	<0.001*
Family history of diabetes	No (reference)	-	-	-
	Yes	0.85 (0.76 to 0.94)	0.001	0.001*
Family history of high blood pressure	No (reference)	-	-	-
	Yes	0.86 (0.76 to 0.95)	0.001	0.002*

Variable	Category	Odds ratio or coefficient (95% CI)[$]	R squared[£]	P value[$]
Marital and cohabiting status	Married and cohabiting (reference[a])	-	-	-
	Not married and cohabiting	1.60 (1.43 to 1.79)	0.009	<0.001*
	Not cohabiting	1.41 (1.25 to 1.58)	0.005	<0.001*
Language	English (reference[a])	-	-	-
	Mirpuri/Punjabi/Urdu	0.65 (0.58 to 0.73)	0.007	<0.001*
Fathers Job	Employed, non-manual (reference[a])	-	-	-
	Employed, manual	0.85 (0.77 to 0.94)	0.001	0.002*
	Self-employed	0.89 (0.78 to 1.01)	0.001	0.074
	Student	0.90 (0.62 to 1.32)	<0.001	0.603
	Unemployed	0.92 (0.78 to 1.08)	<0.001	0.299
Mothers Job	Currently employed (reference[a])	-	-	-
	Previously employed	0.85 (0.77 to 0.94)	0.001	0.002*
	Never employed	0.68 (0.61 to 0.75)	0.07	<0.001*
Fathers education	5 GCSEs (reference[a])	-	-	-
	<5 GCSEs	0.93 (0.82 to 1.07)	<0.001	0.313
	A level equivalent	0.92 (0.78 to 1.07)	<0.001	0.274
	Higher education	0.85 (0.75 to 0.96)	0.001	0.009
Mothers education	5 GCSEs (reference[a])	-	-	-
	<5 GCSEs	0.98 (0.88 to 1.10)	<0.001	0.757
	A level equivalent	0.91 (0.79 to 1.05)	0.001	0.182
	Higher education	0.93 (0.82 to 1.05)	<0.001	0.242
Alcohol consumption in pregnancy or 3 months before	No (reference[a])	-	-	-
	Yes	1.62 (1.48 to 1.77)	0.010	<0.001*
Smoking Exposure in pregnancy or 3 months before	No (reference[a])	-	-	-
	Yes	1.08 (0.99 to 1.18)	<0.001	0.104
Smoking in pregnancy or 3 months before	No (reference[a])	-	-	-
	Yes	1.49 (1.34 to 1.68)	0.006	<0.001*
Gestational age at delivery	Term birth (37-41 weeks) (reference[a])	-	-	-
	Pre-term birth (<37 weeks)	5.89 (4.69 to 7.40)	0.076	<0.001*
	Post-term birth (>42 weeks)	0.53 (0.31 to 0.92)	0.008	0.023*
Mode of delivery	Spontaneous delivery (reference[a])	-	-	-
	C-section	1.67 (1.44 to 1.94)	0.009	<0.001*
	Induction	1.40 (1.25 to 1.55)	0.005	<0.001*

Variable	Category		Odds ratio or coefficient (95% CI)[$]	R squared[£]	P value[$]
GDM	No (reference[a])		-	-	-
	Yes		3.70 (3.07 to 4.43)	0.049	<0.001*
Hypertension in pregnancy	No (reference[a])		-	-	-
	Yes		1.66 (1.37 to 2.00)	0.008	<0.001*
Birthweight (g)		-	-120.16 (-143.84 to -96.48)	0.012	<0.001*
Infant abdominal circumference at birth (cm)		-	-0.17 (-0.29 to -0.05)	0.001	0.005*
Infant head circumference at birth (cm)		-	-0.26 (-0.33 to -0.19)	0.007	<0.001*
Infant mid upper arm circumference at birth (cm)		-	-0.10 (-0.15 to -0.50)	0.002	<0.001*
Infant subscapular skinfold thickness at birth (cm)^		-	<0.001(-0.01 to 0.01)	<0.001	0.899
Infant tricep skinfold thickness at birth (cm)^		-	0.001 (-0.01 to 0.01)	<0.001	0.770
Outcome of Birth	Livebirth (reference)		-	-	-
	Stillbirth		2.15 (1.18 to 3.92)	0.011	0.012*

[£]R squared is the deviance explained calculated by "1-(residual deviance/null deviance) is the variance in variable which is explained by whether or not GWG is missing

[&]Odds ratios provided for categorical variables where logistic regression was used, B coefficients provided for continuous variables where linear regression was used

[$]A p value less than 0.05 is considered statistically significant

*indicates a statistically significant p value

^Indicates a model where residuals were not normally distributed and needed to be transformed. Results shown are a back transformation of the regression output

[a] Indicates the reference groups used in logistic regression for odds ratio, 95% CI and p value calculation. All other categories in variable are compared to this reference category

Note: All ratios for residual deviance to degrees of freedom in logistic regression models (categorical outcomes) were <2 (data not displayed). Therefore, the distribution of residuals was considered acceptable, and no transformations were required

7.3.1 Maternal body mass index at booking

Table 63 compares differences in variables from the BiB Cohort according to whether or not BMI is missing. There is 6.23% of data for BMI missing; n=8,076 with BMI data and n=537 without BMI data. When comparing the demographic characteristics of women with data on BMI with those women with missing BMI data, women with missing BMI were significantly taller and weighed significantly more at booking appointment. Mothers with missing BMI were also significantly more likely to have a partner (father of child) born in the UK, while mother and all four grandparents born in Pakistan compared to all being born in the UK. Those with missing data on BMI were also significantly more likely to have previous diabetes. Although other characteristics differed, no differences reached statistical significance.

7.3.2 Gestational weight gain

Table 64 compares differences in variables from the BiB Cohort according to whether or not GWG is missing. There is 49.32% of the population in the BiB cohort with no data for GWG (complete data for GWG n=4,362, and those with missing GWG data n=4,246).

Compared with women with data on GWG, women with missing GWG were significantly less likely to be Pakistani, had a significantly higher BMI pre-pregnancy BMI, weighed significantly more at booking, and were significantly taller and older. Those with missing GWG were significantly less likely to speak Mirpuri, Punjabi or Urdu compared with English, and women with missing GWG, and their families, were significantly more likely to be born in the UK compared to outside the UK. Women with missing GWG were more likely to have previous diabetes or previous hypertension, and less likely to have a family history of diabetes or a family history of high blood pressure.

Women with missing GWG were more likely to be not married and cohabiting or not cohabiting compared with married or cohabiting. Fathers of infants whose mothers had missing GWG were less likely to be employed in a manual job compared with a non-manual job, and less likely to have higher education than have 5 GCSEs.

Mothers with missing GWG were less likely to be previously employed or never compared with currently employed. Mothers with missing GWG data were significantly more likely to have consumed alcohol in pregnancy, or three months before, and were significantly more likely to have smoked in pregnancy or the three months before.

Compared to term birth, mothers with missing GWG were significantly more likely to have an infant born pre-term, and significantly less likely to have an infant born post-term. Mode of delivery also differed significantly for those with and without GWG data; compared to a spontaneous birth, women with missing GWG data were significantly more likely to have either a C-section or an induction. Women with missing GWG were significantly more likely to have GDM and HDP, and infants born to mothers who had missing GWG weighed significantly less at birth, had significantly smaller abdominal circumference, smaller head circumference and smaller MUAC. However, there were no significant differences in infant subscapular or tricep SFT. Infants born to mothers without GWG data were also significantly more likely to be stillborn.

7.4 Discussion of Chapter 7

This chapter aimed to consider differences between the two ethnic groups in terms of exposures (maternal BMI and GWG), demographic characteristics (e.g. maternal age, parity, etc.) and outcomes. It then aimed to consider unadjusted and adjusted associations between each outcome and exposure. Finally, it aimed to look at the association between GWG and BMI considering both confounders and mediators using SEM. In this discussion section, I will consider how the BiB cohort compares to the UK in terms of ethnicity, maternal BMI and GWG. I will then go on to discuss key findings and the strengths and limitations of the chapter.

Significant interactions were identified between maternal BMI and ethnicity on the following pregnancy outcomes: GDM, pre-term birth, and infant thigh circumference at 3 years of age. This means that the shape of the association between outcome and maternal BMI was significantly different in the two ethnic groups. Compared with White British women and their infants, Pakistani women had significantly higher odds

if GDM, and infants of Pakistani women had significantly higher odds of pre-term birth (following adjustment), and significantly higher amount of thigh circumference associated with increasing BMI. There were no significant associations between either GDM or HDP and early GWG and in either ethnic group. Significant interactions were identified between GWG and ethnicity on infant tricep SFT at birth prior to adjustment only; results shows that infants of Pakistani women had a smaller increase in tricep SFT associated with a 1kg increase in GWG compared with infants of White British women. When GWG per week gestation was considered as the exposure, a significant interaction was identified between GWG and ethnicity for pre-term birth (Appendix 16, Table 1). Results showed that with increasing GWG per week infants of White British women had significantly reduced chances of being born pre-term, infants of Pakistani women appeared to have an increased chance, although results did not reach significance and confidence intervals were wide.

Results of the path analysis (SEM without any latent variables) showed that ethnicity was not found to be a significant predictor of GWG. Maternal MUAC and BMI had the largest total effect on GWG. This suggests that maternal body composition may play a larger role in determining GWG, independent of ethnicity. Importantly, decreasing GWG was associated with BMI, and increasing GWG was associated with increasing MUAC. This suggests that where body fat is stored at individual level is important for predicting GWG.

7.4.1 Comparison of the Born in Bradford cohort and UK population

In the data from the BiB cohort used for this analysis, 52.5% of women were Pakistani, and 47.5% were White British. This compares with 3.0% Pakistani and 97.0% White British in England and Wales excluding all other ethnic groups (2.0% and 80.5%, respectively, when other ethnic groups considered) (312). Compared with the 2016 Health Survey for England (HSE) data (313), in the BiB cohort, 1.8% fewer women had a BMI in the recommended range using the general population BMI criteria. There were also 2.2% fewer women with a BMI in the underweight range, 1.6% more women with a BMI in the overweight range, and 1.2% fewer women with a BMI in the obese range. Compared to the HSE data, when applying the Asian-specific BMI criteria, those with an underweight BMI remained the same.

There were now 9.9% fewer women with a BMI in the recommended range, 3.3% more women with a BMI in the overweight range and 5.2% more women with a BMI in the obese range (Table 65).

Table 65 Comparing proportions of women in BMI categories: comparing data from the BiB cohort with data from Health Survey for England 2016

	Health Survey for England, 2016* - General population BMI criteria (%)	**BiB - General population BMI criteria (%)**	**BiB - Asian specific BMI criteria (%)**
Underweight	3.4	4.2	4.2
Recommended weight	46.6	44.8	36.7
Overweight	27.6	29.2	30.9
Obese	22.4	21.2	27.6

*The age cut offs are based in the groups provided in the data given by Health Survey for England (HSE) 2016 (313), ideally it would have been 15-49, which is reproductive age as defined by the WHO (8).

GWG data in the UK is limited and there is no national data on GWG prevalence. In Europe and the United States, 20-40% of women gain more than the recommended weight during pregnancy (3). This was comparable with that in the BiB cohort (22.9% when using BMI criteria for the general population to calculate GWG, and 27.1% when using the general population BMI criteria for White British women, and Asian specific BMI criteria for Pakistani women to calculate level of GWG). A systematic review and meta-analysis of 1,309,136 women from 23 international studies (four from China, two from Korea, and one each from Taiwan and Japan, Norway, Belgium, Italy, Denmark, and Sweden) found that 23% of women had low GWG, this compared to 43% in the BiB cohort (39% when using Asian specific BMI criteria to calculate GWG) (97) (Table 66). This systematic review found 30% had recommended GWG, this compared with 34% in the BiB cohort (both when using general population, and Asian specific BMI criteria to calculate GWG) (97) (Table 66). In the systematic review, 47% had high GWG compared with 23% in the BiB cohort (27% when using Asian specific BMI criteria) (97) (Table 66). This suggests that in comparison with other countries, fewer women in the BiB cohort gained high

GWG for their BMI. This difference may be due to actual differences in GWG, but may also be explained by how GWG was measured. In the BiB cohort GWG was measured from pre-pregnancy weight to a weight measure in the third trimester. This final weight was not the final weight for the pregnancy, and so the GWG measure used for the BiB cohort was an indicator of GWG, rather than capturing total GWG.

In the BiB cohort, applying the Asian specific BMI criteria to calculate level of GWG reduced the proportion of women with low GWG by 4.7%, and increased the proportions of women with recommended and high GWG by 0.6% and 4.2%, respectively (Table 66).

Table 66 Comparing proportions of women in GWG categories; data from Goldstein *et al* (97) and data from the BiB cohort

GWG	**Data from systematic review and meta-analysis of 23 studies by Goldstein *et al* (%)**	**BiB - GWG calculated using General population BMI criteria (%)**	**BiB - GWG calculated using Asian specific BMI criteria (%)**
Low	23	43	39
Recommended	30	34	34
High	47	23	27

7.4.2 Discussion of the strengths and limitations of the analysis of the data from the Born in Bradford cohort

The data from the BiB cohort is rich as it has many well-collected variables, and has provided me with the information to investigate the association between maternal BMI, an indicator of GWG and a number of pregnancy outcomes in White British and Pakistani women. The BiB cohort provided me with a large sample size (n=11,066 prior to exclusions, and n=8,613 remained following exclusions) with a good distribution of the two ethnic groups of interest; n=4,088 were of White British ethnicity (47.46%) and n=4,525 were of Pakistani ethnicity (52.54%). This largely bi-ethnic population provided a unique opportunity for detailed assessments of the associations between MA, GAC and pregnancy outcomes in Pakistani and White British women. The large sample size is particularly important for SEM. Although the exact sample size required for SEM is dependent on model complexity and the

number of parameters in the model, which require statistical estimation. A typical sample for SEM research is around 200 cases (314). One of the limitations is that despite this large sample size, there was insufficient data for stillbirth, which is a rare outcome, and when looking at GWG as a categorical exposure (low/high compared with recommended) there were very small numbers of other outcomes in these groups. This lead to wide confidence intervals, and caution should be applied when interpreting these results. Missing data for exposure variables was also an issue, in particular GWG. For maternal BMI there was very little missing data (6.23%), and there were very few significant differences in demographic characteristics between populations with and without BMI data (i.e. women with missing BMI were significantly taller, weighed significantly more at booking, were significantly more likely to have a partner born in the UK, significantly more likely that mother and all four grandparents were born in Pakistan compared to all being born in the UK, and significantly more likely to have previous diabetes). Unlike maternal BMI, there was a large proportion of missing data for GWG; 49.32% of the population in the BiB cohort had no data for GWG. This meant that there were many significant differences in between those with and without missing GWG data in terms of demographic characteristics (Chapter 7, Section 7.3, pgs.277-285). One possible way of dealing with missing data is MI. MI is known generally as a relatively flexible method of dealing with unavoidable missing data in epidemiological research (291). However, MI requires that the data is either missing completely at random, or missing at random (as discussed in section 6.2.2, Chapter 6). This means that either the data on the variable of interest is missing randomly (for example because the scales were broken and so the women could not be weighed) or that the missing data on one variable is sufficiently explained by other variables in the dataset. An example given for this by Sterne *et al* is that individuals with high SES are more likely to have their blood pressure measured and less likely to have high blood pressure compared with individuals with low SES (291). In this PhD project, an *a-priori* decision was made not to use MI with the advice from a statistical expert. This was done as I could not be sure that this missing data meets the assumptions for MI (data missing completely at random or at random) and therefore to minimise the bias caused when MI is used where data is missing not at random.

For the BiB cohort, weight in the third trimester was retrospectively extracted from case notes and as it is not a routinely collected measure (NICE advise against

routine monitoring (45)), it is expected to have higher level of missing data than other variables. It is likely some of the data is missing at random; the clinicians just didn't record it because there are no guidelines requiring its measurement. It is also possible that there is a reason the measurement was not taken. It is possible that the data is missing at random; for example, GWG in the missing population might be higher as significantly more White British women were missing data compared with Pakistani women and White British women on average have higher GWG. However, there is no way of knowing this for sure. It is also possible that the data is missing not at random, and there is a difference in the observed and unobserved values of GWG based on either itself (for example women with high GWG refused to be weighed because they had high GWG, or differences are caused by a variable not recorded in this dataset). It may be that clinicians did not always take the weight measurement, or that they only did it for women where they had time. Data from the BiB cohort has shown that GDM was more prevalent in women with missing GWG data, so it is also possible that women with GDM or other complications in pregnancy were referred to specialists and so did not have the measurement taken like the rest of the cohort. This reasoning as to why the data might be missing is all hypothetical. In future, where possible recording reasons why data is not recorded would be useful to gain a better understanding of the study population, and to ease decisions regarding how to deal with missing data.

Missing data may lead to loss of precision and bias but are unavoidable in epidemiological research (315). Ideally, where there is uncertainty about how the data is missing, and a possibility that MI might be appropriate, both complete case analysis and MI should be done. Results from both MI and complete case analysis should then be presented and discussed. However, to complete this project within the specified timeframe, it was not possible for me to do both. As mentioned previously, I only carried out a complete case analysis. As there was so much data missing for GWG, this may have limited the results found. Independent of why the data were missing, compared to women with GWG data, women with missing GWG data appeared to be higher risk women. By this I mean that they were more likely to have previous diabetes or previous hypertension, they were significantly more likely to have consumed alcohol in pregnancy, or three months before, and were significantly more likely to have smoked in pregnancy or the three months before. They also had higher risk of some pregnancy outcomes; compared to a spontaneous

birth, women with missing GWG data were significantly more likely to have either a C-section or an induction. Women with missing GWG were significantly more likely to have GDM and HDP. Having higher risk women missing from the analysis means that the results for GWG may have been underestimated (i.e. the risk I found may be lower than if the higher risk women had been included in the analysis), and this should be taken into consideration when interpreting the results for GWG as an exposure.

There are also strengths and limitations relating to the data collected. As the BiB cohort is embedded within clinical routine it relies on the support from clinical staff to take and record some of the measurements (316) and it has been previously demonstrated that the measurements taken by the clinical staff are valid and reliable (317, 318). However, as this dataset was not collected for the purposes of this project analysis was limited to the variables available. For example, I was also not able to look at all outcomes of interest, as they were not available either in the dataset, or to me, such as congenital anomalies. In addition there are limitations relating to the measure of GWG available to me. I was only able to calculate GWG by subtracting the weight at the booking appointment from the weight in the third trimester, this measure does not quite reflect the total GWG (i.e. subtracting measured preconception weight from final pregnancy weight). Using this measure of GWG may have underestimated the results as it is likely to be slightly lower than true total GWG. While I was able to consider GWG per week which allowed me to account for length of gestation (but not the rate of weight gain). In future, it is recommended that the most accurate way to measure GWG is to calculate total GWG, subtracting final weight from pre-conception weight, using measured weight rather than self-reported, and adjust for the length of gestation (319). If also considering GWG per week gestation, it is important to take into account the rate of weight gain.

A strength of the analysis itself, is the extra detail provided by the SEM analysis. SEM adds to the regression analysis by showing the detail of the direct and indirect predictors of GWG in the BiB cohort. This information may be useful for informing targeted interventions to reduce GWG in this population. This is important because, although regression analysis showed that there was no significant ethnic difference in the shape of the association between GWG and the majority of pregnancy outcomes, there were significant associations within the ethnic groups. For example; GWG was

significantly associated with higher PPWR at 3 years for Pakistani women, meaning that these women are at a higher weight after pregnancy, and may then enter the next pregnancy at a higher BMI. Increased maternal BMI was found to be significantly associated with a number of adverse pregnancy outcomes, for example; GDM and pre-term birth. So although reducing GWG may not impact on the outcomes for this pregnancy, it may mean that the mother enters the next pregnancy at a BMI in the recommended range.

Another point for discussion is how representative the population is, and how generalisable the results are. While the population in the BiB cohort is representative of the population in Bradford when the data was collected (3), Bradford is not representative of the rest of the UK due to the high levels of poverty (67.8% of the population are in the most deprived IMD quintile) (3).This means also that the White population in Bradford is a high risk group compared with the rest of the UK. This may have diluted the effect size observed as both ethnic groups in Bradford are higher risk populations. This means that the difference between the two groups may be smaller than that where there is an ethnic difference in SES. This limits the generalisability of the findings as in other areas of the UK White British populations tend to be lower risk. While there are similarities between Bradford and other cities with high levels of ethnic minority and immigration both in the UK and worldwide (3), caution must be applied when interpreting these results, and applying them to other populations. This data was also collected between 2007 and 2011, and although is still being followed up; the baseline data may be slightly outdated. Therefore, while these results are applicable to those participants from the BiB cohort who were included in my analysis, they may not be applicable to other populations. In conclusion, while there are significant ethnic differences in the shape of the association between pregnancy outcomes: GDM, pre-term birth, and infant thigh circumference at 3 years of age and maternal BMI there were no significant ethnic differences identified for GWG as an exposure following adjustment for confounders. This this was still true when using the Asian specific BMI criteria to calculate level of GWG. SEM analysis suggested that ethnicity was not a significant predictor of GWG, and that maternal body composition may play a larger role in determining GWG, independent of ethnicity.

Chapter 8. Discussion

This PhD project aimed to investigate the relationship between UK ethnic groups (White and South Asian), MA, GAC, and short- and long-term pregnancy outcomes for both mother and child. In the discussion below, I have briefly summarised the main findings from each of the thesis chapters and placed them in context with the most relevant literature. I have also discussed the overall strengths and limitations of the methodology used; the strengths and limitations of each chapter have been discussed within the respective chapters. I then provide recommendations for future research, and for policy and practice in the UK.

8.1 Summary of findings

In Chapter 1, I highlighted that obesity is a growing global health problem for both adults and children (1), and is linked to a number of chronic health conditions such as type II diabetes, cancer, and cardiovascular disease (1, 2). Obesity is also a concern in pregnancy, and is linked to a number of adverse health outcomes for both the mother (for example; GDM) and infant (for example; pre- and post-term birth) (62-64). My introduction also considered GWG, and how outcomes for the mother (for example; PPWR) and the infant (for example; birth weight) are associated with GWG. In the USA, the IoM have developed guidelines for recommended GWG for BMI (underweight, recommended weight, overweight, and obese) based on a review of evidence from a number of ethnic groups (Non-Hispanic White, Black, Hispanic, and Asian where the Asian population reflected a more eastern Asian population i.e. Chinese, Japanese, Phillipino etc.) (94). Evidence shows that a number of other countries also have guidelines for GWG, and that in about half of these countries, the guidelines are the same as, or similar to, the 2009 IoM GWG guidelines (320). Currently, the UK does not have GWG guidelines. Although guidelines for weight management during pregnancy have recently been reviewed, NICE in the UK have decided not to adopt the IoM GWG guidelines due to the lack of evidence relevant to UK populations, in particular for UK ethnic groups (47, 51).

In the UK, the second largest ethnic group is South Asian (Pakistani, Indian, Bangladeshi) (169, 170). Evidence shows that South Asian women have a higher risk of obesity related outcomes, for example type II diabetes, at a lower BMI than the

White population and that this difference in risk is predominantly due to differences in body composition, including body fat distribution (321). This has led to the development of BMI criteria for Asian populations (5, 43). Evidence also suggests that this difference in risk may extend to pregnancy; for example, South Asian women have been found to have a higher risk of GDM at a lower pre-pregnancy BMI compared with the White women (322). This may also be the case for weight gained in pregnancy (i.e. GWG); there may be a higher risk of adverse outcomes for mother and infant at a lower weight gain in South Asian women compared with White women. This PhD research, therefore, aimed to investigate the relationship between UK ethnic groups (White and South Asian), MA, GAC, and short- and long-term pregnancy outcomes for both mother and child.

In Chapter 2, I highlighted the methodology I used for this PhD project which is based on SEM methodology (using existing theory and evidence to generate a conceptual model which is then tested using data), and used a mixed-methods study design. This methodology allowed me to use existing evidence and theory to develop an evidence-based conceptual model of associations between MA, GAC and pregnancy outcomes. The model was developed in three stages; stage 1: systematic review, stage 2: framework based synthesis and stage 3: expert opinion. This model was then used to guide all data analysis. Although full SEM analysis was only carried out for GWG as an outcome, the SEM methodology used in this thesis provided a robust skeleton for the development of an analysis plan using existing data. This allowed me to immerse myself in the published literature, and use this literature to develop the evidence-based conceptual model.

In Chapter 3, I carried out a systematic review of the association between pregnancy outcomes, MA and GAC in South Asian and White women. Results showed that in South Asian women, GAC, HDP, GDM, mode of delivery, birth weight, stillbirth, congenital anomalies, weight retention and postnatal IGT were all associated with MA. GDM was associated with GAC, and both MA and GAC appeared to have a combined effect on GDM and PPWR. The evidence also suggests that there was no significant association between GAC, gestational age at delivery, PPH, admission to the NICU and perinatal death and MA. Since this systematic review was carried out, a review with an updated search (searching finished July 2017) has been published (186). This updated search identified three more studies that were relevant for

inclusion (322-324); one each from Canada (324), Australia (323) and the UK (322). These three studies considered the following; the first study considered maternal weight (kg) and maternal BMI (kg/m^2) as exposures and GWG (kg) as an outcome (324).

Findings showed that there was no significant difference in GWG relative to pre-pregnancy weight for South Asian compared with White women (324). The second study considered maternal BMI (kg/m^2) as an exposure and the presence or absence of diabetes during pregnancy, with the risk equivalent BMI thresholds for each ethnic group (322). Findings showed that, for South Asian women, a BMI of 21kg/m^2 was the risk equivalent to that of a BMI of 30kg/m^2 for White women, again suggesting that South Asian women have a higher risk of GDM at a lower BMI than White women (322). Finally, the third study considered maternal BMI (kg/m^2) as the exposure and the following outcomes; gestational hypertension, pre-term birth, shoulder dystocia, PPH, mode of delivery, birth weight, fetal compromise, admission to NICU, any perinatal morbidity and stillbirth (323). Findings showed that the odds of gestational hypertension, GDM, shoulder dystocia, unplanned C-section, macrosomia (>4kg) fetal distress, admission to NICU and any perinatal morbidity were all positively associated with maternal obesity in South Asian women, and SGA was negatively associated with maternal obesity (323). Of all outcomes considered, there were only significant interactions between ethnicity and maternal obesity on gestational hypertension, GDM and shoulder dystocia (323). The addition of the results of these three studies did not change the overall findings of my systematic review: there is limited evidence for GAC as an exposure, and in South Asian women, and limited evidence for longer-term outcomes associated with both MA and GAC. However, these new results did highlight shoulder dystocia, fetal distress, admission to NICU and any perinatal morbidity as other potential outcomes of interest associated with MA in South Asian women.

In Chapter 4, I carried out a mixed methods systematic review to identify confounding and mediating variables for the associations between pregnancy outcomes MA and GAC identified in Pakistani women. This chapter provided me with evidence of which confounders I should include in adjustments made in the statistical analysis. It also provided me with evidence of any mediators I could explore using SEM (for example evidence showed that GDM is a mediator of the association between MA and GAC).

This chapter also provided me with additional pregnancy outcomes of interest that were identified through statistical adjustments in papers included in the framework based synthesis. These additional outcomes were; cord blood insulin and leptin levels, maternal mental health in pregnancy, maternal mortality, breastfeeding and longer term infant anthropometric measurements in addition to infant BMI (obesity in infants was identified as an outcome of interest by the evidence in the IoM guidelines (94)).

Chapter 5 describes the methods and results from the expert opinion stage, which provided an additional confirmatory step to model development allowing me to get opinions from experts in the field. This final stage of model development highlighted that the experts felt that that the conceptual model of hypothesised associations between MA, GAC and pregnancy outcomes in Pakistani women was theoretically accurate. An additional outcome was also identified: maternal and infant blood pressure in the longer term (i.e. post-partum blood pressure). Chapter 5 also described the final conceptual model used to guide data analysis of data from the BiB Cohort.

Chapter 6 described the statistical methods used to analyse the data from the BiB cohort. In brief, this involved descriptive statistics, generalised linear model regression analysis (logistic for categorical outcomes and linear for continuous outcomes) with interaction terms added to investigate the ethnic difference in the shape of the association between each exposure and each outcome, and SEM for GWG as an outcome. As I did not use any latent variables in the SEM analysis, this can also be described as a path model.

In Chapter 7, I presented the results of the analysis of the data from the BiB cohort. Findings showed that, on average, Pakistani women had a lower BMI and lower GWG compared with White British women. In unadjusted analysis, Pakistani women were also less likely to have HDP or C-section, and more likely to have GDM and breastfeed. Pakistani women also had higher PPWR at three years compared with White British women. Infants of Pakistani women were less likely to be born post-term, and were smaller at birth compared with infants of White British women for all anthropometric measures considered (birth weight, abdominal circumference, head circumference, mid-arm circumference, subscapular SFT and tricep SFT). At three years of age, infant abdominal circumference, tricep SFT and thigh circumference

were significantly lower for infants of Pakistani women compared with infants of White British women but there were no significant differences in weight or subscapular SFT. Regression analysis considering the association between pregnancy outcomes and exposures BMI and GWG found that there were ethnic differences in the shape of the association pregnancy outcomes: GDM, pre-term birth, and infant thigh circumference at three years of age, and maternal BMI. However, there were no significant ethnic differences in the association between any pregnancy outcome and GWG following adjustment for confounders. SEM identified that although ethnicity was a significant predictor of maternal BMI, it was not a significant predictor of GWG. Maternal MUAC and BMI had the largest total effect on GWG.

8.2 Strengths and limitations

SEM methodology is more than just a statistical analysis method; prior to carrying out any statistical analysis, it ensures that the researcher immerses themselves in the topic, and familiarises themselves with the existing evidence base. This knowledge is then used to develop a conceptual model of the evidence-based associations between variables of interest. This approach uses the existing evidence and theory to shape the data analysis. In this PhD project, not only has existing literature been used, but an existing dataset also. The SEM methodology used in this PhD project maximises the use of existing data, is financially efficient and meets the MRC strategic aims of furthering science and understanding, in particular the aim to encourage greater use of existing data (325).

The approach used to develop the conceptual model was rigorous and thorough. Each stage of model development built on the last and tried to overcome any limitations. The systematic review identified associations between exposures and outcomes in the published literature. This review lacked evidence of potentially confounding mediating variables, and there was the potential for associations that had not been published. The framework based synthesis, therefore, identified confounding and mediating variables, and also any other potential outcomes through adjustments (for example, where researchers had adjusted for maternal BMI in a regression between physical activity and mental health in pregnancy, suggesting that maternal BMI is associated with mental health in pregnancy). Despite this, using

existing evidence and theory to guide conceptual model development meant that there may have been limitations relating to gaps in the literature (by which I mean that not all possible outcomes have been investigated by existing published literature). I used an expert panel to try to combat this. Ideally, I would also have included BiB participants on the expert panel but due to time limitations, it was not possible. Despite the steps taken to combat missing any associations of interest, the updated systematic review identified three outcomes of interest in South Asian women; shoulder dystocia, fetal distress, admission to NICU and any perinatal morbidity.

The model development process was rigorous. I identified both outcomes of interest, and also confounding and mediating variables. This involved two systematic reviews and a validation study. This findings from these studies were then used to develop conceptual models for each outcome. This produced complex conceptual models for each outcome. The complexity of the conceptual models developed also meant there were outcomes identified (GDM, HDP, birth weight, gestational age at delivery, stillbirth, mode of delivery, PPWR, breastfeeding and infant anthropometrics) in the model development process that have not yet been explored using SEM. This was due to the complexity of conceptual models developed, availability and quality of data for confounding and mediating variables, and the time required to complete this complex analysis. However, the evidence-based models developed can now be used to guide future research, and could also form the basis for future causal analysis.

These evidence-based models also provided me with a form of causal diagram for each outcome of interest. I found that causal diagrams were a useful way of determining which variables to adjust for in regression analysis, and can also be used to determine which variables are confounders and mediators for SEM analysis (303). Taking the time to consider whether variables were mediators or confounders of associations was an important step in model development, both for SEM, which considers direct and indirect effects, and regression analysis which, considered total effects. For regression analysis, including a mediator in adjustments can increase bias (298). This is sometimes known as “overadjustment”, although this term is poorly defined (298). Including a mediator or a variable on the causal path between exposure and outcome, in an adjustment for the total effect of an exposure on an outcome may increase bias. An example of this is the association between maternal

smoking and neonatal morality, where adjusting for birth weight decreases the risk ratio, rather than raising it as you would expect (298). This is thought to be because smoking is likely to affect an unmeasured factor that effects both neonatal mortality and birth weight separately (298). Unlike in the analysis of total effects, overadjustment bias is not induced where there is a decomposition of effects (i.e. looking at indirect and direct effects), for example in SEM where the correct statistical methods are applied (298). I was, therefore, able to ensure that bias was minimised in regression analysis by not including mediators in my adjustments, and then was able to go on to consider both confounders and mediators of GWG through direct and indirect paths using SEM.

Another strength of this PhD research is the BiB dataset itself. It is a unique dataset. As discussed in Chapter 7, the BiB dataset has many well-collected variables, a large sample size and a good distribution of Pakistani and White British women. The dataset is also unique in that both ethnic groups live in a deprived area. The association between ethnicity and maternal obesity is complicated by the interrelationship between ethnicity and socio-economic group (58, 59). Investigations into whether disparities in health status are due to either “ethnicity and social class”, or “ethnicity or social class” are complicated by this overlap between ethnicity and socioeconomic status (162). However, for this PhD project, this overlap is minimised by the fact that both ethnic groups live in the same area, and any small differences in SES have been accounted for by adjustments carried out in the statistical analysis. Another strength of using the data from the BiB cohort was that it enabled communication and collaboration with the BiB team, enriching my PhD work, particularly in terms of the expert opinion stage of model development.

8.3 Policy and practice

My findings suggest that there is little ethnic difference in the association between GWG and pregnancy outcomes investigated for Pakistani and White British women living in Bradford, in both continuous and categorical analysis. This was also true when calculating level of GWG using the BMI criteria for South Asian women. Due to the lack of ethnic difference, these findings suggest that the IoM guidelines could be relevant for this Pakistani population in the UK. However, due to data availability, the measure of GWG used may have underestimated the results, and I cannot be sure

that the association will remain the same if final weight in pregnancy was used to calculate GWG rather than weigh in the third trimester. Therefore, before I can make clear recommendations for policy and practice, and we can say whether the IoM guidelines for GWG should be implemented in the UK, or whether there should be routine monitoring of, and support for weight change during pregnancy, more research is needed. In particular, we need to examine the association between pregnancy outcomes and GWG for other UK ethnic groups, including other South Asian groups (Indian, Bangladeshi etc.). We must also consider how pregnancy outcomes are affected by other measures of GAC to reflect differences in body composition. The association between childhood anthropometrics, and measures of post-partum anthropometric retention (in addition to PPWR) and MA and GAC should also be explored further in ethnic groups relevant to the UK population.

8.4 Future research

Outcomes were identified (GDM, HDP, birth weight, gestational age at delivery, stillbirth, mode of delivery, PPWR, breastfeeding and infant anthropometrics) in the conceptual model development that have not yet been explored using SEM. This was due to the complexity of conceptual models developed, availability and quality of data for confounding and mediating variables, and the time required to complete this complex analysis. Conceptual models developed for these (both short-, and long-term) pregnancy outcomes (Appendix 9 pgs.355-357) should be used to inform future research; they could be investigated using SEM and could also be used as a basis for causal analysis for example using directed acyclic graphs (DAGs) and Daggity software. There were also some additional pregnancy outcomes identified as relevant by model development. However, due to availability[25] of data from the BiB cohort, I was not able to explore the associations between MA, GAC and some pregnancy outcomes. In particular, congenital anomalies, maternal mental health in pregnancy, maternal mortality, and long term maternal and child blood pressure.

Congenital anomalies were highlighted as an outcome of interest by my systematic review. Pakistani women have a higher risk of congenital anomalies compared with White women (200). The increased risk in Pakistani women is partly due to higher

[25] This was both due to the availability of variables in the dataset, and due to permissions accessing some of the variables.

rates of consanguinity in this population (200). However, it is important to investigate other possible risk factors including MA measures and GAC. It is also important to investigate how congenital anomalies might act as a mediator between MA measures and other pregnancy outcomes. There is a temporal issue with investigating the association between congenital anomalies and GAC, i.e. which occurred first. It might be that it is only possible to look at the association between early GAC and congenital anomalies, rather than the total GAC.

Mental health in pregnancy was highlighted as an outcome of interest by my framework based synthesis. Mental health in pregnancy has been found to be associated with maternal BMI (although mental health prior to pregnancy may affect this association, and in turn may influence maternal BMI)(240), and mental health in pregnancy may affect GAC. The association between mental health in pregnancy and both MA and GAC, and whether or not maternal mental health acts as a mediator of the association between MA and GAC, along with other pregnancy outcomes should be investigated. Maternal mortality was also highlighted as an outcome of interest by my framework based synthesis. The risk of maternal mortality has been found to be increased in ethnic minority women in the UK (326), whether this risk if affected by MA and GAC should be explored further. Maternal and child blood pressure after pregnancy were identified as outcomes of interest by the expert opinion phase of model development. Whether or not these are associated with MA and GAC should be considered.

Although I was able to do some analysis for stillbirth as an outcome, it was limited due to the small sample size (stillbirth n=49; n=17 for White British, n=32 for Pakistani). Future research requires larger samples to enable sufficient power to detect an effect size. This is also the case for other rare outcomes such as congenital anomalies, and when considering gestational age at delivery in subgroups; e.g. extreme pre-term birth; very pre-term birth, pre-term birth, early term, term, late term, prolonged pregnancy and post-term birth, as increasing the number of categories, decreases the sample size in each. There is also an issue around determining how data are missing, particularly for variables that are poorly recorded. In future, where possible, a reason for why data is missing should be recorded. This information would allow researchers to make an informed decision on how data is missing, rather than to make assumptions which potentially incur bias (for example, assuming their

data is missing completely at random, when in fact it is not). It may also be beneficial to run both a complete case analysis (with discussion of how the populations with and without missing data differ) and MI, and report clear methodology and results for both methods comparing findings and discussing the strengths and limitations of each.

This PhD research investigates GWG as an exposure and an outcome. Evidence suggests that there is little success in altering the risk of adverse pregnancy outcomes by reducing GWG through lifestyle and dietary interventions in pregnancy (143). Individual patient data meta-analysis of 12,526 women from randomised trials suggests that reduction of maternal and infant composite outcomes (maternal included pre-eclampsia/pregnancy induced hypertension, GDM, pre-term birth, elective and emergency C-section, and infant included intrauterine death, SGA, LGA and admission to NICU) (327). Despite this, risk of C-section and amount of GWG significantly reduced for women receiving the interventions (327). While GWG may not be a significant factor in predicting adverse pregnancy outcomes, this period between pre-conception and conception through to the child's early years is an important window in terms of behaviour change (319, 328). Evidence shows that women who enter pregnancy healthy are more likely to have a pregnancy with positive outcomes for mother and infant(328). These interventions provide a key window of opportunity for providing health education to the mother and, in the longer term, infant. More research is needed looking at interventions improving women's health prior to conception, and also at how we can support involvement of the women's partner in behaviour change from pre-conception.

It is also important to note that existing research does not consider the effects of these interventions on measures of GAC other than GWG, and how these other measures of GAC effect pregnancy outcomes. Future research also needs to explore other measures of GAC (i.e. change in SFT and MUAC), whether these measures differ between ethnic groups, how these measures affect pregnancy outcomes, and whether the association between different measures of GAC and pregnancy outcomes are different between ethnic groups. Overall, GWG may not be significantly associated with risk of adverse pregnancy outcomes. However, GWG isn't just made up of maternal fat mass; it is also fetal factors (the fetus and amniotic fluid) and other maternal factors (total body water). These other anthropometric measures are better

indicators of body fat, and fat distribution than GWG itself. Therefore, it is important that these measures are investigated further; particularly how they are associated with pregnancy outcomes.

There is a need for research to investigate maternal anthropometric measures and pregnancy outcomes in other South Asian populations, for example; Bangladeshi and Indian populations. Within the South Asian population there is heterogeneity between the populations (i.e. Bangladeshi, Pakistani, Indian); for example in relation to first trimester maternal obesity (18), blood pressure (19), and risk factors for coronary heart disease (20). While my findings represent a UK Pakistani population living in Bradford, the findings cannot be applied to other South Asian women in the UK. There is also a need to investigate the influence of the place of birth of the mother and father, and grandparents and also the length of time spent in the country of settlement (length of time may only apply to those who were born in another country and have moved to country of settlement).

There are also issues around terminology in this area of research. For example; place of birth of parents and grandparents is sometimes referred to as “generation status” i.e. first generation migrants are those who have migrated from e.g. Pakistan and now reside in e.g. UK; second generation migrants are those who are born to first generation migrants; third generation migrants are born to second generation migrants and so on. “Generation status” will not be used here as second and third generation “migrants” are in fact not migrants at all as they are born in country of settlement. This is not the only issue with terminology in research involving ethnicity; there are also issues in the use of individual words, and definitions used to define populations (e.g. White, Caucasian or Anglo-Celtic, South Asian, Asian, Pakistani) (329). Going forward, it is important to use the correct terminology, and definitions, to enable better comparisons to be made. Until these terms are clarified, it is best to think about the terminology used, clearly define any terms used, and ensure they are based on ethnicity and not race.

It is also important that future research developing causal or theoretical models includes patient and public involvement (and engagement (PPI(E)), and uses more rigorous and systematic methods for collating thoughts and opinions from experts. Engaging the public in model development would be a useful stage in addition to expert opinion, especially where there are cultural differences between the

researchers and the study population. One way of incorporating PPIE into study design could be to provide a validation step in model development, For example, a systematic review could be carried out to identify associations, and confounders and mediators of associations of interest. PPIE could then be used to get feedback and thoughts on the model developed from the systematic review from, including advice on any missing variables and associations between variables. A model validation step could then be to use a Delphi survey of experts in the field to come to agreement about the final causal diagram to be tested in the data, which could then be further validated by a secondary survey with a different panel of experts. A Delphi survey is a structured communication method useful for theory building, which relies on a rigorously selected panel of experts familiar to the field of research (330). The challenge of achieving attendance of all members in the expert panel limits this method (331). However, the method provides a structured and rigorous approach to recording the decision making process (332).

8.5 Conclusions

Systematic review evidence highlighted nine outcomes of interest when considering MA and GAC as exposures in Pakistani and White British women. Outcomes for the mother were HDP, GDM, mode of delivery (C-section and induction), breastfeeding at 6 months, and PPWR. Outcomes for the infant were outcome of birth (i.e. stillbirth or livebirth), gestational age at delivery (pre-term birth <37 weeks, and post-term birth ≥42 weeks), infant anthropometrics at birth (birth weight, abdominal circumference, head circumference, mid-arm circumference, subscapular SFT and tricep SFT), and infant anthropometrics at 3 years of age (weight, abdominal circumference, subscapular SFT, tricep SFT, and thigh circumference). Analysis of data from the BiB cohort found significant ethnic differences in the shape of the association between GDM, pre-term birth, and infant thigh circumference at 3 years of age, and maternal BMI. There was little ethnic difference in the shape of the association between any pregnancy outcomes and GWG. Ethnicity was not found to be a significant predictor of GWG in the BiB cohort. More research is needed to consider different measures of MA, and measures of GAC, and considering other South Asian ethnic groups.

Appendices

Appendix 1. The Born in Bradford multi-ethnic pregnancy cohort study

This PhD project will involve analysis of data from the Born in Bradford (BiB) cohort. This section will describe Bradford and the BiB cohort, discuss some of the strengths and limitations of the data from the BiB cohort and explain why the BiB cohort is suitable for this PhD project.

About Bradford

Bradford District is in West Yorkshire in the north of England. It is the fourth largest metropolitan district in England in terms of population, after Birmingham, Sheffield and Leeds although the District's population growth is lower than other major cities (333). In June 2017 an estimated 534,300 people live in Bradford district (334). This was an increase of 3,100 people (0.6%) from the previous year; the rate of increase was similar to the previous year (334).

The population increase between 2016 and 2017 was due to what the Bradford metropolitan district council term "natural change"; there were 3,600 more births than deaths in the time, and a large number of people leaving Bradford to live in other parts of the UK (334). Data shows that in 2015/16, the net international migration (i.e. to and from outside the UK) was 2,600, and the net internal migration (i.e. inside the UK) was -2,300 (334).

The population in Bradford is ethnically diverse; the district has the largest proportion of people who identify themselves as Pakistani in England at 20.3% and 63.9% of the population identify as White British (334). Nearly a quarter of the population are Muslim (24.7%), just under half are Christian (45.9%) and just over a fifth describe themselves as having no religion (20.7%) (334).

Bradford's urban areas are amongst the most deprived in the UK (316, 335). In Bradford in 2016, 67.3% of 16-64 year olds were in employment (334). This was significantly lower than the national rate at 74.3% and meant that one in three adults were not in employment (334). Evidence shows that deprivation in Bradford in 2014 using IMD 2010 was higher than the rest of England (336). Evidence also shows that that were a higher proportion of residents in the most deprived IMD quintile than the

rest of England (336) and that the most deprived residents are found in the more urban areas clustering around Bradford city centre (336).

Deprivation in Bradford is associated with a wide range of public health problems. Bradford's infant mortality rate (IMR) is one of the highest in England and Wales, with between 60 and 70 babies dying every year (337). Childhood obesity is also higher in Bradford, in 2012 20.6% of year six children were classified as obese (336) compared to the national average which was 19.1% in 2013/14 (338). Within Bradford, a third of children with obesity live in the most deprived quintile compared to 10% who live in the least deprived quintile. Obesity is also a significant public health problem in Bradford, in 2012 in 26.7% of adults were classified as obese, this was higher than the 2013 measurement of 24.9% for the rest of England (339). In addition, estimated levels of adult smoking, physical activity, GCSE attainment, breastfeeding and smoking at time of delivery are worse than the average for England (336). Life expectancy in Bradford is lower than the average for England; in the most deprived areas it is 9.6 years lower than the national average for men and for women it is 8.7 years lower (336)

Between 2007 and 2011 when the BiB data was collected; around 20% of the population in Bradford was South Asian[26], 90% of whom were of Pakistani origin (2, 6), almost all being from the Mirpur region of Pakistan (335). Among those of Pakistani origin there was a three-generation community which maintains close links with Pakistan (340). Despite the fact that around 20% of the population were Pakistani, just under half of the babies born in the city had parents of Pakistani origin; 50% of babies born were White, 44% Pakistani, 4% Bangladeshi and 2% other (316). The high proportion of babies of Pakistani origin is thought to be due to the relatively young age of the population of Pakistani origin and their higher fertility rates compared to the White British population (316). Sixty percent of the babies born in Bradford were born into the poorest 20% of the population in England and Wales, based on the IMD (316). Infant mortality in Bradford has consistently been above the national average of 5.5 deaths per 1000 live births at 9.5 deaths per 1000 live births, with babies of Pakistani origin having an even higher infant mortality rate of 12.9

[26] South Asian is referring to people from Pakistani, Bangladeshi, Indian or other South Asian origin

deaths per 1000 live births. In addition, the levels of congenital anomalies and childhood disability are among the highest in the UK (200, 341-347).

BiB cohort

BiB was established in 2007 due to the rising concerns relating to increased rates of childhood morbidity and mortality in Bradford (316). BiB is a multi-ethnic birth cohort study which aims to examine the genetic, nutritional, environmental and social factors that impact on health and development during childhood, and the long-term effects into adult life (316). The main goal of BiB is to develop hypotheses that can be tested for health and social interventions to improve both childhood and adult health (316). Broad aims of the BiB project include describing the health and ill health within a multi-ethnic and economically deprived population (316). Identifying modifiable or causal pathways that lead to ill health or promote well-being (316). Designing, developing and evaluating interventions which promote health (316). Providing a model for integrating epidemiological, operational and evaluative research into health related systems including the National Health Service (316), and also to build and strengthen local research capacity in Bradford (316).

BiB Methods

Women were eligible for recruitment if they planned to give birth at Bradford Royal Infirmary (335), all babies born from March 2007 were eligible to participate (335) and fathers of babies who were recruited into the cohort were also eligible for inclusion (335). The recruitment phase of this cohort ended in December 2010 (335). The majority of women were recruited at their 26-28 weeks gestation oral glucose tolerance test (OGTT), a minority did not attend for OGTT and were recruited by other means (e.g. hospital contacts) (316). Babies were recruited at birth and fathers were recruited whenever possible during the antenatal period or soon after birth. The aim was to recruit 10,000 women, their babies and the babies' fathers (335).

Between 2007 and 2011, detailed information on lifestyle factors, environmental risk factors, socio-economic factors, family trees and ethnicity[27], and physical and mental health was collected from 12,453 women with 13,776 pregnancies and 3448 of their partners (316). At recruitment, women had blood samples taken, completed an administrator completed semi-structured questionnaire, and had height, weight, arm circumference and tricep thickness measured, and fathers had saliva samples taken and self-completed a questionnaire (335). At birth, the babies had umbilical cord blood samples taken, then within two weeks of birth they had head, arm and abdominal circumference measured in addition to subscapular and tricep skinfold thickness measurements (335). Participants were allocated unique identification numbers and NHS numbers have been used to access routine data and also for data linkage (335).

BiB Cohort profile summary

Table 1 summarises the characteristics of the BiB cohort at baseline (at the first stage of data collection following recruitment). The majority of the population are Pakistani (45.0%), aged between 25-29 years of age (32.6%), are nulliparous (38.4%) and living in the most deprived quintile of the Index of multiple deprivation (67.8%) (316).

[27] Ethnicity is a socially constructed phenomenon and the definition differs across different studies. In the context of this PhD project data on ethnicity were collected by BiB and ethnicity has been self-defined by the mother.

Table 1 Baseline characteristics of the BiB cohort

	n	%
Maternal ethnicity		
Pakistani	5127	45.0
White British	4488	39.4
White other	303	2.7
Asian other	326	2.9
Indian	438	3.8
Black	249	2.2
Mixed	217	1.9
Other	199	1.7
Mother's age (years)		
<20	978	7.2
20-24	3692	26.8
25-29	4484	32.6
30-34	2985	21.7
35-39	1376	9.9
≥40	249	1.8
Residence deprivation (IMD 2010)		
1 (most deprived)	9347	67.8
2	2356	17.1
3	1374	10.0
4	312	2.3
5 (Least deprived)	207	1.5
Missing/outside Bradford area	177	1.3
Parity		
0 (nulliparous)	5073	38.4
1	3683	27.9
2	2175	16.4
3	1083	8.2
≥4	736	5.6
Missing	468	3.5

Adapted from Wright J, Small N, Raynor P, Tuffnell D, Bhopal R, Cameron N, et al. Cohort profile: The Born in Bradford multi-ethnic family cohort study. International Journal of Epidemiology. 2013;42(4):978-91.

BiB 1000

BiB1000 is a subgroup of the BiB cohort who have been followed up to investigate growth trajectories and modifiable risk factors for childhood obesity (316). BiB1000 aims to enable a deep understanding of the predictors and influences of health related behaviours in order to develop culturally specific obesity prevention strategies (172). BiB1000 specifically examines determinants of childhood obesity by recruiting women during pregnancy and following the infant up into childhood (172). BiB1000 also collects follow up data for the mother therefore allowing investigation into the determinants of long-term maternal outcomes such as PPWR.

All mothers recruited to the full BiB study between August 2008 and March 2009 who had completed the baseline questionnaire were approached to take part in BiB1000 during their 26-28 week glucose tolerance test (172). In order to detect a difference in infant growth of a one centile band (or 0.67 z-scores) in weight at age over one year, allowing for a 5% annual attrition, it was calculated that a sample size of 1080 was required (172). However once recruitment begun it was found to be highly successful, it was therefore in order to optimise the amount of data that were available, it was decided that oversampling by up to 70% would be carried out (172). Of the 1,916 women who were eligible to participate, 1735 women agreed to take part (172). Of these 1,735 women 1,707 had singleton births between October 2008 and May 2009 (172). Follow up data were collected when the children were aged 6, 12 and 18 months and 2, 3 and 4 years (316).

Information was collected by trained bilingual study administrators from the mother in her home, local Children's Centres or hospital-based clinics (172). Structured questionnaires were self-completed, anthropometric measurements were taken routinely collected data were extracted from the maternity IT system which is known as eClipse and the Child Health system in Bradford and Airedale Primary Care Trust (172). BiB1000 has been found to have similar distributions of age, marital status and parity as of the full BiB cohort (316). Table 2 shows that maternal ethnicity was also similar across BiB and BiB 1000.

Table 2 Maternal ethnicity across BiB and BiB1000

	BiB		BiB1000	
Maternal ethnicity	N	%	n	%
Pakistani	5127	45.0	808	47.3
White British	4488	39.4	652	38.2
White other	303	2.7	30	1.8
Asian other	326	2.9	52	3.0
Indian	438	3.8	73	4.3
Black	249	2.2	34	2.0
Mixed	217	1.9	22	1.3
Other	199	1.7	28	1.6

BiB and BiB1000 data collection

A full list of the data collection forms for both BiB and BiB 1000 are available at http://www.borninbradford.nhs.uk/research-scientific/general-study-documentation-and-questionaires/. Tables 3-5 summarise the data collected for mother, child and father at each stage of the BiB study.

Table 3 Maternal data collection

		N=13,776	BiB1000 Cohort (N=1763)					
	Booking (10-14 weeks)	Baseline (26-28 weeks)	6 months	12 months	18 months	2 years	3 years	4 years
Height								
Weight								
Arm circumference								
Tricep skinfold thickness								
Age of Menarche								
Previous births (stillbirths and deaths included)		For BiB1000 Cohort						
Housing status								
Marital status								
Household structure								
Migration history								
Family relationships								
Education (mother and father)								
Employment status (mother and father)								
Financial status (benefits, income etc)								
Deprivation								
Smoking status								

		N=13,776	BiB1000 Cohort (N=1763)					
	Booking (10-14 weeks)	Baseline (26-28 weeks)	6 months	12 months	18 months	2 years	3 years	4 years
Alcohol and drug use								
Diet (food frequency questionnaire)		Limited data available						
Caffeinated drinks								
Use of vitamin and mineral supplements (Vitamin C,D,E and iron multivitamins)								
Home food availability								
Water consumption								
Mental health								
General health								
Physical activity								
Screen time								
Body image								
Parenting practices								
Caregiver's feeding style								
Blood pressure at booking								
Blood pressure at 28/40 weeks								
Blood pressure at 38/40 weeks								

		N=13,776	BiB1000 Cohort (N=1763)					
	Booking (10-14 weeks)	Baseline (26-28 weeks)	6 months	12 months	18 months	2 years	3 years	4 years
Diabetes								
Obstetric history (Including: gestational diabetes, Gravida and parity, Pre-eclampsia, Delivery information, Adverse outcomes)	Extracted by hand from medical notes							
Ultrasound data (12,20,32 weeks)								

Adapted from Wright J, Small N, Raynor P, Tuffnell D, Bhopal R, Cameron N, et al. Cohort profile: The Born in Bradford multi-ethnic family cohort study. International Journal of Epidemiology. 2013;42(4):978-91 and Bryant M, Santorelli G, Fairley L, West J, Lawlor DA, Bhopal R, et al. Design and characteristics of a new birth cohort, to study the early origins and ethnic variation of childhood obesity: the BiB1000 study. Longitudinal and Life Course Studies. 2013;4(2):119-35.

Table 4 Child data collection

	N=13,776	BiB1000 Cohort (N=1763)						
	Baseline	Birth	6 months	12 months	18 months	2 years	3 years	4 years
Length								
Weight								
Head circumference								
Abdominal circumference								
Skinfold thickness (subscapular, triceps and thigh)								
General Health								
Childhood illness								
Breastfeeding								
Diet								
Sleep duration								
Infant characteristics								
Growth perception								
Physical activity								
Screen time								
Strengths and difficulties questionnaire								

Adapted from Wright J, Small N, Raynor P, Tuffnell D, Bhopal R, Cameron N, et al. Cohort profile: The Born in Bradford multi-ethnic family cohort study. International Journal of Epidemiology. 2013;42(4):978-91.

Table 5 Data collection for the father

	N=3,448	BiB1000 Cohort (N=438)	
	Baseline	6 months	12 months
Height	■	■	■
Weight	■	■	■
Ethnicity	■	■	■
Date of birth	■		
Age completed education	■		
Country of birth	■		
Age of migration	■		
Employment	■		
Lifestyle (smoking and alcohol)	■	■	■
General health		■	■
Parenting		■	■
Mental health		■	■

Adapted from Wright J, Small N, Raynor P, Tuffnell D, Bhopal R, Cameron N, et al. Cohort profile: The Born in Bradford multi-ethnic family cohort study. International Journal of Epidemiology. 2013;42(4):978-91.

Strengths and weaknesses

The population in the BiB cohort was representative of the population in Bradford when the data was collected (316). Although there have been slight changes since 2007-11, those who identify as Pakistani are still the second largest ethnic group, and there are still high levels of deprivation in the district(334). Although Bradford is not representative of the rest of the UK due to the high levels of poverty (67.8% of the population are in the most deprived IMD quintile) (316), there are similarities between Bradford and other cities with high levels of ethnic minority and immigration both in the UK and worldwide (316). In addition, the largely bi-ethnic population provides a unique opportunity for detailed assessments of the associations and potentially causal analyses for differences between Pakistani and White British women in regard to key health outcomes (316), such as the short- and long term pregnancy outcomes associated with maternal BMI and GWG which will be investigated by this PhD project. Results from such analyses could be used to inform interventions aimed at reducing health inequalities and improving health in South Asian populations locally, nationally and internationally (316). In addition,

to bi-ethnic comparisons, this dataset also enables comparisons to be made by country of birth (UK or Pakistan) within the Pakistani population (316).

This PhD project aims to investigate the impacts of direct and indirect risk factors for adverse health outcomes for mother and child using Structural Equation Modelling (SEM). SEM requires a large sample size, and although the exact sample size required is dependent on model complexity and the number of parameters in the model which require statistical estimation, a typical sample for SEM research is around 200 cases (314). Therefore another strength of the BiB dataset is the large sample size (n=13,776 for BiB and n=1,763 for BiB1000, although this will be less once missing cases have been excluded) which should be adequate for structural equation modelling to be carried out. BiB1000 is a longitudinal cohort study and although recruitment at baseline was successful, there was loss to follow up and consequential missing data, which will affect the available sample size. At the initiation of this PhD project, through verbal communication with staff at BiB I was aware that 80% of BiB women completed the baseline questionnaire, that 5-10% of the data are missing for BMI, that birth outcomes are well recorded and that skinfold measurements are missing for around 25-30% (taken at birth for the whole BiB cohort). In addition, I was also provided with some preliminary information on the availability of GWG which is shown in Table 6.

Table 6 Preliminary GWG information

Weight measurements throughout pregnancy

	Early pregnancy (booking weight in eClipse) (n=10,601)	Mid Pregnancy (Questionnaire ~ 26 weeks gestation) (n=10,510)	Late pregnancy ≥28 weeks gestation) (n=5,772)
Mean (SD) weight	68.1 (16.0)	74.0 (19.6)	77.5 (15.4)
Mean (SD) gestational age at recording	12.5 (3.1)	26.3 (2.1)	36.5 (2.1)

(5650 with weight at booking in the third trimester, 125 with weight gain <0kg)

There are also strengths and limitations relating to the data collected. As the BiB cohort is embedded within clinical routine it relies on the support from clinical staff to take and record some of the measurements (316). It has been demonstrated that the

measurements taken by the clinical staff are valid and reliable (317, 318). As this dataset was not collected for the purposes of this PhD project, analysis may be limited to the variables available. For example, pregnancy outcomes of interest may not be available for analysis, or there may be certain confounding or mediation variables that I am not able to consider.

Why the BiB dataset

Although there are some limitations associated with the dataset, it is clear that due to its largely bi-ethnic population, Bradford is an ideal setting for research that investigates the differences in health outcomes between people of White and Pakistani origin. The data collected for the BiB and BiB1000 cohorts provides a unique opportunity to consider the effect of pregnancy weight on both short- and long-term pregnancy outcomes for the mother and infant taking into account lifestyle factors, environmental risk factors, socio-economic factors, family trees and ethnicity, and physical and mental health. This PhD project will therefore utilise the BiB data to investigate the relationship between UK ethnic groups (White and Pakistani), maternal booking BMI, GWG, and both short-and long-term pregnancy outcomes for both mother and infant.

Notes on ethics

Permission has been obtained to use the non-patient identifiable BiB data. Where this project involves the analysis of existing, non-patient identifiable data, BiB ethical approval will operate for use of both the BiB and BiB1000 data. Favourable ethical approval was granted by the Bradford Research Ethics Committee Ref 07/H1302/112.

Appendix 2: Search terms

Search strategy for Medline via OVID

1. *Pregnancy/
2. Obstetrics/
3. Pregnan$.ti,ab.
4. Matern$.ti,ab.
5. Gravid$.ti,ab.
6. Mother.ti,ab.
7. Parent.ti,ab.
8. Or/1-7
9. Ethnic groups/
10. Culture/
11. Continental population groups/
12. (Race OR Races OR Racial OR Ethnic$ OR Intra race OR Intra Races OR Intra racial OR Intra ethnic$ OR Inter race OR Inter races OR Inter racial OR Inter ethnic$).ti,ab.
13. “Emigrants and Migrants”/
14. Generation status/
15. Minority groups/
16. (Asian$ OR Indian$ OR Bengali$ OR Kashmiri$ OR Gujarati$ OR Tamil$ OR Bangladesh$ OR Pakistan$ OR Sri Lanka$).ti,ab
17. (Nonwhite OR minority).ti,ab.
18. Or/9-17
19. *Obesity/ or *obesity, morbid/
20. Obes$.ti,ab.
21. *body composition/
22. *Weight gain/
23. (Overweight or over weight or weight gain).ti,ab.
24. Body mass index/
25. (Bmi or body mass index).ti,ab.
26. Skinfold thickness/
27. Adiposity/ph

28. *adipose tissue/
29. Waist circumference/ph
30. Waist-hip ratio/
31. Body fat percentage.mp.
32. or/19-31
33. 8 and 18 and 32
34. Fertile$.ti,ab.
35. (IVF or in vitro fertili?ation).ti.
36. (PCOS or polycystic ovary syndrome)
37. Or/34-36
38. 33 not 37
39. Limit 38 to Human
40. Limit 39 to English

Search strategy for EMBASE via OVID

1. *Pregnancy/
2. Obstetrics/
3. Pregnan$.ti,ab.
4. Matern$.ti,ab.
5. Gravid$.ti,ab.
6. Mother.ti,ab.
7. Parent.ti,ab.
8. Or/1-7
9. Ethnic group/
10. Ethnicity.ti,ab
11. Race/
12. Cultural anthropology/
13. Ancestry group/
14. (Race OR Racial OR Ethnic$ OR Intra race OR Intra Races OR Intra racial OR Intra ethnic$ OR Inter race OR Inter races OR Inter racial OR Inter ethnic$).ti,ab.
15. Emigrant/

16. Migrant/
17. Cultural factor/
18. Minority group/
19. (Asian$ OR Indian$ OR Bengali$ OR Kashmiri$ OR Gujarati$ OR Tamil$ OR Bangladesh$ OR Pakistan$ OR Sri Lanka$).ti,ab
20. Nonwhite.ti,ab. OR minority.ti,ab.
21. Or/9-20
22. *Obesity/ or *morbid obesity/
23. Obes$.ti,ab.
24. *body composition/
25. *Weight gain/
26. (Overweight or over weight or weight gain).ti,ab.
27. Body mass/
28. BMI or body mass index.ti,ab.
29. Skinfold thickness/
30. *adipose tissue/
31. Waist circumference/
32. Waist-hip ratio/
33. body fat distribution/
34. Body fat percentage.mp.
35. or/22-34
36. 8 and 21 and 35
37. Fertile$.ti,ab.
38. (IVF or in vitro fertili?ation).ti.
39. (PCOS or polycystic ovary syndrome)
40. Or/37-39
41. 36 not 40
42. Limit 41 to Human
43. Limit 42 to English

Search terms for PsychINFO via OVID

1. *Pregnancy/
2. Exp Obstetrics/
3. Pregnan$.ti,ab.
4. Matern$.ti,ab.
5. Gravid$.ti,ab.
6. Mother.ti,ab.
7. Parent.ti,ab.
8. Or/1-7
9. exp "Racial and Ethnic Groups"/
10. ethnic identity/
11. exp "Racial and Ethnic Differences"/
12. exp “Race (Anthropological)"/
13. exp Minority Groups/
14. exp Immigration/
15. (Race OR Racial OR Ethnic$ OR Intra race OR Intra Races OR Intra racial OR Intra ethnic$ OR Inter race OR Inter races OR Inter racial OR Inter ethnic$).ti,ab.
16. (Asian$ OR Indian$ OR Bengali$ OR Kashmiri$ OR Gujarati$ OR Tamil$ OR Bangladesh$ OR Pakistan$ OR Sri Lanka$).ti,ab
17. Nonwhite.ti,ab. OR minority.ti,ab.
18. Or/ 9-17
19. *Obesity/
20. Obes$.ti,ab.
21. Weight gain/
22. Body weight/
23. exp Body Size/
24. exp Body Mass Index/
25. exp Body Weight/
26. exp Body Fat/
27. Or/ 19-26
28. 8 and 18 and 27
29. Fertile$.ti,ab.
30. (IVF or in vitro fertili?ation).ti.

31. (PCOS or polycystic ovary syndrome)
32. Or/29-31
33. 28 not 32
34. Limit 33 to Human
35. Limit 34 to English

Search terms for CINAHL via EbescoHost

(MM "Pregnancy") OR (MH "Delivery, Obstetric+") OR (TI "pregnan*" OR AB "pregnan*") OR (TI “Matern*” OR AB “Matern*”) OR *(TI “Gravid*” OR AB “Gravid”) OR (TI “Mother” OR AB “Mother”) OR (TI “Parent” OR AB “Parent”)
AND
(MH "Ethnic Groups+") OR (TI “Ethnicity” OR AB “Ethnicity”) OR (MH "Race Relations+") OR (MH "Culture+") OR (TI “Race” OR AB “Race”) OR (TI “Racial” OR AB “Racial”) or (TI “Ethnic*” OR AB “Ethnic*) OR (TI “Intra race” OR AB “Intra race”) OR (TI “Intra Races” or AB “Intra races”) OR (TI “Intra Racial” OR AB “Intra racial”) OR (TI “Intra ethnic*” OR AB “Intra ethnic*”) OR (TI “Inter race” OR AB “Inter race”) OR (TI “Inter races” OR AB “Inter Races”) OR (TI “Inter Racial” OR AB “Inter Racial”) OR (TI “Inter ethnic*” OR AB “Inter ethnic”) OR (MH "Emigration and Immigration") OR (MH "Migrants") OR (MH "Generation status") OR (MH "Minority Groups") OR (TI “Asian*” OR AB “Asian”) OR (TI “Indian*” OR AB “Indian*”) OR (TI “Bengali*” OR AB “Bangali*”) OR (TI “Kashmiri*” OR AB “Kashmiri*”) OR (TI “Gujarati*” OR AB “Gujarati*”) OR (TI “Tamil*” OR AB “Tamil*”) OR (TI “Bangladesh*” OR AB “Bangladesh*”) OR (TI “Pakistan*” OR AB “Pakistan*”) OR (TI “Sri Lanka* OR AB “Sri Lanka*”) OR (TI “Nonwhite minority” OR AB “Nonwhite minority”)
AND
(MM "Obesity") OR (MM "Obesity, Morbid") OR (TI “obes*” OR AB “obes*”) OR (MH "Body Weight Changes") OR (MH "Weight Gain") OR (TI “Overweight” OR AB “Overweight”) OR (TI “over weight” OR AB “over weight”) OR (TI “weight gain” OR AB “weight gain”) OR (MH "Body Mass Index") OR (TI “BMI” OR AB “BMI”) OR (TI “body mass index” OR AB “body mass index”) OR (MH "Skinfold Thickness") OR (MH "Adipose Tissue") OR (MH "Waist Circumference") OR (MH "Waist-Hip Ratio") OR (MH "Adipose Tissue Distribution") OR "body fat percentage"

NOT

(TI “fertile* OR AB “fertile*”) OR (TI “IVF” OR TI “In vitro fertili*ation”) OR “PCOS” or “polycystic ovary syndrome”

Search for the JBI database

Pregnan* OR and Ethnicity or "South Asian" and Obesity OR Overweight OR "weight gain" OR weight

Search for Scopus, CRD database (DARE), PROSPERO

Pregnancy OR Pregnant OR Maternal

AND

Ethnicity OR ethnic OR Minority OR race OR OR “South Asian” OR Indian OR India OR Pakistani OR Pakistan OR Bangladesh OR Bangladeshi OR “Sri Lankan” OR “Sri Lanka”

AND

Obesity OR Overweight OR “weight " OR “body mass” OR "Body Weight Changes" OR “BMI” OR “Waist circumference” OR "Waist-Hip Ratio" or “Body Fat percentage”

Search for Cochrane database of systematic reviews

1. Pregnan*.mp
2. Maternal.mp
3. Mother.mp
4. parent.mp
5. Gravid.mp
6. Gravida.mp
7. Or/1-6
8. Ethnicity.mp
9. ethnic.mp
10. Minority.mp
11. Culture.mp

12. Race.mp
13. racial.mp
14. South Asian.mp
15. India*.mp
16. Pakistan*.mp
17. Bangladesh*.mp
18. Sri Lanka*.mp
19. Or/8-18
20. Obesity.mp
21. Overweight.mp
22. adiposity.mp
23. weight.mp
24. body mass index.mp
25. Body Weight Changes.mp
26. BMI.mp
27. Waist circumference.mp
28. Waist-Hip Ratio.mp
29. Body Fat percentage.mp
30. Or/20-29
31. 7 and 19 and 30

Search for federated search engine Epistemonikos

Pregnancy OR Pregnant OR Maternal or Mother OR parent OR Gravid or Gravida AND Ethnicity OR ethnic OR “ethnic group” OR Minority OR culture OR race OR racial OR migrant OR migrant OR “South Asian” OR Indian OR India OR Pakistani OR Pakistan OR Bangladesh OR Bangladeshi OR “Sri Lankan” OR “Sri Lanka”
AND
obesity OR Overweight OR “over weight” OR adiposity OR “adipose tissue” OR “weight gain” OR weight OR "body mass index" OR “body mass” OR "Body Weight Changes" OR “BMI” OR “Waist circumference” OR "Waist-Hip Ratio" or “Body Fat percentage”

BNI (ProQuest)

((((SU.EXACT("Pregnancy") OR SU.EXACT("1:Pregnancy ")) OR SU.EXACT.EXPLODE("Obstetrics")) OR (ti(pregnan* OR matern* OR gravid* OR mother OR parent) OR ab(pregnan* OR matern* OR gravid* OR mother OR parent))) AND ((SU.EXACT.EXPLODE("Ethnic Groups") OR SU.EXACT.EXPLODE("Culture and Religion")) OR (ti(Race OR Races OR Racial OR Ethnic* OR Intra race OR Intra Races OR Intra racial OR Intra ethnic* OR Inter race OR Inter races OR Inter racial OR Inter ethnic*) OR ab(Race OR Races OR Racial OR Ethnic* OR Intra race OR Intra Races OR Intra racial OR Intra ethnic* OR Inter race OR Inter races OR Inter racial OR Inter ethnic*)) OR (ti(Asian* OR Indian* OR Bengali* OR Kashmiri* OR Gujarati* OR Tamil* OR Bangladesh* OR Pakistan* OR Sri Lanka*) OR ab(Asian* OR Indian* OR Bengali* OR Kashmiri* OR Gujarati* OR Tamil* OR Bangladesh* OR Pakistan* OR Sri Lanka*)) OR (ti(Nonwhite OR minority or non-white) OR ab(Nonwhite OR minority or non-white))) AND ((SU.EXACT.EXPLODE("Obesity") OR SU.EXACT("Body Size")) OR (ti(obes* OR overweight OR over weight OR weight gain OR Bmi OR body mass index OR body composition OR Skinfold thickness OR Adiposity OR adipose tissue OR Waist circumference OR Waist-hip ratio OR body fat percentage) OR ab(obes* OR overweight OR over weight OR weight gain OR Bmi OR body mass index OR body composition OR Skinfold thickness OR Adiposity OR adipose tissue OR Waist circumference OR Waist-hip ratio OR body fat percentage)))) NOT (ab(Fertile* OR IVF OR in vitro fertilization OR IVF OR in vitro fertilisation OR PCOS OR polycystic ovary syndrome) OR ti(Fertile* OR IVF OR in vitro fertilization OR IVF OR in vitro fertilisation OR PCOS OR polycystic ovary syndrome))

AMED (Allied and Complementary Medicine) 1985 to September 2015

1. exp pregnancy/
2. Mothers/
3. (pregnan* or matern* or gravid* or mother or parent).ti,ab.
4. exp ethnic groups/
5. "emigration and immigration"/
6. (Race or Races or Racial or Ethnic* or Intra race or Intra Races or Intra racial or Intra ethnic* or Inter race or Inter races or Inter racial or Inter ethnic*).ti,ab.

7. (Asian* or Indian* or Bengali* or Kashmiri* or Gujarati* or Tamil* or Bangladesh* or Pakistan* or Sri Lanka* or minority group*).ti,ab.
8. (Nonwhite or minority or non-white).ti,ab.
9. culture/
10. (Generation status or culture or cultural or cultural characteristics or cross-cultural comparision or socio-cultural).mp.
11. or/1-3
12. or/4-9
13. obesity/
14. Body composition/
15. body mass index/
16. Adipose tissue/
17. (obes* or overweight or over weight or weight gain or Bmi or body mass index or body composition or Skinfold thickness or Adiposity or adipose tissue or Waist circumference or Waist-hip ratio or body fat percentage).ti,ab.
18. or/13-17
19. 11 and 12 and 18

Appendix 3: Data extraction form

ADAPTED COCHRANE COHORT STUDY DATA EXTRACTION TEMPLATE

Reviewer	
Title of paper	
Author and Year	
Setting	Location (region/city, country): Study name or dataset:
Data collection time period (Day, Month, Year if available)	
Methodology (please check relevant box)	☐ Prospective Cohort ☐ Retrospective Cohort ☐ Case Control ☐ Cross sectional

All ethnic groups studied (Please use terminology from the paper)	**Subgroups included**

How was ethnicity assigned? (Please check relevant box)	☐ **Self-report** ☐ **Country of birth** ☐ **Parent's country of birth** ☐ **Investigator assigned** ☐ **Medical records, unspecified** ☐ **Unspecified** ☐ **Other** **If "Other" please specify……..**

Outcome	**Definition** (give definition used to define/diagnose outcome)	**How outcome was determined: measured/self-report/unclear**	**How data was collected: routine medical records/prospectively collected for study/unclear**

Exposure (weight status before or during pregnancy i.e. BMI, weight, skinfold thickness, serum leptin or gestational weight gain)	**Definition** (please give units used and groups if applicable. Also include if Asian specific criteria used)	**How exposure was determined: measured/self-report/unclear**	**When assessed (**Please give as much detail as possible e.g. 1st antenatal appointment, or 16 weeks of pregnancy etc)	**Reference group used**

	Total group	White ethnic group	Asian ethnic group 1	Asian ethnic group 2	Asian ethnic group 3	Asian ethnic group 4
Number Identified						
Number Excluded						
Final Number Included						
All Subjects Accounted for in each ethnic group?	Yes No Unclear	Yes No Unclear	Yes No Unclear	Yes No Unclear	Yes No Unclear	Yes No Unclear

(Note: Relevant Asian populations refer to South Asian, UK studies using the term Asian or any other Asian term which only includes women from South Asia using the definition used by NICE (migrants and descendants from Bangladesh, Bhutan, India, Indian-Caribbean (migrants of South Asian family origin), Maldives, Nepal, Pakistan and Sri Lanka) for example; Indo-Asian, Asian-Indian, Indian, Pakistani, Bangladeshi; Relevant White ethnic groups are White, White European, Caucasian, those containing White British women etc)

Inclusion criteria (e.g. gestation at weight measurement, singleton etc)	
Exclusion criteria	

Baseline Characteristics reported by ethnicity? Yes / No (if no do not complete, if yes populate with the data**)**

Characteristic (include all listed e.g. Maternal Age, Parity, Family history of diabetes, deprivation, etc and definition/unit of measurement N/B: If population split by e.g.GDM please report GDM and Non GDM group)	Total group	White ethnic group	Asian ethnic group 1	Asian ethnic group 2	Asian ethnic group 3	Asian ethnic group 4	P value
e.g. Maternal age GDM Non GDM							

(Note: Relevant Asian populations refer to South Asian, UK studies using the term Asian or any other Asian term which only includes women from South Asia using the definition used by NICE (migrants and descendants from Bangladesh, Bhutan, India, Indian-Caribbean (migrants of South Asian family origin), Maldives, Nepal, Pakistan and Sri Lanka) for example; Indo-Asian, Asian-Indian, Indian, Pakistani, Bangladeshi; Relevant White ethnic groups are White, White European, Caucasian, those containing White British women etc)

Are there any observed differences in baseline characteristics by ethnic group?

Data Analysis: please complete table and note ethnic group term used-if additional analysis or additional Asian ethnic group, please use table over page

Pregnancy outcome	Exposure (Maternal BMI, other pre-pregnancy weight status, GWG, skinfold thickness etc)	White ethnic group				Unadjusted Statistical result …….. and……% Confidence interval	Adjusted Statistical result …….. and…….% Confidence interval	Asian ethnic group				Unadjusted Statistical result …….. and……% Confidence interval	Adjusted Statistical result …….. and…….% Confidence interval
		Mean (SD)	Number with outcome	Number without outcome	Total number			Mean (SD)	Number with outcome	Number without outcome	Total number		
GDM													
Factors adjusted for in analyses (Please only consider analysis presented in table(s) on previous page(s) with results relevant to this systematic review)**:**													
Data Analysis methods (Please only consider analysis presented in table(s) on previous page(s) with results relevant to this systematic review):													
Any other relevant analysis not presented in table? (e.g. graphs and figures where numerical data not presented)													

Appendix 4: Quality assessment

ADAPTED NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT[1] STUDIES

Study (author and year):
Reviewer (initials):

Section 1: Selection

1) Representativeness of the exposed cohort (exposure in this context is the maternal weight risk group used, e.g. obesity ≥30kg/m^2 or the GWG risk group used e.g.>20lb for obese women)

a) truly representative of the average pregnant population in the community □
(Did they report how representative the study population BMI/GWG distribution was to the general maternity population in their setting/location/region/country? If it was reported then was it comparable? Or did they include the entire population in the sample – e.g. all women delivering within a specific maternity unit etc)

b) somewhat representative of the average pregnant population in the community □
(Did they report how representative the study population BMI/GWG distribution was to the general maternity population in their setting/location/region/country? If it was reported then was it a similar enough pattern of distribution and not skewed in comparison?)

c) selected group of users eg nurses, volunteers
(E.g. only first time pregnancy, only teenage pregnancy, only those with GDM, only those requiring a certain procedure during pregnancy etc)

d) no description of the derivation of the cohort
(Not reported or unclear)

2) Selection of the non exposed cohort (non-exposure is the maternal weight group used as reference e.g. recommended BMI (18.5-24.9kg/m^2 or the GWG group used as reference e.g.11-20lbs for obese women)

a) drawn from the same community as the exposed cohort □
(Probably this option most of the time if using a general population of pregnancies and determining exposure status based on splitting the group by BMI)

b) drawn from a different source
(E.g. different maternity unit, different specialist clinic, different time range for recruitment between exposed and non-exposed groups)

c) no description of the derivation of the non exposed cohort
(Not reported or unclear)

3). Ascertainment of exposure (maternal BMI/GWG/ other pregnancy weight measurement e.g. skinfold thickness)

a) secure record □
(Explicitly stated that it was a measured weight used to inform BMI/GWG)

b) structured interview □
(No structured interview method for measuring weight status exists. In our case this option could be if self-reported weight was used but it was subsequently validated by measured weight)

c) written self report
(Any self-report weight not validated with measured weight)

d) no description
(Unclear or not explicitly reported how they derived the BMI measurement)

~~4) Demonstration that outcome of interest was not present at start of study~~ [2]
~~a) yes □~~
~~b) no~~

Section 2: Comparability

1) Comparability of cohorts on the basis of the design or analysis (can select more than one answer) please only consider analysis with results relevant to this systematic review

a) study controls for a measure of socioeconomic status (IMD, Carstairs Index, maternal education, maternal income etc) □
(This could be either excluded or adjusted for in analysis)

b) study controls for any additional factor □
(Any other factors adjusted for in the analysis)

c) no factors controlled for

2) Assessment of pregnancy outcome. (in studies where there are multiple pregnancy outcomes which would have different responses if considered separately, please complete this question to reflect the majority of outcomes)

a) independent blind assessment□
(prospectively collected and measured outcome data for the purposes of the research study)

b) record linkage □
(Outcome data retrieved from medical records that had been informed by routine measured data)

c) self report
(Any self-reported outcome data regardless of method of data collection)

d) no description
(not clear/not reported)

3) Was follow-up long enough for pregnancy outcomes to occur? (in studies where there are multiple pregnancy outcomes which would have different responses if considered separately, please complete this question to reflect the majority of outcomes)

a) Yes (or if retrospective analysis of routine medical records) □
(For example;
-If GDM: follow up until diagnosis of GDM is made following relevant diagnostic test such as oral glucose tolerance test at 24-28 weeks gestation.
-If birth weight: follow up until measurement of weight after birth at neonatal examination.
-If gestational age at delivery: followed up until spontaneous onset of labour, or if there was early intervention of induction of labour or caesarean then this was after the gestational age specified as pregnancy outcome, or these factors accounted for in exclusion criteria or adjustments.)

b) No
(For example;
-If GDM: Failure to follow up until assessment of GDM status during pregnancy.
-If birth weight: failure to follow up until measurement of weight after birth at neonatal examination.
-If gestational age at delivery: early intervention of induction of labour or caesarean before the gestational age specified as pregnancy outcome which was not accounted for in the exclusion criteria or adjustments.)

4) Adequacy of follow up of cohorts or management of missing data

a) Complete follow up – all subjects accounted for or multiple imputation of missing data □
(The total number of eligible participants/recruited participants are reported and the final number included are reported: no loss to follow up or exclusions of cases (e.g. missing data)

b) Subjects lost to follow up unlikely to introduce bias - small number lost to follow up <20% (select an adequate %), or description provided of those lost i.e comparison of characteristics of included participants and those with missing data □
(The total number of eligible participants /recruited participants are reported and the final number included are reported and either: lost or excluded less than 20% so presumed unlikely to introduce bias, or lost or excluded more than 20% but compared groups and no systematic differences so presumed missing at random)

c) follow up rate < 80% (select an adequate %) and no description of those lost
(The total number of eligible participants/recruited participants are reported and the final number included are reported: excluded or lost more than 20% but no comparison of included or excluded groups reported)

d) No statement
(The total number of eligible participants/recruited participants are not reported and only the final number included are reported. No mention of any exclusions or loss to follow up)

Total number of stars (out of a possible 8[3]):

Notes:
[1] All the non-cohort studies were cross sectional and all had groups defined by the exposure variable rather than the outcome variables, therefore cohort design template fits best with these study
[2] Item 4 in Section 1: Selection "Demonstration that outcome of interest was not present at start of study" is not applicable to gestational age at delivery outcomes as women are identified in early pregnancy using their pre/early pregnancy BMI and their pregnancy outcomes are not known at the start of the study. Therefore this item has been removed from the scale
[3] A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability. The denominator value for the possible number of stars using the template Newcastle Ottawa Scale has been reduced from 9 to 8 due to the removal of item 4 in Section 1 (as there was potential for additional star to be awarded based on this item).
Red text: Detail added to the Newcastle-Ottawa scale to make it fit with the context of my research; this is part of the guidelines for using this quality assessment tool.

Appendix 5: Quality assessment scores for Newcastle Ottawa Quality assessment

Paper	Section 1:Selection			Section 2: Comparability				Final score (Max:8)*	Reviewers
	1	2	3	1	2	3	4		
Bissenden a) et al 1981	D	A*	D	C	D	A*	D	2	ES+JR
Bissenden b) et al 1981	D	A*	D	C	D	A*	D	2	ES+NH
Bryant et al 2014	A*	A*	A*	C	B*	A*	C	5	ES + DJ
Dornhost et al 1992	A*	A*	D	C	A*	A*	A*	5	ES+JR
Dunne et al 2000	C	A*	D	C	B*	A*	D	3	ES+DJ
Hernandez-Rivas et al 2013	C	A*	D	C	A*	A*	B*	4	ES+DJ
Makgoba et al 2011	A*	A*	C	C	A*	A*	B*	5	ES+DJ
Makgoba et al 2012	C	A*	C	A+B**	B*	A*	C	5	ES+NH
Oteng-Ntim et al 2013	A*	A*	D	A+B**	B*	A*	B*	7	ES+DJ
Penn et al 2014	A*	A*	D	B*	B*	A*	A*	6	ES+DJ
Pu et al 2015	A*	A*	D	A+B**	B*	A*	B*	7	ES +DJ
Retnakaran et al 2005	C	A*	D	C	A*	A*	D	3	ES+DJ
Sharma et al 2011	C	A*	D	C	A*	A*	B*	4	ES+DJ
Sheridan et al 2013	C	A*	B*	C	B*	A*	B*	5	ES+DJ
Sinha et al 2002	C	A*	D	B*	B*	A*	C	4	ES+DJ
Sommer et al 2015	C	A*	A*	B*	A*	A*	C	5	ES+DJ
Sommer et al 2014	C	A*	A*	B*	A*	A*	B*	6	ES+NH
Wong et al 2011	C	A*	D	C	B*	A*	B*	4	ES+DJ
Yue et al 1996	A*	A*	D	C	A*	A*	D	4	ES+JR

*For the purposes of this review, studies with a quality score above four were deemed to be of reasonable quality.
ES= Emma Slack, DJ= Dan Jones.

Appendix 6: Search terms for Framework based synthesis

Search in Medline

1. *Pregnancy/
2. Obstetrics/
3. Mothers/
4. Pregnan$.ti,ab.
5. Matern$.ti,ab.
6. Gravid$.ti,ab.
7. Mother.ti,ab.
8. Parent.ti,ab.
9. *Women's health/
10. Or/1-9
11. Ethnic groups/
12. Continental population groups/
13. (Race OR Races OR Racial OR Ethnic$ OR Intra race OR Intra Races OR Intra racial OR Intra ethnic$ OR Inter race OR Inter races OR Inter racial OR Inter ethnic$).ti,ab.
14. "Emigrants and Immigrants"/
15. Minority groups/
16. Minority group$.ti,ab.
17. Asian$.ti,ab.
18. (Indian$ OR Bengali$ OR Kashmiri$ OR Gujarati$ OR Tamil$ OR Bangladesh$ OR Pakistan$ OR Sri Lanka$).ti,ab.
19. (Nonwhite OR minority).ti,ab.
20. Or/11-19
21. Culture/
22. Culture.mp.
23. Acculturation/
24. Acculturation.mp
25. Cultural Characteristics/
26. Cross-Cultural Comparison/
27. Cultural.mp.
28. Family Relations/
29. Social support/

30. Socio-cultural.mp.
31. Or/21-30
32. View$.mp
33. Opinion$.mp
34. Perspective$.mp
35. Experience$.mp
36. Voice$.mp
37. Attitude$.mp
38. Feeling$.mp
39. Emotion$.mp
40. Thought$.mp
41. Belief$.mp
42. Influence$.mp.
43. Attitude to Health/ or Health Knowledge, Attitudes, Practice/
44. ((("semi-structured" or semistructured or unstructured or informal or "in-depth" or indepth or "face-to-face" or structured or guide) adj3 (interview* or discussion* or questionnaire*))).ti,ab. or (focus group* or qualitative or ethnograph* or fieldwork or "field work" or "key informant").ti,ab. or interviews as topic/ or focus groups/ or narration/ or qualitative research/
45. Or/32-44
46. 10 and 20 and 31 and 45

Search in EMBASE

1. *Pregnancy/
2. Obstetrics/
3. Pregnan$.ti,ab.
4. Matern$.ti,ab.
5. Gravid$.ti,ab.
6. Mother.ti,ab.
7. Parent.ti,ab.
8. Or/1-7
9. Ethnic group/
10. Race/

11. (Race OR Racial OR Ethnic$ OR Intra race OR Intra Races OR Intra racial OR Intra ethnic$ OR Inter race OR Inter races OR Inter racial OR Inter ethnic$).ti,ab.
12. emigrant/
13. Immigrant/
14. Minority group/
15. Asian$.ti,ab.
16. (Indian$ OR Bengali$ OR Kashmiri$ OR Gujarati$ OR Tamil$ OR Bangladesh$ OR Pakistan$ OR Sri Lanka$).ti,ab
17. Nonwhite.ti,ab. OR minority.ti,ab.
18. Or/9-17
19. Cultural anthropology/
20. Culture.ti,ab.
21. Ancestry group/
22. Cultural factor/
23. Acculturation.mp
24. Cross-Cultural Comparison/
25. Cultural.ti,ab.
26. Family Relations/
27. Social support/
28. Socio-cultural.mp.
29. Or/19-28
30. View$.mp
31. Opinion$.mp
32. Perspective$.mp
33. Experience$.mp
34. Voice$.mp
35. Attitude$.mp
36. Feeling$.mp
37. Emotion$.mp
38. Thought$.mp
39. Belief$.mp
40. Influence$.mp.
41. Attitude to Health/
42. interview:.tw. OR exp health care organization OR experiences.tw.

43. Or/34-42

44. 8 and 18 and 29 and 43

Note: tw. Refers to a Macmaster university filter for qualitative research (http://hiru.mcmaster.ca/hiru/HIRU_Hedges_EMBASE_Strategies.aspx)

Search in PsychINFO

1. *Pregnancy/
2. Obstetrics/
3. Pregnan$.ti,ab.
4. Matern$.ti,ab.
5. Gravid$.ti,ab.
6. Mother.ti,ab.
7. Parent.ti,ab.
8. Or/1-7
9. "Racial and Ethnic Groups"/
10. ethnic identity/
11. "Racial and Ethnic Differences"/
12. “Race (Anthropological)"/
13. Minority Groups/
14. Immigration/
15. (Race OR Racial OR Ethnic$ OR Intra race OR Intra Races OR Intra racial OR Intra ethnic$ OR Inter race OR Inter races OR Inter racial OR Inter ethnic$).ti,ab.
16. Asian$.ti,ab.
17. (Indian$ OR Bengali$ OR Kashmiri$ OR Gujarati$ OR Tamil$ OR Bangladesh$ OR Pakistan$ OR Sri Lanka$).ti,ab
18. Nonwhite.ti,ab. OR minority.ti,ab.
19. Or/ 9-18
20. "Culture (Anthropological)"/
21. South Asian Cultural Groups/
22. cultural.mp
23. culture.mp
24. Family/
25. Cross Cultural Differences/
26. Sociocultural Factors/

27. Social Support/
28. Acculturation/
29. Or/20-28
30. (View$ or Opinion$ or Perspective$ or Experience$ or Voice$ or Attitude$ or Feeling$ or Emotion$ or Thought$ or Belief$ or Influence$).mp
31. (((“semi-structured” or semistructured or unstructured or informal or “in-depth” or indepth or “face-to-face” or structured or guide or guides) adj3 (interview* or discussion* or questionnaire*)).ti,ab,id. or (focus group* or qualitative or ethnograph* or fieldwork or “field work” or “key informant”)).ti,ab,id. or exp qualitative research/ or exp interviews/ or exp group discussion/ or qualitative study.md. not “Literature Review”.md.
32. Or/30-42
33. 8 and 19 and 22 and 43

Search in CINAHL

(MM "Pregnancy") OR (MH "Delivery, Obstetric+") OR (TI "pregnan*" OR AB "pregnan*") OR (TI “Matern*” OR AB “Matern*”) OR *(TI “Gravid*” OR AB “Gravid”) OR (TI “Mother” OR AB “Mother”) OR (TI “Parent” OR AB “Parent”)
AND
(MH "Ethnic Groups+") OR (TI “Ethnicity” OR AB “Ethnicity”) OR (MH "Race Relations+") OR (MH "Culture+") OR (TI “Race” OR AB “Race”) OR (TI “Racial” OR AB “Racial”) or (TI “Ethnic*” OR AB “Ethnic*) OR (TI “Intra race” OR AB “Intra race”) OR (TI “Intra Races” or AB “Intra races”) OR (TI “Intra Racial” OR AB “Intra racial”) OR (TI “Intra ethnic*” OR AB “Intra ethnic*”) OR (TI “Inter race” OR AB “Inter race”) OR (TI “Inter races” OR AB “Inter Races”) OR (TI “Inter Racial” OR AB “Inter Racial”) OR (TI “Inter ethnic*” OR AB “Inter ethnic”) OR (MH "Emigration and Immigration") OR (MH "Immigrants") OR (MH "Acculturation") OR (MH "Minority Groups") OR (TI “Asian*” OR AB “Asian”) OR (TI “Indian*” OR AB “Indian*”) OR (TI “Bengali*” OR AB “Bangali*”) OR (TI “Kashmiri*” OR AB “Kashmiri*”) OR (TI “Gujarati*” OR AB “Gujarati*”) OR (TI “Tamil*” OR AB “Tamil*”) OR (TI “Bangladesh*” OR AB “Bangladesh*”) OR (TI “Pakistan*” OR AB “Pakistan*”) OR (TI “Sri Lanka* OR AB “Sri Lanka*”) OR OR (TI “Nonwhite minority” OR AB “Nonwhite minority”)
AND

(MM “Culture”) (TI “cultur*” OR AB “cultur*”) OR (MM “Cultural diversity”) OR (MM “Cultural Values”) OR (MM “Anthropology, Cultural”) OR (MM “sociocultural”) OR (TI “sociocultural” OR AB “sociocultural”) OR (MM “family”) OR (MM “social support”) OR (MM “acculturation”) OR (TX “acculturation”) (MM “social identity”) OR (TI “social” OR AB “Social”)
AND
(TX “View*”) or (TX “Opinion*”) or (TX “Perspective*”) or (TX “Experience*) or (TX “Voice*”) or (TX “Attitude*) or (TX “Feeling*”) or (TX “Emotion*”) or (TX “Thought*) or (TX “Belief*”) or (TX “Influence*) or (TX “Qualitative”)

Search in Scopus and PROSPERO

Pregnancy OR Pregnant OR Maternal
AND
Ethnicity OR ethnic OR Minority OR race OR OR “South Asian” OR Indian OR India OR Pakistani OR Pakistan OR Bangladesh OR Bangladeshi OR “Sri Lankan” OR “Sri Lanka”
AND
Culture OR cultural OR sociocultural OR acculturation OR family OR social
AND
(View OR views OR Opinion OR opinions OR Perspective OR perspectives OR Experience OR experiences OR Voice OR voices OR Attitude OR attitudes OR Feeling OR feelings OR Emotion OR emotions OR Thought OR thoughts OR Belief OR beliefs OR Influence OR influences OR qualitative OR interview OR interviews)

Search in Applied Social Sciences Index and Abstracts (ASSIA) via ProQuest

(Pregnancy OR Pregnant OR Maternal OR Mother OR parent OR Gravid OR Gravida) AND (Ethnicity OR ethnic OR "ethnic group" OR Minority OR culture OR race OR racial OR migrant OR immigrant OR "South Asian" OR Indian OR India OR Pakistani OR Pakistan OR bangla desh OR bangla deshi OR "Sri Lankan" OR "Sri Lanka") AND (Culture OR cultural OR sociocultural OR acculturation OR family OR social) AND (View OR views OR Opinion OR opinions OR Perspective OR perspectives OR Experience OR experiences OR Voice OR voices OR Attitude OR attitudes OR Feeling OR feelings OR Emotion OR emotions OR Thought OR

thoughts OR Belief OR beliefs OR Influence OR influences OR qualitative OR interview OR interviews)

Search for JBI database

Pregnan* and Ethnicity or "South Asian" and culture* or sociocultural or acculturation and View*or Opinion*OR Perspective* OR Experience* OR Voice* OR Attitude* OR Feeling* OR Emotion* OR Thought* OR Belief* OR Influence* OR qualitative OR interview* OR interviews

Search for Cochrane Database of Systematic Reviews

1. Pregnan*.mp
2. Maternal.mp
3. Mother.mp
4. parent.mp
5. Gravid.mp
6. Gravida.mp
7. Or/1-6
8. Ethnicity.mp
9. ethnic.mp
10. Minority.mp
11. Culture.mp
12. Race.mp
13. racial.mp
14. South Asian.mp
15. India*.mp
16. Pakistan*.mp
17. Bangladesh*.mp
18. Sri Lanka*.mp
19. Or/8-18
20. Culture.mp
21. cultural.mp
22. sociocultural.mp
23. acculturation.mp

24. family.mp
25. social.mp
26. or/20-25
27. View*.mp
28. Opinion*.mp
29. Perspective*.mp
30. Experience*.mp
31. Voice*.mp
32. Attitude*.mp
33. Feeling*.mp
34. Emotion*.mp
35. Thought*.mp
36. Belief*.mp
37. Influence*.mp
38. Qualitative.mp
39. Interview*.mp
40. Or/27-39
41. 7 and 19 and 26 and 40

Search for federated search engine Epistemonikos

Pregnancy OR Pregnant OR Maternal or Mother OR parent OR Gravid or Gravida
AND
Ethnicity OR ethnic OR “ethnic group” OR Minority OR culture OR race OR racial OR migrant OR immigrant OR “South Asian” OR Indian OR India OR Pakistani OR Pakistan OR Bangladesh OR Bangladeshi OR “Sri Lankan” OR “Sri Lanka”
AND
Culture OR cultural OR sociocultural OR acculturation OR family OR social
AND
(View OR views OR Opinion OR opinions OR Perspective OR perspectives OR Experience OR experiences OR Voice OR voices OR Attitude OR attitudes OR Feeling OR feelings OR Emotion OR emotions OR Thought OR thoughts OR Belief OR beliefs OR Influence OR influences OR qualitative OR interview OR interviews

AMED (Allied and Complementary Medicine) 1985 to September 2015

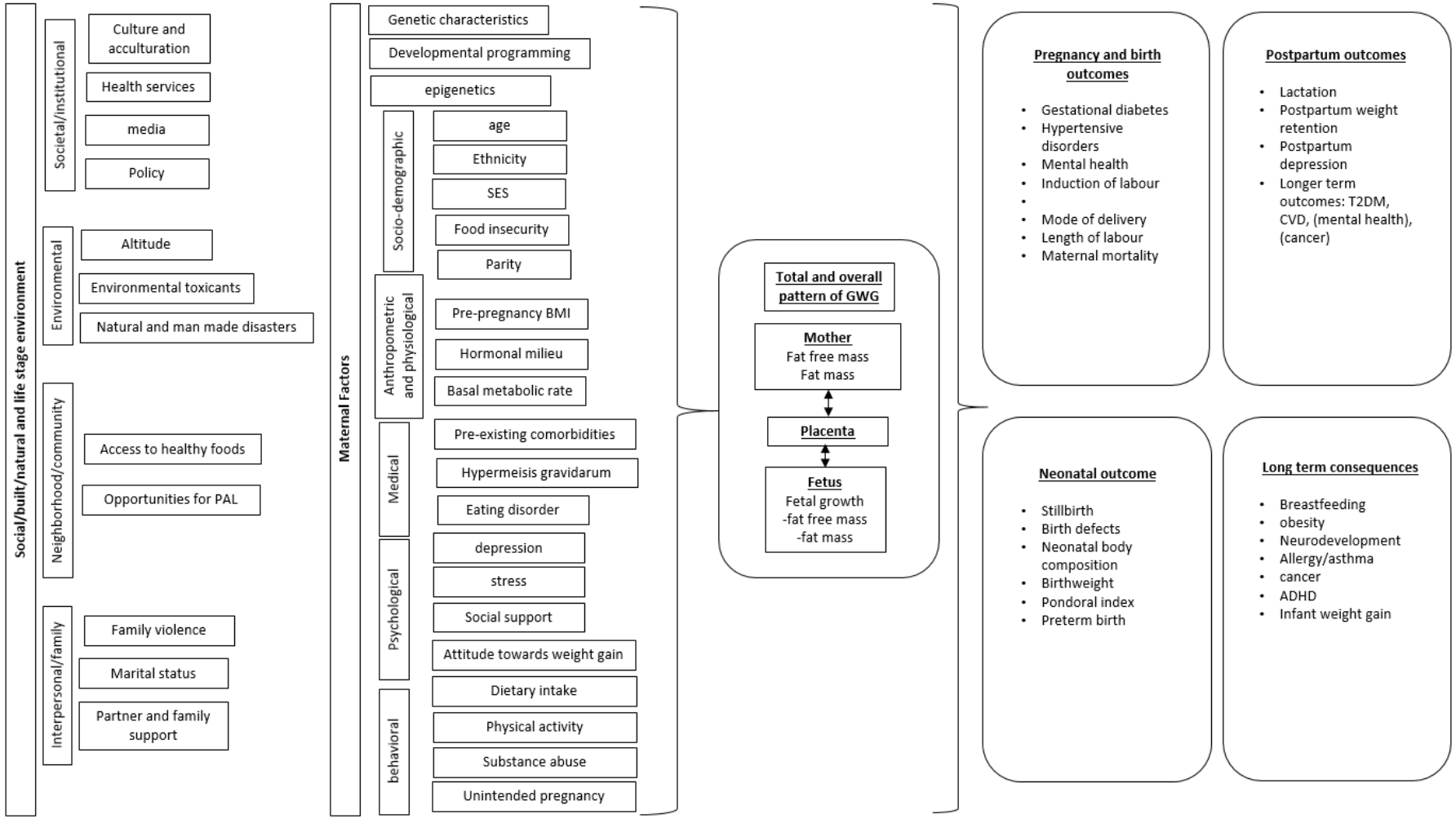
1. exp pregnancy/
2. Mothers/
3. womens health/
4. (pregnan* or matern* or gravid* or mother or parent).ti,ab.
5. or/1-4
6. exp ethnic groups/
7. "emigration and immigration"/
8. (Race or Races or Racial or Ethnic* or Intra race or Intra Races or Intra racial or Intra ethnic* or Inter race or Inter races or Inter racial or Inter ethnic*).ti,ab.
9. (Asian* or Indian* or Bengali* or Kashmiri* or Gujarati* or Tamil* or Bangladesh* or Pakistan* or Sri Lanka* or minority group*).ti,ab.
10. (Nonwhite or minority or non-white).ti,ab.
11. or/6-10
12. culture/
13. Cross cultural comparison/
14. Family relations/
15. Social support/
16. (Acculturation or culture or cultural or cultural characteristics or cross-cultural comparision or socio-cultural).mp.
17. or/12-16
18. attitude to health/
19. (view* or opinion* or perspective* or experience* or voice* or attitude* or feeling* or emotion* or thought* or belief* or influence* or qualitative or interview or interviews).ti,ab.
20. or/18-19
21. 5 and 11 and 17 and 20

Search in British Nursing Index (BNI)

((ti(pregnan* OR matern* OR gravid* OR mother OR parent) OR ab(pregnan* OR matern* OR gravid* OR mother OR parent)) OR ((SU.EXACT("Pregnancy") OR SU.EXACT("1:Pregnancy ") OR SU.EXACT.EXPLODE("Women's Health") OR SU.EXACT("Motherhood")) OR SU.EXACT.EXPLODE("Obstetrics"))) AND (SU.EXACT.EXPLODE("Ethnic Groups") OR (ti(Race OR Races OR Racial OR

Ethnic* OR Intra race OR Intra Races OR Intra racial OR Intra ethnic* OR Inter race OR Inter races OR Inter racial OR Inter ethnic*) OR ab(Race OR Races OR Racial OR Ethnic* OR Intra race OR Intra Races OR Intra racial OR Intra ethnic* OR Inter race OR Inter races OR Inter racial OR Inter ethnic*)) OR (ti(Asian* OR Indian* OR Bengali* OR Kashmiri* OR Gujarati* OR Tamil* OR Bangladesh* OR Pakistan* OR Sri Lanka*) OR ab(Asian* OR Indian* OR Bengali* OR Kashmiri* OR Gujarati* OR Tamil* OR Bangladesh* OR Pakistan* OR Sri Lanka*)) OR (ti(Nonwhite OR minority or non-white) OR ab(Nonwhite OR minority or non-white))) AND (SU.EXACT.EXPLODE("Culture and Religion") OR (Acculturation or culture or cultural or cultural characteristics or cross-cultural comparision or socio-cultural) OR (family relations or social support or social network*)) AND (SU.EXACT("Health Attitudes") OR (view* OR opinion* OR perspective* OR experience* OR voice* OR attitude* OR feeling* OR emotion* OR thought* OR belief* OR influence* or qualitative OR interview OR interviews))

Appendix 7: Starting point for Familiarization



Potential determinants and consequences for GWG according to 2009 IoM guidelines
(Adapted from Institute of Medicine. Weight Gain During Pregnancy: Re-examining the Guidelines. Yaktine A, Rasmussen K, editors. Washington DC: National Academic Press; 2009. Key: Black=information from the 2009 IoM guidelines)

Appendix 8: Table of included studies for framework based synthesis

No.	Author and year	Country of study	Qualitative or quantitative	BiB*/ not BiB	Total sample size and sample size for Pakistani or South Asian population	Ethnic group of interest
1	Bakken *et al* 2015 (246)	Norway	Quantitative	Not BiB	Total n=8524 (n=287 Pakistani; n=211 Pakistani born in Pakistan, n=76 Pakistani born in Norway)	Pakistani
2	Bandyopadhyay et al 2011 (275)	Melbourne, Australia	Qualitative	Not BiB	Total n=17 (n=1 Pakistani)	South Asian
3	Bansal *et al* 2014 (247)	Scotland	Quantitative	Not BiB	Total n 144,344 (n=1,072 Pakistani)	Pakistani
4	Ball et al 2012 (244)	Bradford, UK	Quantitative	BiB	Total n=2560 (n=1,212 Pakistani)	Pakistani
5	Bissenden *et al* 1981 (203)	Birmingham, UK	Quantitative	Not BiB	Total n=39 (n=11 Asian; Pakistani or Bangladeshi)	Asian: Pakistani or Bangladeshi
6	Bissenden *et al* 1981 (202)	Birmingham, UK	Quantitative	Not BiB	Total n=70 (n=39 Asian; Pakistani or Bangladeshi)	Asian: Pakistani or Bangladeshi
7	Bryant *et al* 2014 (171)	Bradford, UK	Quantitative	BiB	Total n=8,478 (n=4,547 Pakistani)	Pakistani
8	Bundey et al 1990 (248)	Birmingham, UK	Quantitative	Not BiB	Total n= 4,394 (n=956 Pakistani)	Pakistani
9	Bundy *et al* 1991 (249)	Birmingham, UK	Quantitative	Not BiB	Total n= 4,394 (n=956 Pakistani)	Pakistani
10	Busk-Rasmussen *et al* 2014 (250)	Denmark	Quantitative	Not BiB	Total n=42420 (n=992 Pakistani)	Pakistani
11	Bowes and Domokos 1998 (276)	Scotland	Qualitative	Not BiB	Total n=205 (n=62 Pakistani women, n=50 health visitors and n=25 general practitioners)	Pakistani
12	Bowler 1993 (282)	South England	Qualitative	Not BiB	15 interviews with midwives to South Asian women	South Asian
13	Cabieses *et al* 2014 (229)	Bradford, UK	Quantitative	BiB	Total n=476 (n=157 Pakistani)	Pakistani

No.	Author and year	Country of study	Qualitative or quantitative	BiB*/ not BiB	Total sample size and sample size for Pakistani or South Asian population	Ethnic group of interest
14	Chitty and Winter 1989 (269)	North West and Thames region, UK	Quantitative	Not BiB	Total n=63,44 (n=3,507 Pakistani)	Pakistani
15	Choudhry and Wallace 2012 (277)	UK	Qualitative	Not BiB	Total n=20 (n=17 Pakistani)	South Asian; mainly Pakistani
16	Dadvand et al (230)	Bradford, UK	Quantitative	BiB	Total n=10,780 (n=4,889 Pakistani)	Pakistani
17	Dornhorst *et al* 1992 (207)	London, UK	Quantitative	Not BiB	Total n=7,273 (n=1164 Indian; from the Indian subcontinent)	Indian; from the Indian subcontinent
18	Dunne et al 2009	Birmingham, UK	Quantitative	Not BiB	Total n=440 (n=128 Indo-Asian)	South Asian
19	Fairley et al 2013 (231)	Bradford, UK	Quantitative	BiB	Total n=1,434 (n=792 Pakistani)	Pakistani
20	Fraser et al 2012 (232)	Bradford, UK	Quantitative	BiB	Total n=1,198 (n= 876 South Asian)	South Asian
21	Gardosi *et al* 2013 (251)	UK	Quantitative	Not BiB	Total n=105, 476 (n=7,834 Pakistani; n=3,426 born in UK and 4,408 not born in UK)	Pakistani
22	Greenhalgh et al (2015) (278)	London, UK	Qualitative	Not BiB	Total n=45 (N=45 South Asian of which N=13 women of North Indian or Pakistani origin)	South Asian
23	Griffiths *et al* 2007 (252)	UK	Quantitative	Not BiB	Total n=18,150 (n=857 Pakistani)	Pakistani
24	Griffiths *et al* 2011 (267)	UK	Quantitative	Not BiB	Total n=13,590 (n=548 Pakistani)	Pakistani
25	Grjibovski et al 2009	Norway	Quantitative	Not BiB	Total n=1962 (n=1,962 Pakistani)	Pakistani
26	Harding *et al* 2004 (253)	England and Wales	Quantitative	Not BiB	Total n=57,674 (n=1,538 Pakistani; n=1,121 born in Pakistan and n=417 born in England or Wales)	Pakistani

No.	Author and year	Country of study	Qualitative or quantitative	BiB*/ not BiB	Total sample size and sample size for Pakistani or South Asian population	Ethnic group of interest
27	Hernandez-Rivas *et al* 2013 (215)	Barcelona, Spain	Quantitative	Not BiB	Total n=271 (n=81 South Central Asian; Pakistan, India, Bangladesh)	South Central Asian: Pakistan, India, Bangladesh
28	Higgins and Dale 2012 (254)	UK	Quantitative	Not BiB	Total n=7,047 (n=522 Pakistani boys and n=523 Pakistani girls)	Pakistani
29	Honeyman *et al* 1987 (255)	Birmingham, England	Quantitative	Not BiB	Total n=260 (n=260 Pakistani)	Pakistani
30	Ibison 2005 (256)	London, UK	Quantitative	Not BiB	Total n=27,667 (n=1009 Pakistani)	Pakistani
31	Ingram *et al* 2008 (279)	Bristol, UK	Qualitative	Not BiB	Total n=22 (n=12 South Asian)	South Asian
32	Ingram *et al* 2003 (281)	Bristol, UK	Qualitative (Mixed methods study but only qualitative part relevant)	Not BiB	Total n=14 (n=5 Pakistani)	Pakistani
33	Kelly *et al* 2006 (268)	UK	Quantitative	Not BiB	Total n=17,474 (n=742 Pakistani)	Pakistani
34	Kelly *et al* 2009 (257)	UK	Quantitative	Not BiB	Total n=16,157 (n=687 Pakistani)	Pakistani
35	Lawlor et al 2014 (233)	Bradford, UK	Quantitative	BiB	Total n=1,415 (n=786 Pakistani)	Pakistani
36	Lawton et al 2012 (234)	Bradford, UK	Quantitative	BiB	Total n=184 (n=115 South Asian)	South Asian
37	Leon *et al* 2010 (258)	England and Wales	Quantitative	Not BiB	Total n=1,315,325 (n=48,053 Pakistani; 28,566 born in Pakistan and 17,583 born in England or Wales)	Pakistani
38	Makgoba *et al* 2011 (205)	London, UK	Quantitative	Not BiB	Total n=134,150 (n=2,749 South Asian)	South Asian
39	Makgoba *et al* 2012 (206)	London, UK	Quantitative	Not BiB	Total n=123,718 (n=15,817 South Asian)	South Asian

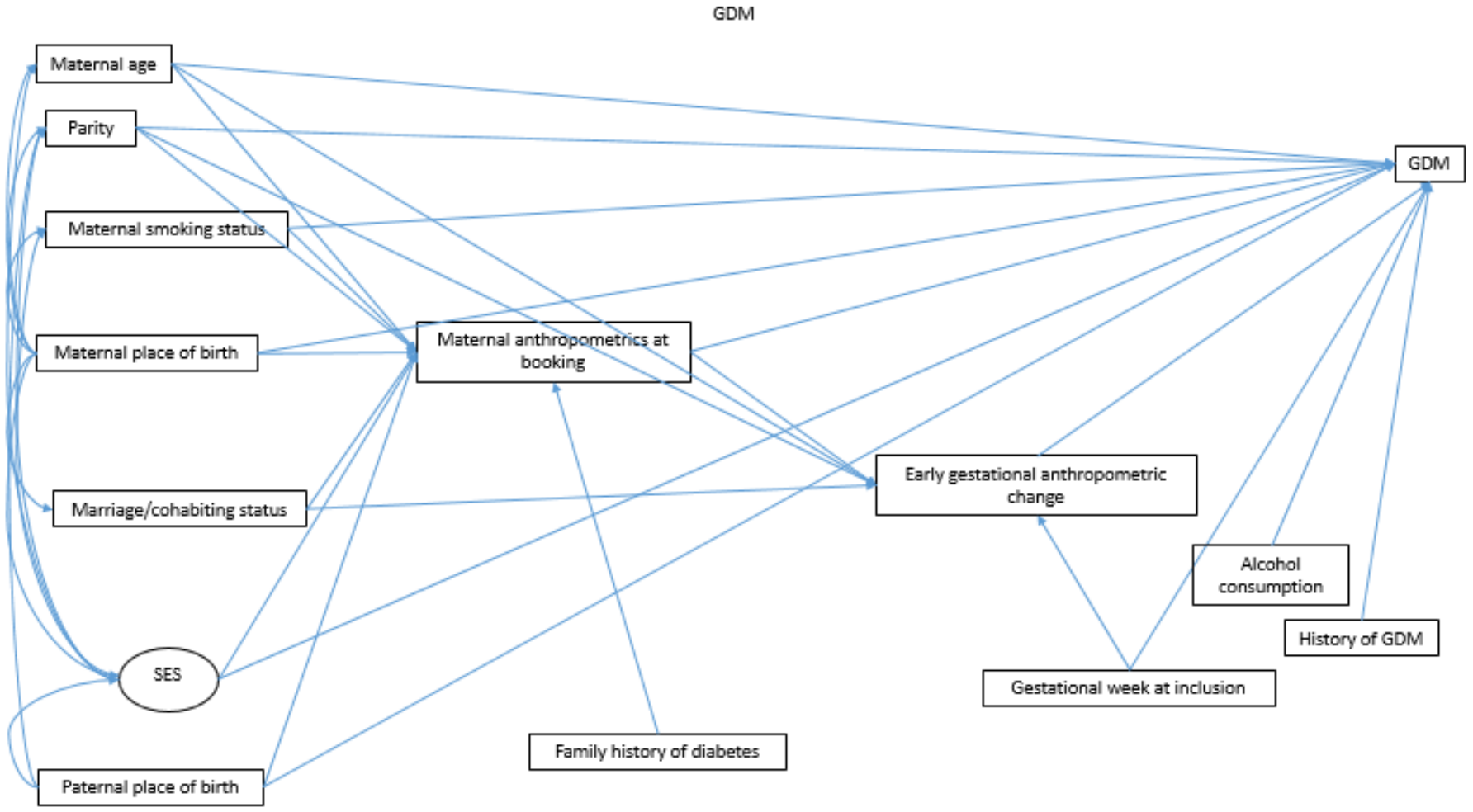
No.	Author and year	Country of study	Qualitative or quantitative	BiB*/ not BiB	Total sample size and sample size for Pakistani or South Asian population	Ethnic group of interest
40	Moser *et al* 2008 (270)	England and Wales	Quantitative	Not BiB	N= 649,371 (n=24,290 Pakistani)	Pakistani
41	Nair *et al* 2015 (259)	UK	Quantitative	Not BiB	Total n=1,796 (n=80 Pakistani)	Pakistani
42	Norris et al 2014 (235)	Bradford, UK	Quantitative	BiB	n=12,453 (n Pakistani not specified in paper)	Pakistani
43	Oteng-Ntim *et al* 2013 (204)	London, UK	Quantitative	Not BiB	Total n=13,580 (n=1162 Asian; Bangladeshi, Indian, Pakistani, other Asian and Asian British)	Asian; Bangladeshi, Indian, Pakistani, other Asian and Asian British
44	Pallan, Parry and Adab 2012 (260)	Birmingham, UK	Qualitative	Not BiB	Total n=68 (n=6 Pakistani)	Pakistani
45	Penn *et al* 2014 (201)	London, UK	Quantitative	Not BiB	Total n=29,347 (Asian; Indian, Pakistani, Bangladeshi, Asian Other n=2,857)	Asian; Indian, Pakistani, Bangladeshi, Asian Other
46	Pedersen *et al* 2012 (261)	Denmark	Quantitative	Not BiB	Total n=1,626,880 (n=10,859 Pakistani)	Pakistani
47	Petherick, Tuffnell and Wright 2014 (236)	Bradford, UK	Quantitative	BiB	Total n=310 (n=161 Pakistani)	Pakistani
48	Prady (245)	Bradford, UK	Quantitative	BiB	Total n=3,261 (n=1,360 Pakistani)	Pakistani
49	Prady et al 2011 (243)	Bradford, UK	Quantitative	BiB	Total n=8,454 (n=2,542 Pakistani)	Pakistani
50	Pu et al 2015 (216)	Northern California, USA	Quantitative	Not BiB	Total n=14,080 (n=5,069 Asian Indian)	Asian Indian
51	Retnakaran et al 2006 (161)	Canada	Quantitative	Not BiB	Total n=147 (n=31 South Asian; India, Pakistan, Sri Lanka and Bangladesh)	South Asian; India, Pakistan, Sri Lanka and Bangladesh

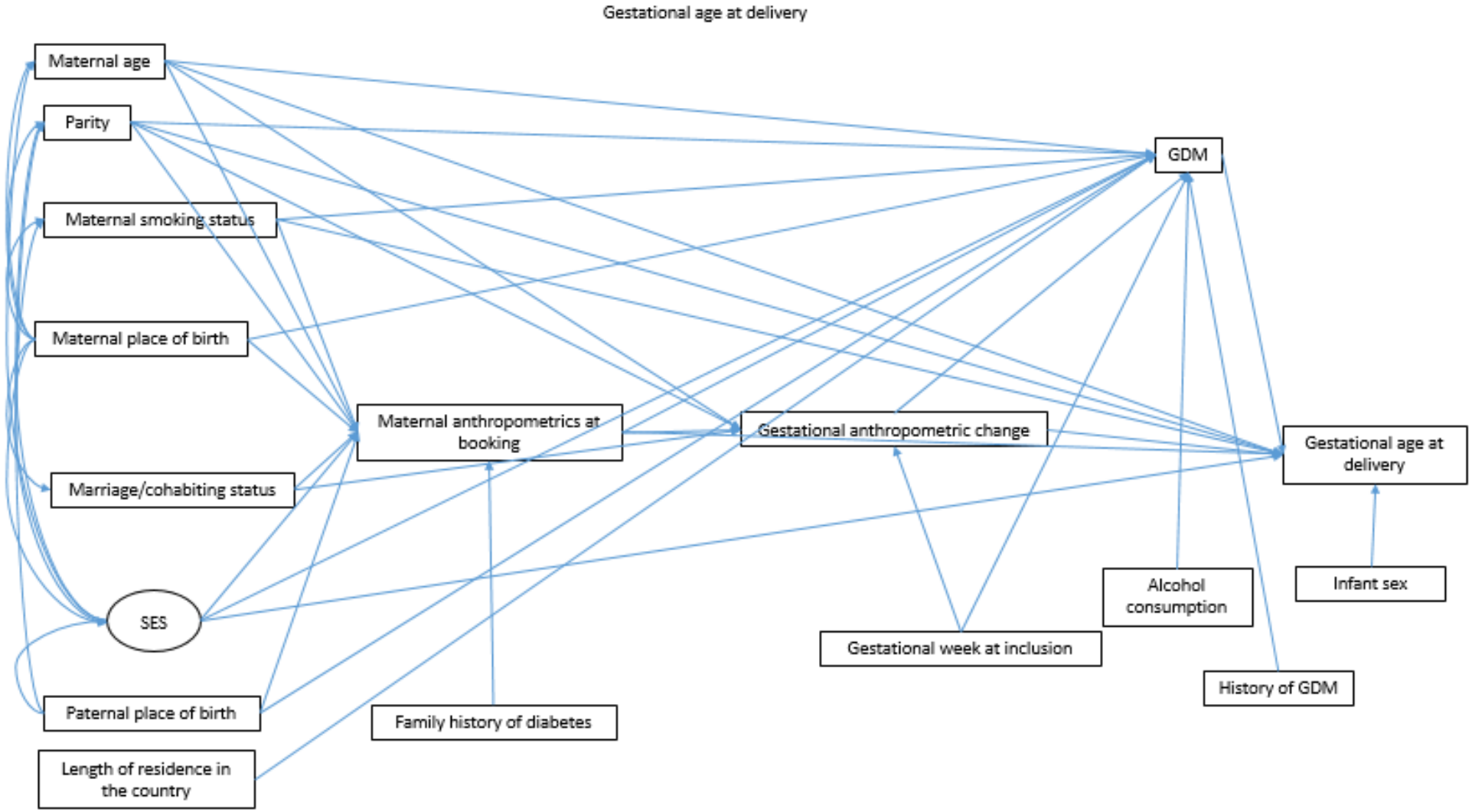
No.	Author and year	Country of study	Qualitative or quantitative	BiB*/ not BiB	Total sample size and sample size for Pakistani or South Asian population	Ethnic group of interest
52	Sacker et al 2012(274)	UK			(Total n = 18,552) (n= Pakistani not specified)	Pakistani
53	Sanchalika and Teresa 2015 (262)	New Jersey, USA	Quantitative	Not BiB	Total n=327,069 (n=2,924 Pakistani)	Pakistani
54	Santorelli et al 2013 (238)	Bradford, UK	Quantitative	BiB	Total n=1,326 (n=646 Pakistani)	Pakistani
55	Santorelli et al 2014 (237)	Bradford, UK	Quantitative	BiB	Total n=1,326 (n=646 Pakistani)	Pakistani
56	Saxena et al 2016 (263)	UK	Quantitative	Not BiB	Total n=5,689 (n=894 Pakistani)	Pakistani
57	Schembari et al 2015 (239)	Bradford, UK	Quantitative	Not BiB	Total n=9,067 (n=4,878 Pakistani)	Pakistani
58	Sharma et al 2011 (208)	Oxford, UK	Quantitative	Not BiB	Total n=958 (N= 249 Asian or Asian British; Indian, Pakistani, Bangladeshi or any other Asian background)	South Asian
59	Sheridan et al 2013 (200)	Bradford, UK	Quantitative	BiB	Total n=9,615 (n=5,127 Pakistani)	Pakistani
60	Sinha et al 2002 (209)	Birmingham, UK	Quantitative	Not BiB	Total n=180 (n=89 Indo Asian; Predominantly Muslim women from the Punjab Region)	Indo Asian; Predominantly Muslim women from the Punjab Region
61	Sommer et al 2015 (212)	Groruddalen, Oslo, Norway	Quantitative	Not BiB	Total n=543 (n=190 South Asian; 63% Pakistani and 31% Sri Lankan)	South Asian; 63% Pakistani and 31% Sri Lankan
62	Sommer et al 2014 (211)	Groruddalen, Oslo, Norway	Quantitative	Not BiB	Total n=529 (n=181 South Asian)	South Asian
63	Sørbye et al 2014 (264)	Norway	Quantitative	Not BiB	Total n=723, 045 (n=10,615 Pakistani; n=8,814 Pakistani born, and n=1,801 Norwegian born)	Pakistani

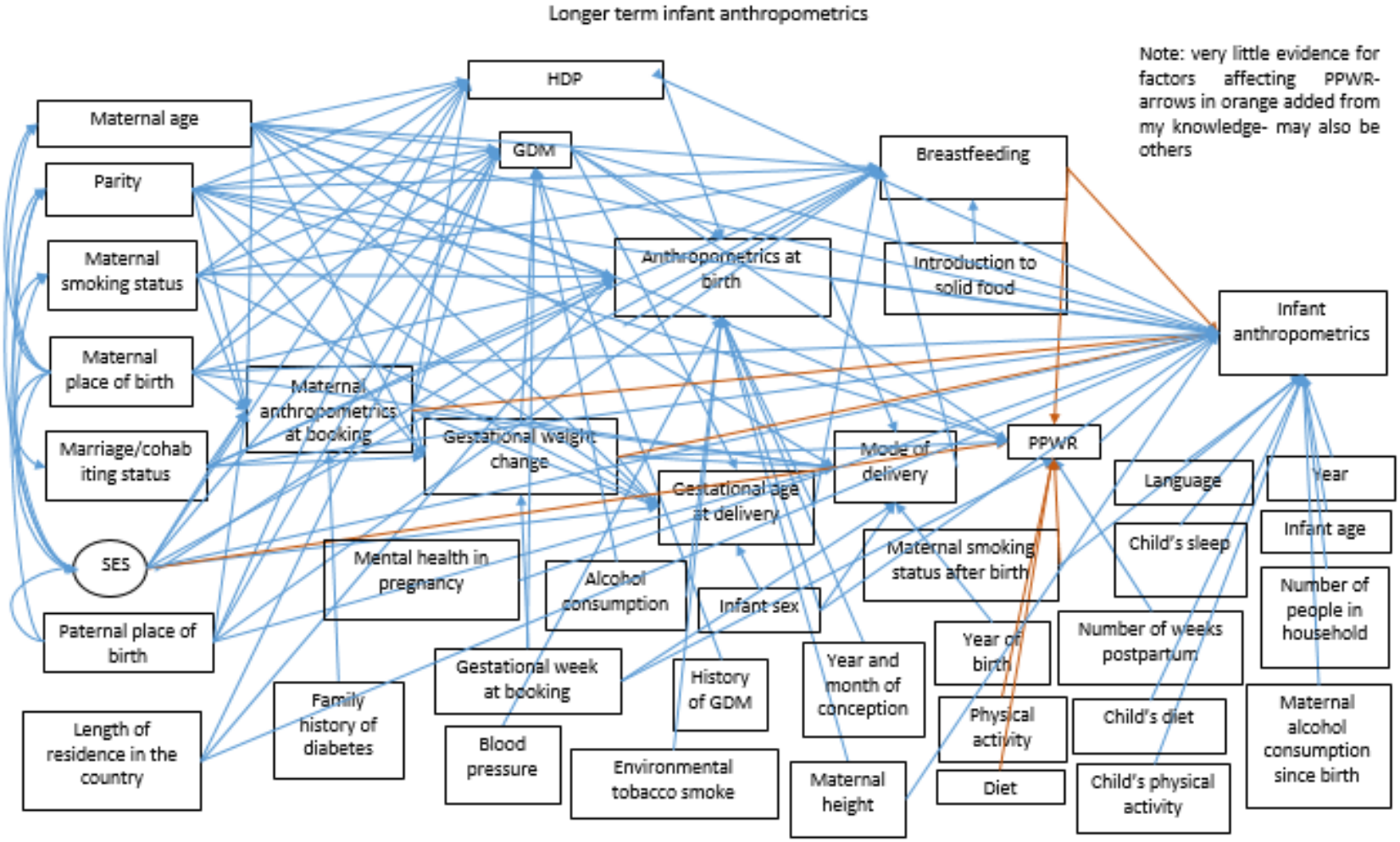
No.	Author and year	Country of study	Qualitative or quantitative	BiB*/ not BiB	Total sample size and sample size for Pakistani or South Asian population	Ethnic group of interest
64	Stoltenberg *et al* 1997 (271)	Norway	Quantitative	Not BiB	Total n=1,566,839 (n=7,494 children with two Pakistani parents)	Pakistani
65	Terry, Condie and Settatree 1980 (265)	Birmingham, UK	Quantitative	Not BiB	Total n=3,996 (n=571 Pakistani)	Pakistani
66	Traviss et al 2012, (240)	Bradford, UK	Quantitative	BiB	Total n=1,716 (n=824 Pakistani)	Pakistani
67	Twamley *et al* 2011 (280)	London and Birmingham, UK	Qualitative	Not BiB	Total n=34 women and N=34 health care professionals (n=4 Pakistani)	Pakistani
68	Uphoff et al 2015 (283)	Bradford, UK and national, UK	Quantitative	BiB and Not BiB	Total n=17,421 (N=5,318 Pakistani) BiB: Total n=8,441 (Pakistani n=4,462) Other cohort: Total n=8,980 (Pakistani n=856)	Pakistani
69	Villadsen, Mortensen and Andersen 2009 (272)	Denmark	Quantitative	Not BiB	Total n=1,333,452 (n=8,481 Pakistani)	Pakistani
70	West et al 2013 (168)	Bradford, UK	Quantitative	BiB	Total n= 8,704 (n=4,649 Pakistani)	Pakistani
71	West et al 2013 (242)	Bradford, UK	Quantitative	BiB	Total n=1,482) (n=823 Pakistani)	Pakistani
72	West et al 2014 (241)	Bradford, UK	Quantitative	BiB	Total n=7,159 (n=3656 Pakistani)	Pakistani
73	Wong et al 2012 (213)	New South Wales, Australia	Quantitative	Not BiB	Total n=375 (n=160 South Asian; Indian, Pakistani, Sri Lankan and Fiji Indian)	South Asian
74	Yue et al 1996 (214)	Sydney, Australia	Quantitative	Not BiB	Total n=2526 (n=114 Indian)	Indian
75	Zilanawala *et al* 2015 (266)	UK	Quantitative	Not BiB	Total n=18,370 (n=926 Pakistani)	Pakistani

*BiB refers to studies using participants that were included in the BiB/BiB 1000 cohort; this may be the whole sample, or a subsample

Appendix 9: Conceptual models for example outcomes using evidence from systematic review (Chapter 3) and framework based synthesis (Chapter 4)




Gestational age at delivery
Maternal age
Parity
Maternal smoking status
Maternal place of birth
Marriage/cohabiting status
SES
Paternal place of birth
Length of residence in the country
Maternal anthropometrics at booking
Family history of diabetes
GDM
Gestational anthropometric change
Gestational week at inclusion
Alcohol consumption
History of GDM
Gestational age at delivery
Infant sex


Longer term infant anthropometrics
Note: very little evidence for factors affecting PPWR- arrows in orange added from my knowledge- may also be others
HDP
Maternal age
GDM
Breastfeeding
Parity
Maternal smoking status
Anthropometrics at birth
Introduction to solid food
Infant anthropometrics
Maternal place of birth
Maternal anthropometrics at booking
Gestational weight change
Mode of delivery
PPWR
Marriage/cohabiting status
Gestational age at delivery
Language
Year
Infant age
SES
Mental health in pregnancy
Alcohol consumption
Infant sex
Maternal smoking status after birth
Child's sleep
Number of people in household
Paternal place of birth
Year of birth
Number of weeks postpartum
Gestational week at booking
History of GDM
Year and month of conception
Physical activity
Child's diet
Maternal alcohol consumption since birth
Length of residence in the country
Family history of diabetes
Blood pressure
Environmental tobacco smoke
Maternal height
Diet
Child's physical activity

Appendix 10: Agenda for expert opinion meeting

Agenda
Conceptual model feedback meeting
Tuesday 4th October 2016, 12-1pm
Gallery room

- **Welcome and introductions**
- **PhD project**
    - This PhD project is part of a 1+3 MRC funded studentship and aims to investigate the association between ethnic groups (White and South Asian), maternal pre-/early pregnancy anthropometrics, change in anthropometrics during pregnancy, and short- and long-term pregnancy outcomes for both mother and infant
    - The project consists of a number of stages:
        - Development of hypothetical conceptual model
            - Systematic review
            - Framework based synthesis
            - Expert opinion
        - Data analysis to test hypothetical conceptual model using BiB Data and structural equation modelling.

- **Purpose of meeting**
    - To ask for your feedback on a hypothetical conceptual model of the associations between maternal pre-/early pregnancy anthropometrics, change in anthropometrics during pregnancy and pregnancy outcomes in South Asian women developed using a systematic review and framework based synthesis
    - To ask for your feedback on a list of variables which may influence the associations in the conceptual model

- **Brief presentation (10 minutes): Description of conceptual model development process**
    - Systematic review
    - Framework based synthesis
    - Expert opinion

- **Discussion of exposures and outcomes**
    - Missing associations?
    - Missing outcomes?
    - Missing interactions between outcomes?

- **Discussion of list of factors influencing associations in the conceptual model**
    - Are there any missing factors?
    - Interactions between factors?

- **Next steps and timeline**

	Oct	Nov	Dec	Jan	Feb	March	April	May	June	July	Aug	Sept
Selection of final variables												
Data request and arrival of data												
Write up systematic review for publication												
Data cleaning and coding												
Data analysis and structural equation modelling												
Write up thesis												

Appendix 11: Information handed out at expert opinion meeting

Summary of variables identified from systematic review and framework-based synthesis for consideration for inclusion in hypothetical conceptual model

Exposures identified: Weight, BMI, tricep skinfold, subscapular skinfold, suprailliac skinfold, sum of skinfolds, serum leptin levels as a measure of adiposity, mid upper arm circumference, total body fat, truncal body fat, weight gain, fat mass gain, truncal fat gain, mean skinfold gain and mid upper arm circumference gain

Outcomes identified: Gestational diabetes, hypertensive disorders of pregnancy, (estimated fetal adiposity), maternal death, anthropometrics at birth, stillbirth, perinatal death, mode of delivery, gestational age at delivery, congenital anomalies, breastfeeding, post-partum impaired glucose tolerance, post-partum weight retention and childhood anthropometrics

Factors influencing: Variables identified by systematic review (purple) and framework based synthesis (white) as associated with exposure, outcome or both

Variable type	Associated with exposure (i.e. maternal pre-early pregnancy anthropometrics/change in anthropometrics during pregnancy) only	Associated with outcome (i.e. pregnancy outcomes) only	Associated with both exposure and outcome	Associated with exposure or outcome not both	Variable not associated with both exposure and outcome to be included? (Yes/No and reason)
Measures of SES	• maternal education • insurance status	• mothers education • insurance status • Carstairs index • father's employment • IMD • highest occupation in household • highest education in household • housing tenure • annual household income • means tested benefits • financial situation • mother's employment	• maternal education • insurance status	• Carstairs index • father's employment • IMD • highest occupation in household • highest education in household • housing tenure • annual household income • means tested benefits • financial situation • mother's employment	
Sociodemographic:	• Maternal age • parity • Marriage /cohabiting status • Maternal anthropometrics	• Maternal age • parity • Marriage/cohabiting status • Maternal anthropometrics • mothers anthropometrics at 6 months post-partum • maternal height • paternal anthropometrics	• Maternal age • parity • Marriage/cohabiting status • Maternal anthropometrics	• marriage/cohabiting status • Mothers anthropometrics at 6 months post-partum • maternal height • paternal anthropometrics	
Infant sociodemographic characteristics		• infant age • infant sex • genetics		• infant age • infant sex • genetics	
Pre-existing comorbidities/physical health status	• HOMA-IR • Insulin	• HOMA-IR • highest diastolic blood pressure	• HOMA-IR • maternal fasting glucose	• highest diastolic blood pressure • Glucose intolerance	

		• Anaemia • maternal hypertension • Glucose intolerance • Insulin • maternal fasting glucose • pre-existing medical conditions	• insulin	• maternal fasting glucose • Insulin • anaemia • maternal hypertension • pre-existing medical conditions	
Behavioural	• Maternal diet • maternal exercise • Smoking • Gestational week at inclusion	• maternal Diet • maternal exercise • smoking • Gestational week at inclusion • Alcohol • Maternal consumption of alcohol since birth • Antenatal care attendance • Mothers smoking after pregnancy • Substance misuse • Timely initiation of prenatal care • Environmental tobacco smoke • Childs diet • Child's physical activity • Bedtime of child at weekdays	• Maternal diet • maternal exercise • Smoking • Gestational week at inclusion	• Alcohol • Maternal consumption of alcohol since birth • Antenatal care attendance • Mothers smoking after pregnancy • Substance misuse • Timely initiation of prenatal care • Environmental tobacco smoke • Childs diet • Child's physical activity • Bedtime of child at weekdays	
Family history relating to ethnicity and acculturation:	• fathers place of birth • mothers place of birth	• length of residence in country of mother • mother's immigration status • migrant generation • fathers place of birth • mothers place of birth	• fathers place of birth • mothers place of birth	• length of residence in country • mother's immigration status • migrant generation	

Family history of illness	• family history of diabetes • family history of type 2 diabetes •	• family history of type 2 diabetes	• family history of type 2 diabetes	• family history of diabetes	
Culture/tradition	• beliefs	• cultural norms/traditions • language spoken at home • Consanguinity		• Beliefs • cultural norms/traditions • language spoken at home • Consanguinity	
Mental wellbeing	• Weight issues • GHQ score in pregnancy	• mothers GHQ score (subscale D) in pregnancy	• GHQ score in pregnancy	• weight issues	
History of pregnancy problems		• previous pregnancy problems, previous history of GDM, previous live and stillbirths		• previous pregnancy problems, previous history of GDM, previous live and stillbirths	
Pregnancy outcomes (evidence of interaction with other pregnancy outcome)		• Anthropometric change during pregnancy • Complications during pregnancy • Augmentation • Birthweight • congenital anomalies • GDM • gestational age at delivery • HDP • induction • Insulin requirement in pregnancy • IUGR		• Anthropometric change during pregnancy • complications during pregnancy • Augmentation • Birthweight • congenital anomalies GDM • gestational age at delivery • HDP • induction • Insulin requirement in pregnancy • IUGR	
Other	• food outlet availability	• conception year and season • year of birth • year of first birth • cord blood insulin • cord blood leptin • hospital of birth • multiple pregnancies • T2DM-GDM age gap		• food outlet availability • conception year and season • year of birth • year of first birth • cord blood insulin • cord blood leptin • Hospital of birth	

		• number of children in household • number of weeks post-partum		• multiple pregnancies • T2DM-GDM age gap • number of children in household • number of weeks post-partum	

Additional variables and reason for inclusion

Additional notes

Appendix 12: Determining which variables are mediators, competing exposures and confounders- additional example where gestational weight gain is also considered an exposure

Determining which variables are mediators, competing exposures and confounders for maternal anthropometrics at booking as an exposure and gestational age at delivery as an outcome.

Variable	Column A: **Precedes exposure maternal anthropometrics at booking**	Column B: **Precedes outcome gestational age at delivery**	Column C: **Follows exposure maternal anthropometrics at booking**	Mediator/ confounder/ competing exposure
Place of birth	X	X	-	Confounder
Family history of diabetes	X	X	-	Confounder
Maternal age	X	X	-	Confounder
Parity	X	X	-	Confounder
Marriage/cohabiting status	X	X	-	Confounder
SES:			-	
Maternal education	X	X		Confounder
Maternal employment	X	X		Confounder
Paternal education	X	X		Confounder
Paternal employment	X	X		Confounder
IMD	X	X		Confounder
Housing tenure	X	X		Confounder
Gestational week at booking	-	X	X	Mediator
Maternal smoking status	X	X	-	Confounder
Length of residence in the country	X	X	-	Confounder
Maternal alcohol consumption	X	X	-	Confounder
Infant sex	-	X	X	Mediator
Environmental tobacco smoke	X	X	-	Confounder
Maternal height	X	X	-	Confounder
GDM	-	X	X	Mediator
GWG	-	X	X	Mediator
History of GDM	X	X	-	Confounder

Note: Those variables that are in columns A and B are confounders, variables that are only in column B are competing exposures, and those that are in columns B and C are mediators

Determining which variables are mediators, competing exposures and confounders for GWG as an exposure and mode of delivery as an outcome.

Variable	Column A: **Precedes GWG**	Column B: **Precedes outcome gestational age at delivery**	Column C: **Follows exposure GWG**	Mediator/ confounder/ competing exposure
Place of birth	X	X	-	Confounder
Family history of diabetes	X	X	-	Confounder
Maternal age	X	X	-	Confounder
Parity	X	X	-	Confounder
Marriage/cohabiting status	X	X	-	Confounder
SES:			-	
Maternal education	X	X		Confounder
Maternal employment	X	X		Confounder
Paternal education	X	X		Confounder
Paternal employment	X	X		Confounder
IMD	X	X		Confounder
Housing tenure	X	X		Confounder
Gestational week at booking	X	X	-	Confounder
Maternal smoking status	X	X	-	Confounder
Length of residence in the country	X	X	-	Confounder
Maternal alcohol consumption	X	X	-	Confounder
Infant sex	-	X	X	Mediator
Environmental tobacco smoke	X	X	-	Confounder
Maternal anthropometrics at booking	X	X	-	Confounder
Maternal height	X	X	-	Confounder
GDM	-	X	X	Mediator
History of GDM	X	X	-	Confounder

Note: Those variables that are in columns A and B are confounders, variables that are only in column B are competing exposures, and those that are in columns B and C are mediators

The majority of GWG follows GDM diagnosis, therefore GDM has been considered as mediator

Appendix 13: Born in Bradford ethical approval

Bradford Research Ethics Committee

NHS

Top Floor
Extension Block
St Lukes Hospital
Little Horton Lane
Bradford
BD5 0NA

Chairman: **Professor Alan C Roberts**
OBE TD DL MPhil PhD DSc LLD FLS CBiol FIBiol
Administrator: Sue Bell

Tel: 01274 365508 **Email:** sue.bell@bradfordhospitals.nhs.uk
Fax: 01274 365509 **Email:** alan.roberts@bradfordhositals.nhs.uk

14 August 2006

Professor John Wright
Consultant in Clinical Epidemiology and Public Health.
Bradford Teaching Hospitals NHS Foundation Trust
Department of Clinical Quality & Research
Bradford Royal Infirmary

Dear Professor Wright

Full title of study: **Born in Bradford: a longitudinal multiethnic birth cohort study to investigate the determinants of childhood growth, development and health.**
REC reference number: **06/Q1202/48**

Thank you for your letter of 26 July 2006, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chairman.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form. [Confirmation of approval for other sites listed in the application will be issued as soon as local assessors have confirmed they have no objection.]

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Application	1	28 April 2006
Investigator CV		19 April 2006
Protocol	1	20 April 2006
Covering Letter		02 May 2006
Questionnaire: Born in Bradford	1	28 April 2006
Questionnaire: Baby's Father	1	28 April 2006

Questionnaire: Health Survey Scoring Demonstration	1	28 April 2006
Letter of invitation to participant	1	19 April 2006
GP/Consultant Information Sheets	1	19 April 2006
Participant Information Sheet: Under 16s	1	26 July 2006
Participant Information Sheet: Born in Bradford	4	26 July 2006
Participant Consent Form: Fathers	2	26 July 2006
Participant Consent Form: Mothers	2	26 July 2006
Response to Request for Further Information		26 July 2006
Data Collection Sheet	1	03 April 2006
DVD script	1	01 December 2005
Protocol Flowchart	1	19 April 2006

Research governance approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/Q1202/48	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project
Yours sincerely

Professor A Roberts
Chairman – Bradford Research Ethics Committee

Enclosures: *Standard approval conditions*
Site approval form

e-mailed copy to: R & D Department
Bradford Teaching Hospitals NHS Foundation Trust
Bradford Royal Infirmary
Duckworth Lane
Bradford

SF1 list of approved sites

Bradford Research Ethics Committee

LIST OF SITES WITH A FAVOURABLE ETHICAL OPINION

For all studies requiring site-specific assessment, this form is issued by the main REC to the Chief Investigator and sponsor with the favourable opinion letter and following subsequent notifications from site assessors. For issue 2 onwards, all sites with a favourable opinion are listed, adding the new sites approved.

REC reference number:	06/Q1202/48	**Issue number:**	1	**Date of issue:**	14 August 2006
Chief Investigator:	Professor John Wright				
Full title of study:	Born in Bradford: a longitudinal multiethnic birth cohort study to investigate the determinants of childhood growth, development and health.				

This study was given a favourable ethical opinion by Bradford Research Ethics Committee on 01 August 2006. The favourable opinion is extended to each of the sites listed below. The research may commence at each NHS site when management approval from the relevant NHS care organisation has been confirmed.

Principal Investigator	*Post*	*Research site*	*Site assessor*	*Date of favourable opinion for this site*	*Notes (1)*
Prof John Wright	Consultant in Clinical Epidermiology and Public Health	Bradford Teaching Hospitals NHS Foundation Trust	Bradford Research Ethics Committee	14/08/2006	

Approved by the Chair on behalf of the REC:

S Ball ..... (Signature of Chair/Administrator)
(delete as applicable)

S BALL ..... (Name)

SF1 list of approved sites

(1) *The notes column may be used by the main REC to record the early closure or withdrawal of a site (where notified by the Chief Investigator or sponsor), the suspension of termination of the favourable opinion for an individual site, or any other relevant development. The date should be recorded.*

Appendix 14: Newcastle University ethical approval

Newcastle University

05 October 2015

Miss Emma Slack
Institute of Health & Society

Faculty of Medical Sciences
Newcastle University
The Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH United Kingdom

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Emma

Title: A life course investigation of maternal ethnic group and pregnancy weight in the development of short- and long-term health outcomes for women and their offspring
Application No: 00908/2015
Start date to end date: 01 August 2015 to 31 August 2017

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: **00908/2015.** If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation.*

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee.*

Best wishes,

Yours sincerely

M. Holbrough

Marjorie Holbrough
On behalf of Faculty Ethics Committee

cc.
Professor Daniel Nettle, Chair of FMS Ethics Committee
Ms Lois Neal, Assistant Registrar (Research Strategy)

*Please refer to the latest guidance available on the internal Newcastle web-site.

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Newcastle University

Faculty of Medical Sciences
Newcastle University
The Medical School
Framlington Place
Newcastle upon Tyne
NE2 4HH United Kingdom

Miss Emma Slack
Institute of Health & Society

FACULTY OF MEDICAL SCIENCES: ETHICS COMMITTEE

Dear Emma

Title: A life course investigation of maternal ethnic group and pregnancy weight in the development of short- and long-term health outcomes for women and their offspring
Application No: 00908_1/2016 Amendment
Start date to end date: 01 August 2015 to 01 September 2018

On behalf of the Faculty of Medical Sciences Ethics Committee, I am writing to confirm that the ethical aspects of your proposal have been considered and your study has been given ethical approval.

The approval is limited to this project: **00908_1/2016.** If you wish for a further approval to extend this project, please submit a re-application to the FMS Ethics Committee and this will be considered.

During the course of your research project you may find it necessary to revise your protocol. Substantial changes in methodology, or changes that impact on the interface between the researcher and the participants must be considered by the FMS Ethics Committee, prior to implementation.*

At the close of your research project, please report any adverse events that have occurred and the actions that were taken to the FMS Ethics Committee.*

Best wishes,

Yours sincerely

K. Sutherland

Kimberley Sutherland
On behalf of Faculty Ethics Committee

cc.
Professor Daniel Nettle, Chair of FMS Ethics Committee
Ms Lois Neal, Assistant Registrar (Research Strategy)

*Please refer to the latest guidance available on the internal Newcastle web-site.

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Appendix 15: Summary for GWG including missing data

		All		White British		Pakistani		P value for ethnic difference
Women with underweight BMI (<18.5kg/m^2)	Low <12.5kg	131	38.76	25	26.04	106	43.80	0.074
	Recommended 12.5-18kg (reference[a])	59	17.48	16	16.67	43	17.77	0.378
	High >18kg	14	4.14	6	6.25	8	3.31	0.078
	Missing[b]	134	39.64	49	51.04	85	35.12	0.007*
Women with recommended BMI (18.5 to <25.0kg/m^2)	Low <11.5kg	1,045	28.68	371	21.95	674	34.50	0.045*
	Recommended 11.5-16kg (reference[a])	655	17.98	267	15.80	388	19.86	0.037*
	High >16kg	247	6.78	93	5.50	154	7.88	0.970
	Missing[b]	1,697	46.57	959	56.75	738	37.77	<0.001*
Women with overweight BMI (25.0 to <30.0kg/m^2)	Low <7.5kg	428	18.06	147	13.39	281	22.09	0.003*
	Recommended 7.5-11.5 (reference[a])	404	17.05	153	13.93	251	19.73	0.284
	High >11.5kg	405	17.09	195	17.76	210	16.51	<0.001
	Missing[b]	1,133	47.81	603	54.91	530	41.67	<0.001*
Women with obese BMI (≥30/m^2)	Low <5kg	314	18.21	158	16.97	156	19.67	0.532
	Recommended 5-9kg (reference[a])	266	15.43	112	12.03	154	19.42	0.008*
	High >9kg	291	16.88	156	16.76	135	17.02	0.050
	Missing[b]	853	49.48	505	54.24	348	43.88	<0.001*
GWG categories for BMI	Low	1,787	20.75	676	16.54	1,111	24.55	0.002*
	Recommended (reference[a])	1,384	16.07	548	13.41	836	18.48	0.377
	High	943	10.95	444	10.86	499	11.03	<0.001*
	Missing[b]	4,499	52.23	2,420	59.20	2,079	45.9	<0.001*

		All		White British		Pakistani		P value for ethnic difference
Women with underweight BMI (<18.5kg/m^2)	Low <12.5kg	131	38.76	25	26.04	106	43.80	0.074
	Recommended 12.5-18kg (reference[a])	59	17.48	16	16.67	43	17.77	0.378
	High >18kg	14	4.14	6	6.25	8	3.31	0.078
	Missing[b]	134	39.64	49	51.04	85	35.12	0.007*
Women with recommended BMI (White British: 18.5 to <25.0kg/m^2) (Pakistani: 18.5 to <23.0kg/m^2)	Low <11.5kg	778	26.06	371	21.95	407	31.40	0.633
	Recommended 11.5-16kg (reference[a])	534	17.88	267	15.80	267	20.60	0.324
	High >16kg	202	6.76	93	5.50	109	8.41	0.493
	Missing[b]	1,472	49.30	959	56.75	513	39.58	<0.001*
Women with overweight BMI (White British: 25.0 to <30.0kg/m^2) (Pakistani: 23.0 to <27.5kg/m^2)	Low <7.5kg	421	16.77	147	13.39	274	19.39	0.456
	Recommended 7.5-11.5kg (reference[a])	448	17.84	153	13.93	295	20.88	0.234
	High >11.5kg	492	19.60	195	17.76	297	21.02	0.060
	Missing[b]	1,150	45.80	603	54.92	547	38.71	0.00*
Women with obese BMI (White British: ≥30/m^2) (Pakistani: ≥27.5kg/m^2)	Low <5kg	393	17.54	158	16.97	235	17.93	0.038*
	Recommended 5-9kg (reference[a])	367	16.38	112	12.03	255	19.47	0.007*
	High >9kg	420	18.74	156	16.76	264	20.15	0.580
	Missing[b]	1,061	47.34	505	54.24	556	42.44	<0.001*
GWG categories for BMI using general population BMI criteria	Low	1,592	18.48	676	16.54	916	20.24	0.384
	Recommended[a]	1,408	16.35	548	13.41	860	19.01	0.363
	High	1,114	12.93	444	10.86	670	14.81	0.999
	Missing[b]	4,499	52.23	2,420	59.20	2,079	45.94	<0.001*

Appendix 16: Tables of Results for gestational weight gain per week

Maternal GWG per week as exposure for pregnancy outcomes for mother and infant in Pakistani and White women: Maternal outcomes

Outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted [B] coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted [B] coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted [B] coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted [B]
Mode of delivery								
C-section	0.93 (0.46 to 1.88)	4.13 (1.48 to 11.55)*	0.49 (0.19 to 1.23)	2.37 (0.52 to 10.76)	1.74 (0.66 to 4.60)	6.52 (1.73 to 24.61)*	0.062	0.077
Induction	2.02 (1.22 to 3.36)*	3.60 (1.71 to 7.57)*	1.38 (0.64 to 3.00)	4.85 (1.47 to 16.00)*	2.64 (1.35 to 5.15)*	3.36 (1.27 to 8.94)*	0.217	0.995
Any breastfeeding at 6 months	2.59 (0.69 to 9.65)	0.54 (0.73 to 4.08)	5.44 (0.63 to 47.09)	0.55 (<0.001 to 112.73)	2.19 (0.39 to 12.23)	0.26 (0.02 to 4.03)	0.518	0.319
Post-partum weight retention at 3 years (kg)	9.97 (5.43 to 14.50)*	10.94 (5.19 to 16.68)*	11.44 (1.48 to 21.39)*	20.75 (5.67 to 35.83)*	10.06 (5.31 to 14.82)*	8.07 (1.10 to 15.05)*	0.782	0.199

*Significant association (p<0.05)

[A] P value for interaction between Ethnicity and BMI on outcome (shows whether or not there is a significant difference in Pakistani women compared with White British women in the shape of association between early GWG and outcome).

[B] Adjustments made for maternal BMI, maternal age, parity, smoking, place of birth of mother, father and their parents, alcohol consumption, exposure to tobacco smoke, marital and cohabiting status, gestational age at booking, history of diabetes, IMD, mothers education, mothers job, fathers education and fathers job

Maternal GWG per week as exposure for pregnancy outcomes for mother and infant in Pakistani and White women: infant outcomes

Outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted [B]
Stillbirth^		-		-		-		-
Gestational age at delivery								
Pre-term (<37 weeks gestation)	0.26 (0.09 to 0.77)*	0.17 (0.04 to 0.79)*	0.08 (0.02 to 0.37)*	0.01 (0.01 to 0.24)*	0.96 (0.19 to 4.87)	2.44 (0.24 to 24.00)	0.030*	0.008*
Post-term (≥42 weeks gestation	0.35 (0.05 to 2.43)	0.57 (0.02 to 15.60)	0.86 (0.06 to 13.23)	-^	0.14 (0.01 to 1.64)	0.25 (0.05 to 13.64)	0.331	-^
Infant anthropometrics at birth								
Birth weight (g)	387.47 (297.31 to 477.63)*	681.53 (564.18 to 798.88) *	422.64 (286.35 to 558.92)*	690.77 (509.24 to 872.29)*	331.09 (216.46 to 445.71)*	654.32 (499.05 to 809.59)	0.311	0.585
Infant abdominal circumference at birth (cm)	0.72 (0.22 to 1.21)*	1.62 (0.97 to 2.29)*	0.62 (-0.90 to 1.33)	1.55 (0.53 to 2.57)*	0.64 (-0.01 to 1.28)	1.68 (0.79 to 2.56)*	0.967	0.734
Infant head circumference at birth (cm)	0.74 (0.47 to 1.01)*	1.03 (0.94 to 1.67)*	0.74 (0.33 to 1.16)*	1.33 (0.76 to 1.90)*	0.66 (0.31 to 1.02)*	1.26 (0.78 to 1.75)*	0.786	0.860
Infant mid- arm circumference at birth (cm)	0.35 (0.14 to 0.55)*	0.87 (0.59 to 1.15)*	0.41 (0.11 to 0.71)*	0.99 (0.57 to 1.41)*	0.27 (<-0.01 to 0.54)	0.80 (0.42 to 1.17)*	0.488	0.606
Infant subscapular SFT at birth (mm)	0.32 (0.08 to 0.56)*	0.67 (0.35 to 1.00)*	0.48 (0.10 to 0.86)*	0.80 (0.26 to 1.34)*	0.19 (-0.11 to 0.50)	0.63 (0.21 to 1.04)*	0.244	0.259

Outcome	Whole cohort		White British		Pakistani		P value for interaction between Ethnicity and BMI on outcome	
	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted [B] coefficient or odds ratio (95%CI)	Unadjusted coefficient or odds ratio (95%CI)	Adjusted [B] coefficient or odds ratio (95%CI)	Unadjusted Coefficient or odds ratio (95%CI)	Adjusted [B] coefficient or odds ratio (95%CI)	Un-adjusted	Adjusted [B]
Infant tricep SFT at birth (mm)	0.40 (0.17 to 0.64)*	0.94 (0.62 to 1.26)*	0.72 (0.34 to 1.01)*	1.31 (0.77 to 1.85)*	0.16 (-0.14 to 0.46)	0.70 (0.29 to 1.10)*	0.022*	0.016*
Anthropometric measures of infant at 3 years								
Weight (kg)	1.19 (-0.09 to 2.47)	1.74 (0.13 to3.35)	0.05 (-1.85 to 1.94)	0.30 (-2.43 to 3.03)	1.74 (0.07 to 3.41)	2.01 (-0.11 to 4.14)	0.228	0.923
Abdominal circumference (cm)	0.96 (-1.65 to 3.57)	1.40 (-1.89 to 4.69)	-1.07 (-4.88 to 2.74)	0.97 (-5.00 to 6.94)	1.88 (-1.58 to 5.32)	2.45 (-2.48 to 7.38)	0.298	0.556
Tricep SFT (mm)	0.79 (-1.35 to 2.92)	0.39 (-2.43 to 3.22)	0.76 (-2.99 to 4.51)	-0.48 (-8.79 to 7.84)	0.53 (-2.01 to 3.07)	2.91 (-0.37 to 6.19)	0.918	0.663
Subscapular SFT (mm)	0.45 (-1.15 to 2.05)	1.26 (-0.90 to 3.42)	0.16 (-2.07 to 2.40)	-0.19 (-5.77 to 5.38)	0.65 (-1.60 to 2.90)	1.47 (-1.46 to 4.39)	0.769	0.683
Thigh circumference (mm)	-0.36 (-3.52 to 2.78)	-0.22 (-4.36 to 3.91)	2.05 (-2.52 to 6.63)	4.90 (-2.32 to 12.12)	-2.19 (-6.35 to 1.98)	1.72 (-5.29 to 8.72)	0.199	0.030*

[A]P value for interaction between Ethnicity and BMI on outcome (shows whether there is a significant difference in Pakistani women compared with White British women in the shape of association between early GWG and outcome).

Adjustments made for maternal BMI, age, parity, smoking, generation, alcohol consumption, exposure to tobacco smoke, marital and cohabiting status, gestational age at booking, history of diabetes, mothers education, mothers job, fathers education and fathers job

*significant p<0.05

^Insufficient numbers to run adjusted model

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