Ethnic differences in the trajectories of physical growth in contemporary children in the United Kingdom: development and early life influences

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Thesis submitted for the degree of Doctor of Philosophy

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June, 2019

DECLARATION

I, Yi Lu, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

ACKNOWLEDGEMENT

Undertaking this PhD has been an invaluable training experience. It not only equipped me with epidemiology and statistics knowledge and skills, but also taught me independence, patience and resilience. I am grateful for my two supervisors, Dr Leah Li and Dr Anna Pearce, for their guidance, support and encouragement throughout this journey. Thank you both for always making the time for me when I needed help.

I would also like to thank Professor Mario Cortina Borja for his advice and support. I am inspired by his passion for research and generosity with his time and knowledge in helping others. I would also like to thank fellow students and colleagues (Laura Busert, Birgit Pimpel, Emeline Rougeaux, Amal Khanolkar and many others) for their friendship, support, and stimulating coffee conversations. I would like to give special thanks to my two examiners, Professor Amanda Sacker and Dr Sarah Crozier, for their careful reading of this thesis and helpful suggestions for improving the presentation and discussion.

I greatly appreciate my friends Nicola Zaghen and Ilaria Martinelli for proofreading many parts of this thesis. I am grateful for the Great Ormond Street Institute of Child Health at University College London for offering me the PhD studentship. Gratitude extends to the Medical Research Council for providing the funding for this project.

Lastly, a special thank goes to Kim Svensson, without whose endless support this PhD journey would not have been as enjoyable.

ABSTRACT

Background: Child growth has important health and socio-economic implications. Cross-sectional studies suggest that there are marked ethnic differences in children's height and body mass index (BMI) in the United Kingdom (UK). This thesis aimed to investigate ethnic differences in growth trajectories in height and adiposity of contemporary UK children and the potential explanatory role of early life factors.

Methods: Using longitudinal data from the UK Millennium Cohort Study (total n=18,107 singletons), mixed effects fractional polynomial models were applied to estimate height and BMI trajectories (3-14 years) and several early life factors were examined. Multiple imputation as well as attrition weights were used to handle missing data.

Results: Compared with White children, South Asians had a comparable height growth and lower BMI in childhood with the BMI difference reducing with age; in adolescence, South Asian boys had similar height and BMI to White children, while girls were slightly shorter and remained to have a slightly lower BMI. Notwithstanding, body fat measure revealed that South Asians had much greater levels of body adiposity, especially in boys. Black African-Caribbeans had the highest height and BMI trajectories. The BMI difference between Black African-Caribbean and White children emerged at 5 years and increased to 0.5 kg/m^2 (95% confidence interval (CI)0.02, 1.01) in boys and 1.46 kg/m^2 (0.90, 2.02) in girls at 14 years; similar patterns were also seen in the other adiposity measures. Their greater BMI was largely explained by maternal pre-pregnancy BMI and infant weight gain. Socio-economic patterns in BMI also differed by ethnicity. Contrary to the White and South Asian groups, lower socio-economic position was associated with lower BMI in Black African-Caribbean children.

Conclusions: Public health policies need to take a whole-system and life course approach to improve health disparities and reduce childhood obesity, with an emphasis on early intervention and the consideration of varying needs of their target population especially in areas of high ethnic diversity.

IMPACT STATEMENT

There is considerable variation in health across ethnic groups in the UK (1). The pathways to these health disparities are complex (1), with a wide range of factors involved across different stages of the life course (1-3). Child growth is a good indicator of general health in children and reflects early life influences. The study of ethnic differences in child growth is important to gain a better understanding of the development of ethnic disparities in health. A further concern is the alarmingly high levels of overweight and obesity, which are associated with an increased risk of several cardio-metabolic diseases (4) and projected to cost the National Health Services £10 billion per year by 2050 (5). A better understanding of the development of differences in adiposity between socio-demographic groups, will help to identify potential areas for obesity prevention and to reduce unfair differences.

Within academia, this thesis provides a better understanding of the development of ethnic differences in child growth, how they change with age and potential explanatory factors, which contribute to better our understanding of the development of ethnic disparities in health. Many of the previous studies on this subject are restricted by small sample sizes (6), cross-sectional nature of the data (7), and their short follow-up periods (8, 9). This thesis also identified distinctively different socio-economic patterns across ethnic groups. In Black African-Caribbean children, higher socio-economic position was associated with higher BMI. Furthermore, several gaps of knowledge were identified and recommendations for future research were made.

Beyond academia, findings from this thesis are important and relevant to healthcare professionals and policymakers. Evidence from the thesis supports a whole-system and life course approach to improve health disparities and reduce childhood obesity, with an emphasis on early intervention. The thesis also highlights that higher socio-economic position is not universally associated with lower BMI. Therefore, the varying needs of target groups should be taken into consideration when planning and providing health services and interventions, especially in areas of high ethnic diversity. Additionally, this thesis identified that large-for-gestational-age children with rapid infant weight gain had substantially higher BMI in childhood and adolescence which exceeded the international references for overweight. Given the strong association between obesity and cardio-metabolic health, it is of public health significance to monitor infant growth and prevent excessive weight gain in infancy.

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ABBREVIATIONS

AIC	Akaike Information Criterion
AGA	Appropriate for Gestational Age
BIC	Bayesian Information Criterion
BIA	Bioelectrical Impedance Analysis
BF	Body Fat
BMI	Body Mass Index
CAPI	Computer Assistant Personal Interview
CI	Confidence Interval
HSE	Health Survey of England
IOTF	International Obesity Task Force
LGA	Large for Gestational Age
MAR	Missing At Random
MCAR	Missing Completely At Random
MCS	Millennium Cohort Study
MICE	Multiple Imputation by Chained Equation
MNAR	Missing Not At Random
NCMP	National Child Measurement Programme
OECD	Organisation for Economic Co-operation and Development
OR	Odds ratio
PDS	Pubertal Development Scores
RRR	Relative Risk Ratio
RWG	Rapid Weight Gain
SD	Standard Deviation
SDS	Standard Deviation Score
SECs	Socio-Economic Circumstances
SEP	Socio-Economic Position
SGA	Small for Gestational Age
UK	United Kingdom
US	United States
WC	Waist Circumference
WHO	World Health Organisation

1 BACKGROUND

1.1 The concept of ethnicity

Ethnicity is a state of belonging to a social group on the basis of shared geographical region, nationality or cultural traditions (e.g., language, heritage and religion); whereas race is a biological concept referring to people with common sets of phenotypical features, such as skin colour, hair colour and facial features (1). One of the distinct differences between ethnicity and race is the ability of self-identification. Race indicates the differences between people that are fixed and passed through generations (1), while ethnicity is most often self-identified nowadays. Although phenotypical differences have some genetic basis, race is considered to be a poor marker for genetic variation (2). The use of race has been discouraged by some journals (3, 4).

The ethnic group that an individual self-identifies with may change as their perceptions change. An individual can learn another language and different social norms and assimilate into a culture to belong to a different ethnic group. Therefore, the definition of ethnicity is more subjective. As McKenzie and Crowcroft has described:

> "*For instance, a black Baptist born in the UK but whose parents were born in Jamaica might be called Afro-Caribbean, black British, of Caribbean origin UK born, West Indian, and, of course, Jamaican*."(3)

Classification of ethnicity from state bureaucracy is commonly adopted in population health research, such as the UK Census (5). Ethnicity was first used in the 1991 Census in England, Scotland and Wales. The classification has been updated at every new Census to make it more acceptable and relevant to the ever changing society but also easier for the respondents to complete (6).

1.2 Immigration history in the United Kingdom (UK)

Prior to the 20th century, episodes of non-European migration to the UK were small scale and their impact on the demographic diversity was minor (7). The number of migrants arriving in the UK increased markedly after the Second World War and when British colonies started to gain their independence. Large waves of migrants arrived in the 1950s and 1960s from new Commonwealth countries, such as the Caribbean Islands and the Indian subcontinent, in order to fill the increasing demands for cheap labour in the construction and manufacturing industries as well as in the public services (8). A second wave of Indian migrants fled from East Africa (e.g., Uganda, Kenya) to the UK in the 1970s. Asian communities were discriminated against by the ruling governments, in part due to their disproportionate success in business and enterprise (7). There were small episodes of movements of Black African migrants to the UK prior to the 20th century, initially as seamen and later for educational purposes. The number of Black African migrants only started to increase markedly in the 1970s and 1980s to seek asylum due to political instability in their home countries (9). From the 1980s onwards to today, more African students arrived in the UK for educational purposes.

The first wave of Pakistani migration started in the 1960s to fill unskilled jobs in the textile manufacturing industry and decreased when the British government stopped issuing employment vouchers in 1965 (10). Migration of Bangladeshi started in the 1960s and peaked in the late 1970s after Bangladesh declared independence from Pakistan. The arrivals of migrants from Commonwealth countries continued into the 1980s and 1990s (11). More recent migrations to the UK are largely influenced by the flow of refugees and asylum seekers, mainly from African and Middle Eastern countries with continuing civic conflicts (11). Migration for economic and educational reasons to the UK is still common place (11).

Minority ethnic groups living in the UK differ greatly in the country of origin, period of arrival, social and political environment at arrival, motivations for migration and their socio-economic circumstances prior to migration. These factors shape and influence their social experience, employment and integration into the society post migration. The complex interaction between these factors can have a great influence on their socio-economic circumstances and health. For example, the initial post-war migrants to the UK were primarily motivated by economic opportunities and encouraged by the British government to support the expanding needs in the labour force (7). In later decades, there were changes in public and political attitudes towards migrants, especially those for political reasons. These migrants had notably different settlement patterns and were more likely to live in segregated and deprived neighbourhoods, while most of the migrants for educational purposes experienced better employment opportunities and more upward social mobility (9).

Migrants may modify their beliefs and behaviours to adapt to their new host country's values, culture and environment (12). This process is referred to as acculturation. The length of residence in the host country is thought to influence migrants' health through behavioural changes and neighbourhood effects (13, 14). There are now second-generation and even third-generation descendants of the initial post-war immigrants in the UK. Indian children born in the UK in the 1990s and 2000s had taller height than their counterparts in India (15). Time spent in the UK was found to be positively associated with height among Indian children who were not born but were living in the UK (16). A number of US and UK studies have shown that immigrants have lower BMI relative to the native-born counterparts in the host country upon arrival, but longer residence in the host country is associated with adoption of unhealthy dietary elements (e.g. fast food consumption) and higher BMI (13, 17-19).

1.3 Changing demographics in the UK and health inequalities

The UK population is growing, ageing and becoming more diverse (20). Minority ethnic groups are projected to make up 20% of the UK population by 2051, compared with only 8% in 2001 and just under 6% in 1991 (21). There are considerable ethnic differences in health, the pattern of which varies across health conditions (22). Most minority ethnic groups in the UK have poorer general health than the White British group (23). For example, the rates of heart diseases are greater in South Asian groups, particularly among Bangladeshis and Pakistanis (22, 24). The prevalence of adult non-insulin dependent (type 2) diabetes is three to five times higher among South Asians and Black African-Caribbeans than in the general population (25).

Health inequalities are differences in people’s health driven by factors that are considered to be both avoidable and unfair (26). Closing the gap in health and reducing health inequality between socio-demographic groups has been one of the biggest public health challenges in the UK and is emphasised in several government reports and guidances (27-29). The pathways to health disparities between ethnic groups are complex (22), and involve a wide range of factors across the life course, such as biological factors (e.g. genetic variation), social and economic circumstances, cultural differences in health behaviours as well as experiences of immigration and racial discrimination (22, 30, 31). The development of many chronic conditions has their roots in the early life (32). One of the high priorities to reduce health inequalities is, as highlighted in *the Marmot review*, to give every child the best start in life through for example reduction in inequalities in the early development of physical and emotional health (31).

1.4 Child growth and its health and socio-economic implications

Child growth, as reflected in increases in height and weight and other body changes with age, is a dynamic statement of a child’s general health and is influenced by both genetic and environmental (non-genetic) factors (33). After a rapid growth in infancy, height growth (velocity) in childhood continues at a steady pace of about 5-6 cm per year, before reaching adolescent growth spurt (Figure 1.1) (34). Girls enter puberty on average 2 years earlier than boys at the age of around 11 years (35) and are slightly taller than boys between the ages of 11 and 13 years

(36). Once final height is achieved, it changes little in adulthood, apart from a small shrinkage in late middle life (37). Therefore, height is often considered as a marker of early life experiences as well as genetic height potential, and increasingly used by health researchers to investigate the association between early life experiences and later health outcomes (38, 39).

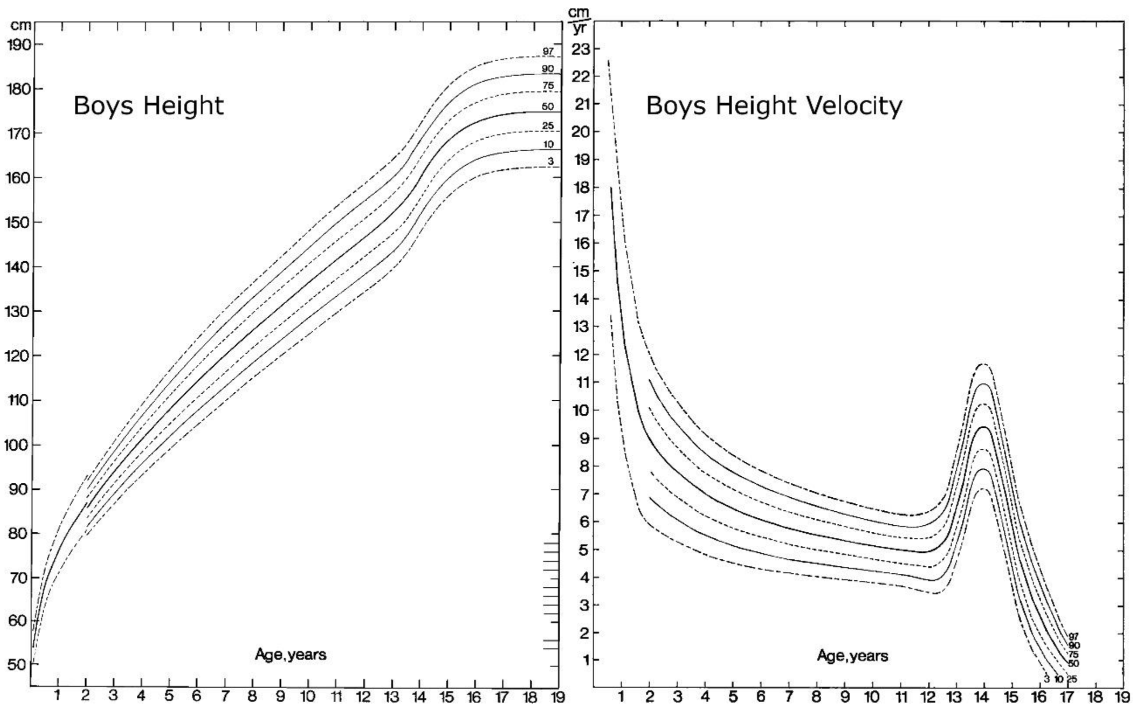

Figure 1.1: Height (cm) and height velocity (cm/year) with age for boys, within 3rd - 97th percentiles
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A common finding from large cohort studies is that children who were born small or premature, especially followed by accelerated weight gain in infancy, had an elevated cardiovascular and metabolic disease risk in later adult life (32). Shorter achieved adult height has been repeatedly associated with an increased risk of cardiovascular diseases (41-46). It is possible that socio-economic circumstances, e.g. income and education, may confound part of the association between adult height and disease risks (39). A prospective study in Japan found no association between height and coronary heart disease, after adjustment for education (47). However, a number of other studies which controlled for potential socio-economic confounders found the association between height and cardiovascular diseases remains (48-54), suggesting that they are possible biological, biochemical and genetic mechanisms underlying this association (39, 55).

Height growth is also associated with a number of social and economic outcomes, such as productivity, social skills and participation in labour market (56, 57). It has been observed that taller people on average earn more and perform better in cognitive tests (58-60). There are a few possible explanations for these associations. They may be partially confounded by parental socio-economic factors, that parents from more advantaged backgrounds provide their children with better nutrition and also invest more in their education (61). Tallness as a preferred social trait may have boosted taller people's confidence and social skills which later serve them well in the labour market (62-64). It is also possible that people who are tall as a result of robust growth also have better health and had better cognitive development (39, 65, 66).

Another important feature of child growth is the change in body adiposity with age. The level of body adiposity declines in the early childhood, and at around 6-8 years rebounds to an increasing trend in late childhood and adolescence (Figure 1.2) (67). There is a tendency that children with an early adiposity rebound are more likely to have a higher level of body adiposity and become obese at the end of growth (68). In adulthood, weight continues to be influenced by dietary and lifestyle factors.

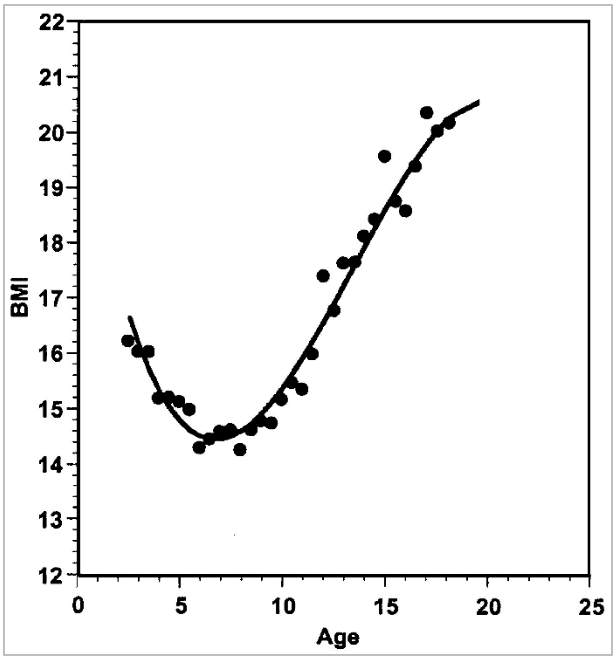

Figure 1.2: An example of a girl's observed BMI and predicted BMI curve from 2 to 20 years
BMI: body mass index. Reproduced with permission from Guo *et al*. *International Journal of Obesity*, 2000 [(69)].

Childhood obesity, as a result of excessive weight gain, is a growing public health problem worldwide (70, 71). In the UK, one in three children in Year 6 (aged 10-11 years) were either overweight or obese (72). Obesity and high levels of body adiposity in childhood tend to persist into adolescence and adulthood (73). A large body of high-quality studies have documented a strong association between obesity and cardiovascular risk factors in childhood (73). The long-term effects of obesity on cardio-metabolic health are also well established (73, 74). Childhood obesity is strongly associated with type 2 diabetes, hypertension, ischaemic health disease and stroke in adulthood, with a pooled hazard ratio ranging from 1.1 to 5.1 (74).

Obese children and adolescents are more likely to be bullied and have lower self-regard and quality of life compared with those with normal weight (75), which can have adverse effects on educational attainment and lifetime achievement. In adults, obesity is inversely associated with socio-economic achievement, which is more evident in women than men (76). Although part of this association may be confounded by family socio-economic background, people with obesity often experience other health conditions (73), reduced physical performance (76) and higher level of social discrimination (77) which may constrain their socio-economic performance.

1.5 Variation in child growth across ethnic groups

1.5.1 Ethnic differences in height growth in the UK

Large ethnic differences in British children's height were first reported in the National Study of Health and Growth by Rona and Chinn in 1985 (78). Since then, a number of studies (largely cross-sectional studies) have reported ethnic differences in height in UK children, including the Health Survey of England (HSE) (79-83). Black African and Caribbean children tend to be taller than their White peers at all ages throughout the childhood (84-86), apart from one study which found no difference in mean age-adjusted height between Black African boys and boys in the general population (87). Findings on height differences between South Asian and White children are less consistent (15, 79-81, 83, 84, 88), with studies showing that South Asian children were shorter (79), similar (15) or taller (83) compared with White children.

Ethnic differences in height appear to vary by age and the time period of when the observation was made. Hancock *et al* showed that in Reception year (aged 4-5 years) Bangladeshi children had similar height to White children, however, among Year 6 children (aged 10-11 years) Bangladeshi children were slightly shorter than White children (84). In the HSE 1999, Bangladeshi boys and Indian girls were both shorter than their same-sex peers in the general population, by 2.15 cm and 1.57 cm respectively (89). Nevertheless, in the HSE 2004 Bangladeshi boys and Indian girls had similar mean heights to their counterparts in the general population (90). It is unclear whether these findings were due to: 1) different height growth trajectories in childhood across ethnic groups, i.e. the pattern of ethnic differences in height changes with age; and 2) the era when the comparison was made, i.e. ethnic differences in height growth have changed over time.

The challenge of using cross-sectional data to study child growth is that body size changes with age. Therefore, cross-sectional studies may result in inconsistent conclusions and be insufficient to study ethnic differences in growth patterns. Few studies have used longitudinal data to investigate height trajectories across ethnic groups, possibly due to small proportions of ethnic minority children in most cohort studies (91). Bansal *et al* found that infants of South Asian backgrounds born in the early 2000s in Manchester were on average about 1cm shorter in birth length, but they grew more rapidly in the first year and had a similar mean length at 12 months compared to White infants (92). Similar findings were reported by Fairley and colleagues (81). In the Born in Bradford cohort study, Fairley *et al*. found that despite being shorter in length at birth, Pakistani infants were taller than their White counterparts by the age of two years, after adjusting for preterm birth, maternal smoking and parental height. In a more recent study, Bécares *et al* (86) reported that Black children were taller than White children from 3 to 7 years; Indian and Pakistani children also had a higher mean height standard deviation score (SDS) during this age period, with the magnitude of differences reducing with age; whereas Bangladeshi children who had similar height to White children at 3 and 5 years became shorter at 7 years by 0.14 SDS. Ethnic differences in height growth throughout childhood into adolescence remain largely unclear.

1.5.2 Potential contributing factors to ethnic differences in height growth

Height is a polygenetic trait with an estimated heritability of 60%-80% in high-income countries (93, 94). Parental height is often used as an indicator of genetic potential to assess child growth (33). However, parental height also reflects the growth environment of parents (83). In England, apart from Black Caribbean and Black African adults who have a similar mean height to the general population, adults from minority ethnic backgrounds in general have a shorter mean height than the general population (80).

Despite the genetic component to height growth, the extent to which individuals achieve their height potential depends on a range of environmental factors, including prenatal factors, nutrition and family socio-economic circumstances. A summary of reported findings on key influencing factors of height growth and ethnic differences in these factors is provided below.

Prenatal factors

Several maternal characteristics and health behaviours during pregnancy are found to be associated with child growth. The adverse effects of maternal smoking on child height growth are well documented. Infants born to mothers who smoked during pregnancy are about 1 cm shorter in birth length than those born to non-smokers (95, 96). The effect is possibly mediated by prenatal growth retardation (97) and appears to stay relatively stable in childhood (98). In the UK, women from minority ethnic backgrounds are less likely to smoke during pregnancy than White women (99).

Several UK studies have associated older maternal age and fewer children (or lower parity) with increased childhood height (61, 100, 101). The proportion of infants born to mothers under 20 years of age ranged from 1.6% in the Indian group to 9.5% in the Black Caribbean group in 2005 (102). Similar findings are reported by recent studies (99). Pakistani, Bangladeshi and Black African mothers are more likely to give birth to three or more children than White, Indian and Black Caribbean mothers (99).

Birthweight

There is a positive association between birthweight and height in childhood (101, 103). Low-birth-weight infants have shorter height in childhood than their normal-birth-weight counterparts, and very low-birth-weight infants may remain as short adults (104, 105). In the UK, Asian and Black babies are born on average up to 300 g lighter than White babies (106, 107).

Infant feeding and childhood nutrition

Infants who are breast-fed are longer in length than those who are formula-fed in the first 4-6 months, after which formula-fed infants grow slightly faster (108). However, some evidence suggests that the height difference due to different feeding practices disappears after 2 years of age (109). Overall, mothers from minority ethnic groups are more likely than White mothers to initiate breastfeeding and breastfeed their child for at least 4 months (99). Good nutrition is fundamental to support growth. Prolonged undernutrition can result in growth faltering (110-112). If nutrition supply is limited only for a short period of time, affected children may recover and return to normal growth once it is corrected (113).

Family socio-economic circumstances (SECs)

Socio-economic gradient in height is observed in many populations, with children and adults from more privileged backgrounds being taller as assessed by a range of indicators, such as family income (114), father's social class (115-117), or mother's education (118). The gradient tends to be relatively smaller in developed countries than developing countries (119, 120) and recent evidence suggests that the socio-economic gradient in achieved adult height has narrowed across generations in the UK (121). UK children born to mothers with an education level in the "university degree and above" category were on average 0.15 SDS longer at birth and 0.30 SDS taller at the age of 15 years, compared with those in the "below O-level" category (122). The association between family SECs and height growth is likely to be confounded by factors such as parental height, and mediated by many factors including maternal age, parental health, parity, maternal smoking during pregnancy, knowledge of feeding and dietary matters, and access to healthcare (39).

The distribution of most socio-economic measures differs by ethnic groups. Around two-fifths of people from minority ethnic groups lived in low-income families, especially Pakistanis (60%) and Bangladeshis (70%), compared with only one-fifth of White people (123). In 2012/13, over 50% of Asian and Black children in England lived in the most deprived 20% areas (124). Pakistani and Bangladeshi mothers were also more likely to not have any formal academic qualifications (107).

1.5.3 Ethnic differences in body adiposity in childhood

Body mass index (BMI), calculated as weight in kilograms divided by the square of height in metres, is a measure of weight in relation to height (125). In adults, BMI achieves relative independence of height, while in childhood and adolescence BMI remains to be positively associated with height (126). There is also an ongoing debate on the appropriateness of using BMI to compare obesity risk across ethnic groups (127). BMI correlates well with body fatness (128, 129), but it does not distinguish between lean (e.g. muscle) and fat body mass (130). At a given BMI, Asians have been found to have a higher level of body fat and are more prone to developing abdominal obesity than White Europeans (131-133). Black people, in contrast, have lower abdominal fat than Caucasians at the same BMI (134, 135). Hence, health implications for a given BMI can vary across different ethnic groups (136).

Other more sophisticated and accurate measures of body adiposity are available (125), such as dual-energy X-ray absorptiometry. However, they are either more difficult to obtain or poorly suited for population health research (137). Therefore, BMI remains the most commonly used measure in national studies such as the HSE and surveillance programmes such as the English National Child and Measurement Programme (NCMP) (127). Using BMI in combination with additional easy-to-obtain adiposity measures, such as waist circumference, may help to facilitate comparisons of obesity risks across ethnic groups in relation to their risk of metabolic syndrome at population level (138-142).

There is are large number of studies, mainly cross-sectional studies, comparing body adiposity across ethnic groups in the UK. However, in a systematic review conducted in 2011, El-Sayed *et al* reported that current findings on ethnic differences in childhood obesity in the UK are not sufficiently consistent to draw conclusions (143). The obesity risk of minority ethnic groups relative to White children among reviewed studies appears to vary according to age and differ by sex (143), which suggests childhood BMI trajectories may differ by ethnicity. In school year 2015-2016, the prevalence of obesity among children aged 4-5 years was only slightly higher in the Asian and Asian British group than in the White group (10% vs. 9%); however the difference in obesity prevalence was much higher among children aged 10-11 years (25% vs. 18%) (144).

Limited studies have used longitudinal data to investigate the development of ethnic differences in BMI in the UK (143), especially in late childhood and adolescence. A recent study by Martinson and colleagues showed that Asian children in England had a slightly lower mean BMI than White children at the age of 3 years by 0.63-0.76 kg/m^2, while Black children had a mean BMI similar to White children (145). Both Asian and Black children then gained BMI more rapidly than White children between the ages of 3 and 7 years with Black children having the highest mean BMI at 7 years; these differences were hardly affected after adjustment for maternal age at birth, low birthweight, parity and maternal education. However, several questions remain unanswered by the study, including whether BMI trajectories of South Asian and White children would intersect after the age of 7 years, whether there are any substantial differences in BMI trajectories between ethnic subgroups (e.g. between Indians and Bangladeshis), and whether the differences can be explained by maternal BMI, infant weight gain, family income and other early life factors.

1.5.4 Potential contributing factors to ethnic differences in adiposity

Genetic variants

The estimated heritability of BMI from twin studies ranges from 41% to 85% across different populations (146). The genetic effect varies over age and is relatively low during the preschool and mid-puberty periods, possibly due to the stronger influence of shared environmental factors in the family during these periods, such as culture and education (147). There is some evidence suggesting that the heritability of BMI is lower in Asian countries than western countries (146, 148).

Maternal pre-pregnancy BMI and gestational weight gain

Consistent evidence has found a positive association between maternal pre-pregnancy BMI and offspring's weight status (149-151). Hawkins *et al* (152) found that children born to mothers who were overweight before pregnancy were 1.37 times more likely to be overweight at the age of 3 years than those born to mothers who had normal weight before pregnancy. Risk of childhood overweight or obesity increases by 1% to 23% for every additional kilogram weight gained during pregnancy, after adjustment for potential confounding factors (153). Women from Black African, Black Caribbean and Pakistani groups are more likely to have BMI in the obese category than women in the general population (127).

Maternal smoking during pregnancy

Several studies have associated maternal smoking during pregnancy with low birthweight (154, 155) and rapid weight gain in late infancy and childhood (98, 156, 157). Infants of smoking mothers are on average about 200g lighter than those of non-smokers, even after controlling for differences in socio-economic status, maternal size and maternal alcohol consumption (155). This effect of maternal smoking on birthweight is possibly through causing foetal hypoxia and interfering with regulating mechanisms and cellular growth (158). Studies looking at the benefits of stopping smoking at difference stages during the pregnancy found that quitting smoking at any time before 16 weeks is most beneficial and thereafter makes little difference in birthweight (159, 160).

Birthweight and infant weight gain

Higher birthweight has been associated with earlier adiposity rebound and greater BMI in infancy and childhood, independent of maternal weight status and gestational weight gain (150). Reilly *et al* found that for every 100g increase in child birthweight, the odds of being overweight at the age of 7 years increased by 1.05 (161).

Infant weight gain is strongly and positively associated with later BMI and risk of overweight and obesity (162-165). A recent meta-analysis showed that rapid weight gain between birth and 2 years (defined as a change in weight z-scores >0.67 SDS) was associated with 4.16 higher odds of overweight/obesity in childhood and adolescence (162). Rapid weight gain is more common among low birthweight babies, especially following intrauterine growth restriction, although rapid weight gain is not confined only to low birthweight children (162, 166). Whether the association between infant rapid weight gain and raised BMI differs by birthweight status is not well studied. While some studies (167, 168) found no evidence of an interaction between birthweight and rapid weight gain (RWG), a recent cohort study showed that the association of RWG with BMI at 7 years was stronger for boys with low or high birthweight (169).

Infant feeding

Inconclusive observational evidence suggests that breastfeeding or exclusive breastfeeding for the first 4-6 months may have a protective effect against childhood overweight and obesity (150, 170). Early introduction of solid foods before three to four months may increase the level of body fat in childhood (150, 171). World Health Organisation recommends that infants should be exclusively breastfed for the first 6 months of life, which was adopted by the UK in 2003 (172). The previous UK advice was to exclusively breastfeed for the first 4 months and introduce solid foods between 4 and 6 months (172).

Diet and physical activity

Dietary behaviours can have a great influence on a child's weight status. Although many people from minority ethnic groups have a healthy diet, there is evidence suggesting that South Asian children (particularly Bangladeshis) have higher mean total energy and fat intakes than White European children, while Black African children have markedly lower total and saturated fat intakes (173). Younger generations from minority ethnic groups, especially those who were born in the UK, are likely to adopt unhealthy elements of British diets and engage in poor dietary behaviours, such as consumption of fast food and skipping breakfast (174-176).

Physical activity is an important factor for maintaining body energy balance and regulating body adiposity. Children who are physical active tend to have less body fat than those less physically active (177, 178) and have a better metabolic profile (179). Studies using objectively measured physical activity (PA) outcomes showed South Asian children are less active than White and Black children, particularly among children of Indian and Bangladeshi origin (180, 181).

Family socio-economic circumstances

Family socio-economic circumstances are strongly associated with child weight status. The prevalence of obesity in Year 6 children in the UK between 2010 and 2011 increased from 18% in the least deprived areas to 24% in the most deprived areas (182). The findings are consistent across a number of socio-economic measures (e.g. maternal education, head-of-household occupational social class and area-level deprivation measures) and different data sources (143, 182-184).

Socio-economic patterning of childhood obesity is a result of complex interrelationships between multiple risk factors at individual, family and area-level (185). Two important factors may be diet qualities and physical activity levels. Maintaining a healthy diet is less achievable for families from less privileged socio-economic backgrounds in current obesogenic environments, where the costs of high-fat, high-sugar and energy-dense foods are relatively cheaper than those of healthy foods such as fish, fruit and vegetables (186). Lower household income is associated with lower spending on fruit and vegetables as proportion of total family food and non-alcoholic beverage expenditure as well as lower physical activity levels in children (187).

Recent research, mainly from the United States (US), suggests that the inverse association between socio-economic position and BMI in children and adolescents is less evident for Asian Americans and inconsistent for Hispanic and non-Hispanic Black populations, compared with their non-Hispanic White counterparts (188-190). This may be attributable to the fact that cultural, environmental and biological factors related to obesity development are likely to have different socio-economic patterns across different ethnic populations (191). Evidence from the UK is limited. Only one study, of which I am aware, used data from the National Child Measurement Programme and found that the negative socio-economic gradient in obesity risk by area deprivation is smaller in South Asian and less clear for Black children compared with White children in London (192). However, it is unclear whether the pattern of socio-economic disparities in BMI differs by ethnicity using indicators of family-level socio-economic position (SEP), since that over 50% of Asian and Black children in England live in the most deprived 20% areas (124).

1.6 Summary of background and aim of current PhD study

Child growth influences many aspects of health and socio-economic performance in later life. Ethnic minorities represent a rapid growing group in the UK population (21). There is considerable variation in health across ethnic groups (22). The pathways to these health disparities are complex (22), with a wide range of factors involved across different stages of the life course (22, 30, 31). Child growth is a good indicator of general health in children and reflects early life influences. The study of ethnic differences in child growth is important to gain a better understanding of the development of ethnic disparities in health.

Previous research, mainly from cross-sectional studies, have suggested that there are marked ethnic differences in height and BMI in children. One of the challenges of studying child growth is that height, BMI and other adiposity measurements change with age. Studies on ethnic differences in child growth using cross-sectional data measured at one age can result in inconsistent and potentially misleading findings. Longitudinal studies which investigate ethnic differences in growth trajectories and the development of these differences are limited. This is possibly due to small proportions of ethnic minorities naturally present in cohort studies.

In the UK, levels of overweight and obesity are alarmingly high, with one in three children aged 10-11 years (193) and more than half of the adults in England are either overweight or obese (194). BMI (195, 196) and obesity (197) have strong social patterns, with people from more disadvantaged backgrounds having higher mean BMI and a greater obesity risk. Recent research, mostly from the US, suggests that the inverse association between socio-economic position and

BMI in children and adolescents is less evident for Asian Americans and inconsistent for Hispanic and non-Hispanic Black populations, compared with their non-Hispanic White counterparts (188-190). Yet little evidence is available in UK children.

A number of influencing factors of child growth were found to differ by ethnic groups. However, the relationships are not straightforward, with some of the factors operating in opposite directions for different ethnic groups. While many minority ethnic children are more likely to live in less advantaged socio-economic circumstances (124) and be born with a low birthweight (106, 107), they have some other favourable early life factors, such as mothers are less likely to smoke during pregnancy (99) and more likely to breastfeed in accordance to recommendations (99).

Therefore, the aim of the current PhD study was to investigate ethnic differences in growth trajectories in height and adiposity of contemporary UK children and to explore the potential explanatory role of early life factors. Data from the Millennium Cohort Study, a UK national cohort study which for the first time oversampled minority ethnic groups, were used. The specific objectives were

1. To investigate whether height trajectories from the age of 3 to 14 years differed by ethnic group; and whether the observed differences were explained by early life factors.

2. To explore whether socio-economic patterns in BMI trajectories between 3 and 14 years differed across ethnic groups; and whether early-life obesity risk factors can explain any of the observed socio-economic disparities in each ethnic group.

3. To investigate the development of ethnic differences in BMI trajectories between 3 and 14 years; whether the differences can be explained by early-life risk factors; and whether the pattern of ethnic differences was also seen in overweight/obesity and other adiposity measures (i.e. waist circumferences and body fat).

Several early life factors were considered in this thesis, with a special focus on those that are identifiable by infancy, including

- Prenatal factors: parental height, and maternal age, pre-pregnancy BMI, parity, and smoking behaviour during pregnancy.
- Indicators of foetal and infant growth: birthweight and weight gain in early life.
- Infant feeding practices: breastfeeding and early introduction to solid foods.
- Family SECs: family income and maternal education level.

Both birthweight and infant growth differ by ethnicity (Chapter 3). Excessive infant weight gain is more common among low birthweight infants, especially following intrauterine growth restriction. Whether the association between infant rapid weight gain and raised BMI differs by birthweight status is not sufficiently understood, with some evidence suggesting that the adverse effect of rapid weight gain on BMI may be stronger for boys with low or high birthweight compared with normal birthweight (169). Understanding whether particular groups of children are more susceptible to adverse consequences of rapid weight gain in early life will provide information for improving infant growth monitoring practice and designing cost-effective early interventions. Therefore, an additional objective was added during the PhD study

4. To examine the association of rapid weight gain in the first 3 years of life with later BMI trajectories (5-14 years); and whether the association differed by birthweight group.

1.7 Structure of this thesis

The remainder of the thesis is structured as follows. Chapter 2 'Methodology' describes the Millennium Cohort Study, data used for analyses and methodological considerations for modelling growth and dealing with missing data. Chapter 3 provides an overview of ethnic differences in early life factors and associations between early life factors with height and BMI in the Millennium Cohort Study. Chapters 4-7 provide details on statistical analysis, results and discussion in addressing each of the four objectives. Chapter 8 summarises key findings and implications of the present PhD study. A summary of manuscripts and conference presentations resulting from this PhD study is provided in Chapter 9.

2 METHODOLOGY

2.1 Millennium Cohort Study

2.1.1 Study population

The Millennium Cohort Study (MCS) is a contemporary and nationally representative cohort study of children born at the turn of the 21st century in the UK. Rich information was collected on physical, socio-emotional, cognitive and behavioural development over time, daily life and experiences, as well as parental characteristics, family socio-economic circumstances, relationships and family life. It oversampled children from areas with high level of deprivation and, in England, areas with high proportions of ethnic minorities. The MCS is well suited for investigating the objectives of the present PhD project.

The study population of the MCS are all children who were born between 1 September 2000 and 31 August 2001 in England and Wales, and between 24 November 2000 and 11 January 2002 in Scotland and Northern Ireland (198). The MCS included children who were living in the UK at the age of nine months and registered for 'Child Benefit', which at the time was a universal benefit in the UK. Therefore, only a small percentage of the population was not included in the sampling process, due to their temporary or uncertain residency status in the UK, such as refugees.

2.1.2 Sampling methods

A clustered, geographically and disproportionately stratified sampling method was applied, to oversample children who lived in the less advantaged socio-economic circumstances and, in England, those who lived in areas with high proportions of ethnic minorities (198). The stages of sampling are illustrated in Figure 2.1.

The population was first stratified by country with a target sample size of 15,000 children at first contact. The target size as proportionate to the population size in each country of the UK would be 12,600 in England, 750 in Wales, 1,200 in Scotland and 450 in Northern Ireland. To increase the sample size in the three smaller countries, a sample of 1,500 children was allocated to each of these countries, leaving 10,500 for England.

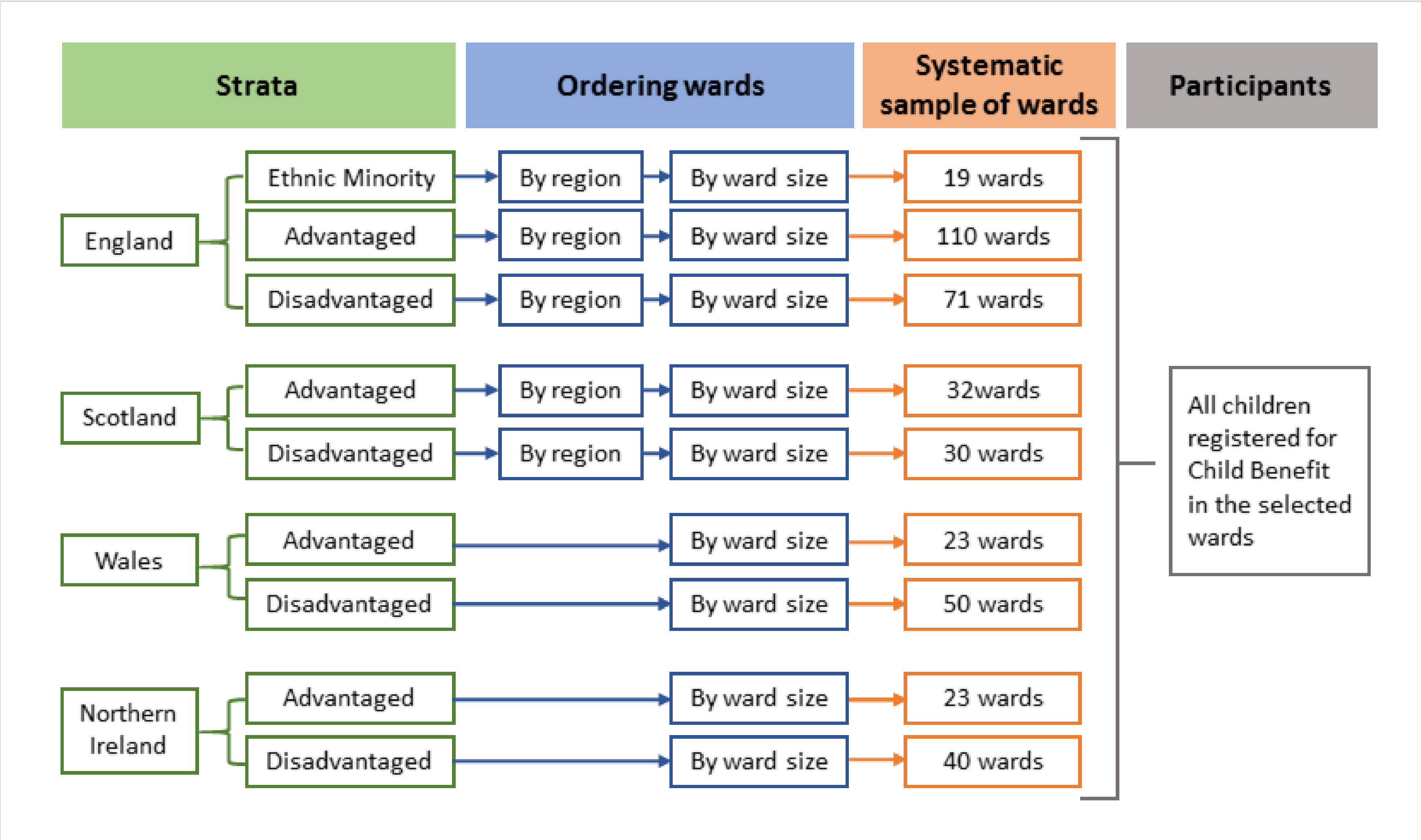

Figure 2.1: MCS sampling process

Wales, Scotland and Northern Ireland each had an *advantaged* and a *disadvantaged* strata, with half of the target sample in each. The wards that were in the upper quartile of the Child Poverty Index (i.e. the poorest 25%) fell into the *disadvantaged* stratum, and the remaining wards were in the *advantaged* stratum. Therefore, the term *advantaged* is relative. England had three strata with half in the *advantaged* stratum, a quarter in the *disadvantaged* stratum and a quarter in the *ethnic minority* stratum. The *ethnic minority* stratum captured children who lived in wards with at least 30% of the population from 'Black' and 'Asian' ethnic groups. Wards that were not in the *ethnic minority* stratum were then placed into the *advantaged* or *disadvantaged* stratum using the Child Poverty Index cut-off point. After the initial allocation of the target sample was agreed, additional resources were available to boost sample sizes in different ways in each of the four UK countries. The final target sample size was 13,146 in England, 3,000 in Wales, 2,500 in Scotland and 2,000 in Northern Ireland (198).

Within each stratum in each country, the populations were ordered first by region and then by ward size. Due to the small size of Wales and Northern Ireland populations, each stratum was ordered by ward size only. Wards with few births were combined into 'super-wards'. After the ordering, wards were systematically selected to achieve the target sample size (Table 2.1). A list of all eligible children in the selected wards was generated from the Child Benefit register and families were invited to take part in the study.

Table 2.1: Number of sample wards required by stratum to achieve expected sample size

Country (Stratum)	No. of Sample Wards	Expected births per ward, Mean (SD)	Expected response rate, %	Expected sample size before ward selection
England (Advantaged)	110	68 (43)	75	5610
England (Disadvantaged)	71	108 (63)	70	5368
England (Ethnic minority)	19	197 (117)	65	2433
Wales (Advantaged)	23	48 (27)	75	828
Wales (Disadvantaged)	50	62 (40)	70	2170
Scotland (Advantaged)	32	52 (18)	75	1248
Scotland (Disadvantaged)	30	61 (22)	70	1281
Northern Ireland (Advantaged)	23	46 (20)	75	794
Northern Ireland (Disadvantaged)	40	48 (27)	70	1344

*SD: Standard Deviation

2.1.3 Achieved sample size at each sweep

The total sample size for the MCS study is 19,517 children from 19,224 families (18,552 were in the first sweep and 692 joined the study in the second sweep as they were not identified in the Child Benefit records until after the completion of the first sweep).

At the time of writing up this thesis, data from the first six sweeps were available and therefore included in the analysis. They were conducted when cohort members were 9 months, 3, 5, 7, 11, and 14 years old. The achieved sample size was 18552, 15590, 15246, 13857 and 13287 families, respectively (Figure 2.2).

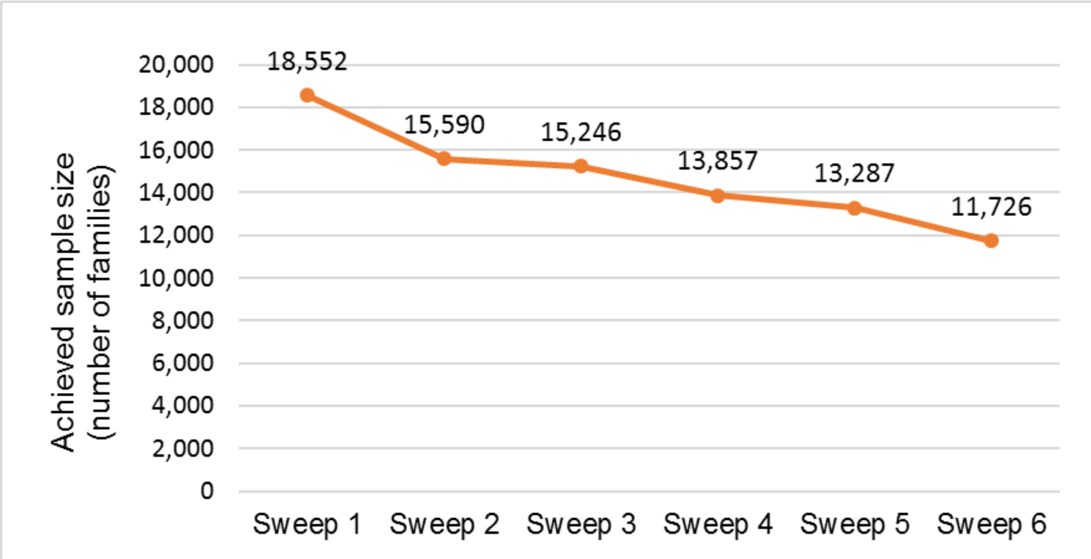

Figure 2.2: Achieved sample size at each MCS sweep (total *n*=19,244 families)
*MCS: millennium cohort study. Sweeps were conducted when cohort members aged 9 months, 3, 5, 7, 11 and 14 years old. 692 families were not issued at sweep 1, hence the productive sample size was 18,552 at first contact.

2.2 Modes of data collection at each MCS sweep

At each sweep, computer assisted personal interviews (CAPI) were carried out at home with main (usually the mother) and partner (usually the father) respondents by trained interviewers (Table 2.2). For example, at 9 months nearly all main respondents were natural mothers (e.g. 99.9%), although the proportion decreased in successive sweeps with growing numbers of fathers or male partners being the main respondent. The overall respondent rate of partner interviewers at 9 months (sweep 1) was 72%, of which 98% of the partner respondents were fathers. Therefore, the CAPI interviewers are referred as parental interviews hereafter.

From 3 years, cognitive assessments and anthropometric measurements were conducted with cohort members. As cohort members aged, the focus of data collection gradually shifted from their parents/carers to cohort members themselves, and more elements were introduced, e.g. young person questionnaires at 7, 11 and 14 years and time use record at 14 years. Saliva samples and objectively measured physical activity data were also collected at some sweeps (Table 2.2).

Table 2.2: Key survey elements at each MCS data collection

	9 months	3 years	5 years	7 years	11 years	14 years
Parental interviews*	✓	✓	✓	✓	✓	✓
Cognitive assessments		✓	✓	✓	✓	✓
Physical measurements		✓	✓	✓	✓	✓
Young person questionnaire				✓	✓	✓
Older siblings		✓	✓			
Interviewer observations		✓	✓	✓	✓	✓
Teacher survey			✓	✓	✓	
Consent to data linkage	✓	✓	✓	✓	✓	
Saliva samples		✓				✓
Time use record						✓
Activity monitors				✓		✓

*Most of the main and partner respondents for the household interviews were mothers and fathers. Therefore, they are referred as parental interviews here.

2.3 Key variables used in this PhD project

2.3.1 Ethnicity

Child's ethnicity was reported by parents at baseline parental interviews (9 months), using the 2001 UK Census ethnicity categories. Ethnic composition of the MCS sample is provided in Table 2.3. Only 26 children had missing data. Due to the small numbers in the minority ethnic groups, 'Indian', 'Pakistani' and 'Bangladeshi' were collapsed into the 'South Asian' group, and 'Black African' and 'Black Caribbean' into the 'Black African-Caribbean' group in some of the analysis.

Table 2.3: Ethnic composition of the MCS population (unweighted)

Ethnicity	N	%
White	15,982	81.9%
Mixed	603	3.1%
Pakistani	961	4.9%
Indian	502	2.6%
Bangladeshi	397	2.0%
Black African	427	2.2%
Black Caribbean	263	1.3%
Others (including Chinese)	356	1.8%
Missing	26	0.1%
Total	19,517	100%

2.3.2 Anthropometric measurements

A number of anthropometric measures are available in the MCS and were used as outcome variables in the present PhD project, including height, body mass index (BMI), body fat percentage and waist circumference. They were all measured by trained interviewers. An overview of anthropometric data used in the analysis is provided in Table 2.4.

Table 2.4: Anthropometric measurements in the MCS

Measures	Tools	Measured at follow-up visit				
		3y	5y	7y	11y	14y
Height, cm	Leicester Stadiometer	✓	✓	✓	✓	✓
Weight, kg	Tanita HD-305 scale	✓	✓	✓	✓	✓
BMI (weight/ height^2), kg/m^2		✓	✓	✓	✓	✓
Body fat, %	Tanita HD-305 scale			✓	✓	✓
Waist circumference, cm	SECA tape		✓	✓		

*BMI: Body Mass Index.

Height (to the nearest millimetre) was measured without shoes at 3-, 5-, 7-, 11- and 14-year visits (sweeps 2-6) using a Leicester Height Measure Stadiometer following standard protocols (199). The interviewer could repeat the measurement, if they were not satisfied with the accuracy of the first measurement and the child and parent were happy to cooperate. Height data are approximately normally distributed. Histograms of heights across different sweeps are provided in Appendix 1 Figure S1.

Weight (to the nearest 0.1 kg) at 3- and 5–year visits was measured using a TANITA HD-305 scale with light clothing and without shoes. At 7-, 11- and 14–year visits, both *weight* (to the nearest 0.1 kg) and *body fat percentage* (to the nearest 0.1%) were measured using a TANITA BF-522W scale. If the parent or child did not want body fat to be measured, the scale had a 'weight only' mode for weight measurement. If the child was unwilling or unable to stand for the measurement, the scale was reset to zero with the parent standing on the scale. The child's weight measurement was then taken with the parent holding the child while standing on the scale. *BMI* (kg/m^2) was calculated as weight divided by height squared. BMI data from 3-, 5- and 7-year visits are approximately normally distributed; the distribution of BMI data from 11- and 14-year visits are slightly positively skewed (Appendix I Figure S2). To take the body fat percentage measurement, the interviewer first needed to enter the age, sex and height of the child into the scale. The child was then asked to stand on the scale barefoot. The TANITA scale, a leg-to-leg bioelectrical impedance machine, estimates body fat percentage by sending a weak electric current through the feet and measuring the resistance. The interviewer could repeat the weight and body fat measurements, if they were not satisfied with the accuracy of the first measurements as long as the child and parent were happy to cooperate.

Waist circumference (to the nearest 0.1 cm) was measured against the skin using a seca measuring tape at 5- and 7-year visits. Interviewers first located the costal margin (lower ribs) and the iliac crest on the mid-axillary line with their fingers, then estimated the mid-point between the two, and marked the point with a pen or a sticker. The tape was placed around the waist at the marked mid-point. Two measurements were taken. If the difference between the two measurements was 2 cm or more, a third measurement was taken and the mean of the closest two measurements was taken. If the child or mother did not permit measuring the waist against bare skin, waist measurements over light clothing were allowed instead.

2.3.3 Early life factors

Rich data on parental characteristics, family socio-economic circumstance, birthweight and infant feeding practices were collected at the baseline interviews (9 months) and were considered in this PhD project.

Prenatal factors

Parental heights were self-reported or reported by partners at interviews and converted to sex-specific standard deviation scores (SDSs), derived internally based on the MCS sample. Mid-parental height SDS was calculated by taking the average of both natural parent's height SDSs. Where only one parent's height was available (19%), due to lone parenthood or other reasons, only their height SDS was used as mid-parental height SDS. Maternal weight before pregnancy was self-reported at baseline (9 months) interviews. Maternal pre-pregnancy BMI was calculated using maternal pre-pregnancy weight and maternal height.

Perinatal factors

Mother's age at the birth of cohort members in years was recalled by respondents.

Detailed information on mothers' smoking habits before pregnancy as well as any changes made to their smoking habit during pregnancy were collected. The average number of cigarettes smoked per day at the end of fourth month of pregnancy was derived and used to capture maternal smoking during pregnancy. The fourth month was used because previous studies have found that a change in maternal smoking behaviour by the end of fourth month of pregnancy places their baby into a birthweight and perinatal mortality category appropriate to her new changed behaviour (200).

Gestational age in weeks was obtained from the hospital records. If not available, gestational age was derived using the parent-reported due date and the date of childbirth, assuming the due date was calculated based on 280 days of gestation.

Birthweight was obtained from birth registration through data linkage. In the cases where parents did not give consent for data linkage or data linkage attempts were unsuccessful, parents' recall of their child's birthweight was used (32%). A validation study showed a high level of agreement between birthweight data from parental reports and birth registration records (201).

Factors in infancy

At baseline interviews, parents were also asked about the initiation of breastfeeding and timing of introducing formula milk and solid foods. This was used to estimate the duration of any breastfeeding and exclusive breastfeeding as well as the age at introduction of solid foods.

To calculate infant weight gain, birthweight and weight at 3 years were first converted into age- and sex-specific SDS using UK-WHO growth charts adjusting for gestational age, to take into account variation in gestation age and actual age at 3-year visits across cohort members. Infant weight gain was calculated as the change in weight SDS between birth and 3 years.

Family socio-economic circumstances

Family income was derived from self-reported income at parental interviews and was then weighted using OECD (Organisation for Economic Co-operation and Development) scales to take into account family size. The OECD scales set the needs of a family relative to those of a couple without children whose scale is one. For example, a single adult has a scale of 0.67, while a family of one parent with one child under 14 years has a scale of 0.87. More details on the calculation of OECD weighted family income can be found elsewhere (202). Mother's highest academic qualification level was self-reported. Qualifications gained overseas that do not fall in any of the categories in UK education systems were categorised into the 'others' group.

2.4 Role of early life factors in ethnic differences in child growth

In epidemiological research, a confounder is a variable that is associated with both an exposure and an outcome variable, but it is not an intermediate variable that is on the pathway between the exposure and outcome (203). Thus a confounder may be a cause, but cannot be an effect, of the exposure (204). Bias caused by measured confounders can be controlled through adjustment or matching during statistical analysis. A mediator or intermediate variable is defined as a variable on the causal pathway from the exposure to the outcome (203). It causes variation in the outcome and itself is caused to vary by the exposure variable.

Effect modification occurs when the effect of the exposure on the outcome varies depending on the level of a third variable (203). This third variable is referred as an effect modifier. For example, the effect of salt intake on cardiovascular disease risk differs across age groups (i.e. the effect modifier), which is particularly greater among older adults (205). A common way of dealing with effect modification is to examine the strength of association between the exposure and outcome variables across different levels of the effect modifier, by including an interaction term or stratifying the statistical analysis.

In the context of studying ethnic differences in children's physical growth, ethnic identity of the child is not considered as a causal effect on the early life factors (e.g. early introduction to solid foods or family income) included in this thesis. These early life factors do not meet the conventional definition of mediators. Hence, a broader term, "explanatory factors", is used to refer to variables that are associated with both the exposure and outcome variables and explain the association between the exposure and outcome. The adjustment for these explanatory factors can be interpreted as the amount of ethnic differences in the outcome after accounting for different distributions of early-life factors across ethnic groups.

In each of the results chapters (Chapters 4-7), the role of each set of covariates considered in the statistical analysis are detailed.

2.5 Data handling

Datasets for each of the six MCS sweeps were downloaded and merged into a master copy. To minimise the proportion of missing data in time-invariant variables (i.e. variables that are not expected to change greatly with time, e.g. maternal height), values from later sweeps were used if the variables were missing at the baseline and were collected at later sweeps.

Height data was cleaned in two steps. First, implausible values greater than mean+5SD or less than mean-5SD were treated as missing. In the second step, changes in height SDS between sweeps were summarised. Impossible height growth between sweeps (e.g. height decreased with age) were plotted to ascertain erroneous values, which were then treated as missing. Weight data were cleaned in a similar approach to height data. First, cut-offs of ±5 SD were used to identify implausible data, which were treated as missing. Second, weight changes between sweeps were calculated and examined. Implausible weight growth (i.e. weight changes <-3 SD or >3 SD) were plotted to ascertain erroneous values. BMI, waist circumference and body fat data had a slightly, positively skewed distribution, the cut-offs of -4 SD and 5 SD were used to remove extreme values.

In general, continuous covariates are used as continuous variables, and categorical covariates are included as categorical variables in statistical models. However, categorisation of continuous variables is considered if the relationship between the covariate and outcome is non-linear. The choice of reference category is informed by previous research (e.g. conventional cut-off value used for defining low birthweight), the number of observations available in each category and the biological/public health interpretation of the estimated association (e.g. BMI categories).

2.6 Methodological considerations

2.6.1 Multilevel models for growth trajectories

Several methodological challenges are present when modelling longitudinal data. First, the correlation of repeated measurements (e.g. height and BMI measurements) within an individual needs to be taken into consideration to correctly estimate standard errors for parameters of interest. Second, the variance and measurement errors increase with age as children grow older. Additionally, unit non-response and loss to follow-up are common in longitudinal studies, therefore the number of growth measurements available for each child also varies across individuals.

To address some of these challenges, mixed effects models as described by Singer and Willet (206) were used to model height and BMI trajectories, with individuals as level-2 units and measurement occasions as level-1 units. Mixed effects models take into account the within-individual correlations of repeated measurements and allow different timing of measurements between individuals. Models contain both *fixed* and *random effects*, where the *fixed effects* describe population average curve, while the *random effects* allow individual growth curves to be different from the population average (206).

For example, consider a single-level linear regression model with age as the predictor:

$$\boldsymbol{Y_i = \beta_0 + \beta_1 age_i + \epsilon_i}$$
$$\boldsymbol{\epsilon_i \sim N(0, \sigma^2)} \quad [1]$$

where Y_i is the outcome for individual i ($i = 1, 2 \ldots n$); age_i is age at the outcome measurement for individual i; β_0 is the intercept and β_1 is the coefficient for age_i (i.e. slope). ϵ is the residual, the part of Y that is not explained by the model, and follows a normal distribution with a mean zero and variance σ^2.

For a 2-level mixed effects linear model (level 2: individuals, level 1: measurement occasions) with <u>a random intercept only</u>:

$$\boldsymbol{Level\ 1: Y_{ij} = \beta_{0i} + \beta_1 age_{ij} + \epsilon_{ij}}$$
$$\boldsymbol{Level\ 2: \beta_{0i} = \beta_0 + \mu_{0i}}$$
$$\boldsymbol{\epsilon_{ij} \sim N(0, \sigma^2)\ and\ \mu_{0i} \sim N(0, \sigma_0^2)} \quad [2]$$

Here Y_{ij} denotes the outcome for individual i $(i = 1, 2 \dots n)$ at occasion j $(j = 1, 2 \dots n_i)$; age_{ij} denotes the age of j-th measurement occasion for individual i. μ_{0i} is the random part of the intercept which represents the variation of the intercept for individual i from the population mean intercept (*fixed effect* β_0). β_1 is the slope for ith individual (same as population mean slope), as no random effects are specified for the slope. ϵ_{ij} is the residual for subject i at occasion j, the part of Y_{ij} that is not explained by the model, follows a normal distribution with mean zero and variance σ^2 and μ_{0i} follows a normal distribution with mean zero and variance σ_0^2.

For a mixed effects linear model with both random intercept and slope:

$$\boldsymbol{Level\ 1}: \boldsymbol{Y_{ij} = \beta_{0i} + \beta_{1i} age_{ij} + \epsilon_{ij}}$$

$$\boldsymbol{Level\ 2}: \boldsymbol{\beta_{0i} = \beta_0 + \mu_{0i}}$$

$$\boldsymbol{Level\ 2}: \boldsymbol{\beta_{1i} = \beta_1 + \mu_{1i}} \qquad [3]$$

Where additional *random effects* are specified for the slope (β_{1i}): β_1 is the population mean slope (*fixed effect*), while μ_{1i} is the random part of the slope which represents the variation of the slope for individual i from the mean slope of the population. The level-1 residual ϵ_{ij} and level-2 random effects (μ_{0i}, μ_{1i}) follow the assumptions:

$$\boldsymbol{\epsilon_{ij} \sim N(0, \sigma^2)\ and \begin{bmatrix} \mu_{0i} \\ \mu_{1i} \end{bmatrix} \sim N\left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_0^2 & \sigma_{01} \\ \sigma_{10} & \sigma_1^2 \end{bmatrix} \right)}$$

Combine level 2 and level 1 equations, equation [3] can be re-written into a composite model:

$$\boldsymbol{Y_{ij} = (\beta_0 + \mu_{0i}) + (\beta_1 + \mu_{1i}) age_{ij} + \epsilon_{ij}} \qquad [4]$$

Additional covariates or explanatory variables can be included in the model with or without random effects specified. Unstructured covariance matrix for the random effects are specified and maximum likelihood estimation were used when fitting the models.

2.6.2 Selecting appropriate functions for age to capture non-linear growth curves

Modelling growth trajectories requires fitting appropriate functions for age to describe the changes in growth measurements. Several methods have been developed over the years and can be broadly sub-divided into structural and non-structural models (207). Structural models include Jenss-Bayley, Count, Preece-Baines and Reed models, which summarise the growth process using several parameters that have biological interpretation (207). Non-structural models include polynomial, fractional polynomial and spline models. There are advantages and disadvantages connected with the functional forms of these models (207). The choice of model depends on the type of growth data (e.g. height, weight or BMI), period of growth (e.g. infancy, childhood or adolescence), the number of measurements available per individual and the frequency of measurements.

In this thesis, fractional polynomial models were considered to model height growth trajectories between ages of 3 and 14 years for a number of reasons. First, in the present study, the purposes of growth modelling were to compare growth patterns between sub-groups in the population and examine early life factors that may influence or be associated with growth. Non-structural models are comparably easier to fit and more flexible in shape than structural models (207) and more suitable for the age period under investigation in this thesis. Second, the number of growth measurements available per child ranges from one to five, therefore parameter parsimony is important. The period under investigation spans from early childhood into adolescence, during which time height and BMI growth is a non-linear function of age and characterised with a general deceleration in childhood and a rapid growth in adolescence with the onset of puberty. Fractional polynomial models are much more flexible than polynomial models with the same degrees of freedom (208). Additionally, piecewise linear spline models are good alternative non-structural models which are parsimonious. However, this method divides growth into a set of linear growth phases, which are less biologically sounds than smooth curves produced by fractional polynomial models.

Briefly, 2-level fractional polynomial models estimate outcome as a function of age as

$$\boldsymbol{E(Y_{ij}) = \beta_{0i} + \sum_{j=1}^{m}\left(\beta_k \cdot age_{ij}^{fp_k}\right) + \epsilon_{ij},\ k = 1, 2, \dots m} \qquad [5]$$

where Y_{ij} , β_{0i} and ϵ_{ij} are defined as in equation [3]; m is the degree of the fractional polynomial, e.g. m=2 for a second-order fractional polynomial model; k is the number of fractional power. The age fractional polynomial power age^{fp_k} is selected from a set of 8 candidates $\{-2, -1, -0.5, 0, 0.5, 1, 2, 3\}$, and β_k is the coefficient for age^{fp_k}. Power (0) (i.e. age^0) is the term $\ln(age)$. The automatic selection process of best-fitting fractional polynomial powers was performed using the *-fp-* command in Stata. The procedure started with fitting all possible combinations of powers, then examined deviance statistics to select the best-fitting model for each degree of fractional polynomial and tested whether the inclusion of an additional fractional polynomial term significantly improves the model. For example, to select the best-fitting second-order fractional polynomials (m=2), it fits 8 first-order fractional polynomial models (m=1) and 32 second-order fractional polynomial models (m=2). The best-fitting models of degrees 1 and 2 are selected based on deviance statistics. A partial F test or likelihood-ratio test is used to compare the best-fitting models of degrees 1 and 2 to test whether the additional fractional polynomial term significantly improves the model. Powers are allowed to repeat in the same model. Each time a power is repeated, it is multiplied by $\ln(age)$. For example, power (1, 1) is interpreted as age and $age \cdot \ln(age)$.

For visual illustration, in results Chapters 4-7, estimated trajectories are plotted to illustrate the changes of height and BMI with age as well as by subgroup. Outcome data are usually sparse near the two ends of the age range, where the estimates are likely to be unstable (209). To remove these “end effects”, a restricted age range, instead of the full observed age range, was used for plotting the trajectories. Further details are provided in the methods section within each of the results chapters.

2.6.3 Missing data in multilevel data

Missing data patterns

Missing data are common in longitudinal studies, due to lost to follow-ups (i.e. attrition) and unit/item non-response (e.g. participants failed to respond to certain sweeps or survey items). Rubin (210) differentiated between three important missing data mechanisms (see Table 2.5). When missingness is unrelated to observed or unobserved data, the missing mechanism is considered as *missing completely at random* (MCAR). Under MCAR assumption, conventional analysis methods, such as complete case analysis and likelihood-based analysis, produce unbiased estimates. When missingness is related to variables in the observed data but not unobserved data, the mechanism is considered at *missing at random* (MAR). When missingness is related to unobserved data, it is considered as *missing not at random* (MNAR). In practice, it is nearly impossible to test for MAR and MNAR mechanisms based on observed data, as data needed for such a test are by definition missing.

Table 2.5: Missing mechanisms

Missing mechanism	Description
Missing completely at random (MCAR)	Probability of missingness is not related to observed or unobserved data
Missing at random (MAR)	Probability of missingness is related to observed data but not unobserved data
Missing not at random (MNAR)	Probability of missingness is related to unobserved data

Strategies for handling missing data

For the present PhD project, the main exposure variable (i.e. ethnicity) is nearly fully observed with a low percentage of missing data (0.1%). Missing data are more likely to occur in repeatedly measured anthropometric outcome variables and some of the early life factors measured at baseline interviews. Missing data in individual-level early life factors at baseline is likely to be due to item non-response, while missing data in outcome variables at follow-up is likely to be the result of both attrition and item non-response. Previous literature has shown that attrition and item non-response in longitudinal studies most often have systematic elements and are unlikely to be MCAR (211). In the MCS, factors such as child's ethnicity, maternal age and family socio-economic indicators, have been shown to be associated with participants' response to follow-up surveys (199). Item non-response is commonly caused by respondents' refusal or inability to respond. For example, maternal pre-pregnancy BMI may be missing because the mother was concerned about her weight and refused to report her weight. It may also be a result of the mother not being able to recall her weight prior to the pregnancy. Table 2.6 summarises the strategies used to handle missing data in outcome variables and early life factors. For missing data in repeatedly measured outcome variables such as height and BMI trajectories, mixed effects models were used assuming they were MAR, for example participants who had BMI measured at 3, 5 and 14 years but not at 7 and 11 years. Likelihood-based methods to fit mixed effects models can product unbiased estimates, providing that covariates that predict the missing values are included in the model (206). For cross-sectional analysis which only used outcome measured at a specific sweep, e.g. obesity at 11 years, inverse probability weighting was used to correct for the unequal probabilities of participants present at the selected sweep. Sampling weights as well as attrition weights at each sweep were calculated by the MCS team and provided with the datasets (202). The sampling weights are proportionate to the inverse of sampling fractions (i.e. the probabilities of wards being selected in each stratum). The attrition weights are proportionate to the inverse of the probabilities of participant present at each sweep.

Table 2.6: Strategies for handling missing data in the present PhD project

Missing data	Strategies
Outcome variables	• For repeated outcome measurements, mixed effects models can handle missing data in the outcome variable under a MAR assumption (Chapters 4-7) • For cross-sectional analysis, inverse probability weighting was applied using sampling and attrition weights provided with MCS datasets (Chapters 3 and 6)
Level-2 early life factors	• Complete case analysis was performed, when the proportion of missing data was small. Relevant comparison of characteristics of complete and incomplete data as well as sensitivity analysis were provided (Chapter 4) • Multiple imputation with chained equation was applied to impute missing data in early life factors, if the proportion of missing data was relatively high (Chapters 5-6)

*MAR: missing at random.

When missing data were in early life factors and the proportion of missing data was small, the missing data were considered inconsequential (212) and complete case analysis was performed. However, comparison of participant characteristics between complete and incomplete data as well as relevant sensitivity analysis were conducted. When the proportion of missing data in early life factors was relatively high, multiple imputations by chained equations (MICE) were used. The MICE method is a flexible imputation method that can be used to impute multiple variables of different types at the same time (213). MICE works on a variable-by-variable approach and it is possible to specify a different imputation method for each variable with missing data.

2.7 Statistical analyses

Twins and triplets have been shown to have different growth in early life, therefore, only singletons were included in the analysis in this thesis (214, 215). The analysis sample, variables and statistical methods used for each aim will be outlined separately within each results chapter, alongside a description of any relevant sensitivity analysis performed. All analyses were conducted in Stata V.13.1 (Stata Corp., College Station, TX, USA).

2.8 Ethics approval

Medical research ethical clearance was obtained by the MCS team for each sweep of data collection. Details can be found in MCS guides to the datasets (202). Informed consent for each relevant element at each sweep was sought from carers (usually parents) as well as the children themselves as they grew older. This thesis uses data from the MCS to perform secondary data analysis, which was approved by the Research and Development Office at UCL Great Ormond Street Institute of Child Health (15PL05). Further ethical approval was not required.

2.9 Role of the researcher

I downloaded and merged MCS datasets from each survey into a master copy, performed data cleaning, as well as derived relevant variables required for the analyses in this thesis. I designed the study, alongside my supervisors, and performed all analyses presented in this thesis.

Datasets from each survey of the MCS were downloaded from the UK Data Service (University of Essex and University of Manchester). The persistent identifiers for MCS datasets are:

- First survey http://dx.doi.org/10.5255/UKDA-SN-4683-1;
- Second survey http://doi.org/10.5255/UKDA-SN-5350-3;
- Third survey http://doi.org/10.5255/UKDA-SN-5795-3;

- Fourth survey http://doi.org/10.5255/UKDA-SN-6411-6;
- Fifth survey http://doi.org/10.5255/UKDA-SN-7464-2;
- Sixth survey http://doi.org/10.5255/UKDA-SN-8156-2.

3 OVERVIEW OF EARLY LIFE FACTORS IN MILLENNIUM COHORT STUDY

Several prenatal, neonatal and infancy factors, which may influence children's physical growth, have been identified by previous studies (Chapter 1 Background). This chapter compares the distributions of these early life factors by ethnic group, examines the associations of these factors with height or BMI outcome, and whether the associations changed between outcome measured at 3 years and at 14 years (i.e. first and last available measure in the MCS).

Of the total 18,107 singletons in the MCS, around 82% were White, 5.0% were Indian, 2.1% were Pakistani, 1.3% were Black Caribbean, 2.2% were Black African, 3.1% were from mixed ethnic backgrounds and 1.9% were from other ethnic groups (including Chinese) (Table 3.1). The weighted proportion, after accounting for disproportionate representation of children from minority ethnic groups and disadvantaged backgrounds, was 87.2%, 1.8%, 2.9%, 1.0%, 1.0%, 1.5%, 3.1% and 1.4% respectively (Table 3.1).

Table 3.1: Weighted and unweighted ethnic composition of all MCS singletons

	Unweighted (total *n* = 18,982)		**Weighted*** (total *n*=18,919)	
	n	%	*n*	%
White	15,516	81.7%	16,490	87.2%
Indian	492	2.6%	339	1.8%
Pakistani	948	5.0%	558	2.9%
Bangladeshi	395	2.1%	185	1.0%
Black Caribbean	255	1.3%	184	1.0%
Black African	411	2.2%	279	1.5%
Mixed	585	3.1%	593	3.1%
Others	355	1.9%	268	1.4%
Missing	25	0.1%	24	0.1%

*Sampling weights were applied to take into account disproportionate representation of children from minority ethnic groups and disadvantaged backgrounds.

3.1 Ethnic differences in early life factors

Parental characteristics

Maternal age: The mean maternal age at the birth of MCS cohort member differed between ethnic groups. Compared to White mothers (28.9 years), Pakistani and Bangladeshi mothers were on average younger by about 2 years and Black African mothers were older by 2 years; while Indian and Black Caribbean mothers had a similar mean age to White mothers (Table 3.2).

Parental height: White mothers and fathers had a mean height of 164.4 cm and 178.7 cm, respectively. Compared with White parents, South Asian parents (especially Bangladeshis) were considerably shorter. Bangladeshi mothers and fathers were on average shorter than their White counterparts by 8.0 cm and 9.3 cm ($p<0.001$), respectively. Black African (165.0 cm) and Black Caribbean mothers (164.8 cm) had a similar mean height to White mothers, while Black African and Caribbean fathers were on average about 3 cm shorter than White fathers ($p<0.001$) (Table 3.2).

Maternal pre-pregnancy BMI: The mean reported maternal BMI pre-pregnancy ranged from 22.1 kg/m^2 in the Indian group to 25.5 kg/m^2 in the Black African group. Pakistani and Bangladeshi mothers had a similar mean pre-pregnancy BMI to White mothers (23.5 kg/m^2 vs. 23.7 kg/m^2), but they were more likely to be in the 'thin' category. Black Caribbean and Black African mother had a higher mean BMI by 0.9 kg/m^2 and 1.8 kg/m^2 respectively and were more likely to be in the 'overweight' or 'obese' BMI category before pregnancy ($p\leq0.01$) (Table 3.2).

Maternal smoking: The prevalence of self-reported smoking at the end of fourth month of gestation was 23% among White mothers. Mothers of ethnic minorities were much less likely to smoke during pregnancy than White mothers, with the prevalence ranging from 1% to 3%, with the exception of Black Caribbean mothers who had a similar proportion of mothers smoked during pregnancy (20%, p-value for the difference with White mothers = 0.29) (Table 3.2).

Birth order: In the White group, 43% of the MCS children were first-born children in their families. The proportion of first-born children was lower among Pakistanis (34%), Bangladeshis (29%) and Black Africans (33%) ($p<0.001$) (Table 3.2).

Neonatal factors

Birthweight: White children had a mean birthweight of 3.41 kg. Mean birthweight was generally lower among children in minority ethnic groups by 300-390 g in South Asian groups ($p<0.001$), 220 g in Black Caribbean group ($p<0.001$) and 80 g in Black African group ($p=0.002$). After taking into account gestational age, 8% of White children were born small for gestational age and 11% were born large for gestational age. Among children in minority ethnic groups, the proportion of children born small for gestational age was much higher (14%-26%) and the proportion of children born large for gestational age was lower (3%-9%) ($p<0.01$), with the exception for Black Caribbean children who had similar proportions of children in different birthweight for gestational age categories as White children (Table 3.2).

Infant feeding and weight gain

Breastfeeding: In the White group, 32% of mothers reported that they had never exclusively breastfed their MCS children, 65% reported that they had exclusively breastfed their children for less than 4 months and 3% reported to have exclusively breastfed their children for 4 months or more. Mothers from minority ethnic groups were more likely to exclusively breastfeed their children than White mothers ($p<0.001$). The proportion of mothers who had never exclusively breastfed was lowest in the Black African group (5%), followed by Black Caribbean (7%), Bangladeshi (13%), Indian (16%) and Pakistani (25%) (Table 3.2).

Introduction to solid food: The proportion of children who had early introduction to solid food (at age of less than 4 months) was much higher in the White group (10%), compared with minority ethnic groups (1%-4%) ($p<0.01$) (Table 3.2).

Weight gain: The mean change in weight SDS between birth and 3 years was lowest in the White group (-0.09 SDS), followed by South Asian groups (0.21-0.28 SDS) and highest in the Black African and Black Caribbean groups (0.65-0.75 SDS), indicating that minority ethnic groups had greater weight gain between birth and 3 years ($p<0.001$) (Table 3.2).

Family socio-economic circumstances at baseline (9 months)

Family income quintiles: The distribution of family income was overall similar between White and Indian families, apart from that the income of Indian families was slightly less likely to be in the top two quintiles (21% and 14% vs. 22% and 22% in Whites, $p=0.04$). However, Pakistani, Bangladeshi, Black Caribbean and Black African families were much more likely to have family income in the lowest two quintiles ($p<0.001$). For example, 49% and 40% of Bangladeshi families had income in the lowest and second lowest quintiles, while the proportions were 17% and 19% in the White group, respectively (Table 3.2).

Maternal education: At 9 months, 28% of mothers in the White group had a higher education diploma or degree qualification and 13% had not obtained any formal academic qualification. The proportion of mothers who did not have any formal academic qualifications was higher in the minority ethnic groups than in the White group, especially among Pakistani and Bangladeshi mothers (43%-45%). Higher proportion of Indian (35%) and Black African (38%) mothers had obtained a qualification at higher education level at 9 months (Table 3.2).

Table 3.2: Overview of early life factors by ethnic group, based on weighted analysis (total *n*=18,017 singletons, weighted *n*= 18,035)

	% missing†	White *n*=15516 mean(SD)	Indian *n*=492 mean(SD)	*p*‡	Pakistani *n*=948 mean(SD)	*p*‡	Bangladeshi *n*=395 mean(SD)	*p*‡	Black Caribbean *n*=255 mean(SD)	*p*‡	Black African *n*=411 mean(SD)	*p*‡
Prenatal factors												
Maternal age at MCS birth (years)	0.3%	28.9(5.7)	28.6(6.3)	0.47	26.5(6.8)	***	26.4(7.5)	***	29.5(8.2)	0.18	30.8(7.0)	***
Mid-parental height (SDS)	0.4%	0.12(0.75)	-0.53(0.96)	***	-0.37(1.00)	***	-1.04(1.18)	***	0.08(1.02)	0.30	0.07(1.21)	0.22
Maternal height (cm)	0.8%	164.4(6.7)	159.4(7.6)	***	160.7(8.5)	***	156.4(10.8)	***	164.8(8.0)	0.18	165.0(9.5)	0.13
Paternal height (cm)	21%	178.7(6.9)	174.1(9.6)	***	175.2(9.9)	***	169.4(11.0)	***	175.9(8.7)	***	175.6(11.8)	***
Maternal pre-pregnancy BMI (kg/m^2)	12%	23.7(4.3)	22.1(4.1)	***	23.5(6.1)	0.29	23.5(6.2)	0.68	24.6(5.2)	**	25.5(6.2)	***
Median (IQR)		22.7 (20.9-25.5)	21.1 (19.7-23.8)		22.5 (20.3-26.1)		22.9 (20.6-26.1)		23.8 (21.5-27.1)		24.5 (22.5-28.6)	
Maternal pre-pregnancy BMI category, n(%)	12%			***		***		***		**		***
Thin (<18.5 kg/m^2)		728(5%)	28(10%)		42(10%)		12(11%)		8(5%)		9(5%)	
Normal (18.5-24.9 kg/m^2)		9977(67%)	202(72%)		249(59%)		60(55%)		79(52%)		91(51%)	
Overweight (25.0-29.9 kg/m^2)		2922(20%)	44(16%)		91(21%)		29(26%)		46(31%)		46(26%)	
Obese (≥30 kg/m^2)		1285(9%)	7(2%)		41(10%)		8(8%)		18(12%)		33(18%)	
Maternal smoking during pregnancy, n(%)	2.0%			***		***		***		0.29		***
No		12363(77%)	330(99%)		539(97%)		180(98%)		141(80%)		267(97%)	
Yes		3680(23%)	4(1%)		16(3%)		4(2%)		35(20%)		9(3%)	
Birth order, n(%)	2.7%			0.67		***		***		0.26		***
First born child		7144(44%)	140(45%)	***	161(34%)	***	41(29%)	***	70(39%)	***	84(33%)	**
Second born or higher		9226(56%)	172(55%)		314(66%)		99(71%)		109(61%)		168(67%)	
Neonatal factors												
Birthweight (kg)	0.5%	3.41(0.55)	3.02(0.72)	***	3.11(0.73)	***	3.07(0.82)	***	3.19(0.75)	***	3.33(0.69)	**
Birthweight for gestational age, n(%)	5.3%			***		***		***		**		0.21
Small for gestational age		1191(8%)	79(26%)		102(20%)		34(20%)		25(14%)		26(11%)	
Appropriate for gestational age		12837(82%)	219(71%)		379(75%)		129(77%)		132(77%)		193(80%)	
Large for gestational age		1718(11%)	9(3%)		24(5%)		5(3%)		15(9%)		21(9%)	

	% missing†	White *n*=15516	Indian *n*=492		Pakistani *n*=948		Bangladeshi *n*=395		Black Caribbean *n*=255		Black African *n*=411	
		mean(SD)	mean(SD)	*p*‡	mean(SD)	*p*‡	mean(SD)	*p*‡	mean(SD)	*p*‡	mean(SD)	*p*‡
Infant feeding and weight gain												
Exclusive breastfeeding, n(%)	3.5%			***		***		***		***		***
None		5030(32%)	51(16%)		133(25%)		22(13%)		12(7%)		14(5%)	
< 4 months		10316(65%)	247(78%)		357(68%)		141(82%)		151(88%)		228(90%)	
≥ 4 months		509(3%)	18(6%)		33(6%)		8(5%)		8(5%)		11(4%)	
Early introduction to solid foods, n(%)	3.3%			***		***		***		***		**
Yes		14210(90%)	312(98%)		516(99%)		168(98%)		170(99%)		243(96%)	
No		1666(10%)	6(2%)		8(1%)	***	3(2%)	***	2(1%)	***	11(4%)	***
Weight gain (birth-3 years), SDS	25%	-0.09(1.10)	0.21(1.51)	***	0.28(1.76)	***	0.27(2.06)	***	0.75(1.95)	***	0.65(1.60)	***
Family socio-economic circumstances (at 9 months)												
OECD weighted family income quintiles, n(%)	0.1%			0.04		***		***		***		***
Highest quintile		3566(22%)	72(21%)		23(4%)		5(3%)		17(9%)		35(13%)	
Fourth quintile		3559(22%)	46(14%)		27(5%)		7(4%)		26(14%)		30(11%)	
Third quintile		3418(21%)	79(24%)		49(9%)		10(5%)		30(17%)		38(14%)	
Second quintile		3058(19%)	88(26%)		217(39%)		73(40%)		35(19%)		57(21%)	
Lowest quintile		2880(17%)	52(15%)		241(43%)		90(49%)		76(41%)		118(42%)	
Maternal highest academic qualification, n(%)	0.5%			***		***		***		0.03		***
Degree or higher education diploma		4588(28%)	116(35%)		55(10%)		15(8%)		46(25%)		104(38%)	
A-level		1632(10%)	34(10%)		42(8%)		13(7%)		12(7%)		18(6%)	
GCSE grades A*-C		5976(36%)	64(19%)		103(19%)		37(20%)		64(35%)		30(11%)	
GCSE grades D-G		1873(11%)	18(5%)		41(7%)		13(7%)		22(12%)		12(4%)	
Other academic qual.		217(1%)	40(12%)		75(14%)		22(12%)		5(3%)		32(12%)	
None		2142(13%)	63(19%)		237(43%)		82(45%)		34(19%)		81(29%)	

*Values are mean(SD), unless otherwise stated, from weighted analysis to take into account of oversampling of children from minority ethnic groups and less advantaged backgrounds. OECD: Organisation for Economic Co-operation and Development. SD: standard deviation. SDS: standard deviation score. IQR: interquartile range. †% of missing data in the variable (unweighted). ‡P-value for difference in characteristics between each ethnic group and Whites, based on linear regression for continuous variables and Chi-squared tests for categorical variables. ** p≤0.01; *** p≤0.001.

3.2 Descriptive associations between early life factors and height/BMI at 3 and 14 years

Table 3.3 presents descriptive associations between each of the key early life factors and height growth, and describes whether the associations changed between 3 years and 14 years (i.e. first and last available height measurement in the MCS).

Adjusting for sex and actual age at measurement, height at 3 years was higher in children whose parents were taller, mothers did not smoke during pregnancy and had a higher education diploma or degree qualification, and in children who had higher birthweight and lived in families with income in the highest quintile. A similar pattern of associations between the early life factors and height at 14 years was found. Apart from birth order, associations of most of these early life factors with height appeared to strengthen at 14 years compared with at 3 years.

Table 3.3: Associations between early life factors and height (cm) at 3 and 14 years, estimated from linear regression models

	Height at 3 years		Height at 14 years	
Early life factors	b*	95% CI	b*	95% CI
Mid-parental height, per 1 SDS increase	1.75	[1.68, 1.82]	4.08	[3.93, 4.24]
Mother's height, per 1 cm increase	0.17	[0.16, 0.18]	0.39	[0.37, 0.40]
Father's height, per 1 cm increase	0.15	[0.14, 0.16]	0.35	[0.33, 0.37]
Birth order				
First born child	Ref		Ref	
Second born or higher	-0.48	[-0.61, -0.36]	-0.43	[-0.72, -0.15]
Maternal smoking during pregnancy				
No	Ref		Ref	
Yes	-0.67	[-0.82, -0.51]	-0.83	[-1.18, -0.48]
Birthweight, per 1 kg increase	1.74	[1.63, 1.85]	2.96	[2.72, 3.20]
Birthweight for gestational age				
Small for gestational age	Ref		Ref	
Appropriate for gestational age	1.65	[1.43, 1.87]	3.09	[2.61, 3.57]
Large for gestational age	3.34	[3.05, 3.63]	5.94	[5.31, 6.57]
Family income quintiles				
Highest quintile	Ref		Ref	
Fourth quintile	-0.08	[-0.29, 0.13]	-0.45	[-0.90, -0.01]
Third quintile	-0.28	[-0.49, -0.07]	-0.79	[-1.24, -0.35]
Second quintile	-0.58	[-0.79, -0.38]	-1.64	[-2.08, -1.21]
Lowest quintile	-0.73	[-0.94, -0.53]	-2.44	[-2.87, -2.00]
Maternal highest academic qualification				
Degree or higher education diploma	Ref		Ref	
A-level	-0.17	[-0.41, 0.06]	-0.77	[-1.28, -0.26]
GCSE grades A*-C	-0.39	[-0.56, -0.23]	-1.06	[-1.42, -0.71]
GCSE grades D-G	-0.75	[-0.98, -0.52]	-1.46	[-1.97, -0.95]
Other academic qualification	0.37	[-0.03, 0.77]	-0.82	[-1.65, 0.02]
None	-0.55	[-0.75, -0.36]	-2.64	[-3.07, -2.21]

*Estimated coefficient from unweighted linear regression of height at 3 or 14 years on each of the key early life factors which influences height growth, with adjustment for age at measurement and sex. CI: confidence interval.

Table 3.4 shows the associations between each of the key early life risk factors which may influence adiposity and BMI at 3 and 14 years. Adjusting for sex and age at measurement, BMI at 3 years was higher in children whose mother smoked during pregnancy, had higher pre-pregnancy BMI, and in children who had higher birthweight, never been exclusively breastfed, were introduced to solid food early and lived in families with income in the lower quintile groups (third and fourth quintiles compared with the highest income quintile). Lower family income and maternal education were more consistently associated with higher BMI at 14 years and a negative socio-economic gradient in BMI was shown. Apart from birthweight, associations between other early life factors and BMI strengthened at 14 years, compared to at 3 years.

3.3 Summary

To summarise, the distributions of several early life factors differed by ethnic group. Although there was some variation between ethnic subgroups, South Asian subgroups (Indian, Bangladeshi and Pakistani) were more similar to each other, than to Black Africans and Black Caribbeans. Compared to their White counterparts, South Asian parents were on average shorter and mothers were slightly younger at MCS child birth (except for Indian mothers) and more likely to have a BMI in the 'thin' category prior to pregnancy. However, Black African and Caribbean mothers had a similar mean height to White parents and fathers were slightly shorter than White fathers. Black mothers were older at the birth of the MCS child (except for Black Caribbean mothers) and were more likely to be in the 'overweight' or 'obese' BMI category before pregnancy. Compared to White children, ethnic minority children were less likely to be first-borns, had a lower mean birthweight, and were more likely to be born small for gestational age, have been exclusively breastfed, experience more weight gain in the first three years of life, and live in a family with lower family income and mothers having no formal academic qualification.

Consistent with existing literature (Chapter 1), parental height and birthweight were positively associated with height at 3 years in the MCS, adjusting for sex and age at height measurement. Not being a first-born, maternal smoking during pregnancy and less advantaged family socio-economic circumstances were associated with lower mean height at 3 years. Apart from birth order, these associations were strengthened at older age at 14 years, compared to at 3 years.

BMI at 3 years was positively associated with maternal pre-pregnancy BMI, maternal smoking during pregnancy, birthweight, infant weight gain and early introduction to solid foods, after adjusting for sex and age at the BMI measurement. Exclusive breastfeeding and advantaged family socio-economic circumstances were associated with lower mean BMI at 3 years. With the exception of birthweight, the associations between these early life factors and BMI were stronger at 14 years, compared to at 3 years. A clear negative socio-economic gradient in BMI was shown at 14 years.

Table 3.4: Associations between early life factors and BMI at 3 and 14 years, estimated from linear regression models

	BMI at 3 years		BMI at 14 years	
Early life factors	b*	95% CI	b*	95% CI
Maternal smoking during pregnancy				
No	Ref		Ref	
Yes	0.21	[0.15, 0.28]	0.93	[0.75, 1.12]
Maternal pre-pregnancy BMI, kg/m²	0.06	[0.05, 0.07]	0.26	[0.24, 0.27]
Maternal pre-pregnancy BMI category				
Thin (<18.5 kg/m²)	Ref		Ref	
Normal (18.5-24.9 kg/m²)	0.43	[0.31, 0.55]	1.12	[0.77, 1.46]
Overweight (25.0-29.9 kg/m²)	0.77	[0.65, 0.90]	2.68	[2.31, 3.05]
Obese (≥30 kg/m²)	1.05	[0.91, 1.20]	4.18	[3.76, 4.60]
Birthweight, per 1 kg increase	0.56	[0.52, 0.61]	0.41	[0.28, 0.54]
Birthweight for gestational age				
Small for gestational age	Ref		Ref	
Appropriate for gestational age	0.55	[0.46, 0.64]	0.40	[0.14, 0.66]
Large for gestational age	1.09	[0.98, 1.21]	1.19	[0.85, 1.54]
Exclusive breastfeeding				
None	Ref		Ref	
< 4 months	-0.09	[-0.14, -0.03]	-0.67	[-0.84, -0.50]
≥ 4 months	-0.21	[-0.36, -0.07]	-1.07	[-1.48, -0.65]
Early introduction to solid foods				
No	Ref		Ref	
Yes	0.31	[0.22, 0.39]	1.02	[0.76, 1.27]
Weight gain (birth-3 years), per 1 SDS increase	0.62	[0.60, 0.64]	0.86	[0.80, 0.93]
Family income quintiles				
Highest quintile	Ref		Ref	
Fourth quintile	0.18	[0.09, 0.26]	0.68	[0.44, 0.92]
Third quintile	0.09	[0.01, 0.17]	0.89	[0.65, 1.13]
Second quintile	0.03	[-0.05, 0.12]	1.12	[0.89, 1.36]
Lowest quintile	0.07	[-0.01, 0.15]	1.38	[1.14, 1.61]
Maternal highest academic qualification				
Degree or higher education diploma	Ref		Ref	
A-level	-0.08	[-0.17, 0.02]	0.26	[-0.01, 0.54]
GCSE grades A*-C	0.02	[-0.04, 0.09]	0.76	[0.57, 0.95]
GCSE grades D-G	0.04	[-0.05, 0.13]	1.07	[0.80, 1.35]
Other academic qualification	-0.28	[-0.44, -0.12]	0.47	[0.02, 0.92]
None	-0.07	[-0.14, 0.01]	0.90	[0.67, 1.13]

*Estimated coefficient from unweighted linear regression of BMI at 3 or 14 years on each of the key early life risk factors of obesity, with adjustment for age at measurement and sex. CI: confidence interval, SDS: standard deviation score.

4 ETHNIC DIFFERENCES IN HEIGHT GROWTH AND THE ROLE OF EARLY LIFE FACTORS (OBJECTIVE 1)

4.1 Introduction

A number of cross-sectional studies have suggested ethnic differences in children's height in the UK (124, 216-218) (Chapter 1), although there is a considerable variation in sizes and sometimes the directions of the reported differences. For example, in a multi-ethnic cohort in London (219), South Asian boys and girls aged 11-13 years were reported to be 2-3 cm shorter than their White counterparts. In the Health Survey for England 1999, Bangladeshi boys and Indian girls aged 2-15 years were both shorter than their peers in the general population, and the age adjusted difference was 2.15 cm and 1.57 cm respectively (89). In the Health Survey for England 2004, Bangladeshi boys and Indian girls had mean heights similar to their counterparts in the general population (90). The discrepancies across these studies may be partly due to variation in study samples and the use of ethnic categories across studies. It is also possible that these discrepancies were partly attributable to: 1) ethnic differences in height trajectories, i.e. the pattern of height differences changes with age; or 2) the era when the comparison was made, i.e. ethnic differences in height growth have changed over time. Longitudinal studies are needed to understand ethnic differences in height trajectories. Using data from the Born in Bradford (England) cohort study, Fairley and colleagues (220) found that Pakistani infants were shorter than White infants at birth, but had more rapid postnatal growth in the first four months and were taller by 0.6 cm in boys and 1.1 cm in girls at the age of two years. However, growth patterns from childhood to adolescence across ethnic groups are largely unclear.

Although there is a strong genetic element to height growth, the extent to which genetically determined height potential is achieved is shaped by environmental factors (221). A number of early life factors were found to influence height growth, including maternal smoking during pregnancy, birthweight, and family socio-economic circumstances (SECs) in early life (222). Sub-optimal growth and shorter achieved adult height have been associated with adverse health outcomes, e.g. cardiovascular diseases (41, 43), and poor social performance (56, 57). Therefore, it is important to understand whether any potential ethnic differences in height growth are due to their differences in early life factors, which can be used for public health intervention.

This chapter aims to investigate 1) whether height trajectories from the age of 3 to 14 years differed by ethnic group; and 2) whether any height differences were explained prenatal factors, birthweight and early-life family SECs.

4.2 Methods

Analysis sample

The analysis in this chapter included singletons who had at least one height measurement and were from the six major ethnic groups in the UK (i.e. White, Indian, Pakistani, Bangladeshi, Black African and Black Caribbean) (*n*=16,138, eligible sample). This analysis further excluded children who were not living with either of their natural parents (e.g. adopted children), because they were unlikely to have information on their natural mother's characteristics required for this analysis (*n*=41). Children who had missing data on the covariates were excluded (*n*=671). A total of 15,426 children with 60,935 height measurements were included in the analysis (analysis sample, 96% eligible sample).

Variables

Details on how relevant variables were collected and derived are provided in Chapter 2. A brief description is provided below.

Outcome: Height (cm) was measured at ~3, 5, 7, 11 and 14 years of age and included as a continuous variable.

Exposure: Ethnicity was categorised as 'White', 'South Asian' and 'Black African-Caribbean'. Indian, Pakistani and Bangladeshi were collapsed into the 'South Asian' group, and Black African and Black Caribbean into the 'Black African-Caribbean' group, due to their small sample sizes. The observed height differences between specific sub-groups are provided in Appendix II Table S1. There was some variation between ethnic subgroups. Bangladeshi appeared to be the shortest among the South Asian subgroups. Black Africans were taller than Black Caribbeans. Due to small sample sizes in the Bangladeshi and Pakistani groups, many of their differences to White children had wide conference intervals. Overall, South Asian subgroups were more similar to each other, than to Black African-Caribbeans.

Covariates: A number of explanatory factors were considered in the analysis, which are suggested by existing literature to be predictive of height growth and are closely associated with ethnicity, including maternal age (99, 223), maternal smoking during pregnancy (99, 224), birth order (99, 223), birthweight (225, 226), maternal education and family income (227-229). These factors were examined to understand the extent of ethnic differences in height growth that would remain if the distribution of these factors were equalised across ethnic groups (230).

Maternal age at childbirth in years was used as a continuous variable. Maternal smoking in pregnancy was used as a binary variable, defined as smoking >0 cigarette/day at the end of fourth months of gestation. Birth order was categorised as ‘first’ and ‘second or later’ born. Birthweight was adjusted to explore whether any ethnic differences in height growth were due to differences in intrauterine growth. Birthweight in kilograms was used as a continuous variable. Maternal highest educational qualification at baseline (9 months) was classified as ‘degree or higher education diploma’, ‘A-level’, ‘GCSE grades A*-C’, ‘GCSE grades D-G’, ‘others’ (e.g. qualifications obtained overseas that cannot be categorised into any of the above groups) and ‘no qualifications’. OECD weighted family income (9 months) was used as quintiles.

Statistical analysis

Early life factors were compared between each minority ethnic group and the White group using t-tests for continuous variables and Chi-squared tests for categorical variables. Mixed effects third-order fractional polynomial models were used to capture the non-linear trends for height growth from childhood to adolescence (231). Models were fitted separately for boys and girls, due to known sex differences in height growth (232). The best-fitting fractional polynomial age powers were age, age^3 and $age^3 * \ln(age)$ for boys and $\sqrt{age}$, age^2 and age^3 for girls. Random coefficients were allowed for age and age^3 in boys, and age^2 and age^3 in girls. Inclusion of an additional age term for random effects led to non-convergence (i.e. $age^3 * \ln(age)$ in boys and $\sqrt{age}$ in girls). The fitted height trajectories were:

for boys

$$Height_{ij} = (\beta_0 + \mu_{0i}) + (\beta_1 + \mu_{1i})age_{ij} + (\beta_2 + \mu_{2i})age_{ij}^3 + \beta_3 age_{ij}^3 * \ln(age_{ij}) + \epsilon_{ij}$$

for girls

$$Height_{ij} = (\beta_0 + \mu_{0i}) + (\beta_1 + \mu_{1i})age_{ij}^2 + (\beta_2 + \mu_{2i})age_{ij}^3 + \beta_3\sqrt{age_{ij}} + \epsilon_{ij}$$

where $Height_{ij}$ denotes height for subject i (level-2) at measurement occasion j (level-1); $\beta_0, \beta_1, \beta_2$ and β_3 denote the fixed parts of the intercept and coefficients for age terms; μ_{0i}, μ_{1i} and μ_{2i}denote the respective random parts; and ϵ_{ij} is the error term for subject $i = 1, 2 \ldots n$ at measurement occasion $j = 1, 2 \ldots n_i$. Deviance, Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) statistics were used to assess goodness of fit and to compare models. Differences between observed and predicted height (level-1 residuals) are summarised in Appendix II Table S2. Q-Q (quantile-quantile) plots for random intercepts and coefficients are provided in Appendix II Figure S3.

The unadjusted model (model 1) included fractional polynomial age terms, ethnicity, and interaction terms between ethnicity and all age terms to estimate ethnic differences in height trajectories between 3 and 14 years. The White group was the largest ethnic group and considered as the reference group. Models were further adjusted for potential explanatory factors according to life stages, first for prenatal factors (model 2), then additionally for birthweight (model 3), and further for family SECs (family income and maternal education) (model 4). Height trajectories for each ethnic group as well as height differences between ethnic groups by age were estimated. To remove the "end effects" caused by sparse data, instead of the full observed age range (2.7 - 15.3 years), a restricted age range from 3 to 14 years was used for plotting the trajectories.

Sensitivity analysis

A number of sensitivity analyses were conducted. **First**, there was a small proportion of participants (4%) who had missing data on covariates and were excluded from the main analysis. Models 1-4 were repeated using the maximum available sample for each model to compare with the results from the main analysis using complete cases. **Second**, to explore the role of potential genetic influence in ethnic differences in height growth, model 4 was further adjusted for mid-parental height SDS. Parental height was considered as a proxy for genetic influence. **Third**, a number of pubertal development measures (i.e. parent-rated stage of voice change at 11 years in boys, self-reported age at first menstruation in girls, and derived pubertal development score at 14 years) were examined to explore whether ethnic differences in height growth could be due to differences in growth tempo (i.e. children mature at different rates). The method used for deriving the pubertal development score is described in Appendix II Table S3.

All analyses were conducted in Stata V.15.1 (Stata Corp., College Station, TX, USA).

4.3 Results

Participant characteristics by ethnic group

Of the 15,426 children included, 87.7% were White, 8.8% South Asian and 3.2% Black African-Caribbean children. South Asian mothers (mean age: 26.9 years) were on average younger than White mothers (28.5 years) at the birth of the MCS child, while Black African-Caribbean mothers (30.1 years) were slightly older (Table 4.1). About 36% of South Asian and 33% of Black African-Caribbean children were first-borns compared with 43% among White children. Ethnic minority children had a lower mean birthweight by 320 g in South Asians and 110 g in Black African-Caribbeans and their mothers were much less likely to smoke at four months of pregnancy compared with the White group (3-10% vs. 26%). They were also more likely to live in a family with lower maternal education level and family income than White children. For example, 40% of mothers in the South Asian and 31% in the Black African-Caribbean groups had no formal academic qualification, compared with only 16% in the White group. *P* values for the above described ethnic differences were all ≤0.001.

The mean mid-parental height SDS was lower in the South Asian group than in the White group (-0.57 SDS vs. 0.07 SDS, $p<0.001$) (Table 4.1) and was similar between the White and Black African-Caribbean group (0.07 SDS vs. 0.10 SDS, $p=0.35$).

Table 4.1: Description of participant characteristics by ethnic group (total *n*=15,426 singletons)

Characteristics	**White (*n*=13,528)**	**South Asian† (*n*=1,382)**	**Black African-Caribbean† (*n*=516)**
Maternal age at childbirth (y), mean(SD)	28.5(6.0)	26.9(5.2)	30.1(6.3)
First born, n(%)	5,970(43.1%)	495(35.6%)	174(32.8%)
Maternal smoking (>0 cigarette/day), n(%)	3,492(25.8%)	45(3.3%)	49(9.5%)
Birthweight (kg), mean(SD)	3.41(0.56)	3.09(0.56)	3.30(0.60)
Maternal education, n(%)			
Higher education	3,584(25.9%)	220(13.6%)	156(27.4%)
A-level	1,366(9.9%)	124(7.7%)	39(6.8%)
GCSE grades A*-C	5,005(36.1%)	307(19.0%)	111(19.5%)
GCSE grades D-G	1,561(11.3%)	129(8.0%)	43(7.5%)
Others	199(1.4%)	192(11.9%)	44(7.7%)
No qualification	2,151(15.5%)	641(39.7%)	177(31.1%)
Household income quintiles, n(%)			
Lowest	2,981(21.4%)	666(40.9%)	270(46.9%)
Second lowest	2,878(20.7%)	581(35.6%)	132(22.9%)
Middle	2,830(20.3%)	175(10.7%)	72(12.5%)
Second highest	2,732(19.6%)	108(6.6%)	56(9.7%)
Highest	2,509(18.0%)	100(6.1%)	46(8.0%)
Mid-parental height SDS‡, mean(SD)	0.07(0.77)	-0.57(0.81)	0.10(0.94)

* Cell values are unweighted mean(SD) or n(%). SD: standard deviation. SDS: standard deviation score
† All characteristics differed between each ethnic group and Whites: $p≤0.001$ for t-tests for continuous variables and Chi-squared tests for categorical variables, except the difference in mid-parental height SDS between Black African-Caribbean and White groups ($p=0.354$).
‡ *n*=15,398

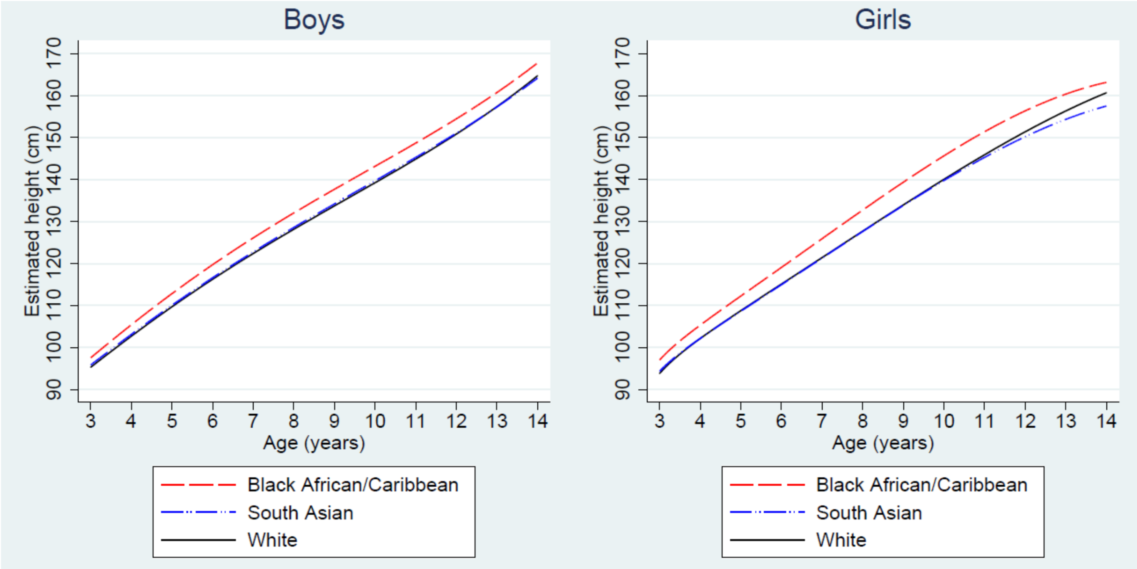

Figure 4.1: Estimated mean height trajectories (3-14y) for boys and girls by ethnic group, from unadjusted mixed effects fractional polynomial models

Differences in height trajectories between White and South Asian groups

Mean height trajectories by ethnicity are illustrated in Figure 4.1. Estimated height differences between ethnic groups at 3, 5, 7, 11 and 14 years with 95% confidence intervals (CIs) are presented in Table 4.2. At 3 years, South Asian children were slightly taller than their White counterparts by 0.5 cm [95% CI: (0.2, 0.8) in boys and (0.2, 0.9) in girls]. South Asian and White boys had similar growth trajectories in childhood and adolescence with a small (≤0.5 cm) or no height difference. However, in girls South Asians appeared to have a slower growth in adolescence than Whites, with a height deficit of 0.6 cm (0.0, 1.2) at 11 years increasing to 3.2 cm (95% CI 2.6, 3.7) at 14 years (Table 4.2 model 1).

The pattern of changes in estimated ethnic height differences after adjustment for early life factors is shown in Figure 4.2. Differences in height trajectories between White and South Asian children were largely unchanged after adjusting for prenatal factors in Model 2. Adjusting for birthweight increased South Asians' height relative to White (Figure 4.2 and Table 4.2), for example, estimated height difference between South Asian and White (as reference) girls at 3 years was 0.5 cm (0.2, 0.9) in model 2 which increased to 1.3 cm (0.9, 1.6) in model 3, while the difference at 14 years was -3.2 cm (-3.7, -2.7) which reduced to -2.4 cm (-2.9, -1.9) in model 3. Ethnic differences in height trajectories remained similar when further including family SECs in the model 4.

Difference in height trajectories between White and Black African-Caribbean groups

The pattern of height differences between White and Black African-Caribbean groups was distinctly different from the pattern between White and South Asian children. Black African-

Caribbean children were markedly taller than other ethnic groups between the ages of 3 and 14 years (Figure 4.1). Compared with White boys, Black African-Caribbean boys were taller at 3 years, had a more rapid growth in childhood but less height gain from 9 to 14 years: the difference in mean heights was 2.2 cm (1.7, 2.7) at 3 years, widened to 4.0 cm (3.2, 4.7) at 9 years and narrowed to 3.1 cm (2.0, 4.2) at 14 years. This pattern was more evident in girls: the height difference between Black African-Caribbean and White girls was 3.2 cm (2.6, 3.8) at 3 years, widened with age to 5.6 cm (4.7, 6.5) at 10 years, but substantially reduced to 2.5 cm (1.6, 3.3) at 14 years.

Adjusting for prenatal factors in model 2 did not alter these estimated differences between White and Black African-Caribbean children. Height advantage among Black children relative to White increased by about 10% when birthweight was controlled for in model 3 and remained largely the same with additional adjustment for family income and maternal education in model 4 (Table 4.2).

Sensitivity analysis

Results from the analyses using the maximum available sample for each model were similar to those from the main analyses using complete cases (Appendix II and Table S4).

South Asian parents were considerably shorter than White parents (Table 4.1). Additional adjustment for mid-parental height in the sensitivity analysis (Table 4.2, final column) increased the height of South Asians relative to White children. The estimated height difference between South Asian and White (reference) boys increased from 1.3 cm (1.0, 1.7) at 3 years and 0.2 cm (-0.5. 0.9) at 14 years in model 4, to 2.1 cm (1.8, 2.4) and 1.0 cm (0.4, 1.7), respectively. In girls, the height advantage of South Asians relative to Whites at 3 years increased from 1.4 cm (1.1, 1.8) in model 4 to 2.3 cm (2.0, 2.6) in the sensitivity analysis; and the height deficit of South Asian girls at 14 years narrowed from -2.2 cm (-2.8, -1.7) to -1.4 cm (-1.9, -0.9) in the sensitivity analysis. However, height advantage among Black African-Caribbeans remained similar after additional adjustment for mid-parental height SDS.

Table 4.2: Estimated ethnic differences in height (cm) from unadjusted and adjusted models

	Model 1		Model 2		Model 3		Model 4		Sensitivity Analysis	
age	diff	95% CI	diff	95% CI	diff	95% CI	diff	95% CI	diff	95% CI
South Asian vs. White (reference) boys										
3	0.5	(0.2, 0.8)	0.6	(0.2, 0.9)	1.3	(1.0, 1.6)	1.3	(1.0, 1.7)	2.1	(1.8, 2.4)
5	0.4	(0.0, 0.7)	0.4	(0.0, 0.7)	1.1	(0.8, 1.5)	1.2	(0.8, 1.5)	2.0	(1.6, 2.3)
7	0.4	(0.0, 0.8)	0.4	(0.0, 0.8)	1.1	(0.7, 1.5)	1.2	(0.8, 1.6)	2.0	(1.6, 2.4)
9	0.4	(0.0, 0.9)	0.5	(0.0, 0.9)	1.2	(0.7, 1.7)	1.3	(0.8, 1.7)	2.1	(1.6, 2.5)
11	0.4	(-0.2, 0.9)	0.4	(-0.2, 0.9)	1.1	(0.6, 1.7)	1.2	(0.6, 1.7)	2.0	(1.5, 2.5)
14	-0.6	(-1.3, 0.1)	-0.6	(-1.3, 0.1)	0.1	(-0.5, 0.8)	0.2	(-0.5, 0.9)	1.0	(0.4, 1.7)
South Asian vs. White (reference) girls										
3	0.5	(0.2, 0.9)	0.5	(0.2, 0.9)	1.3	(0.9, 1.6)	1.4	(1.1, 1.8)	2.3	(2.0, 2.6)
5	-0.1	(-0.5, 0.2)	-0.1	(-0.5, 0.2)	0.6	(0.3, 1.0)	0.8	(0.4, 1.2)	1.6	(1.3, 2.0)
7	-0.1	(-0.5, 0.3)	-0.1	(-0.6, 0.3)	0.6	(0.2, 1.1)	0.8	(0.4, 1.2)	1.6	(1.2, 2.0)
9	-0.1	(-0.6, 0.4)	-0.2	(-0.7, 0.4)	0.6	(0.1, 1.1)	0.8	(0.3, 1.3)	1.6	(1.1, 2.1)
11	-0.6	(-1.2, 0.0)	-0.6	(-1.2, -0.1)	0.1	(-0.4, 0.7)	0.3	(-0.3, 0.9)	1.1	(0.6, 1.7)
14	-3.2	(-3.7, -2.6)	-3.2	(-3.7, -2.7)	-2.4	(-2.9, -1.9)	-2.2	(-2.8, -1.7)	-1.4	(-1.9, -0.9)
Black African-Caribbean vs. White (reference) boys										
3	2.2	(1.7, 2.7)	2.2	(1.7, 2.7)	2.5	(2.0, 3.0)	2.6	(2.1, 3.0)	2.4	(1.9, 2.8)
5	3.1	(2.6, 3.7)	3.1	(2.5, 3.6)	3.4	(2.8, 3.9)	3.4	(2.9, 3.9)	3.2	(2.7, 3.7)
7	3.7	(3.1, 4.4)	3.6	(3.0, 4.3)	4.0	(3.3, 4.6)	4.0	(3.4, 4.6)	3.8	(3.2, 4.4)
9	4.0	(3.2, 4.7)	3.9	(3.1, 4.6)	4.2	(3.5, 4.9)	4.2	(3.5, 5.0)	4.1	(3.4, 4.8)
11	3.8	(3.0, 4.7)	3.8	(2.9, 4.6)	4.1	(3.2, 4.9)	4.1	(3.3, 5.0)	4.0	(3.2, 4.8)
14	3.1	(2.0, 4.2)	3.0	(1.9, 4.1)	3.3	(2.2, 4.4)	3.4	(2.3, 4.5)	3.2	(2.2, 4.3)
Black African-Caribbean vs. White (reference) girls										
3	3.2	(2.6, 3.8)	3.1	(2.5, 3.7)	3.4	(2.9, 4.0)	3.6	(3.1, 4.2)	3.4	(2.8, 3.9)
5	3.5	(2.9, 4.0)	3.4	(2.8, 3.9)	3.7	(3.2, 4.3)	3.9	(3.4, 4.4)	3.6	(3.1, 4.2)
7	4.5	(3.8, 5.2)	4.4	(3.7, 5.1)	4.7	(4.1, 5.4)	4.9	(4.2, 5.6)	4.7	(4.0, 5.3)
9	5.4	(4.6, 6.3)	5.3	(4.5, 6.1)	5.6	(4.8, 6.4)	5.8	(5.0, 6.6)	5.6	(4.8, 6.3)
11	5.5	(4.5, 6.4)	5.4	(4.4, 6.3)	5.7	(4.8, 6.6)	5.9	(4.9, 6.8)	5.6	(4.8, 6.5)
14	2.5	(1.6, 3.3)	2.4	(1.5, 3.2)	2.7	(1.8, 3.5)	2.9	(2.0, 3.7)	2.7	(1.9, 3.5)

*Estimated from mixed effects fractional polynomial models. Diff: estimated difference in mean height; 95% CI: 95% confidence interval.
Model 1: unadjusted model.
Model 2: model 1 + adjusted for prenatal factors (maternal age, smoking during pregnancy, birth order).
Model 3: model 2 + adjusted for birthweight.
Model 4: model 3 + adjusted for family SECs (maternal education, family income).
Sensitivity analysis: model 4 + adjusted for mid-parental height SDS.

Preliminary analysis shows little differences in pubertal development score in boys across ethnic groups (Appendix II Table S3). However, voice change appeared to occur earlier in ethnic minority boys. At 11 years, 6% of Black African-Caribbean and 4% of South Asian boys were reported by their parents to 'have definitely started voice change', compared with only 3% in White boys; about 15% of Black African-Caribbean and 12% of South Asian boys were reported to 'have barely started voice change', compared with 10% in White boys (p=0.002). South Asian and Black African-Caribbean girls started menstruation on average at a younger age than White girls (11.7 and 11.9 vs. 12.1 years, p<0.001). However, the mean pubertal development score at 14 years indicates that South Asian girls were less mature than White and Black African-Caribbean girls (p<0.001). Results on ethnic differences in height trajectories were largely unaltered when the model 4 was further adjusted for these crude pubertal measures (Appendix II Table S5).

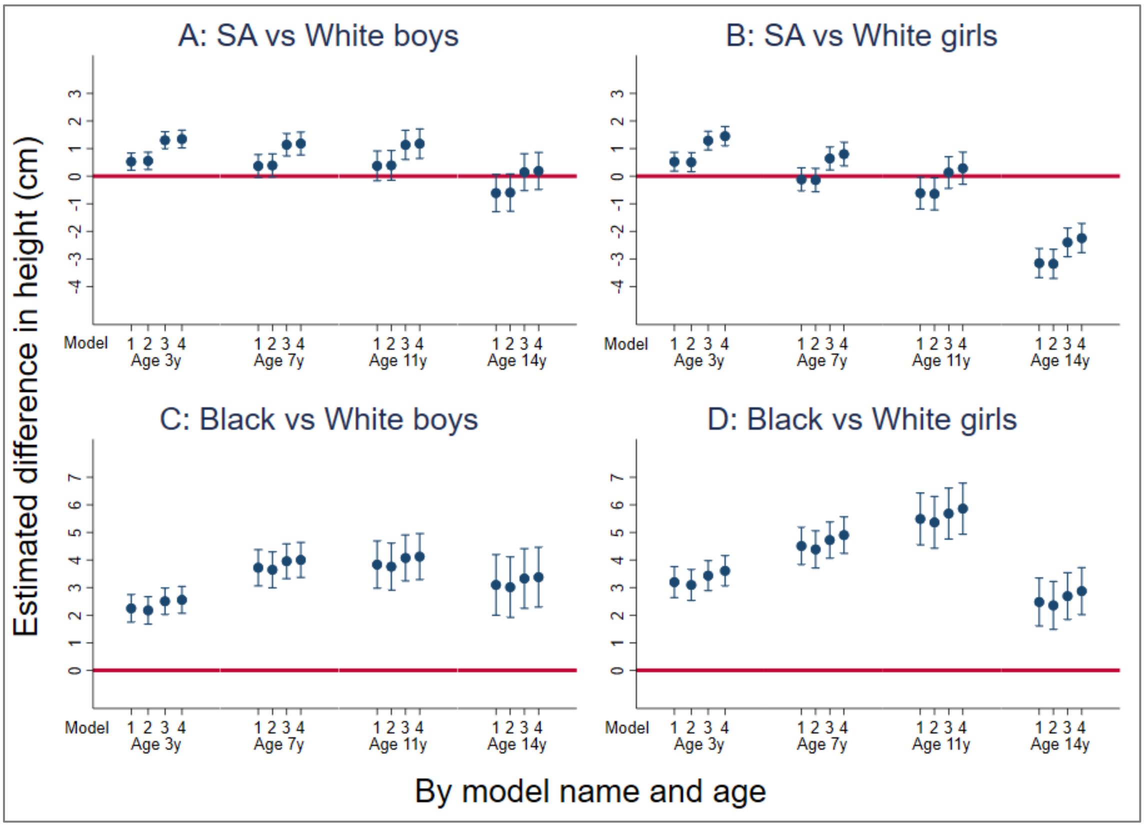

Figure 4.2: Estimated height differences with 95% confidence interval between each ethnic minority group and White at age 3, 7, 11 and 14 years, based on models 1-4

Reference line (y=0) indicates no height difference between ethnic groups. SA: South Asian. Black: Black African-Caribbean.

Model 1: unadjusted model.

Model 2: model 1 + adjusted for prenatal factors (maternal age, smoking during pregnancy, birth order).

Model 3: model 2 + adjusted for birthweight.

Model 4: model 3 + adjusted for family SECs (maternal education, family income).

4.4 Discussion

Summary of key findings

This study shows that contemporary South Asian children were slightly taller than their White counterparts at 3 years and had similar height growth during childhood and adolescence, apart from that South Asian girls grew slightly slower and were shorter than their White counterparts in adolescence. South Asians' height relative to White children increased after adjustment for birthweight and further increased when adjusting for mid-parental height in sensitivity analysis. Adjusting for prenatal factors and family socio-economic circumstances had little effects on the estimated differences in height between South Asian and White children. Black African-Caribbean was the tallest ethnic group from 3 to 14 years. Height differences between Black African-Caribbean and White children increased with age during childhood but reduced slight in adolescence, especially in girls. Adjusting for prenatal factors, birthweight, family socio-economic factors and parental height did not alter these differences.

Strengths and limitations

This is the first study, to my knowledge, to investigate ethnic differences in height growth trajectories from early childhood to adolescence among contemporary UK children. The present study also explored the role of prenatal factors, birthweight and family socio-economic factors in these ethnic differences. However, there are a few limitations. Although the MCS oversampled children from minority ethnic backgrounds, the numbers of children in some ethnic sub-groups were still small, which resulted in the use of broader ethnic categories. Preliminary analysis shows that there was some variation in mean height between specific sub-groups. However, the patterns of ethnic differences (relative to White children) are similar to those using broader ethnic groups in the main analysis. The MCS is an ongoing cohort study and cohort members (born in 2000-2) were still in their adolescence at the time of data analysis, therefore achieved adult height of these cohort members were unobserved. Data on their birth length was not available to investigate the full height growth trajectory from birth to adulthood. Furthermore, due to the crude and incomplete (~40% missing) measures of pubertal development in the MCS, the role of growth tempo in ethnic differences in height was not further investigated.

Comparison with previous studies and implications

Few longitudinal studies have investigated height growth trajectories across ethnic groups in the UK, possibly because few cohorts have sufficient numbers of children from minority ethnic groups and follow-up visits (233). In the Born in Bradford study (220), Pakistani children were found to be lighter in weight and shorter in length at birth compared with their White counterparts. However, they experienced more rapid postnatal weight and length growth in infancy and were slightly taller than White children at 2 years by 0.6 cm (0.02, 1.21) in boys and 1.1 cm (0.48, 1.64) in girls. Similarly in our study, South Asian children had a lower mean birthweight but were slightly taller than White children at 3 years; thus South Asians in the present study may also have experienced rapid growth in infancy. Accelerated early growth has been associated with poor cardio-metabolic health profile (234). Given the greater risk of coronary heart diseases and type 2 diabetes among South Asians in the UK (24, 25), it would be informative to investigate whether ethnic differences in cardio-metabolic health outcomes are attributable to different growth patterns in early life.

The present study further illustrates that they maintained a comparable growth in childhood. However, in adolescence South Asian girls became shorter than White girls. South Asian parents were considerably shorter than White parents. Adjusting for parental height increased South Asian children's height relative to White children, suggesting that contemporary South Asian children in the UK may have experienced a greater generational height gain. Despite being commonly used as an indicator of height growth potential of offspring, parental height reflects both genetic influence and parents' own growth environments (235). A greater intergenerational height gain for South Asian children may indicate improvements in growth environments, i.e. South Asian parents may have had sub-optimal growth environments.

A social gradient in height has been repeatedly reported by previous studies among children and adults, with those from more advantaged socio-economic backgrounds having a higher mean height than their less advantaged counterparts (229, 236-238), although more recent evidence suggests that the gradient in adult height has narrowed across successive generations (121). In the present study, ethnic differences in height did not appear to be explained by family income and maternal education.

Consistent with findings from cross-sectional studies (124, 239), Black African-Caribbean children were found to be taller than their White and South Asian counterparts from childhood into adolescence, although on average Black African-Caribbean children were born lighter than White children. Height differences between Black African-Caribbean and White children widened in childhood but narrowed in adolescence. These conclusions remained similar when analyses were repeated using height z-scores (Appendix II Figure S4), apart from the pattern of height differences widening in childhood being less evident. The early life factors considered in this analysis did not seem to explain their height advantage to White children. In addition, Black African-Caribbean parents had similar height as White parents. It is possible that biological patterns of height growth differ between ethnic groups. Studies to examine the role of genetic factors and the contribution of later modifiable factors (such as diet) will help to understand this further.

4.5 Conclusion

Child-to-adolescent height growth trajectories differed by ethnic group among contemporary UK children. Compared with White children, South Asian children had much shorter parents and a lower birthweight on average, but maintained a comparable childhood height growth, suggesting that contemporary South Asian children in the UK may have experienced a greater intergenerational height gain. Black African-Caribbean children were taller than their White and

South Asian peers from 3 to 14 years, which was not explained by the prenatal, birthweight and family socio-economic factors. Further research to follow this cohort into adulthood and to understand the role of genetic and other environmental factors (e.g. diet) in these ethnic differences is warranted. It is also informative for future studies to investigate the role of different growth patterns in the development of ethnic differences in cardio-metabolic health profile.

5 SOCIO-ECONOMIC DISPARITIES IN BMI TRAJECTORIES ACROSS ETHNIC GROUPS (OBJECTIVE 2)

5.1 Introduction

In the UK and many other higher-income countries, BMI (195, 196) and the level of obesity (143, 197) in childhood and adulthood are socially patterned with people from disadvantaged backgrounds having higher BMI and more likely to be obese, which are likely to be due to their disproportionally higher exposure to risk factors such as physical inactivity and high consumption of energy-dense foods (240) (see Chapter 1).

Recent research, mainly from the US, suggests that the inverse association between socio-economic factors and BMI in children and adolescents is less evident for Asian Americans and inconsistent for Hispanic and non-Hispanic Black populations, compared with their non-Hispanic White counterparts (188-190). This may be attributable to reports that cultural, environmental and biological factors related to obesity development are likely to have different socio-economic patterns across different ethnic populations (191). Yet little evidence is available in UK children. Only one study, of which we are aware, used data from the National Child Measurement Programme and found that the variation in BMI by area deprivation group is smaller in South Asian and Black children than White children in London(192). It is not clear whether patterns of socio-economic disparities in BMI differ by ethnicity using family-level SEP indicators, since over 50% of Asian and Black children in England live in the most deprived 20% areas (124). It is necessary to gain a full understanding of how socio-economic disadvantage impacts on adiposity across different ethnic groups and provide information for public health policies and targeted interventions.

This chapter aims to investigate 1) socio-economic patterns in BMI trajectories between 3 and 14 years across ethnic groups; and 2) whether early-life obesity risk factors can explain any socio-economic disparities.

5.2 Methods

Analysis sample

The analysis included singletons from White, South Asian and Black African-Caribbean backgrounds with at least one BMI measurement at follow-up visits (eligible sample *n*=16,082), excluding participants whose ethnicity was 'mixed' (*n*=510, 3.0%), 'others (e.g. Chinese)' (*n*=297, 1.8%) or missing (*n*=11, 0.07%). After removing participants who had missing data on exposure variables (i.e. family income or maternal education, *n*=86), a total of 15,996 participants (99% of eligible sample) with 62,051 BMI measurements were included in the analysis.

Variables

Details on how relevant variables were collected and derived are provided in Chapter 2. A brief description is provided below.

Exposure (family socio-economic position at ~9 months): Income poverty was a binary variable and defined by OECD equivalised family income below 60% of national median household income, a commonly used measure of relative poverty (241). Maternal education was defined using the highest academic qualification obtained by the mother and classified as: 'higher (GCSE grades A*-C & above)', 'lower (GCSE grades D-G & below)' and 'others (e.g. qualifications gained overseas)'.

Outcome: BMI at 3-, 5-, 7-, 11- and 14-year visits was calculated using measured height and weight and included as a continuous variable (242).

Ethnicity: was considered as a potential effect modifier of the association between family socio-economic position (SEP) and later BMI. Participants' ethnicity was grouped as 'White', 'South Asian (Indian, Bangladeshi and Pakistani)' and 'Black African-Caribbean (Black African and Black Caribbean)'.

Covariates: A number of intermediate factor of obesity which are identifiable by infancy (150) were included in the analysis, including maternal pre-pregnancy BMI, maternal smoking during pregnancy (98, 156), duration of exclusive breastfeeding, and early introduction to solid foods. Maternal pre-pregnancy BMI (kg/m^2) was classified as 'thinness (<18.5 kg/m^2)', 'healthy (≥18.5 kg/m^2, <25 kg/m^2)', 'overweight (≥25 kg/m^2, <30 kg/m^2)' and 'obesity (≥30 kg/m^2)'. Maternal smoking during pregnancy was defined as any smoking (>0 cigarette/day) by the end of the first trimester. Duration of exclusive breastfeeding was grouped as 'none', 'less than 4 months' and '4 months or longer', according to the recommendation on breastfeeding at the time. Early introduction to solid foods was defined as introducing solid foods before the age of 4 months.

Statistical analysis

Preliminary analysis showed that the pattern of ethnic differences in socio-economic disparities in BMI trajectories was similar for boys and girls. Therefore, the analysis was performed for boys and girls combined and adjusted for sex. The best-fitting third-order fractional polynomials for age were age^2, age^3 and $age^2 * \ln(age)$. Random effects were allowed for intercept and coefficients for age^2 and age^3. Inclusion of random effects for the additional age term $age^2 * \ln(age)$ led to convergence issues. Therefore, only fixed effects were adopted for $age^2 * \ln(age)$. The fitted BMI trajectories were:

$$BMI_{ij} = (\beta_0 + \mu_{0i}) + (\beta_1 + \mu_{1i})age_{ij}^2 + (\beta_2 + \mu_{2i})age_{ij}^3 + \beta_3 age_{ij}^2 * \ln(age_{ij}) + \epsilon_{ij}$$

Where BMI_{ij} denotes BMI for subject i at measurement occasion j; $\beta_0, \beta_1, \beta_2, \beta_3$ denote the fixed intercept and coefficients for age terms; $\mu_{0i}, \mu_{1i}, \mu_{2i}$ denote the random intercepts and coefficients. ϵ_{ij} is the error term for subject $i = 1, 2 \dots n$ at measurement occasion $j = 1, 2 \dots n_j$. Unstructured covariance matrix for the random effects was specified and maximum likelihood estimation were used. Q-Q (quantile-quantile) plots for level-1 residuals and random intercepts and coefficients are provided in Appendix III Figure S5.Model selection was guided by deviance, Akaike and Bayesian Information Criterion statistics.

Model 1 included sex, age terms, income poverty and interaction between poverty and all age terms to estimate differences in mean BMI trajectories between poverty and non-poverty groups. To remove the “end effects” caused by sparse data, instead of the full observed age range (2.7 - 15.3 years), a restricted age range from 3 to 14 years was used for plotting the trajectories. After testing the interaction between ethnicity and poverty (*p*-value <0.01), the analysis was stratified by ethnic group (i.e. model 1 was fitted for each ethnic group separately) (**model 2**). Early-life risk factors of obesity were adjusted to assess whether they could explain any socio-economic disparities in BMI in each ethnic group – first for maternal characteristics (i.e. pre-pregnancy BMI and smoking during pregnancy) in **model 3**; and additionally for infant feeding (i.e. exclusive breastfeeding and early introduction to solid food) in **model 4**. Models 1-4 were repeated using maternal education level as an alternative SEP indicator (instead of income poverty in the main analysis), to assess whether similar patterns persisted.

As a sensitivity analysis, models 1 and 2 were repeated using income quintiles variable instead of the binary poverty variable in the main analysis. Mean BMI differences between highest and lowest income quintile groups were estimated and compared with those between poverty and non-poverty groups from the main analysis.

Multiple imputation

There was missing data in some of the covariates (2%-11%), with 89% of participants having complete data on all covariates (see Table 5.1). The distributions of key variables in the sample with incomplete cases and the sample with complete cases are provided in Table 5.2. Compared with completed cases, participants with missing data on covariates were more likely to be ethnic minorities, from families living in poverty and with lower level of maternal education, have a mother who had never exclusively breastfed but did not smoke during pregnancy or introduce solid foods to their child before the age of 4 months (Table 5.2).

Multiple imputation with chained equation (MICE) was performed to account for these missing data in 30 datasets, under a missing at random (MAR) assumption (213, 243). Imputation models included all analysis variables as well as auxiliary variables (i.e. maternal age and birthweight). Maternal age and birthweight were included as they predicted both the probability of missingness and values of covariates. A set of imputation models were specified with one for each variable with missing data: logistic regression for binary variables (i.e. maternal smoking and early introduction to solid foods) and ordered logistic regression for categorical variables (i.e. maternal pre-pregnancy BMI and duration of exclusive breastfeeding). Distributions of the observed and imputed data were compared and largely similar (Appendix III Table S6)

Mixed effects models 1-4 were fitted to each of the imputed datasets separately, and estimates across the 30 imputed datasets were combined using Rubin's rules (244). Fraction of missing information (%) and Monte Carlo error estimates were examined to assess whether an adequate number of imputations were performed.

5.3 Results

A higher proportion of South Asian (64%) and Black African-Caribbean (59%) children were living in poverty, compared with White children (32%). Table 5.3 shows early life factors by poverty across ethnic groups. Distributions of early life factors were socially patterned with less variation in the South Asian and Black African-Caribbean groups. For White children, those in the poverty group were more likely to have a mother who smoked during pregnancy and had pre-pregnancy BMI in the 'thinness category (<18.5 kg/m^2), to have never been exclusively breastfed and an early introduction to solid foods, than their counterparts in the non-poverty group (p<0.001). Among South Asians, mothers from the poverty group were more likely to have pre-pregnancy BMI in the 'obesity' category, smoke during pregnancy and have not exclusively breastfed their child (p<0.01). Among Black African-Caribbean children, mothers from poverty families were more likely to smoke during pregnancy (p=0.04); *P* values for other differences between poverty and non-poverty groups were very large, which may be in part due to the small sample size of Black ethnic group.

Table 5.1: Patterns of missing data in covariates (total *n*=15,996)

N (%)	Maternal smoking during pregnancy	Early introduction to solid foods	Exclusive breastfeeding	Maternal pre-pregnancy BMI
14,158 (88.5%)	1	1	1	1
1,281 (8.0%)	1	1	1	0
279 (1.7%)	0	0	0	0
260 (1.6%)	1	0	0	0
18 (<1%)	Other missing patterns			

*1 indicates value is present and 0 indicates value is missing. Sex, ethnicity, income and maternal education were not included in the missing data patterns, because they were completely observed in the analysis sample.

Table 5.2: Differences between incomplete and complete cases on key variables

	Incomplete cases (total *n*=1,838)	Complete cases (total *n*=14,158)	*P**
Poverty, *n*(%)			<0.001
No	830 (45%)	9,435 (67%)	
Yes	1,008 (55%)	4,723 (33%)	
Maternal education, *n*(%)			<0.001
Higher (GCSE grades A*-C & above)	915 (50%)	9,961 (70%)	
Lower (GCSE grades D-G & below)	813 (44%)	3,875 (27%)	
Others (e.g. qualifications gained overseas)	110 (6%)	322 (2%)	
Ethnicity, *n*(%)			<0.001
White	1,233 (67%)	12,600 (89%)	
South Asian	421 (23%)	1,178 (8%)	
Black African and Caribbean	184 (10%)	380 (3%)	
BMI 3 years (kg/m^2), mean(SD)	16.7 (1.6)	16.8 (1.5)	<0.001
BMI at 14 years (kg/m^2), mean(SD)	21.9 (4.3)	21.3 (3.9)	<0.001
Maternal pre-pregnancy BMI, *n*(%)			0.87†
Thin	0 (0%)	757 (5%)	
Healthy	8 (80%)	9,256 (65%)	
Overweight	1 (10%)	2,893 (20%)	
Obese	1 (10%)	1,252 (9%)	
Maternal smoking during pregnancy, *n*(%)			<0.001
No	1,267 (82%)	10,767 (76%)	
Yes	279 (18%)	3,391 (24%)	
Duration of exclusive breastfeeding, *n*(%)			<0.001
None	499 (39%)	4,709 (33%)	
Less than 4 months	764 (59%)	8,968 (63%)	
4 months or longer	29 (2%)	481 (3%)	
Early introduction to solid foods, *n*(%)			<0.001
No	913 (70%)	9,104 (64%)	
Yes	383 (30%)	5,054 (36%)	

* *P*-value for difference between incomplete and complete cases based on *t*-test for continuous variables and on chi-squared test for categorical variables.
† Fisher's exact test.

Table 5.3: Early life factors by poverty across ethnic groups (total n= 15,996)

	% missing	White (*n*=13833)			South Asian (*n*=1599)			Black African-Caribbean (*n*=564)		
		Poverty*			Poverty*			Poverty*		
		Yes (32%)	No (68%)	*p*†	Yes (64%)	No (36%)	*p*†	Yes (59%)	No (41%)	*p*[b]
Maternal pre-pregnancy BMI group	11%			<0.001			<0.001			0.32
Thinness		324 (9%)	293 (3%)		84 (11%)	42 (10%)		10 (5%)	4 (2%)	
Healthy		2387 (63%)	5967 (68%)		420 (56%)	297 (69%)		106 (51%)	87 (50%)	
Overweight		716 (19%)	1822 (21%)		168 (23%)	77 (18%)		62 (30%)	49 (28%)	
Obesity		348 (9%)	751 (9%)		74 (10%)	17 (4%)		29 (14%)	34 (20%)	
Maternal smoking in pregnancy	2%			<0.001			0.003			0.04
No		2199 (52%)	7788 (83%)		988 (96%)	559 (99%)		288 (88%)	212 (93%)	
Yes		2022 (48%)	1548 (17%)		39 (4%)	7 (1%)		39 (12%)	15 (7%)	
Duration of exclusive breastfeeding	3%			<0.001			<0.001			0.19
None		2352 (56%)	2510 (27%)		224 (23%)	80 (15%)		29 (9%)	13 (6%)	
less than 4 months		1769 (42%)	6395 (69%)		704 (73%)	409 (77%)		268 (88%)	187 (89%)	
4 months and more		58 (1%)	349 (4%)		42 (4%)	41 (8%)		9 (3%)	11 (5%)	
Introduction to solid foods <4 months	3%			<0.001			0.17			0.16
No		2411 (58%)	5871 (63%)		848 (87%)	450 (85%)		264 (87%)	173 (82%)	
Yes		1772 (42%)	3384 (37%)		122 (13%)	80 (15%)		41 (13%)	38 (18%)	

***** Numbers are unweighted N (%).

† *p* value for between poverty and non-poverty.

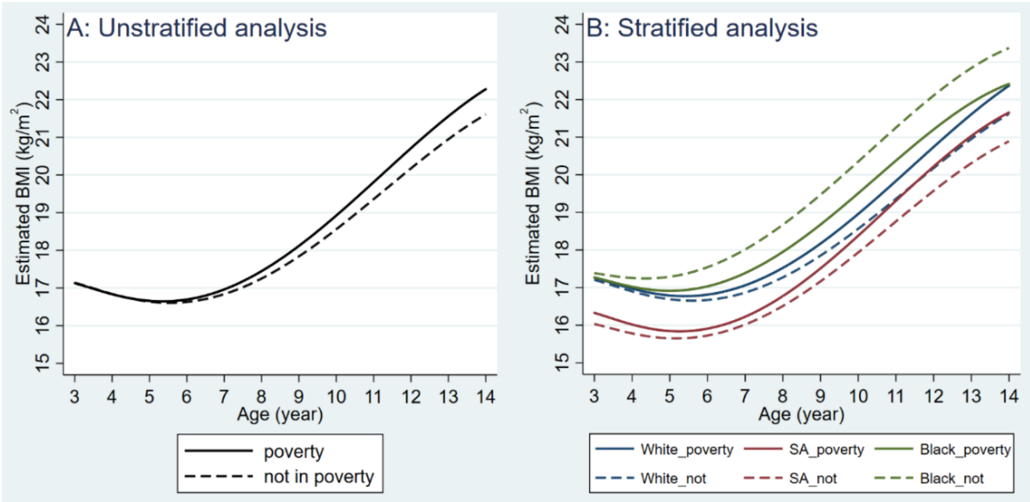

Figure 5.1: Estimated BMI trajectories between 3 and 14 years by income poverty group, from unstratified (model 1) and stratified (model 2) mixed effects fractional polynomial models.
Models were adjusted for sex. The solid (—) lines represent poverty groups while the dashed (– –) lines represent non-poverty groups. SA: South Asian; Black: Black African-Caribbean; not: not in poverty. In panel B, each colour represents one ethnic group.

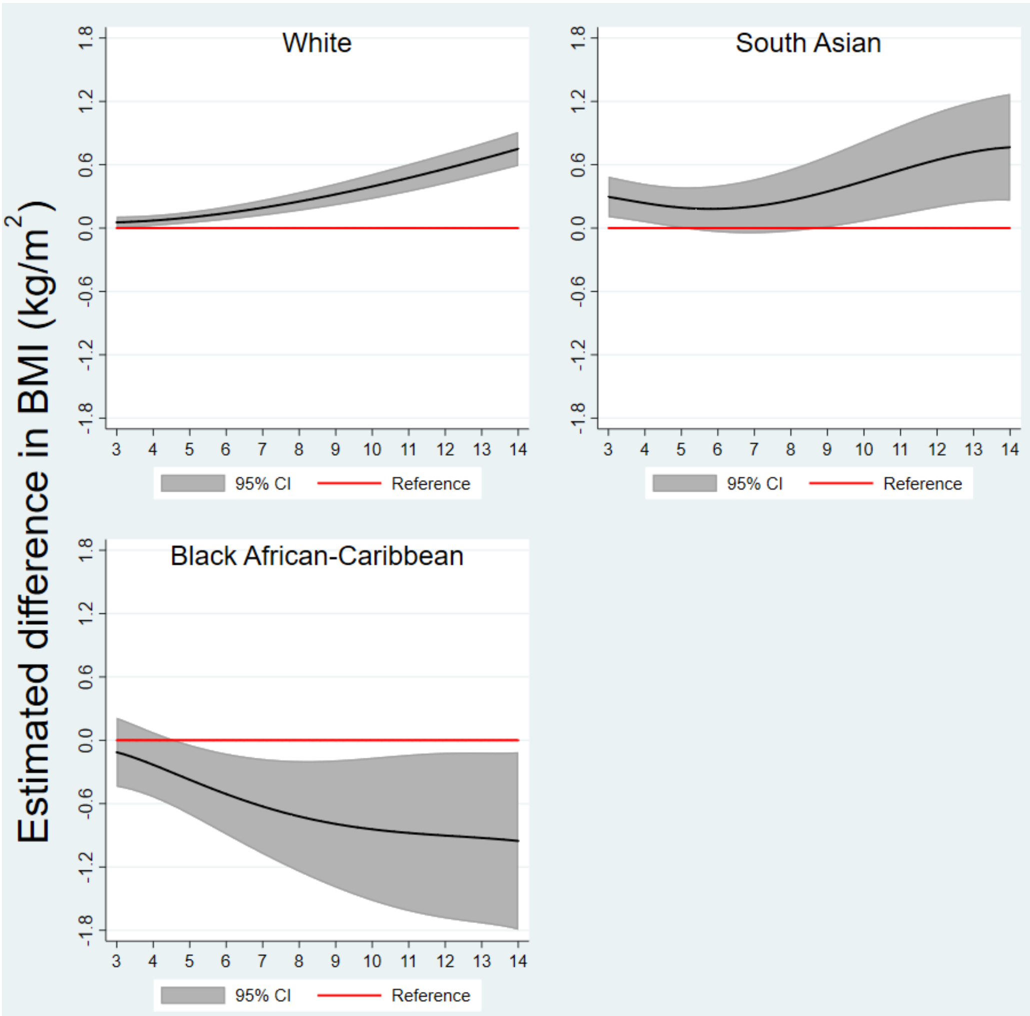

Figure 5.2: Estimated mean BMI differences with 95% confidence intervals from 3 to 14 years between poverty and non-poverty groups
Models were adjusted for sex. The non-poverty group was used as the reference.

BMI trajectories between 3 and 14 years by income group

Figure 5.1 shows estimated mean BMI trajectories by income poverty group. At 3 years, there was no difference in mean BMI between poverty and non-poverty groups (Figure 5.1 panel A). However, a difference started to emerge at the age of about 6 years with children from the poverty group having a higher mean BMI by 0.06 kg/m^2 (95% CI: 0.01, 0.12) which widened with age to 0.67 kg/m^2 (0.52, 0.82) at 14 years.

The patterns of differences in BMI trajectories between poverty groups differed across ethnic groups (Figure 5.1 panel B). Among White children, the pattern was largely similar to that in the whole sample analysis: a small BMI difference between poverty and non-poverty groups was established at 3 years by 0.05 kg/m^2 (0.00, 0.11) which increased to 0.75 kg/m^2 (0.59, 0.91) at 14 years (Figure 5.2). South Asian children in the poverty group had a higher BMI at 3 years by 0.30 kg/m^2 (0.10, 0.49) than their counterparts in the non-poverty group. This difference persisted through childhood but widened in adolescence. The estimated BMI at 14 years was 0.77 kg/m^2 (0.26, 1.27). In the Black African-Caribbean group, the pattern of BMI differences between poverty and non-poverty groups reversed: poverty was associated with lower BMI. A BMI difference emerged at 5 years by -0.37 kg/m^2 (-0.71, -0.04) and widened with age to -0.95 kg/m^2 at 14 years (-1.79, -0.11). The confidence intervals of estimates in the South Asian and Black African-Caribbean groups were noticeably wider than those in the White group, which may be in part due to their smaller sample sizes (Table 5.4 model 2).

Adjustment for maternal characteristics and infant feeding: In the White and South Asian groups, estimated BMI differences attenuated slightly after adjustment for maternal characteristics (i.e. maternal pre-pregnancy BMI and maternal smoking in pregnancy). For example, the BMI difference at 14 years reduced from 0.75 kg/m^2 and 0.77 kg/m^2 before adjustment to 0.72 kg/m^2 and 0.73 kg/m^2 after adjustment, for White and South Asian groups respectively (Table 5.4 model 3). Further adjustment for infant feeding had little effect on these differences (Table 5.4 model 4). BMI differences in the Black African-Caribbean group remained largely unaltered after adjustment for maternal characteristics and infant feeding.

Sensitivity analysis using income quintiles showed very similar results. The distinct patterns of income differences across ethnic groups persisted: lower income was associated with higher BMI in White and South Asian children, but with lower BMI in Black African-Caribbean children; estimated BMI differences between lowest and highest income quintile groups widened with age in White and Black African-Caribbean groups and in the South Asian group stayed stable in childhood and widened in adolescence (Appendix III Table S7).

Table 5.4: Estimated mean BMI differences (kg/m^2) with 95% confidence intervals at each year of age between poverty and non-poverty groups from unadjusted and adjusted models

	Model 2: unadjusted		**Model 3:** model 2 + maternal BMI & smoking		**Model 4:** model 3 + infant feeding	
Age	**diff***	**95% CI**	**diff***	**95% CI**	**diff***	**95% CI**
			White			
3	0.05	(0.00, 0.11)	0.02	(-0.03, 0.08)	0.01	(-0.05, 0.07)
4	0.07	(0.02, 0.12)	0.04	(-0.01, 0.09)	0.03	(-0.02, 0.09)
5	0.10	(0.05, 0.16)	0.07	(0.01, 0.13)	0.06	(0.00, 0.12)
6	0.14	(0.08, 0.21)	0.11	(0.05, 0.18)	0.10	(0.04, 0.17)
7	0.19	(0.12, 0.27)	0.16	(0.09, 0.24)	0.15	(0.08, 0.23)
8	0.25	(0.16, 0.34)	0.22	(0.14, 0.31)	0.21	(0.12, 0.30)
9	0.32	(0.22, 0.42)	0.29	(0.19, 0.39)	0.28	(0.18, 0.39)
10	0.39	(0.28, 0.51)	0.37	(0.25, 0.48)	0.36	(0.24, 0.47)
11	0.47	(0.34, 0.61)	0.45	(0.32, 0.58)	0.44	(0.31, 0.57)
12	0.56	(0.42, 0.70)	0.53	(0.39, 0.68)	0.52	(0.38, 0.67)
13	0.65	(0.50, 0.80)	0.63	(0.48, 0.78)	0.62	(0.47, 0.77)
14	0.75	(0.59, 0.91)	0.72	(0.56, 0.88)	0.71	(0.55, 0.87)
			South Asian			
3	0.30	(0.10, 0.49)	0.26	(0.07, 0.45)	0.26	(0.07, 0.46)
4	0.24	(0.05, 0.42)	0.20	(0.02, 0.38)	0.21	(0.02, 0.39)
5	0.19	(0.00, 0.39)	0.16	(-0.03, 0.35)	0.16	(-0.03, 0.36)
6	0.18	(-0.04, 0.40)	0.15	(-0.07, 0.37)	0.15	(-0.07, 0.37)
7	0.21	(-0.05, 0.46)	0.17	(-0.08, 0.43)	0.18	(-0.08, 0.43)
8	0.26	(-0.03, 0.56)	0.23	(-0.06, 0.52)	0.23	(-0.06, 0.53)
9	0.35	(0.01, 0.68)	0.31	(-0.02, 0.65)	0.32	(-0.02, 0.65)
10	0.44	(0.06, 0.83)	0.41	(0.03, 0.79)	0.41	(0.04, 0.79)
11	0.55	(0.13, 0.97)	0.51	(0.10, 0.93)	0.52	(0.10, 0.93)
12	0.65	(0.19, 1.10)	0.61	(0.16, 1.06)	0.61	(0.16, 1.06)
13	0.72	(0.25, 1.20)	0.69	(0.21, 1.16)	0.69	(0.22, 1.16)
14	0.77	(0.26, 1.27)	0.73	(0.23, 1.23)	0.73	(0.23, 1.24)
			Black African-Caribbean			
3	-0.11	(-0.44, 0.21)	-0.10	(-0.43, 0.22)	-0.10	(-0.43, 0.22)
4	-0.23	(-0.54, 0.08)	-0.22	(-0.52, 0.09)	-0.22	(-0.52, 0.09)
5	-0.37	(-0.71, -0.04)	-0.35	(-0.68, -0.03)	-0.35	(-0.68, -0.03)
6	-0.51	(-0.89, -0.13)	-0.49	(-0.86, -0.11)	-0.49	(-0.86, -0.11)
7	-0.63	(-1.08, -0.18)	-0.61	(-1.05, -0.16)	-0.60	(-1.05, -0.16)
8	-0.72	(-1.25, -0.20)	-0.70	(-1.22, -0.19)	-0.70	(-1.22, -0.18)
9	-0.79	(-1.40, -0.19)	-0.78	(-1.37, -0.18)	-0.77	(-1.37, -0.18)
10	-0.84	(-1.52, -0.17)	-0.83	(-1.50, -0.16)	-0.83	(-1.50, -0.16)
11	-0.88	(-1.62, -0.14)	-0.87	(-1.60, -0.14)	-0.87	(-1.60, -0.13)
12	-0.90	(-1.69, -0.12)	-0.90	(-1.67, -0.12)	-0.89	(-1.67, -0.12)
13	-0.93	(-1.73, -0.12)	-0.92	(-1.72, -0.12)	-0.92	(-1.72, -0.11)
14	-0.95	(-1.79, -0.11)	-0.94	(-1.77, -0.11)	-0.94	(-1.77, -0.11)

***estimated mean BMI difference in kg/m^2. CI: confidence interval. Model 2 included sex, poverty, age terms and poverty-age interactions, stratified by ethnic group. Model 3: model 2 + maternal pre-pregnancy BMI and smoking during pregnancy. Model 4: model 3 + exclusive breastfeeding and early introduction to solid foods.

BMI trajectories between 3 and 14 years by maternal education group

Results from analysis repeated using maternal education as an alternative SEP indicator are provided in Appendix III Figure S6 and Figure S7. The overall patterns of the association between maternal education and BMI across ethnic groups were comparable to those between income and BMI. However, the increment in BMI differences with age was smaller with wider confidence intervals for minority ethnic groups.

Lower maternal education was associated with higher BMI in White and South Asian children. In White children, a BMI difference emerged at 5 years by 0.07 kg/m^2 (0.01, 0.13) and increased with age to 0.71 kg/m^2 (0.54, 0.88) at 14 years; among South Asian children, there was a BMI difference of 0.30 kg/m^2 (0.10, 0.50) at 3 years which widened slightly with age. Estimated BMI differences attenuated after adjustment for maternal characteristics and were no longer evident after further adjustment for infant feeding (Appendix III Table S23). For Black African-Caribbean children, there is a trend that children from the lower maternal education group ahve lower BMI, though the 95% confidence intervals were wide and contained zero.

5.4 Discussion

Summary of key findings

There are three key findings from this analysis. First, in the overall sample, income deprivation was associated with higher child-to-adolescent BMI trajectories from 6 to 14 years. Second, the socio-economic pattern in BMI trajectories differed across ethnic groups. Poverty was associated with higher BMI in the White and South Asian groups, with a BMI difference established as early as 3 years. However, among Black African-Caribbeans, poverty was associated with lower BMI from 5 to 14 years. Income differences in BMI overall increased with age across all ethnic groups. Third, adjusting for prenatal and infancy risk factors had little effects on these BMI differences. Similar results were found when using income quintiles or maternal education as an alternative SEP indicator.

Comparison with previous studies and implications

Comparison with previous research is hindered by the dearth of studies that have investigated whether the pattern of socio-economic disparities in child and adolescent BMI differs by ethnicity, especially in the UK. A negative association between SEP and BMI was found in the overall sample (emerged at 6 years) and among White children (established at 3 years) in the present study, which strengthened with age. These findings are in line with previous studies based on the general population in the UK, which suggested social-economic differences in BMI are emerging at younger ages (245, 246) and widened with age (247). Using data from a cohort in the Bristol area of the UK with 96% of the cohort members being White (248), Howe and colleagues found that a socio-economic difference in BMI began to emerge at around 4 years and increased with age to 0.38 kg/m^2 and 0.89 kg/m^2 at 10 years, for boys and girls respectively (247).

The present study found that poverty was associated with higher BMI in White and South Asian children, but with lower BMI in Black African-Caribbean children. Available studies on ethnic differences in social patterns of child and adolescent BMI are mainly from the US and reported mixed findings: some studies reported a negative (249, 250) or no association (188, 251, 252) between SEP and BMI for non-Hispanic Black children, while other studies found a positive association (189, 253) as shown in the present study. These inconsistent findings may be partly due to variation in study samples, age groups, ethnic composition and settings. A number of early-life risk factors identifiable by infancy were considered in the analysis, including maternal pre-pregnancy BMI, maternal smoking during pregnancy and infant feeding. However, they explained only a small amount of the socio-economic disparities in child-to-adolescent BMI. It is possible that factors in childhood and adolescence (such as diet and possibly physical activity levels) may play a bigger role in explaining the development of these socio-economic disparities (254). However, Griffiths *et al* used objective accelerometer-based measurements collected in the MCS at 7 years and found no clear socio-economic gradients in physical activity levels and adherence to national guidelines among MCS children (255).

Black African-Caribbean children in the poverty group had lower BMI than their peers in the non-poverty group. The difference began to emerge at 6 years and increased with age to 14 years. This pattern was also seen when the analysis was repeated using income quintiles or maternal education, despite the wider confidence intervals. It is not well understood why Black African-Caribbean children had a different socio-economic pattern from South Asian and White children. Height is positively correlated with BMI in children and adolescents (126). Although Black African-Caribbean children in the non-poverty group had higher mean height than their counterparts in the poverty group, preliminary analysis adjusting for height did not explain this socio-economic pattern in BMI (Appendix III Table S9). This pattern may be attributable to variation in perceptions of childhood obesity and body size (256, 257), biological factors (191), cultural differences in diet and processes of acculturation among different immigrant groups (13, 18). There is some evidence from qualitative studies that parents from certain minority ethnic groups, including Black African and older Black Caribbean parents, consider 'big' body sizes as desirable and a sign of health and wealth (257). Studies from the US suggest that greater acculturation is associated with higher income (18), but also poorer dietary practices and health behaviours (such as smoking) (13). Further studies are needed to replicate these findings and to elaborate on the relationship between acculturation and diet as well as the mechanisms of how socio-economic disadvantage interacts with BMI in different ethnic groups in the UK.

Income differences in BMI were established by 3 years in White and South Asian children and increased with age. Childhood BMI levels tend to track into adolescence and adulthood and affect later cardio-metabolic outcomes (258). A previous study found that by the age of 10 years there was not only a marked difference in BMI but also evidence of disparities in cardiovascular risk factors between maternal education groups (259). There is an urgent need for early intervention to address socio-economic disparities in BMI.

The present study suggests that lower SEP may not be universally associated with higher BMI, which should be taken into consideration when planning public health interventions. Addressing socio-economic disadvantage will benefit the health of less advantaged socio-economic groups in many ways, but other approaches may be needed to address the higher BMI among Black African-Caribbeans.

Strengths and limitations

The present study benefits from using family-level socio-economic indicators collected at baseline, which are more accurate than those collected retrospectively (260). Other key strengths include the use of a nationally representative cohort and repeated measured BMI to explore the development of socio-economic disparities in BMI across different ethnic groups. However, a few limitations need to be considered. Although the MCS oversampled minority ethnic groups, the sample sizes are still relatively small, which led to wide confidence intervals of the estimated BMI differences for these groups. Maternal pre-pregnancy BMI was derived using height and pre-pregnancy weight self-reported when the child was 9 months old, which may be subjected to report and recall bias (261).

5.5 Conclusions

Low SEP may not be universally associated with higher child and adolescent BMI. In Black African-Caribbean children, low SEP was associated with lower BMI. Income differences in BMI were established as early as 3 years in White and South Asian children and generally widened with age to 14 years, which highlights the need of early interventions to reduce socio-economic disparities in BMI. The reversed direction of SEP-BMI association in Black children requires replication in other studies and warrants further investigation to provide insights into underpinning biological and cultural mechanisms. Public health interventions to address obesity need to consider the different needs of their target populations, especially in areas of high ethnic diversity.

6 ETHNIC DIFFERENCES IN BMI AND OTHER ADIPOSITY MEASURES, AND THE ROLE OF EARLY LIFE FACTORS (OBJECTIVE 3)

6.1 Introduction

Despite a large body of literature documenting childhood BMI across ethnic groups in the UK, few studies have investigated ethnic differences in BMI trajectories and its development using longitudinal data (143). Ethnic disparities in BMI trajectories may have their origin in early life (262). A recent study by Martinson *et al* found substantial variation in BMI trajectories from the ages of 3 to 7 years between White, Black and South Asian children (145). South Asian children had lower BMI than White children during this age period but experienced more BMI gain. It is unclear whether BMI trajectories of South Asian and White children would intersect after the age of 7 years. Obesity and higher BMI in childhood are associated with an increased risk of cardio-metabolic diseases in adulthood (73, 74). In the UK, South Asian adults have greater rates of heart diseases (22, 24) and three to five times higher risk of type 2 diabetes compared with the general population (25). Therefore, it is important to understand whether South Asian children would continue to experience greater BMI gain and develop higher BMI after 7 years.

A number of early life factors which influence levels of body adiposity also differ by ethnicity, and may contribute to ethnic differences in BMI (262), including family socio-economic circumstances (SECs), maternal pre-pregnancy BMI, smoking during pregnancy, birthweight, and infant feeding practice and weight gain. BMI is a measure of weight in relation to height (125). In adults, BMI achieves relative independence from height, while in children there is residual correlation between height and BMI (126). As shown in Chapter 4, there are marked differences in children's height growth across ethnic groups in the UK, which are often not taken into account in previous studies (143). An analysis of the latest National Child and Measurement Programme data found that the higher prevalence of obesity at 10-11 years in Black (as compared to White) children was partially explained by their taller height (263).

There is an ongoing debate on the appropriateness of using BMI to assess cardio-metabolic risks across ethnic groups (126, 127). In adults, for a given BMI, South Asians tend to have a higher level of body fat and are more prone to developing abdominal obesity than White Europeans (131-133). South Asians also have higher risks of type 2 diabetes and cardiovascular morbidity (264). In a multi-ethnic sample of children aged 9-10 years in England, BMI was lower in South Asians and similar in Black African-Caribbeans, compared with White Europeans at the same fat mass (265). Pooling data from four recent UK studies, Hudda *et al* found that BMI underestimates body fat in South Asian children and overestimates body fat in Black African-Caribbean children (266).

Therefore, this chapter aims to investigate 1) ethnic differences in BMI trajectories between 3 and 14 years; 2) whether the differences can be explained by maternal characteristics, family socio-economic factors, and indicators of foetal and early growth (birthweight and infant weight gain); and 3) whether the pattern of ethnic differences was also seen in overweight/obesity and other adiposity measures (i.e. waist circumferences and body fat).

6.2 Methods

Study population

This analysis included singletons from White, Indian, Bangladeshi, Pakistani, Black African and Black Caribbean backgrounds with at least one BMI measurement at follow ups (*n*=16,083, eligible sample). A small number of participants who had missing data on maternal education and family income were excluded from the analysis (*n*=89). In total, 15,994 children with 62,039 BMI measurements were included.

Variables

Details on how relevant variables were collected and derived are provided in Chapter 2. A brief description is provided below.

Exposure (ethnicity): ethnicity of each child was reported by parents at baseline interview and grouped as 'White', 'South Asian' and 'Black African-Caribbean'. Indian, Pakistani and Bangladeshi were combined into the 'South Asian' group, and Black African and Black Caribbean into the 'Black African-Caribbean' group, due to their small sample sizes. Mean BMI for each ethnic subgroup at each age is provided in Figure S8 and Table S10.

Outcome: height to the nearest mm and weight to the nearest 0.1 kg were measured at around 3, 5, 7, 11 and 14 years by trained interviewers following a standard protocol and were used to calculate BMI. International Obesity Task Force (IOTF) BMI-for-age cut-offs (267) were used to define overweight and obesity. *Waist circumference* (WC) to the nearest 0.1 cm was measured against bare skin using a seca measuring tape at ages 5 and 7 years. *Body fat percentage* (BF%) to the nearest 0.1% was measured with light clothing and without shoes using a leg-to-leg bioelectric impedance analysis machine (TANITA BF-522W) at ages 7, 11 and 14 years. BMI standard deviation scores (SDS), WC SDS as well as BF SDS were calculated using British 1990 references (139, 268, 269).

Covariates: A number of explanatory factors were considered in the analysis, which are suggested by existing literature to be predictive of BMI and are closely associated with ethnicity. These factors include height, family socio-economic circumstances (i.e. family income and maternal education), maternal pre-pregnancy BMI and smoking during pregnancy, indicators of foetal and early growth (i.e. birthweight and infant weight gain), and infant feeding (i.e. duration of exclusive breastfeeding and early introduction to solid foods).

In childhood and adolescence, BMI is positively associated with height (126) (correlation coefficient r=0.09-0.30 in the analysis sample). Therefore, height was considered in the analysis to take into account residual correlation between height and BMI. Family income was weighted according to family size and used as quintiles. Maternal highest academic qualification was reported at baseline and grouped as 'higher education diploma or degree', 'A-level', 'GCSE grades A*-C', 'GCSE grades D-G', 'others' and 'none of these'. Maternal pre-pregnancy BMI (kg/m^2) was calculated using self-reported height and pre-pregnancy weight recalled at 9 months, and used as a continuous variable. Maternal smoking during pregnancy was defined as any smoking (>0 cigarette/day) at four months of gestation. There were substantial ethnic differences in birthweight and infant weight gain, both of which are positively associated with later BMI trajectories as shown in Chapter 3. Birthweight (kg) was used as a continuous variable. Infant weight gain was calculated as the change in weight-for-age z-scores between birth and 3 years using UK-WHO growth references, to take into account variation in age at weight measurements (270). Duration of exclusive breastfeeding was categorised into 'none', '<4 months' and '4 months and longer', according to the duration of exclusive breastfeeding recommended at that time. Early introduction of solid foods was defined as introducing solid foods before the age of 4 months.

Estimating BMI trajectories

The best combination of third-order fractional polynomial functions to describe BMI changes were age^2, age^3 and $age^2 * \ln(age)$. Random effects were allowed for intercept and coefficients for age^2 and age^3. Inclusion of random effects for the additional age term $age^2 * \ln(age)$ led to convergence issues. Therefore, only fixed effects were adopted for $age^2 * \ln(age)$. The fitted BMI trajectories were the same as described in the previous chapter (Chapter 5). Unstructured covariance matrix for the random effects and maximum likelihood estimation were used. Model selection was guided by deviance, Akaike and Bayesian

Information Criterion statistics. Ethnicity and interactions between ethnicity and all age terms were included in the models as fixed effects to estimate ethnic-specific mean BMI trajectories. To remove the "end effects" caused by sparse data, instead of the full observed age range (2.7 - 15.3 years), a restricted age range from 3 to 14 years was used for plotting the trajectories.

Adjustment for early life factors

In the first step, early life factors (both main effects and their interaction with all age terms) were included in the models, one at a time, to assess their role in explaining any ethnic differences in BMI trajectories. Weight gain was defined by the change in weight-for-age z-scores between birth and 3 years, while BMI trajectories were modelled from 3 years to 14 years. Therefore, only interactions between infant weight gain and age terms (i.e. no main effect) were included in the model to estimate the effect of early-life weight gain on later BMI. Family SECs did not explain BMI differences between White and South Asian children. Maternal smoking and infant feeding practices did not explain BMI differences between White and Black African-Caribbean children (Appendix IV Table S11).

The differences between South Asian and White groups, and between Black African-Caribbean and White groups were explained by different sets of covariates. For that reason, models were fitted for South Asian group and Black group separately in the next step. For the comparison between South Asian and White groups, **model 1** was an unadjusted model; **model 2** was adjusted for height; **model 3** was further adjusted for maternal characteristics; **model 4** was additionally adjusted for indicators of foetal and early growth; and **model 5** additionally included infant feeding. For the comparison between Black African-Caribbean and White groups, **model 1** was unadjusted for covariates; **model 2** was adjusted for height; **model 3** was further adjusted for family SECs; **model 4** additionally included maternal BMI; and **model 5** further included indicators of foetal and early growth. All models were fitted for boys and girls separately.

Multiple imputation

Multiple imputation with chained equation was performed to account for missing data in covariates under a missing at random (MAR) assumption, following the guidelines provided by Sterne *et al* (271). The proportion of missing data was high in maternal pre-pregnancy BMI (11%) and infant weight gain (16%), and very low in maternal smoking (2%) and birthweight (0.2%). Differences in key variables between participants with and without missing data in maternal BMI and infant weight gain were examined to assess missing patterns (Appendix IV Table S12). Imputation model included all variables in the analysis models as well as an auxiliary variable (i.e. maternal age). Maternal age was included because it predicted both the missing values and missing patterns in maternal pre-pregnancy and weight gain variables. Pairwise correlation coefficients between variables are provided in Appendix IV Table S13.

A total of 30 datasets were created. A general linear regression imputation method was specified for birthweight and infant weight gain SDS, a logistic regression for binary variables (i.e. maternal smoking and early introduction to solid foods), an ordered logistic regression for duration of exclusive breastfeeding, and a predictive mean matching imputation method using subsets of 10 nearest values was specified for maternal pre-pregnancy BMI due to its skewed distribution. Distributions of the observed and imputed data were compared and largely similar (Appendix IV Figure S9). Models were fitted to each of the imputed datasets separately, and estimates from the 30 imputed datasets were combined using Rubin's rules (244). Fraction of missing information (%) and Monte Carlo error estimates were examined to assess whether an adequate number of imputations were performed.

Ethnic differences in overweight and obesity at 3, 5, 7, 11 and 14 years

Logistic regression models were used to estimate ethnic differences in the odds of being overweight or obesity at each age with White group as the reference. Additional multinomial logistic regression models using 3-category BMI variables ('healthy', 'overweight' and 'obesity') were also performed. Estimated relative risk ratios (RRR) of 'overweight' and 'obesity' (versus 'healthy') in each minority ethnic group compared with the White group are provided in Appendix IV Table S14.

Relationships between BMI and other adiposity measures across ethnic groups

Ethnic differences in the relationship between BMI and WC at 5 and 7 years were explored using linear regression models, while differences in the relationship between BMI and BF at 7, 11 and 14 years were explored using quadratic models due to the curvilinear relationship between BMI and BF. Ethnic differences in BMI SDS, WC SDS and BF SDS at each age were estimated using weighted linear regression to account for disproportionate sampling design and attrition. Adiposity on the SDS scale was used to improve comparability of ethnic differences across different adiposity outcomes.

6.3 Results

Participant characteristics

Of the 15,994 included children, 87.4% were White, 10.1% South Asian and 3.5% Black African-Caribbean children (Table 6.1). Participant characteristics were similar as reported in previous chapters (Chapters 3-4): compared with White children, minority ethnic children had a lower mean birthweight, greater weight gain in infancy and less advantaged family SECs; their mothers were less likely to smoke during pregnancy and more likely to breastfeed in accordance to national guidelines. South Asian mothers had a slightly lower mean BMI before pregnancy by 0.6 kg/m^2 than White mothers, and Black African-Caribbean mothers had a higher mean BMI pre-pregnancy by 1.7 kg/m^2. *P*-values for the above described ethnic differences were all <0.001.

Ethnic differences in BMI trajectories

South Asian vs. White children: Figure 6.1 shows estimated BMI trajectories by sex and ethnic group. At 3 years, South Asian boys and girls had a lower BMI than White counterparts by -0.79 kg/m^2 (95% CI: -0.90, -0.67) and -0.58 kg/m^2 (-0.70, -0.46) respectively (Figure 6.1). Thereafter, their trajectories started to converge. By 9 years, there was little difference in mean BMI in boys. In girls, although the BMI difference narrowed slightly with age in childhood (3 -12 years), a small difference of around -0.4 kg/m^2 persisted throughout childhood into adolescence. Estimated BMI differences with 95% CIs at each age are provided in Appendix IV Table S15 (model 1).

Estimated BMI differences remained largely unaltered after adjusting for height in model 2, but attenuated slightly when including maternal smoking and pre-pregnancy BMI in model 3 (Figure 6.2). South Asian mothers were less likely to smoke during pregnancy and had a lower mean BMI prior to pregnancy, which partially explained the lower BMI trajectories in South Asian children. Adjustment for birthweight and weight gain in model 4 and infant feeding in model 5 further attenuated these BMI differences, but to a lesser extent compared with maternal characteristics. Estimated BMI differences with 95% CIs from adjusted models are provided in Appendix IV Table S15.

Table 6.1: Participant characteristics by ethnic group (total *n*=15,994)

Characteristics	% missing	White (*n*=13,822)	South Asian (*n*=1,607)	Black African-Caribbean (*n*=565)
Maternal smoking (>0 cigarette/day), n(%)	2%	3503(25.9%)	45(2.8%)	52(9.4%)
Maternal pre-pregnancy BMI (kg/m^2)	11%	23.7(4.4)	23.1(4.5)	25.4(5.1)
Family income quintiles, n(%)	n/a			
Highest quintile		2500(18.1%)	100(6.2%)	46(8.1%)
Fourth quintile		2721(19.7%)	108(6.7%)	56(9.9%)
Third quintile		2816(20.4%)	174(10.8%)	71(12.6%)
Second quintile		2840(20.6%)	577(35.9%)	131(23.2%)
Lowest quintile		2945(21.3%)	648(40.3%)	261(46.2%)
Maternal highest academic qualification, n(%)	n/a			
Higher education diploma or degree		3582(25.9%)	220(13.7%)	156(27.6%)
A-level		1360(9.8%)	124(7.7%)	37(6.6%)
GCSE grades A*-C		4988(36.1%)	307(19.1%)	109(19.3%)
GCSE grades D-G		1557(11.3%)	128(8.0%)	43(7.6%)
Others		199(1.4%)	192(12.0%)	43(7.6%)
None of these		2136(15.5%)	636(39.6%)	177(31.3%)
Birthweight (kg)	0.2%	3.40(0.56)	3.08(0.57)	3.28(0.60)
Weight gain between birth and 3 years (SDS)	16%	-0.08(1.14)	0.25(1.30)	0.66(1.40)
Duration of exclusive breastfeeding, n(%)	3.4%			
None		4859(35.2%)	306(19.0%)	42(7.4%)
Less than 4 months		8160(59.0%)	1114(69.3%)	455(80.5%)
4 months or longer		407(2.9%)	83(5.2%)	30(3.5%)
Early introduction of solid foods	3.4%			
No		8275(59.9%)	1301(81.0%)	437(77.4%)
Yes (<4 months)		5151(37.3%)	202(12.6)	79(14.0%)

*Cell values are unweighted mean(SD), unless otherwise stated. SD: standard deviation. SDS: standard deviation score. n/a: not applicable, a small number of participants who had missing data on maternal education and family income were excluded from the analysis (*n*=89). All characteristics differed between each minority ethnic group and White: $p \leq 0.001$ for t-tests for continuous variables and Chi-squared tests for categorical variables.

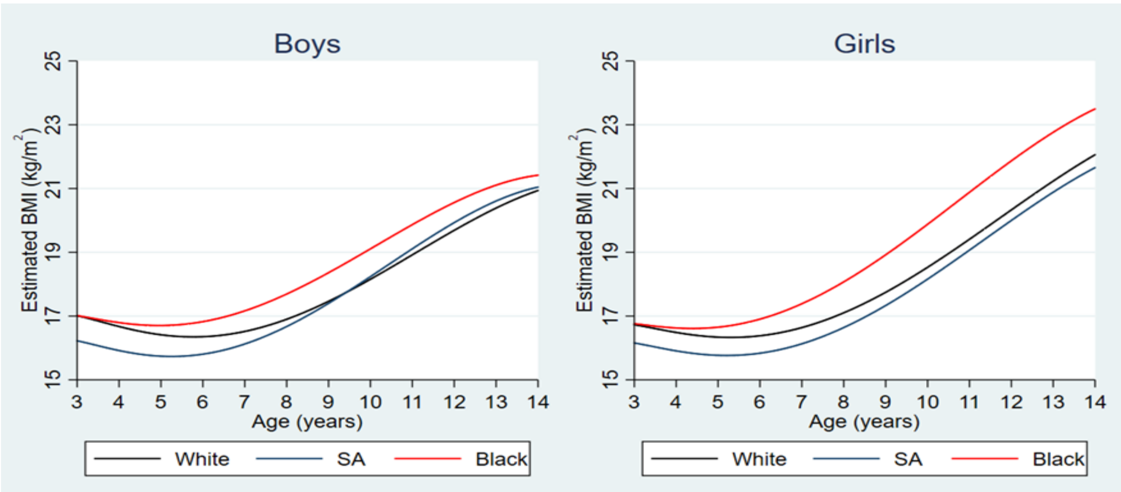

Figure 6.1: Estimated BMI trajectories by sex and ethnic group from unadjusted mixed effects fractional polynomial models

*SA: South Asian; Black: Black African-Caribbean. Models included fractional polynomial age terms, ethnicity, and interaction between ethnicity and all age terms. Analysis was repeated for boys and girls separately.

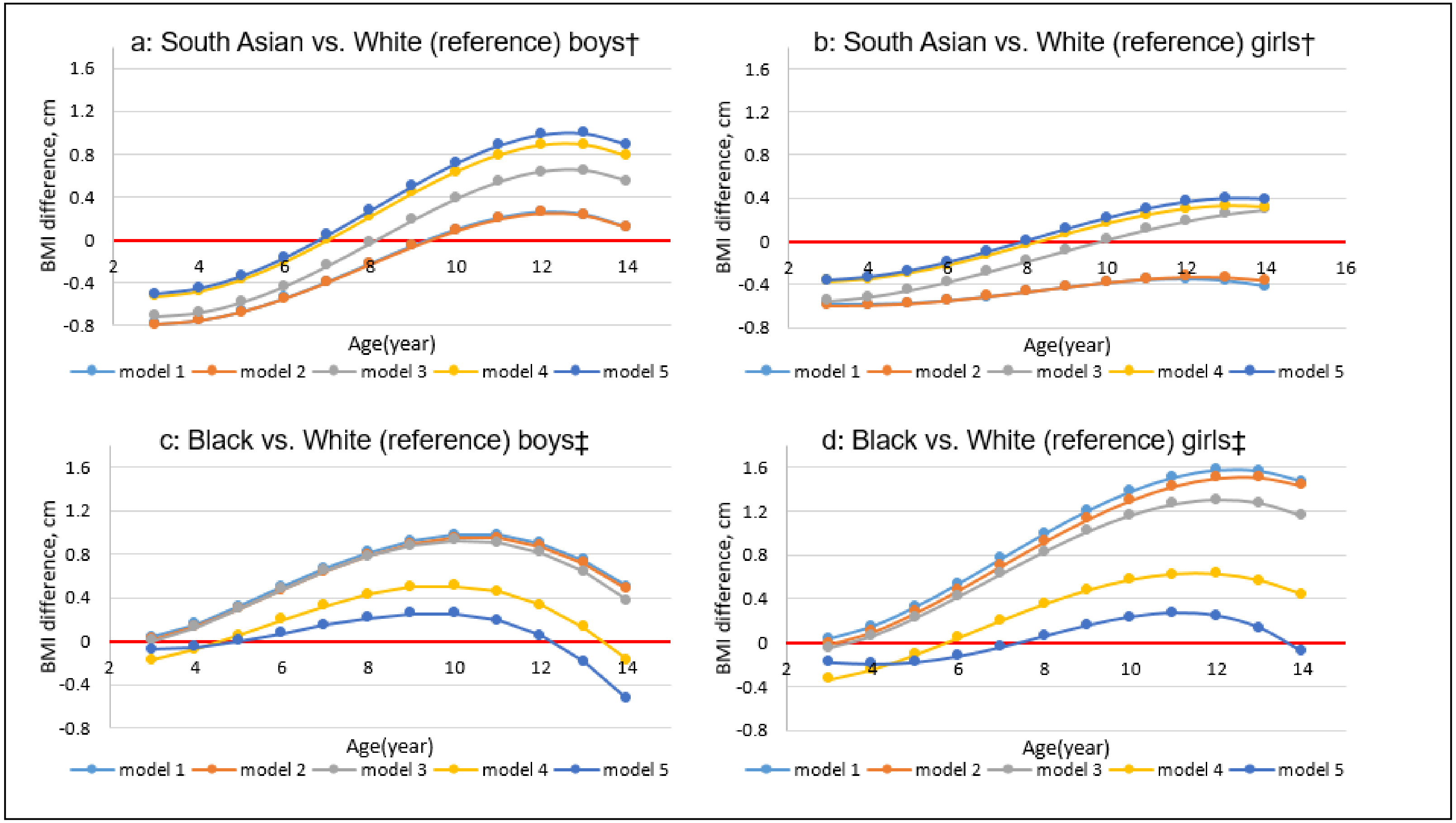

Figure 6.2: Estimated BMI differences in cm between ethnic groups from unadjusted and adjusted mixed effects models

* Black: Black African-Caribbean. White was used as the reference group. The red reference line indicates no difference between minority ethnic group and the White group.

† **South Asian models**: Model 1 was unadjusted; model 2 adjusted for height; model 3 additionally adjusted for maternal smoking and BMI; model 4 additionally adjusted for birthweight and infant weight gain; model 5 further adjusted for infant feeding. Estimated BMI differences for models 1 and 2 overlap.

‡ **Black African-Caribbean models:** model 1 was unadjusted; model 2 adjusted for height; model 3 adjusted for family SECs; model 4 adjusted for maternal BMI; model 5 adjusted for birthweight and infant weight gain.

Black African-Caribbean vs. White children: Black African-Caribbean children had higher BMI trajectories than the other two ethnic groups (Figure 6.1). At 3 years, there was no difference in mean BMI between White and Black African-Caribbean children. A difference began to emerge at about 5 years with Black African-Caribbean children having higher BMI by 0.32 kg/m^2 [95% CI in boys: (0.14, 0.49); in girls: (0.12, 0.52)]. In boys, this difference widened with age to 0.89 kg/m^2 (0.44, 1.35) at 12 years, and narrowed slightly to 0.49 kg/m^2 (-0.02, 1.01) at 14 years. In girls, the BMI difference increased rapidly to 1.57 kg/m^2 (1.06, 2.07) at 12 years and remained at a similar level thereafter. Estimated BMI differences with 95% CIs at each age are provided in Appendix IV Table S16.

BMI differences between Black African-Caribbean and White children attenuated slightly after adjustment for height in model 2 (Figure 6.2c and Figure 6.2d), and further reduced slightly when family SECs were included in model 3. BMI differences reduced substantially after additional adjustment for maternal BMI in model 4, and were only evident at ages 7 to 11 years in boys and 8 to 13 years in girls. In the final model with further adjustment for birthweight and infant weight gain, the higher BMI among Black African-Caribbeans was only evident in boys at 8 and 9 years, by 0.21 kg/m^2 (0.00, 0.42) and 0.25 kg/m^2 (0.01, 0.49) respectively; there was no evidence of higher BMI in Black African-Caribbean girls. Estimated BMI differences with 95% CIs from adjusted models are provided in in Appendix IV Table S16.

Ethnic differences in overweight or obesity at 3, 5, 7, 11 and 14 years

Figure 6.3 shows the odds of being overweight/obese among minority ethnic children compared with their same-sex White counterparts (i.e. OR). The patterns of ethnic differences were similar to those seen in BMI trajectories. South Asian boys had lower odds of being overweight/obese than White boys at 3 years [OR=0.62 (0.49, 0.78)], similar odds at 5 years, but higher odds at 7, 11 and 14 years (Figure 6.3a). South Asian girls were less likely to be overweight/obese than White girls at 3 years [OR=0.77 (0.61, 0.97)], but had similar levels of risk thereafter, except at age 7 [OR= 1.37 (1.07, 1.75)] (Figure 6.3b).

There was some evidence that Black African-Caribbean children may be more likely to be overweight/obese at 3 years [OR in boys 1.34 (0.92, 1.95); in girls 1.41 (0.98, 2.03)] (Figure 6.3c and Figure 6.3d). At 5, 7 and 11 years, the odds of overweight/obesity among Black African-Caribbean children were around twofold of their same-sex White counterparts (OR ranged from 1.92 to 2.09 in boys, and from 2.07 to 2.61 in girls). However, at 14 years, Black African-Caribbean boys no longer had higher odds of overweight/obesity than White boys, while Black African-Caribbean girls remained to have an increased odds of overweight/obesity [OR= 2.03

(1.42, 2.90)]. Estimated OR with 95% CI for each of minority ethnic group compared with the White group is provided in Appendix IV Table S17.

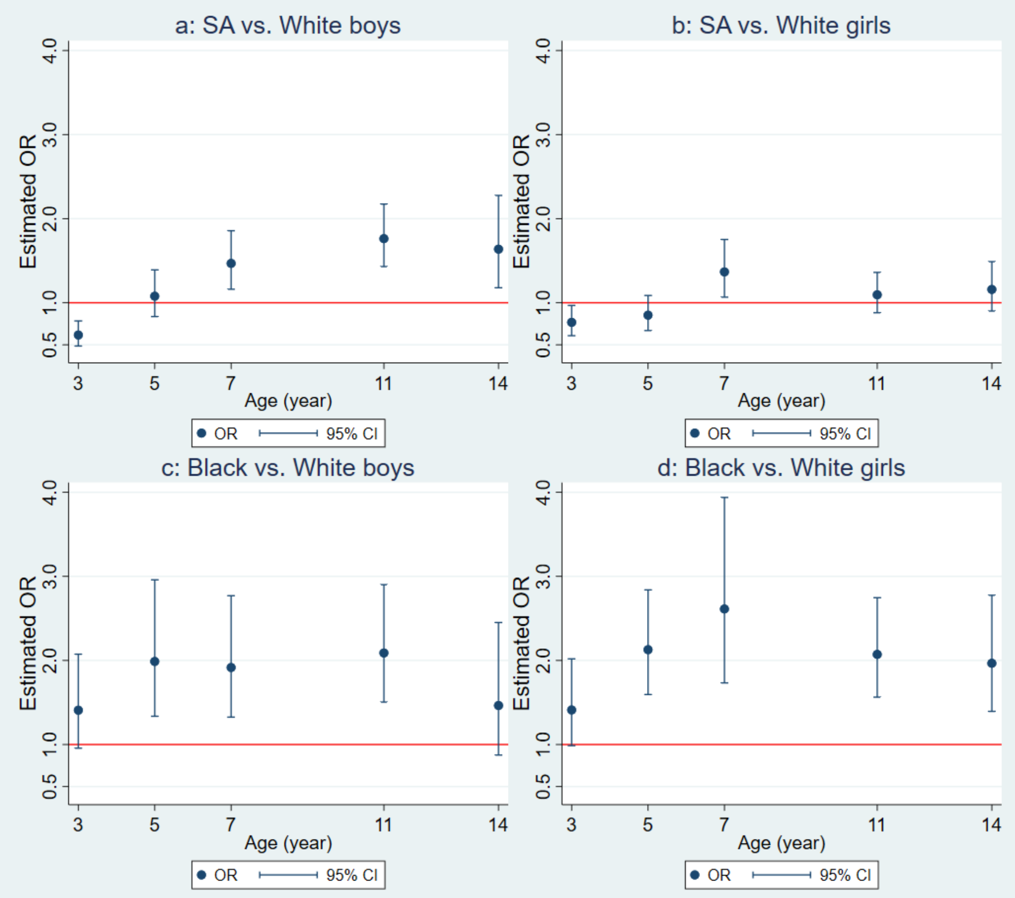

Figure 6.3: Estimated odds ratios (OR) of overweight or obesity with 95% confidence intervals (CIs) by sex, from unadjusted logistic regression

*Overweight was defined using IOTF references and included obesity. OR indicates how the odds of overweight in the minority ethnic group compared with the White (reference) group. The reference line (OR=1) represents no difference between minority ethnic group and the White group. Analysis was weighted to account for disproportional sampling and attrition. SA: South Asian; Black: Black African-Caribbean.

Ethnic differences in BMI, waist circumference, and body fat

The relationships between BMI and WC at 5 and 7 years are shown in Figure 6.4. The slopes for South Asians were steeper than for Black and White children, i.e. mean WC at a given BMI was greater for South Asians, which was more evident at 7 years than 5 years. At a given BMI, Black African-Caribbean boys in general had a slightly lower WC than their White counterparts, and Black girls had very similar WC to White girls at 5 and 7 years.

The relationships between BMI and BF% at 7, 11 and 14 years are shown in Figure 6.5. For a given BMI, South Asian children had higher percentage of BF than White children, but the magnitude of differences was much smaller in girls. Black African-Caribbean children had similar or slightly higher levels of BF compared with White children of the same BMI. Coefficient estimates are provided in in Appendix IV Table S18 and Table S19.

Figure 6.6 illustrates differences in SDS for BMI, WC and BF between each ethnic group and White by age. The estimates with 95% CIs are provided in in Appendix IV Table S20.

South Asian vs. White: South Asians had lower mean BMI SDS than their White counterparts at ages 5 and 7; they also had similarly lower mean WC SDS but to a lesser extent, with the exception of girls at 7 years. However, the mean BF SDS of South Asian children at 7 years was higher than that of White children, by 0.20 SDS (0.11, 0.29) in boys and 0.28 SDS (0.16, 0.41) in girls. At 11 and 14 years, there was no difference in BMI SDS between South Asian and White children; nevertheless, South Asian boys and girls had higher levels of BF than their White counterparts, and the differences were much greater in boys than girls (Figure 6.6 and Appendix IV Table S20).

Black African-Caribbean vs. White: The mean BMI SDS was greater in Black African-Caribbean children than in White children from 5 to 14 years, with the exception for Black boys at 14 years who had similar mean BMI to White boys (Figure 6.6). However, there was no difference in mean WC SDS between Black African-Caribbean and White boys at 5 and 7 years. Black African-Caribbean boys had higher levels of body fat at 7 and 11 years by 0.35 SDS (0.18, 0.53) and 0.60 SDS (0.30, 0.90), respectively, but not at 14 years. In similar comparisons, Black African-Caribbean girls had greater WC than White girls at 5 years by 0.27 SDS (0.10, 0.43), which increased to 0.50 SDS (0.32, 0.68) at 7 years; they also had similarly higher levels of BF with a difference of 0.61 SDS (0.36, 0.87) at 7 years reducing slightly to 0.58 SDS (0.38, 0.77) at 14 years (Figure 6.6 and Appendix IV Table S20).

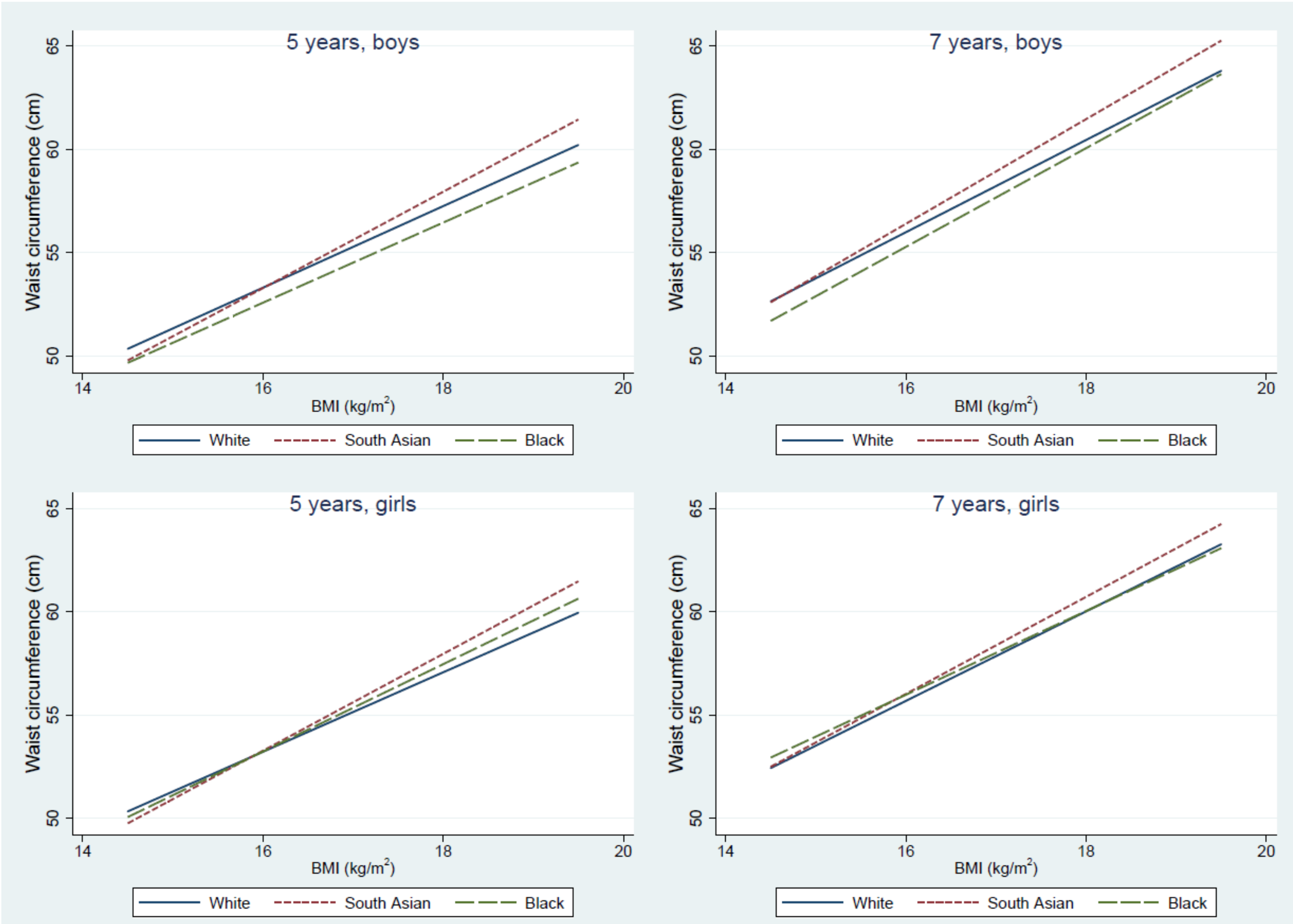

Figure 6.4: Fitted linear regression lines between waist circumference (cm) and BMI (kg/m^2) at 5 and 7 years, by sex and ethnicity

* Black: Black African-Caribbean. Linear regression models included age at measurement, ethnicity, BMI and ethnicity*BMI.

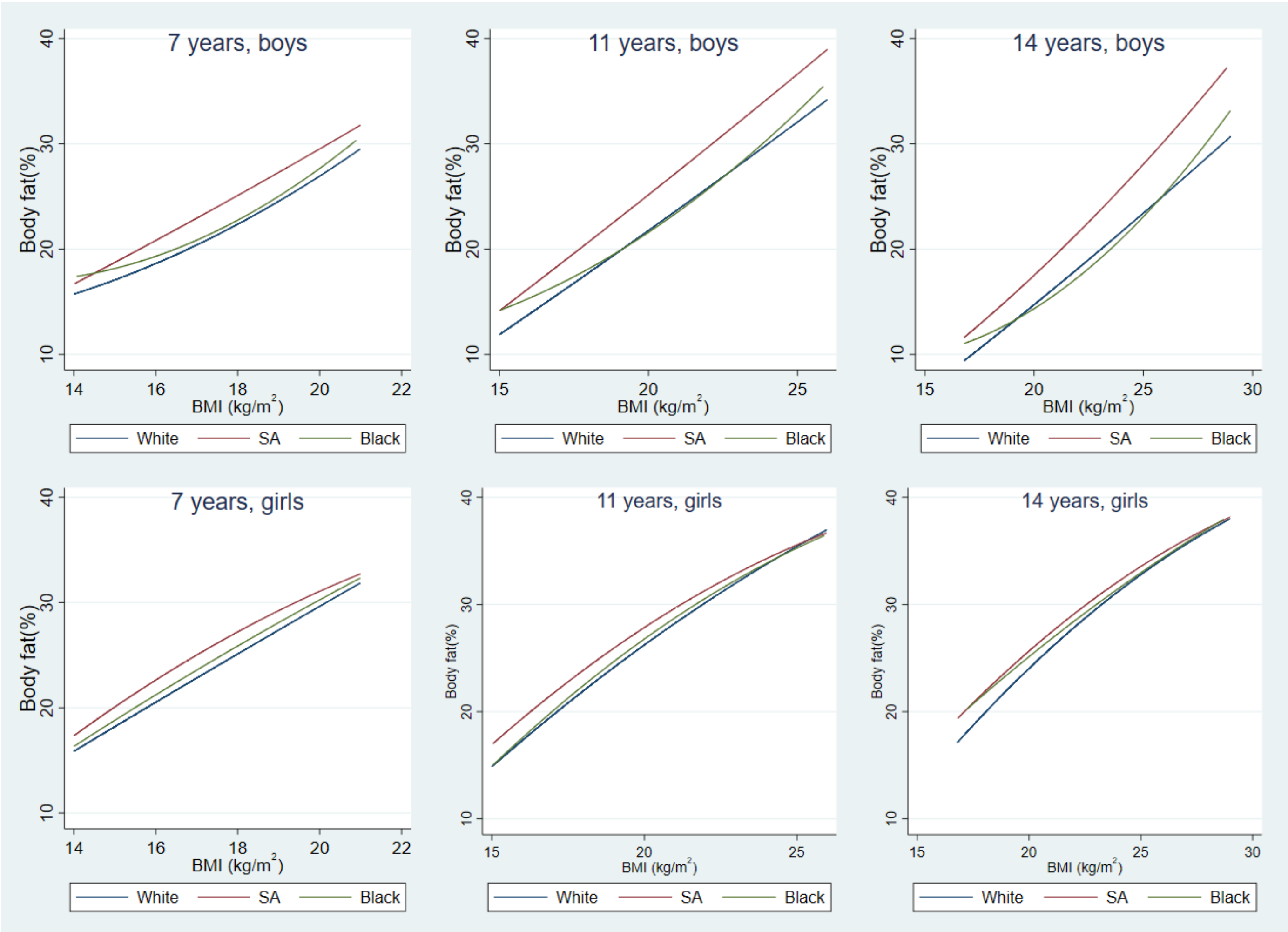

Figure 6.5: Fitted quadratic curves between body fat (%) and BMI (kg/m^2) at 7, 11 and 14 years, by sex and ethnicity

* SA: South Asian. Black: Black African-Caribbean. Models were unweighted and included age at measurement, BMI, BMI quadratic term, ethnicity, and interaction between ethnicity and BMI terms.

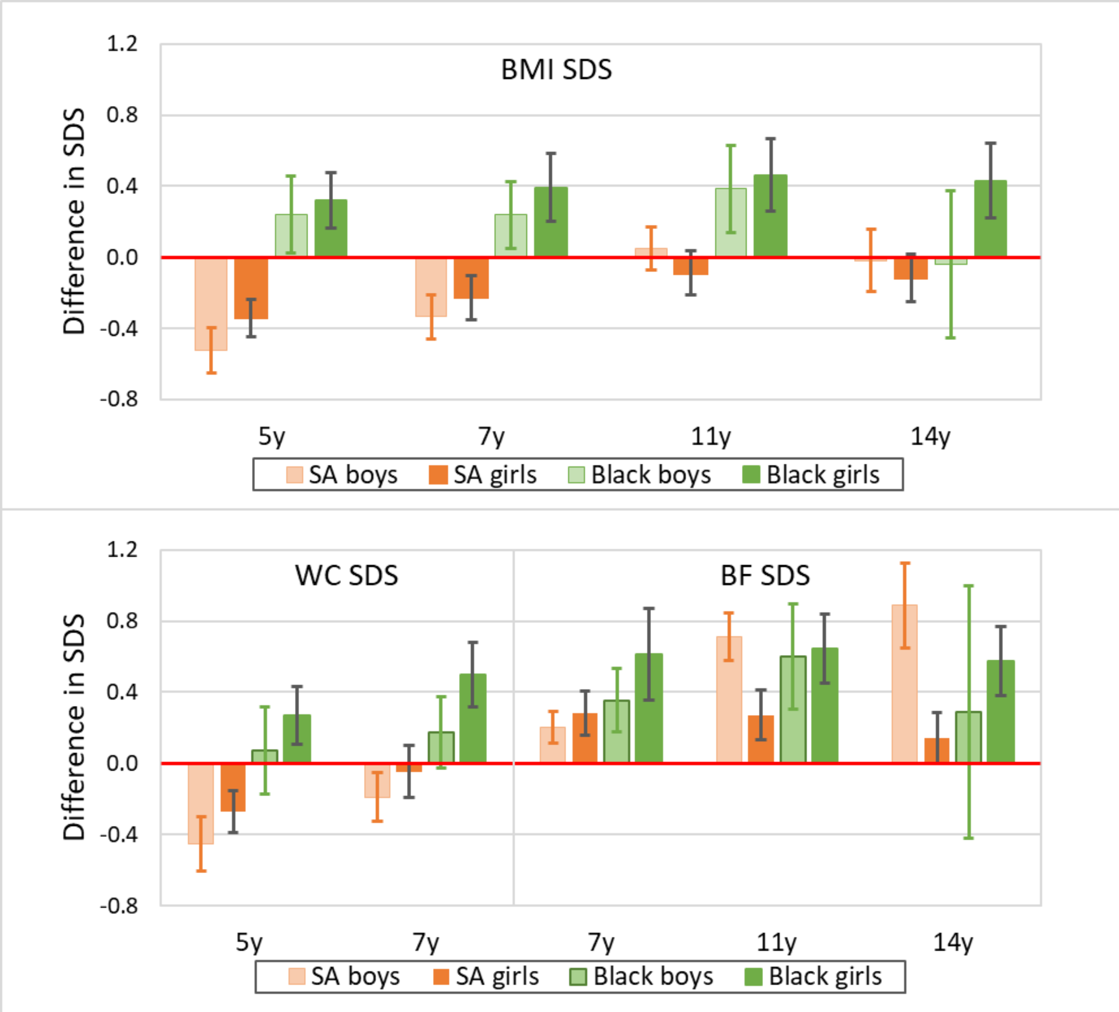

Figure 6.6: Ethnic differences with 95% confidence intervals in WC SDS, BF SDS and BMI SDS, based on weighted linear regression models

*SDS: standard deviation score. Estimates are based on linear regression of each adiposity outcome on age at measurement and ethnicity. Analysis was weighted to account for disproportional sampling and attrition.

6.4 Discussion

Summary of key findings

There are several key findings: 1) South Asian children had lower BMI than White children at 3 years, with the differences narrowing with age. For boys, there was no BMI difference by 9 years, and for girls a small difference persisted in girls to 14 years. 2) Black African-Caribbean children had similar mean BMI as White children at 3 years, but a difference emerged at 5 years and in general widened with age, especially in girls. 3) The lower BMI found among South Asian children was partially explained by maternal characteristics and birthweight, while the higher BMI found in Black African-Caribbean children was almost fully explained by height, family SECs, maternal BMI and infant weight gain. 4) Patterns of ethnic differences in overweight or obesity were largely consistent with the findings in BMI trajectories. 5) Compared with White counterparts of the same BMI, South Asians had higher levels of BF, especially boys, while Black children had similar BF% at 7, 11 and 14 years. South Asians had higher levels of BF at these ages, despite the fact that they had favourable BMI.

Comparison with previous studies

Few studies have investigated ethnic differences in child-to-adolescent BMI trajectories in the UK. One study using the MCS data up to 7 years found that compared with White children, South Asians had lower BMI between 3 and 7 years, but experienced greater BMI growth during this age period; while Black children had similar BMI as White children at 3 years but higher BMI thereafter to 7 years (145). The present study extended these findings to adolescence and showed that the BMI trajectories of South Asian and White boys converged after 9 years with no difference between 9 and 14 years, while a small difference between South Asian and White girls persisted into adolescence. The BMI differences between Black African-Caribbean and White boys further increased after 7 years, but narrowed slightly between 12 and 14 years in boys. Therefore, cross-sectional analysis which combines sex groups or uses data from a wide range of ages may overlook these patterns of ethnic differences with age, resulting in inconsistent findings on obesity risk of minority ethnic groups relative to White groups (143).

Explanations of ethnic differences in BMI

A number of early life factors have been identified to be associated with high BMI in childhood (272, 273). The majority of previous studies which investigated the role of early life factors in ethnic disparities in adiposity did not explore these factors for each minority ethnic group separately (143). The present study showed that BMI disparities between Black African-Caribbean and White groups were explained by different early life factors compared with those between South Asian and White groups. The lower BMI found among South Asian children was partially explained by their lower maternal BMI, better maternal smoking behaviour and lower birthweight. Family SECs were negatively associated with BMI in White and South Asian groups (as shown Chapter 5) and therefore did not explain the lower mean BMI in South Asian children relative to White children. It remains unclear how much of the remaining differences was due to biological differences or dietary factors (127), which warrants further research.

The higher BMI in Black African-Caribbeans relative to White children was nearly fully explained by their taller height, lower family SECs, and especially higher maternal BMI and greater infant weight gain. The Black African-Caribbean group had better maternal smoking behaviour in pregnancy and infant feeding practice, hence these factors did not explain their higher BMI trajectories relative to White children during preliminary analysis.

Ethnic differences in BMI, WC and BF

Relationships between BMI and other adiposity measures (i.e. WC and BF) also differed by ethnicity. However, the patterns of these differences appeared to be complex and vary by sex and age. South Asians in general had greater WC and BF than White children at a given BMI, especially in boys, which is consistent with other UK studies comparing body composition in children and adolescents across ethnic groups (265, 266). In a group of children aged 9-10 years, for any given fat mass, BMI was found to be lower in South Asians compared with White European while Black African-Caribbean children had a similar BMI to White children (265).

Hudda *et al* found that BMI overestimated BF in Black African-Caribbean children aged 4-12 years compared with White Europeans (266). In contrast, this study found Black African-Caribbean children had slightly higher or similar levels of BF to White children of the same BMI. The slight discrepancy between the present and Hudda *et al*'s study may be partially due to the different methods used to measure BF. In the MCS, bioelectric impedance analysis machines were used to measure body fat; the accuracy of this method has been shown to vary and can be greatly affected by recent food and fluid intake (268). Isotope dilution was used in Hudda *et al*'s study, which is considered to have less measurement error in populations where the normality of hydration can be assumed (125).

Despite the fact that at 11 and 14 years South Asian boys had similar BMI and girls had slightly lower BMI compared with their White peers, the BF measure revealed that South Asians had much higher levels of adiposity at these ages. These findings are supported by reports from other UK studies using dual-energy x-ray absorptiometry (274), bioelectrical impedance analysis (265, 275) and deuterium dilution (275) methods.

Implications for population health

Marked ethnic differences in BMI are established at very young ages. The greater BMI in Black African-Caribbean children was largely explained by maternal pre-pregnancy BMI and infant weight gain. These findings highlight the needs for early intervention starting even before pregnancy to reduce childhood obesity and improve ethnic disparities in BMI and obesity (276). Although BMI may be misleading in comparing body adiposity in multi-ethnic population, it remains a widely used method in population studies, due to its convenience. The BMI adjustments proposed by Hudda and colleagues, so that adjusted BMI values are related to fat mass index in the same way across ethnic groups, could be a way forward in addressing this problem (268). However, such adjustments have only been developed for UK South Asian and Black African children aged 4 to 12 years. Furthermore, previous reviews carried out in addressing the ongoing debate for ethnic-specific BMI thresholds for overweight and obesity concluded that there is little to be gained by using ethnic-specific BMI thresholds based solely on BMI-adiposity relationship (277, 278). The BMI thresholds were developed based on their association with morbidity and mortality outcomes (279, 280). How best to assess body adiposity in relation to long-term health risks across ethnic groups in children populations continues to be an area of active research.

Strengths and limitations

Strengths of the study are the use of longitudinal data to examine ethnic differences in child-to-adolescent BMI trajectories among UK children and the role of several key influencing factors in early life. The present study further benefited from additional WC and BF data collected to explore ethnic differences in body composition. Some limitations need to be acknowledged. Due to small sample sizes in some of the ethnic groups, aggregated ethnic groups were used. Preliminary analysis showed that there was some variation in BMI between ethnic subgroups; however, overall South Asian subgroups were more similar to each other than to Black Africans and Black Caribbeans (Appendix IV Figure S8 and Table S10). Another limitation is infant weight growth can only be assessed using the weight change between the period of birth and 3 years, due to data availability in the MCS. Birthweight, weight change between birth and 3 years as well as BMI at 3 years are closely related. Caution is required when interpreting the results with adjustment for infant weight gain. Furthermore, BF was measured using a bioelectrical impedance analysis (BIA) machine in the MCS, which may not be suitable for comparison across ethnic groups (275, 281). BIA works by sending a weak electric current through the body to calculate the resistance (i.e. bioimpedance), which is then used to predict BF. However, the inbuilt equations used to predict BF were validated predominantly in White European populations and have been shown to underestimate fat mass in Asians and White Europeans but overestimates fat mass in Black females (281). Bioimpedance index was not available in the MCS datasets, which prevents further investigation of using ethnic-specific equations as proposed by previous researchers (281).

6.5 Conclusion

There were marked ethnic differences in BMI and in the relationships between BMI and other adiposity measures. South Asian children had lower BMI than White children at 3 years, but the difference narrowed with age and only a small difference remained in girls by 14 years. South Asians also had similarly lower WC at 5 and 7 years, but had much greater proportions of BF at 7, 11 and 14 years especially in boys, which was not revealed by BMI. The lower mean BMI in South Asians was partially explained by maternal BMI, maternal smoking during pregnancy and birthweight. Black African-Caribbeans had a higher BMI than White children from 5 years onwards with the difference widening with age. Their greater BMI was largely explained by maternal pre-pregnancy BMI and infant weight gain, and was also reflected in their greater WC and BF. These results highlight the importance of early interventions to reduce childhood obesity and improve ethnic disparities in BMI/obesity. Future research is needed to understand how best to assess body adiposity in relation to later cardio-metabolic health risks across different ethnic groups in children.

7 ASSOCIATION BETWEEN RAPID WEIGHT GAIN IN EARLY LIFE AND LATER BMI TRAJECTORIES ACROSS BIRTHWEIGHT GROUPS (OBJECTIVE 4)

7.1 Introduction

The development of obesity is complex and multifactorial (282). Infant weight gain has been identified as one of the important early life factors and is strongly associated with later BMI and risk of overweight and obesity (162-165). A recent meta-analysis showed that rapid weight gain (RWG) between birth and 2 years (defined as a change in weight z-scores >0.67 SDS) was associated with 4.16 higher odds of overweight/obesity in childhood and adolescence (162). Most of the existing studies are cross-sectional and only used BMI or other adiposity measure at one age; few have considered repeated measures (283-285). It is not well studied how RWG in early life influences later BMI development trajectories. In a group of 206 German children with an appropriate-for-gestational-age birthweight, those who experienced RWG in the first 2 years of life had a higher mean BMI SDS at 2 years than those who did not experience RWG and the BMI difference persisted at a similar level until 7 years (285). A recent US study used latent class analysis and showed that infant weight gain was positively associated with a 'high-rising' or 'median-stable' BMI growth pattern between 2 and 13 years, compared with the 'low-stable' pattern (286). It remains largely unknown how RWG is associated with BMI at different ages and the rate of BMI gains from childhood to adolescence in a population sample.

Rapid weight gain is more common among low birthweight babies than babies born with a normal or high birthweight, especially following intrauterine growth restriction (162). However, overall birthweight is positively associated with childhood BMI (150), that is, children born with a higher birthweight on average have higher BMI in childhood. As shown in Chapter 3 Table 3.2, children from South Asian and Black Caribbean ethnic backgrounds were more likely to be born small for gestational age than White children. It is not well studied whether the association between RWG and raised BMI differs by birthweight status. Therefore, as an additional objective, this chapter aims to examine 1) the association between RWG in the first 3 years of life and child-to-adolescent BMI trajectories (5-14 years); and 2) whether the association differed by birthweight group.

7.2 Methods

Analysis sample

This analysis included term singletons who entered the MCS at baseline survey at 9 months (*n*=16,581). Further inclusion criteria are participants with available information on weight gain between birth and 3 years as well as at least one BMI measurement at follow-up between 5- and 14-year visits (*n* = 11,606, eligible sample). After excluding a small proportion of participants who had missing data on the covariates (*n* =895, 7.7% of the eligible sample), a total of 10,711 children with 38,502 BMI measurements were included in the analysis (analysis sample). A comparison of participant characteristics between the analysis sample and the excluded eligible sample is provided in Appendix V Table S21. The distributions of BMI at 5- and 7-year visits as well as maternal pre-pregnancy BMI were similar between included and excluded samples. Compared with the analysis sample, participants excluded from the analysis had slightly higher BMI at 11- and 14-year visits, and were more likely to experience RWG, born small for gestational age, never have been exclusively breastfed, come from a minority ethnic background and a family with low maternal education level and household income.

Variables

Details on how relevant variables were collected and derived are provided in Chapter 2. A brief description is provided below.

Exposure (RWG between birth and 3 years): In accordance with previous research (166), RWG was defined as a change in weight SDS between birth and 3 years greater than +0.67 SDS, which represents an upward crossing of one major percentile (i.e. 2nd, 9th, 25th, 50th, 75th, 91st and 98th) band on the standard growth charts.

Outcome (repeated measure of BMI from 5 to 14 years): Weight at 3 years was used for calculating weight gain between birth and 3 years (i.e. the exposure variable). Therefore, BMI trajectories were modelled from 5 to 14 years, not including BMI at 3 years.

Birthweight status was categorised into small-, appropriate- and large-for-gestational age (SGA, AGA and LGA) groups based on conventional cut-offs of 10th and 90th percentile (equivalent to ±1.28 SDS) (287). Birthweight for gestational age was considered as a potential effect modifier in the analysis.

*Covariates***:** A number of potential confounders which may bias the estimation of the association between RWG and BMI were considered. They were selected based on previous literature on their associations with infant weight gain (288-290) and with BMI (150), including maternal pre-pregnancy BMI, maternal smoking during pregnancy, duration of exclusive breastfeeding, early introduction of solid foods, maternal education, family income, and ethnicity. Gestational diabetes was also considered during preliminary analysis. The overall prevalence of gestational diabetes in the MCS sample was very low (0.24%). Gestational diabetes was not associated with BMI in univariate analysis (at 14 years *b* = -0.16 [95% CI: -1.83, 1.51] in boys and *b* = 0.33 [-2.05, 2.72] in girls with no gestational diabetes as the reference). Therefore, it was not included in the final analysis.

Maternal pre-pregnancy BMI (kg/m^2) was calculated using mother's self-reported height and recalled weight immediately prior to pregnancy. Maternal smoking in pregnancy was defined as smoking >0 cigarette/day by the end of the first trimester. Duration of exclusive breastfeeding was categorised into 'none', '0-<4 months' and '4 months and longer' (the duration of exclusive breastfeeding recommended at that time). Early introduction of solid foods was defined as introducing solid foods before the age of 4 months. Maternal highest academic qualification was classified as: 'diploma or degree', 'A-level', 'GCSE grades A*-C', 'GCSE grades D-G', 'others (e.g. qualifications gained overseas)' and 'no qualification'. OECD weighted family income was used as quintiles (202). Cohort members' ethnicity was grouped as 'White', 'South Asian' (including Indian, Pakistani and Bangladeshi), 'Black African-Caribbean' (including Black African and Black Caribbean) and 'Others'.

Estimating BMI trajectories

Second-order fractional polynomials were used to capture the non-linear trend of BMI increases with age. The best-fitting second-order fractional polynomials for age were $\sqrt{age}$ and $\sqrt{age} * \ln(age)$ for boys; and age and $\ln(age)$ for girls, based on the deviance statistics. Third-order fractional polynomials were also considered, which did not improve the model substantially (see Appendix V Table S22). Random effects were allowed for intercept and coefficients for $\sqrt{age}$ in boys and age in girls. Models did converge when random effects for an additional age term were included (i.e. $\sqrt{age} * \ln(age)$ in boys and $\ln(age)$ in girls). The fitted BMI trajectories were:

for boys $$BMI_{ij} = (\beta_0 + \mu_{0i}) + (\beta_1 + \mu_{1i})\sqrt{age_{ij}} + \beta_2 \sqrt{age_{ij}} * \ln(age_{ij}) + \epsilon_{ij}$$

for girls $$BMI_{ij} = (\beta_0 + \mu_{0i}) + (\beta_1 + \mu_{1i})\mathrm{age_{ij}} + \beta_2 \ln(age_{ij}) + \epsilon_{ij}$$

where BMI_{ij} denotes BMI for subject i (level-2) at measurement occasion j (level-1); $\beta_0, \beta_1, \beta_2$ denote the fixed parts of the intercept and coefficients for age terms; μ_{0i}, μ_{1i} denote the respective random parts; and ϵ_{ij} is the error term for subject $i = 1, 2 \dots n$ at measurement occasion $j = 1, 2 \dots n_i$. Diagnostics checks of level-1 residuals and level-2 random effects are provided in Appendix V Figure S10.

Effect modification by birthweight and adjustment for early life factors

In the first step, RWG and interactions between RWG and both age terms were included as fixed effects to estimate the mean effect of RWG on later BMI trajectories (model 1). Potential confounders were controlled for in model 2, including maternal BMI, maternal smoking during pregnancy, infant feeding (i.e. duration of exclusive breastfeeding and early introduction of solid foods), family SECs (i.e. maternal education and family income) and ethnicity.

After testing for the interaction between RWG and birthweight group (p<0.001), models were stratified by birthweight group (i.e. SGA/AGA/LGA) (model 3). Difference in mean BMI between RWG and non-RWG groups with 95% confidence interval at each age was estimated. Estimated BMI trajectories for each subgroup were mapped onto International Obesity Task Force (IOTF) BMI reference bands to illustrate their BMI status at each age. To remove the “end effects” caused by sparse data, instead of the full observed age range (4.4 - 15.3 years), a restricted age range from 5 to 14 years was used for plotting the trajectories.

Sensitivity analyses

To assess whether the associations between RWG and BMI were affected by the choice of growth references used to derive the RWG variable, models were repeated by using an alternative RWG variable derived using UK 1990 growth references (232). To assess the robustness of findings on effect modification by birthweight group, the cut-offs of 20th and 80th percentiles (instead of 10th and 90th percentiles in the main analysis) were used to categorise birthweight SDS into SGA, AGA and LGA groups, which resulted in larger SGA and LGA groups (Table 7.1). Models were repeated using this alternative birthweight group variable.

Table 7.1: Comparison of the birthweight for gestational age variable used in the main and sensitivity analyses, based on UK-WHO growth references

Analysis	Cut-offs used	% of children in each group
Main analysis	10th (i.e. -1.28 SDS) and 90th (equiv. 1.28 SDS) percentiles	SGA (<10th percentile): 9.1% AGA (≥10th percentile, ≤90th percentile): 81.0% LGA (>90th percentile): 9.9%
Sensitivity analysis	20th (i.e. -0.842 SDS) and 80th (i.e. 0.842 SDS) percentiles	SGA (<20th percentile): 19.2% AGA (≥20th percentile, ≤80th percentile): 62.0% LGA (>80th percentile): 18.8%

7.3 Results

Prevalence of RWG

Overall, 45% of boys and 40% of girls experienced RWG between birth and 3 years respectively. The prevalence was highest among boys and girls born small for gestational age (88% and 84% respectively), followed by those born appropriate (45% and 39%) and large for gestational age (8% and 5%) (Figure 7.1).

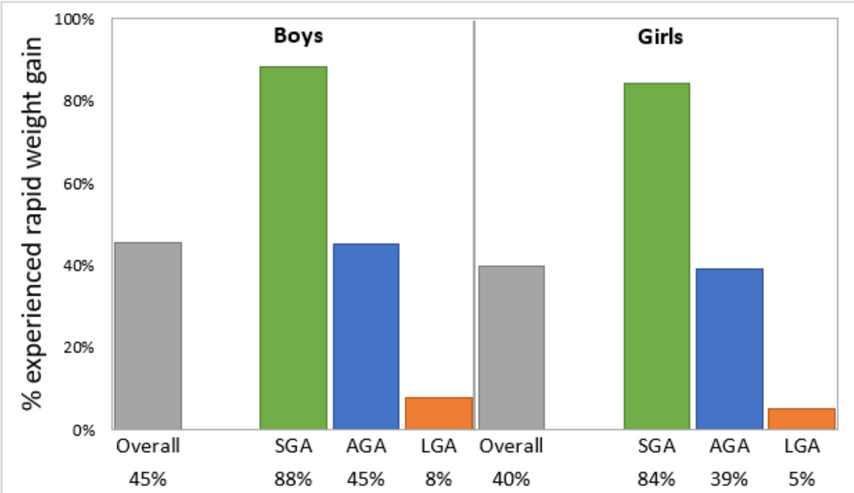

Figure 7.1: Proportion of children experienced RWG between birth and 3 years in each gender and birthweight group, unweighted

SGA/AGA/LGA: small/appropriate/large for gestational age. RWG: rapid weight gain, defined as a change in weight z-scores greater than 0.67 SDS.

Participant characteristics by RWG group

Compared with those in the non-RWG group, children who had RWG were more likely to be first-borns, never exclusively breastfed and from minority ethnic backgrounds (Table 7.2). Their mothers had a slightly lower BMI pre-pregnancy and were more likely to smoke during pregnancy, have no formal academic qualifications, and come from a family with income in the lowest quintile.

BMI trajectories by RWG group

Figure 7.2 shows estimated BMI trajectories for RWG and non-RWG groups mapped onto IOTF BMI reference bands. Mean BMI trajectories for both groups were in the IOFT healthy weight reference range. Children who experienced RWG on average had higher mean BMI than their sex-specific counterparts who did not experience RWG, with a difference of 0.75 kg/m^2 (95% CI: 0.66, 0.84) and 0.89 kg/m^2 (0.79, 0.99) at 5 years for boys and girls respectively. The BMI difference between RWG and non-RWG widened with age slightly to 1.36 kg/m^2 (1.16, 1.56) and 1.77 kg/m^2 (1.54, 1.99) at 14 years. Adjusting for potential confounders did not alter these estimated differences (Table 7.3 Model 2).

Table 7.2: Mean (SD) and frequency (%) for maternal and child characteristics by RWG group (total *n*=10 637)

	non-RWG* (*n*=6 137)	RWG* (*n*=4 500)	***P***†
Birthweight for gestational age			<0.001
SGA	130 (2.1%)	801 (17.8%)	
AGA	5010 (81.6%)	3635 (80.7%)	
LGA	997 (16.2%)	64 (1.4%)	
Maternal pre-pregnancy BMI (kg/m^2)	23.81 (4.41)	23.61 (4.40)	0.01
Any maternal smoking in pregnancy			<0.001
No	5029 (82.0%)	3204 (71.2%)	
Yes	1108 (18.1%)	1296 (28.8%)	
Duration of exclusive breastfeeding			0.011
None	1858 (30.3%)	1427 (31.7%)	
0 – 4 months	4034 (65.7%)	2938 (65.3%)	
4 months or longer	245 (4.0%)	135 (3.0%)	
Early introduction to solid foods (<4 months)			0.52
Yes	2252 (36.7%)	1624 (36.1%)	
No	3885 (63.3%)	2876 (63.9%)	
Mother's highest academic qualifications			<0.001
Diploma or degree	1801 (29.4%)	1197 (26.6%)	
A-level	666 (10.9%)	450 (10.0%)	
GCSE grades A*-C	2117 (34.5%)	1541 (34.2%)	
GCSE grades D-G	600 (9.8%)	490 (10.9%)	
Others	138 (2.3%)	98 (2.2%)	
None	815 (13.3%)	724 (16.1%)	
Family income quintiles			<0.001
Lowest quintile	1074 (17.5%)	973 (21.6%)	
Second quintile	1297 (21.1%)	938 (20.8%)	
Third quintile	1270 (20.7%)	857 (19.0%)	
Fourth quintile	1274 (20.8%)	923 (20.5%)	
Highest quintile	1222 (19.9%)	809 (18.0%)	
Ethnicity			<0.001
White	5503 (90.0%)	3798 (84.4%)	
South Asian	339 (5.5%)	369 (8.2%)	
Black	71 (1.2%)	135 (3.0%)	
Others	224 (3.7%)	198 (4.4%)	

* Values are unweighted n (%).
† *p*-value for difference between RWG and non-RWG groups based on *t*-test for continuous variables and on chi-squared test for categorical variables. RWG: rapid weight gain; SGA/AGA/LGA: small-/appropriate-/large-for-gestational age.

BMI trajectories by RWG and birthweight group

Similar results were found in the analysis stratified by birthweight group (Figure 7.3): within each birthweight category, children who had RWG in early life had a higher mean BMI trajectory than their counterparts in the non-RWG group; the BMI difference between RWG and non-RWG groups in general increased with age from 5 to 14 years, except for SGA boys (Table 7.3 Model 3). The RWG-BMI association was stronger in the LGA group than in the AGA and SGA groups. For example, the estimated BMI difference between RWG and non-RWG groups was 3.5 kg/m^2 (2.3, 4.8) in the LGA group, compared with 1.7 kg/m^2 in the AGA group and 0.7 kg/m^2 in the SGA group. These patterns were more evident in girls than in boys. Children who were born LGA and had RWG in early life had BMI trajectories exceeding IOTF cut-offs for overweight, and in girls exceeding cut-offs for obesity at some ages.

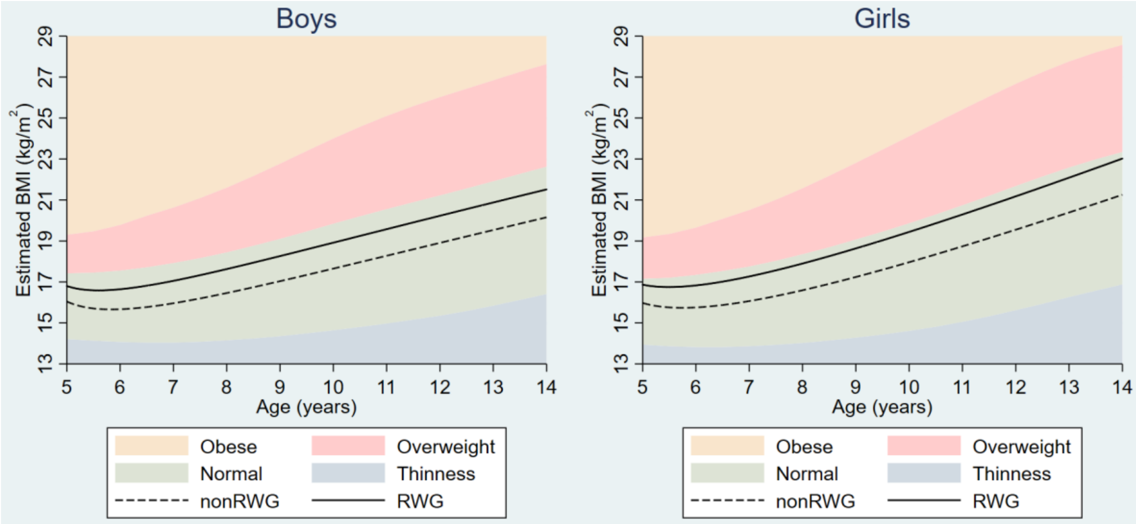

Figure 7.2: BMI trajectories (5-14 years) by RWG group and IOTF BMI reference bands
Estimated from unadjusted mixed effects fractional polynomial models. RWG: rapid weight gain; IOTF: International Obesity Task Force.

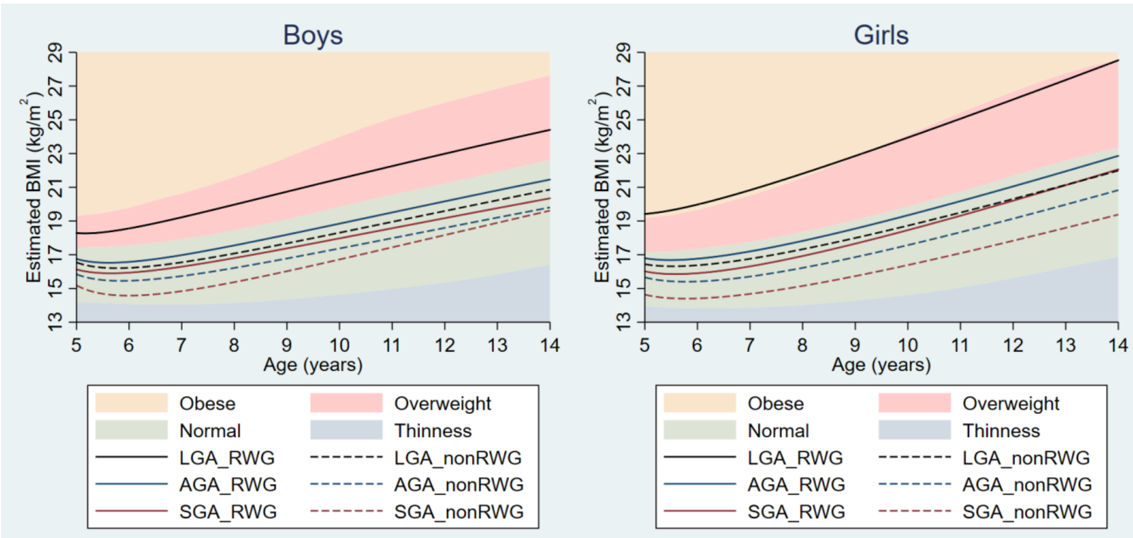

Figure 7.3: BMI trajectories (5-14 years) by RWG and birthweight groups, mapped onto IOTF BMI reference bands
Estimated from mixed effects fractional polynomial models, adjusted for maternal pre-pregnancy BMI, maternal smoking during pregnancy, duration of exclusive breastfeeding, early introduction of solid foods, and ethnicity. RWG: rapid weight gain; IOTF: International Obesity Task Force.

Sensitivity analysis

Sensitivity analysis using alternative RWG variable which was derived using UK 1990 growth references showed a slightly lower prevalence of RWG (40% in boys and 37% in girls). Findings on the association between RWG and BMI across birthweight groups were largely similar to those in the main analysis (Appendix V Table S23). When birthweight for gestational age groups were categorised using the cut-offs of 20th and 80th percentiles (i.e. 0.842 SDS), the association between RWG and BMI remained stronger in the LGA group compared with the AGA and SGA groups (Appendix V Figure S11). The estimated mean BMI trajectories for LGA boys and girls who experienced RWG between birth and 3 years remained in the IOTF overweight range.

Table 7.3: Estimated mean BMI difference at each age between RWG and non-RWG (reference) groups, from unadjusted and adjusted mixed effects fractional polynomial models

	Model 1		**Model 2**		**Model 3 (stratified analysis)**					
	Unadjusted		Adjusted		SGA		AGA		LGA	
age	diff	95%CI	diff	95%CI	diff	95%CI	diff	95%CI	diff	95%CI
Boys										
5	0.8	(0.7, 0.8)	0.8	(0.7, 0.9)	1.0	(0.4, 1.5)	0.9	(0.8, 1.0)	1.7	(1.1, 2.3)
6	1.0	(0.9, 1.1)	1.0	(0.9, 1.1)	1.4	(0.9, 1.9)	1.1	(1.0, 1.2)	2.3	(1.8, 2.9)
7	1.1	(1.0, 1.2)	1.1	(1.0, 1.2)	1.5	(0.9, 2.1)	1.2	(1.1, 1.4)	2.7	(2.0, 3.3)
8	1.2	(1.1, 1.3)	1.2	(1.0, 1.3)	1.4	(0.7, 2.1)	1.3	(1.2, 1.5)	2.9	(2.2, 3.6)
9	1.2	(1.1, 1.4)	1.2	(1.1, 1.3)	1.4	(0.6, 2.1)	1.4	(1.3, 1.6)	3.1	(2.3, 3.9)
10	1.3	(1.1, 1.4)	1.3	(1.1, 1.4)	1.3	(0.4, 2.1)	1.5	(1.3, 1.6)	3.2	(2.3, 4.1)
11	1.3	(1.1, 1.5)	1.3	(1.1, 1.5)	1.1	(0.3, 2.0)	1.5	(1.4, 1.7)	3.3	(2.3, 4.3)
12	1.3	(1.2, 1.5)	1.3	(1.1, 1.5)	1.0	(0.1, 2.0)	1.6	(1.4, 1.8)	3.4	(2.4, 4.5)
13	1.3	(1.2, 1.5)	1.4	(1.2, 1.5)	0.9	(-0.2, 1.9)	1.6	(1.4, 1.8)	3.5	(2.3, 4.6)
14	1.4	(1.2, 1.6)	1.4	(1.2, 1.6)	0.7	(-0.4, 1.8)	1.7	(1.4, 1.9)	3.5	(2.3, 4.8)
Girls										
5	0.9	(0.8, 1.0)	0.9	(0.8, 1.0)	1.4	(0.9, 1.8)	1.1	(1.0, 1.2)	3.0	(2.3, 3.7)
6	1.1	(1.0, 1.2)	1.1	(1.0, 1.2)	1.5	(1.1, 1.9)	1.4	(1.3, 1.5)	3.6	(2.9, 4.3)
7	1.2	(1.1, 1.3)	1.2	(1.1, 1.3)	1.6	(1.1, 2.1)	1.5	(1.4, 1.6)	4.1	(3.3, 4.8)
8	1.3	(1.2, 1.4)	1.3	(1.2, 1.5)	1.8	(1.2, 2.3)	1.6	(1.5, 1.7)	4.5	(3.6, 5.4)
9	1.4	(1.3, 1.5)	1.4	(1.3, 1.6)	1.9	(1.3, 2.6)	1.7	(1.5, 1.8)	4.9	(3.9, 5.8)
10	1.5	(1.3, 1.6)	1.5	(1.4, 1.7)	2.1	(1.4, 2.8)	1.8	(1.6, 1.9)	5.2	(4.2, 6.3)
11	1.6	(1.4, 1.7)	1.6	(1.4, 1.8)	2.2	(1.5, 3.0)	1.8	(1.7, 2.0)	5.6	(4.4, 6.7)
12	1.6	(1.4, 1.8)	1.7	(1.5, 1.9)	2.4	(1.5, 3.2)	1.9	(1.7, 2.1)	5.9	(4.6, 7.2)
13	1.7	(1.5, 1.9)	1.7	(1.5, 1.9)	2.5	(1.6, 3.5)	2.0	(1.8, 2.2)	6.2	(4.8, 7.7)
14	1.8	(1.5, 2.0)	1.8	(1.6, 2.0)	2.7	(1.6, 3.7)	2.0	(1.8, 2.3)	6.5	(4.9, 8.1)

*Values are estimated mean BMI differences with 95% confidence interval (CIs) at each age in kg/m^2. SGA/AGA/LGA: small/appropriate/large for gestational age. Model 1 is the unadjusted model. Model 2 adjusted for maternal pre-pregnancy BMI, maternal smoking during pregnancy, duration of exclusive breastfeeding, early introduction of solid foods, and ethnicity. Model 3 is model 2 stratified by birthweight group.

7.4 Discussion

Summary of key findings

There are four key findings: 1) boys and girls who experience RWG between birth and 3 years on average had higher BMI between 5 and 14 years than their non-RWG counterparts, but their average BMI trajectories remained in the healthy weight range. 2) Mean BMI differences between RWG and non-RWG groups increased slightly with age and were largely unaltered after controlling for potential confounders. 3) The association between RWG and BMI was substantially stronger in the LGA group, compared with the SGA and AGA groups. 4) Children who were born LGA and subsequently experienced RWG had mean BMI trajectories in the IOTF overweight range.

Comparison with other studies

Despite a large body of cross-sectional studies documenting the positive association of early-life RWG with later BMI, few studies have used longitudinal data to examine the association between RWG and BMI trajectories. In the present study, RWG between birth and 3 years was associated with higher BMI in childhood and adolescence, with the estimated BMI differences between RWG and non-RWG groups increasing with age, especially in childhood (5-11 years) These findings are in line with previous studies. A study of 206 term AGA babies in Germany showed that RWG was associated with higher BMI at 2 and 7 years, by about 1.8 kg/m^2 and 2.7 kg/m^2 respectively (285). In a nationally representative Swedish cohort, Thoren and colleagues found that the association between RWG (birth - 1 year) and risk of overweight was slightly stronger at 18 years than at 16 years (odds ratio=1.63 vs. 1.47) (291).

The present study illustrated that the association between RWG and BMI was substantially stronger in the LGA group, compared with the SGA and AGA groups. Children who were born LGA and subsequently experienced RWG had mean BMI trajectories in the IOTF overweight range, and in girls in the obesity range at some ages. Similar findings persisted in the sensitivity analysis using a more conservative cut-off of '>0.84 SDS' to define LGA, instead of '>1.28 SDS' in the main analysis. Limited studies have examined how the association between infant RWG and later BMI differs across birthweight groups. Only three previous studies were identified and the findings were inconsistent. Two papers by Stettler and colleagues published in 2002 found no evidence of effect modification by birthweight in the US and Seychelles (167, 168), which may be due to a lack of statistical power (169). A later study using data from the 1997 Hong Kong birth cohort found that the effect of infant RWG on later childhood BMI was greater among term boys in the low and higher birthweight groups than in the normal birthweight group (169). The slight discrepancy between the present and their studies may be partly attributable to different study populations and birthweight categories used. Children were evenly divided into low, medium and high birthweight groups in their study (169). Whereas in the present study, birthweight groups were defined using conventional cut-offs; SGA were defined as infants below the 10^{th} percentile of birthweight for gestational age and LGA as above the 90^{th} percentile. Percentiles are widely used in clinical and public health settings for monitoring and assessing infant growth, therefore, have greater implications in practice. Indeed, birthweight for gestational age percentiles are included in UK-WHO growth charts used for preschool infants and toddlers in primary and secondary care (292). Due to the limited number of studies on this subject, future study on the RWG-BMI association across different birthweight groups in other populations is needed.

Public health implications

The potential mechanism of the positive RWG-BMI association may be due to that RWG in infancy programmes changes in hormonal axes which influence long-term regulation of appetite and energy expenditure (293, 294). While potential benefits of infant RWG for neurocognitive development among preterm babies is well accepted, evidence on the benefits for term SGA babies to 'catch up' growth in high-income settings is limited and not conclusive (295-297). The present study shows that the mean child-to-adolescent BMI trajectories of LGA children with infant RWG exceeded international references for overweight. Given the strong association between obesity and cardio-metabolic health (298), it is of public health significance to prevent excessive weight gain in infancy, especially among those born LGA.

Strengths and limitations

This is the first study, to my knowledge, to investigate the effect of RWG in early-life on child-to-adolescent BMI trajectories across birthweight groups. This analysis benefited from the use of IOTF BMI reference bands to facilitate visual comparison. A number of potential confounders were collected in the MCS and considered in the analysis. A few limitations need to be considered. There was a small proportion of participants with missing data on covariates who were excluded from the analysis. Although the characteristics of these excluded participants were slightly different from the analysis sample, the distributions of RWG and BMI were very similar between the total eligible sample and the analysis sample. Hence, the impact of missing data on the estimates is likely to be small. Weight was first measured at 3 years during follow up, therefore the period from birth to 3 years was used to define RWG and it was not possible to further investigate any other critical period of RWG. Caution is needed when comparing results from the present study with other studies which observed RWG over a shorter period of time (e.g. in the first 6 months, 1 year or 2 years). It was suggested that the effect of RWG on later adiposity is greater when RWG is measured over longer periods (163).

7.5 Conclusion

In conclusion, children who experienced RWG between birth and 3 years had higher BMI at 5 years and a slightly more rapid BMI gain between 5 and 14 years. The association between RWG and BMI was stronger for children born LGA (than those born AGA or SGA), with mean BMI trajectories exceeding international references for overweight. It is of public health importance to prevent excessive infant weight gain, especially among children who had an adequate growth *in utero* (i.e. born AGA or LGA).

8 SUMMARY OF FINDINGS, IMPLICATIONS AND CONCLUSIONS

This thesis aimed to investigate ethnic differences in height and adiposity growth in contemporary UK children and the role of early life factors using data from the Millennium Cohort Study (MCS), to understand how early life factors act on later health for different ethnic groups. A wide range of factors that are identifiable by infancy were considered. This final chapter summarises main findings reported throughout the thesis, discusses the key strengths and limitations, and considers the implications of these findings in light of the wider social and policy context.

8.1 Summary of principal findings

Although South Asian children were born lighter at birth and had considerably shorter parents, they had similar height growth trajectories to White children, except that South Asian girls were slightly shorter in adolescence. For BMI, South Asians had a lower BMI than White children at 3 years with the difference reducing with age. From 10 years onwards, South Asian boys had a similar BMI to White children and girls remained to have a slightly lower BMI. However, the body fat measure revealed that South Asian boys had much higher levels of adiposity at 7, 11 and 14 years, and girls at 7 and 11 years.

Black African-Caribbean children had higher height and BMI trajectories than White and South Asian children. Their taller height was not explained by prenatal factors, birthweight and family socio-economic circumstances explored in this thesis. The BMI difference between Black African-Caribbean and White children emerged at 5 years and widened with age in childhood, but narrowed slightly in boys between 11 and 14 years. These differences were nearly fully explained by Black African-Caribbean children's taller height, less advantaged family socio-economic circumstances, and especially higher maternal BMI and greater infant weight gain. The pattern of differences in waist circumference and body fat between Black African-Caribbean and White children was consistent with the pattern seen in BMI.

Rapid weight gain in the first 3 years of life was associated with higher BMI trajectories between 5 and 14 years. The association was substantially stronger for children who were born large at birth (compared with those who had an appropriate or lower birthweight). Large-for-gestational-age children who experienced rapid weight gain had mean BMI trajectories exceeding international references for overweight throughout childhood and adolescence.

While lower family income and maternal education were associated with higher BMI in the White and South Asian groups, they were associated with lower BMI in the Black African-Caribbean group. Socio-economic differences in BMI were established as early as 3 years, such as in White and South Asian children, and in general widened with age into adolescence.

8.2 Key strengths and limitations of current thesis

Strengths and limitations of the methods and data used in addressing each of the research aims were discussed previously in relevant chapters (Chapters 4 to 7). The overarching strengths and limitation of this thesis are discussed here.

Strengths

One of the key strengths of this thesis is the use of data from a large, nationally representative cohort study, which oversampled children from minority ethnic backgrounds. There are few epidemiological data sources available in the UK which support the investigation of ethnic differences in child growth and health, as summarised in Table 8.1. Many previous studies on ethnic differences in child growth are restricted by small sample sizes (127), cross-sectional nature of the data (143), and their short follow-up periods (81, 145). The MCS is considered to be the most comprehensive longitudinal data source available in the UK, which provides an adequate representation of children from South Asian and Black African-Caribbean backgrounds. Using longitudinal anthropometric data, it was possible to investigate the development of ethnic differences in child growth (e.g. the age when ethnic differences emerged) and examine how the patterns change with age (i.e. the age effect). In longitudinal studies such as the MCS, respondents are asked to provide information on their current or relatively recent circumstances, which is less subjected to recall errors and bias compared with cross-sectional studies (299). For example, maternal pre-pregnancy weight and breastfeeding practice used in this thesis were collected at baseline interviews when children were about 9 months old. The use of MCS data also makes the findings broadly generalisable to the wider population. Although the MCS also oversampled children living in less advantaged background, family socio-economic circumstances were taken into account in the data analyses.

Table 8.1: Summary of key studies with an ethnically diverse sample in the UK

Study name	Description
National Child Measurement Programme (NCMP) (300)	The NCMP measures the height and weight of over one million children in Reception (aged 4-5 years) and Year 6 (aged 10-11 years) each year in primary schools in England.
Health Survey for England (HSE) (301)	The HSE is an annual cross-sectional survey, which samples a representative proportion of the England population, around 8,000 adults and 2,000 children. Boosted sample for ethnic minorities were included in some years, i.e. in 1999 and 2004.
Born in Bradford study (BiB) (302)	The BiB study is a cohort study which was established in 2007 and tracks the health and wellbeing of over 13,500 children and their parents in the Bradford area of England. Around 50% of the cohort members are of South Asian origin, 87% of whom are from Pakistani origin.
Millennium Cohort Study (MCS) (303)	The MCS is a nationally representative, longitudinal study of over 19,000 children across four UK countries which oversampled children from ethnic minority and less advantaged socio-economic backgrounds. Cohort members were recruited into the study at 9 months in 2001/03 and last followed up at 17 years in 2018/19
Research with East London Adolescence Community Health Survey (RELACHS) (304)	The RELACHS is a school-based longitudinal study of health and wellbeing of adolescents from 3 deprived boroughs of East London, with about 73% of the participants from minority ethnic backgrounds. Participants were recruited into the study at Year 7 (aged 11-12 years) and Year 9 (aged 13-14 years) in 2003 and followed up for two years.
The Child Heart And Health Study in England (CHASE) (305)	The CHASE is a school-based, cross-sectional survey of cardio-metabolic health among 5,000 Year 5 children (aged 9-10 years) living in London and the Midlands. Data collection was conducted between 2004 and 2007. Balanced numbers of children of South Asian, Black African-Caribbean and White European origin were invited to take part.
The Determinants of Adolescent Social well-being and Health Study (DASH) (306)	The DASH is a longitudinal study of social and biological influences on ethnic differences in health and well-being. Over 6,500 children from inner London boroughs were recruited at age 11–13 years in 2003, and were last followed up in 2012/14.
The Health and Behaviour in Teenagers Study (HABITS) (307, 308)	The HABITS is a 5-year longitudinal study of health and behaviour of over 5,000 children from South London. They were assessed annually from ages 11 to 16 years (Years 7 to 11). The sampling procedure was designed to ensure a socio-economically and ethnically diverse sample. Data collection started in 1999 and was completed in 2003.

*****Adapted from National Obesity Observatory – *Obesity and Ethnicity* (127).

This thesis benefited from a wide range of early life factors collected in the MCS, such as parental characteristics, socio-economic circumstances, maternal behaviours during pregnancy and infant feeding practices, which provides a unique opportunity to investigate ethnic differences in growth trajectories and influencing factors (95, 115, 272, 273). To my knowledge, this is the first study to investigate 1) ethnic differences in growth trajectories for height, from early childhood to adolescence, 2) the effect of rapid weight gain in early-life on BMI trajectories across different birthweight groups, and 3) social disparities in BMI trajectories in different ethnic groups. This study is one of the very few studies, which demonstrated strikingly distinct socio-economic patterns in BMI across ethnic groups – in Black African-Caribbean children, higher family income and better maternal education were associated with higher BMI. Only one previous study, of which I am aware, used data from the NCMP and reported that the variation in BMI by area deprivation in London was smaller in South Asian and Black children than in White children (192). In addition to BMI, other adiposity measures are available at some ages in the MCS. This permits the investigation of ethnic differences in body composition to triangulate findings on ethnic differences in body adiposity and potential health implications.

Another strength of this thesis is the use of mixed effects fractional polynomial models to capture the complex non-linear age trends for height and BMI in childhood and adolescence. There are several advantages of using fractional polynomial models. Fractional polynomial models are considerably more flexible to capture non-linear growth trends than polynomial models (207). The smoothed curves can be estimated which are easy to interpret visually and more biologically plausible than piecewise linear splines. Using fractional polynomial functions, it was also possible to examine the age when differences in outcome between groups started to emerge. However, one limitation of fractional polynomial models is that the coefficient estimates for age terms are not easy to interpret, compared with other methods such as piecewise linear spline models where a set of slopes are estimated (207). Therefore, throughout this thesis, results from fractional polynomial models have been presented in the form of both estimated mean trajectories by subgroup of interest and differences in mean outcome between subgroups at each age.

A common problem in longitudinal studies is sample attrition due to loss in follow-ups and missing data due to non-response. Several steps were taken to mitigate the potential for bias and loss of information due to missing data. Missing data in the outcome variables was dealt with by using mixed effects models in longitudinal analysis or using surveys weights in cross-sectional analysis. The mixed effects models take into account within-individual correlations and allow individuals with missing data in outcome variables at some ages to be included in the analysis under a missing at random assumption (309). Cross-sectional analyses were weighted using sampling and attrition weights provided by the MCS. Missing data in covariates was dealt with by using multiple imputation with chained equation. However, when the proportion of missing data was small (in Chapter 7), only complete cases were used in the final analysis, with the expectation that the impact of missing data on estimates is likely to be small.

Limitations

Several limitations of this thesis need to be acknowledged. Although the MCS oversampled children from minority ethnic backgrounds, the sample sizes for some ethnic groups were relatively small, compared to White children. This limited statistical power to test between-group differences and associations. As a result, this thesis considered six main ethnic groups in the UK and the aggregated ethnic groups were used in most of the analyses. Preliminary analyses showed there was some variation between ethnic subgroups. For example, Pakistani and Bangladeshi children were slightly shorter and heavier than Indian children. These results were provided in the appendices for relevant chapters (Chapter 4 and Chapter 6). The MCS only included children who were born and living in the UK at 9 months, therefore recent immigrant populations, asylum seekers and refugees were not included in the study.

Anthropometric measurements were conducted from 3 years onwards, therefore, growth data in infancy were not available, which prevents the ability to investigate height and BMI trajectories from birth. Additionally, the measurements of BMI were not sufficiently frequent to further characterise BMI trajectories, such as age and BMI at adiposity rebound in childhood, and to investigate differences in these characteristics between groups. The analysis on ethnic differences in adiposity would have benefited from body fat measured from more accurate methods such as deuterium dilution (275). In-built equations for predicting body fat in the bioelectrical impedance analysis machines were validated largely on White populations (281). There is a concern that it may not be appropriate for comparison across ethnic groups (275, 281). However, due to its low cost and convenience, it remains to be a popular choice for measuring body fat in large population studies.

A further limitation is that most of the early life factors, including maternal smoking during pregnancy and pre-pregnancy weight, were recalled and self-reported when the child was 9 months old, which may be subjected to recall and report bias. Important factors, such as diet and physical activity, are also collected in the MCS. However, only a subset of cohort members has valid accelerometer data (255) and the sample sizes for minority ethnic groups are substantially smaller. Therefore, physical activity variables were not considered in this thesis. Methods for dietary data collection changed across sweeps and only crude measures of diet patterns and quality are available. For example, at 3-year visits, parents were asked to report the frequency in a week that their child consumed fresh fruit or vegetables at least once a day; between 5- and 11-year visits, parents were asked to report the average number of portions of fruit their child consumed per day; and in 14-year visits, the cohort members themselves were asked how frequently they had at least two portions of fruit per day. During preliminary analysis, available dietary factors were explored, but they explained little of the ethnic differences in BMI. It was not clear whether it was due to the crude nature of these variables, or the small variation in diet across ethnic groups. Therefore, they were not included in the final analysis. Parental immigration and acculturation were not explored in this thesis. Better understanding of how immigration and acculturation interact with income and other social factors and how they may impact on dietary practices and health behaviours may help explain the positive association between socio-economic factors and BMI in Black African-Caribbean children. Moreover, some other important early life factors such as maternal gestational weight gain were not collected in the MCS and therefore were not explored.

This thesis set out to investigate ethnic differences in height and adiposity growth and used mixed effects fractional polynomial models. Due to methodological complexity, it was not possible to incorporate mediation analysis into the growth models. However, future studies using mediation analysis would be beneficial to shed light on the pathways of the development of these ethnic differences in height and adiposity. Furthermore, there may be reverse causality in the association between some of the early life factors. For example, while infant feeding affects growth, parents may alter feeding practices in response to infant size (310). Additionally, possibility of unmeasured confounding factors cannot be ruled out which may contribute to the associations observed in this thesis.

8.3 Discussion and implications for population health, health inequalities and policies

The UK population is becoming increasingly diverse (20). Minority ethnic groups are projected to make up 20% of the UK population by 2051 (4). There is considerable variation in health across socio-demographic groups in the UK (22). The pathway to the development of health inequalities is a complex interplay of factors at multiple levels of influences and across different stages of life (22, 30, 31). The prevalence of chronic conditions is relatively low in children compared with adult populations (311, 312). Child growth serves as a good indicator of general health for the study of early life influences.

Ethnicity is a state of belonging to a social group based on shared geographical region, nationality or cultural traditions (1). The concept of ethnicity is fluid and subjective. The ethnic group that an individual self-identifies or is identified by the society may change over time. In population studies, ethnicity reflects differences in social experiences and cultural traditions (such as health beliefs and dietary practices) and, to some extent, genetic variations between groups. Ethnicity is closely associated with several socio-economic factors.

Many of the minority ethnic groups are more likely to have family income in the lowest two quintiles and a higher proportion of mothers without any formal academic qualification, especially Pakistani and Bangladeshi (Chapter 3). The Indian group shares similar socio-economic characteristics as the White group, which may be explained by their longer residence in the UK, compared with other South Asian groups. In the MCS, about 41% of mothers in the Indian group were born in the UK (i.e. second-generation immigrants or later), compared with 38% in the Pakistani group and only 10% in the Bangladeshi group[1]. Indians are more likely to be in professional positions and have experienced more social upward mobility; there is also a higher proportion of Indian women in the labour market, which contributes to their higher household income (7). By contrast, large waves of Bangladeshi immigrants arrived during the 1980s at a time of a rising unemployment rate in the UK (313), which may have impacted their occupational mobility. Mothers of minority ethnic backgrounds are less likely to smoke during pregnancy and are more likely to breastfeed their children in accordance with national guidelines than the White group (Chapter 3). However, Hawkins *et al.* (314) found that these positive behaviours among minority ethnic groups worsen with their time spent in the UK to become more similar to those found in the general population.

Contemporary South Asian children in the UK were found to have a comparable height growth in childhood as their White peers in Chapter 4, despite the fact that South Asian parents were considerably shorter. This suggests that South Asian children may have experienced a greater intergenerational height gain, possibly owing to the improvements in the living conditions compared with their parents' growth environment (235, 315). Older UK studies of children born in the 1970s and 1980s tend to find South Asian children being shorter than their White peers (78, 85), which may suggest that ethnic differences in growth conditions in the UK have also improved over the decades. Additional analysis showed that Indian children were the tallest and Bangladeshi children were the shortest among South Asian subgroups. This observation is consistent with the pattern of socio-economic circumstances and length of residence - the Indian group shares more similarities with the White group and have longer residence in the UK than the other two South Asian groups. Black African-Caribbean boys and girls were taller than their counterparts from other ethnic groups. Adjustment for important early life factors which influence height growth did not explain these ethnic differences in height. They may be explained by genetic variations captured in the ethnicity variable.

Compared with White children, children of minority ethnic groups on average have a lower birth weight than White children and are more likely to experience rapid postnatal growth (Chapter 3), which is associated with obesity and poorer cardio-metabolic health profile in later life (316-

[1] Among singletons in the MCS, the proportion of mothers who were born in the UK is 95% in the White group, 41% in the Indian group, 38% in the Pakistani group, 10% in the Pakistani group, 78% in the Black Caribbean group and 18% in the Black African group.

318). Chapter 7 shows that the effect of rapid weight gain between birth and 3 years on later BMI trajectories was greater in children born large-for-gestational-age than those born appropriate- and small-for-gestational-age. However, the implications of the "born small and grow fast in infancy" pattern for cardiovascular health outcomes may be different. Cohort studies with longer follow-ups (319, 320) found that the risk for coronary heart disease was greatest in adults who were small or thin at birth but subsequently in the upper BMI distribution in childhood. This growth pattern is more common in ethnic minorities and may help to explain their greater rates of heart diseases and type 2 diabetes in the UK (22, 24, 25). Studies to date have not assessed whether this growth pattern has different cardiovascular health implications across ethnic groups. Continued funding is needed to follow up MCS cohort members into adulthood, which would provide a valuable data source to support such investigation.

Importance of early intervention to tackle childhood obesity and reduce health disparities

The prevalence of childhood overweight and obesity remains alarmingly high in the UK, despite government's ambition to curb high levels of overweight and obesity (321-323). In 2016/17, 22.6% of children in Reception year (aged 4-5 years) and 34.3% of children in Year 6 (aged 10-11 years) in England were either overweight or obese (193). Chapter 7 demonstrated the strong tracking of BMI from infancy to childhood and adolescence. Children who had excessive weight gain in the first 3 years of their life continued to have greater BMI between 5 and 14 years. Marked differences in BMI between socio-economic (Chapter 5) and ethnic groups (Chapter 6) were found to emerge at very young ages, as early as 3 years. These findings highlight the importance of early intervention to address risk factors before and in infancy, which will not only contribute to reducing childhood obesity but also reducing health inequalities between socio-demographic groups.

Early years are an important period for intervention. Healthcare professionals, such as health visitors, paediatricians and school nurses, are well placed to deliver key health messages to expectant and new parents, including breastfeeding, healthy eating and lifestyle. Training and support for healthcare professionals to carry out these health conversations are needed. It has been suggested that health visitors may lack the confidence to intervene and raise sensitive issues with families that have infants at risk of developing obesity (324).

The rates of breastfeeding in the UK is one of the lowest in Europe (325). The latest Infant Feeding Survey in 2010 showed that 81% of UK mothers initiated breastfeeding but the rates of breastfeeding declined markedly in the first few weeks (326). Only 17% of mothers were exclusively breastfeeding at four months; and 1% was exclusively breastfeeding at six months (326), which is recommended by the World Health Organisation and the current UK recommendation (327). The high proportion of infants with rapid weight gain in the first 3 years of life and its potential long-term health implications (Chapter 7) support the needs to promote breastfeeding, monitor infant growth and prevent excessive infant weight gain.

Children are spending an increasing amount of time in childcare facilities. In 2017, 95% of children aged 3-4 years in the UK were enrolled in formal care, spending an average of 21.7 hours per week (328). Children in childcare especially those spending a large amount of time in formal care, rely on carers to provide significant proportions of their dietary intakes and physical activity. Therefore, non-healthcare professionals at these settings also have an important role in promoting health messages and to help children form positive dietary and lifestyle behaviours.

A whole-system and life course approach

Obesity, as a consequence of energy imbalance, is determined by a broad range of multi-faceted and inter-related factors, as demonstrated in the Foresight obesity system map (329). There is no single and straightforward solution to tackle higher levels of obesity and a whole-system and life course approach is needed. Indeed, in this thesis, greater BMI in Black African-Caribbean children were largely explained by their higher maternal pre-pregnancy BMI and greater infant weight gain. This finding supports that childhood obesity prevention needs to tackle high rates of obesity in adult population at the same time. In the 2014 Health survey for England, 65% of men and 58% of women were either overweight or obese (194).

The development of ethnic health disparities is equally complex with an interplay of socio-economic factors, biological susceptibility, immigration, racism and discrimination, cultural differences in diet and lifestyles, access to and take-up of health services (22, 30, 31). A number of policies have been developed with the aim to improve health inequalities (27-29). The contribution of wider social determinants is well recognised (27-29). However current health inequalities policies have largely focussed on socio-economic inequalities rather than ethnic inequalities(27-29).

The positive association between socio-economic position and BMI in Black African-Caribbean children suggests that better family socio-economic circumstances may not be universally associated with lower BMI (Chapter 5). The underlying mechanisms are not clear and may be due to that influencing factors of BMI have different a socio-economic pattern in the Black African-Caribbean group, which could be associated with immigration and acculturation.

Evidence from qualitative studies suggests that parents from certain minority ethnic groups, including Black African and older Black Caribbean parents, consider ‘big’ body sizes as desirable and a sign of health and wealth (257). Some US studies found that greater acculturation is associated with higher income (18), but also poorer dietary practices and health behaviours (such as smoking) (13). This aligns with a growing recognition that public health interventions to address obesity and ethnic inequalities need to consider the varying needs of their target population, especially in areas of high ethnic diversity (127, 330). Addressing socio-economic disadvantage will benefit the health and wellbeing of children and families in lower socio-economic positions in many ways, but other approaches may be needed to reduce the higher levels of BMI and obesity among Black children.

8.4 Gaps in knowledge and future research directions

Future research is needed to address the following questions:

1. To what extent are the height and BMI differences between South Asian and White children driven by genetic factors?
2. Given the strong association between child growth and later health, how much can the ethnic differences in growth explain the ethnic differences in cardio-metabolic health?
3. How best to assess body adiposity in children in relation to health risks across different ethnic groups?
4. How best to promote breastfeeding and monitor infant growth in practice and how can it be embedded in existing NHS Healthy Child Programme services?
5. What are the underpinning mechanisms of the positive association between socio-economic circumstances and BMI in Black African-Caribbean children? How does the socio-economic disadvantage across different ethnic groups interact with BMI?

8.5 Concluding remarks

The UK population is becoming increasingly diverse. There is considerable variation in health across ethnic groups. The pathway to the development of health inequalities is a complex interplay of factors at multiple levels of influences and across different stages of life. This thesis used longitudinal data to examine ethnic differences in child growth across ethnic groups with the focus on early life factors identifiable in infancy. Marked differences in BMI and other adiposity measures were found at young ages and several key contributing factors were identified. This thesis contributed to improving our understanding of the development of ethnic inequalities in health from a life course perspective and emphasised the importance of taking a whole system approach with early interventions to reduce childhood obesity and health inequalities.

9 RESEARCH OUTPUTS AND DISSEMINATION RESULTING FROM THIS THESIS

A manuscript based on Chapter 4 (objective 1) has been submitted to the *Longitudinal and Life Course Studies* and accepted for publication. These results were disseminated at the following conferences:

- The Society for the Study of Human Biology Symposium 2016 (poster presentation)
- The Nutrition and Growth conference 2017 (oral presentation)
- The Society for Social Medicine conference 2017 (oral presentation)
- International Society for Developmental Origins of Health and Disease (DOHaD) 2017 (poster presentation)

A manuscript based on Chapter 7 (Objective 4) has been submitted to *the European Journal of Public Health* and accepted for publication. These results were disseminated at the following conferences:

- European Public Health Conference 2018 (oral presentation)
- The Society for Social Medicine conference 2018 (oral presentation)
- The Nutrition and Growth conference 2019 (oral presentation)
- UCL Populations & Lifelong Health Domain Symposium 2019 (oral presentation)

A manuscript based on Chapter 5 (Objective 3) has been submitted to the *Pediatric Obesity* and accepted for publication. These results have been presented at the Society for Social Medicine conference 2019.

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APPENDICES

Appendix I: Supplementary materials for Chapter 2

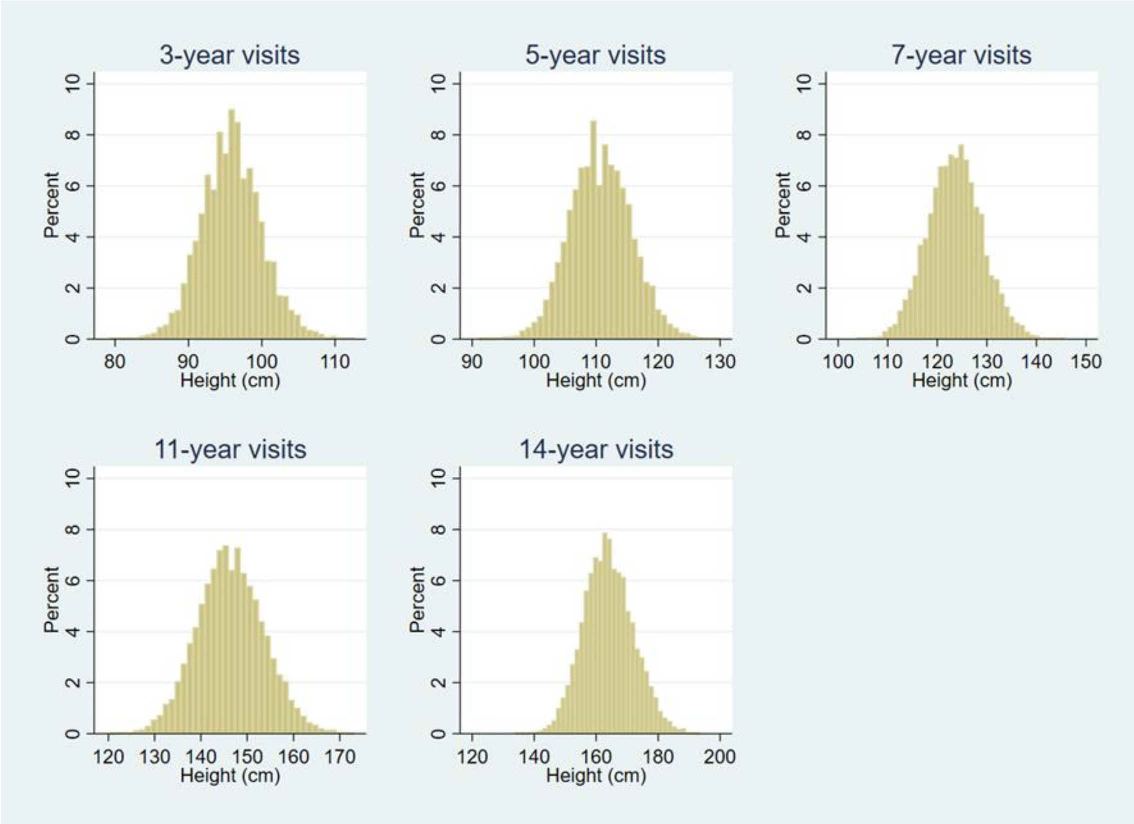

Figure S1: Distribution of observed height (cm) data by sweep

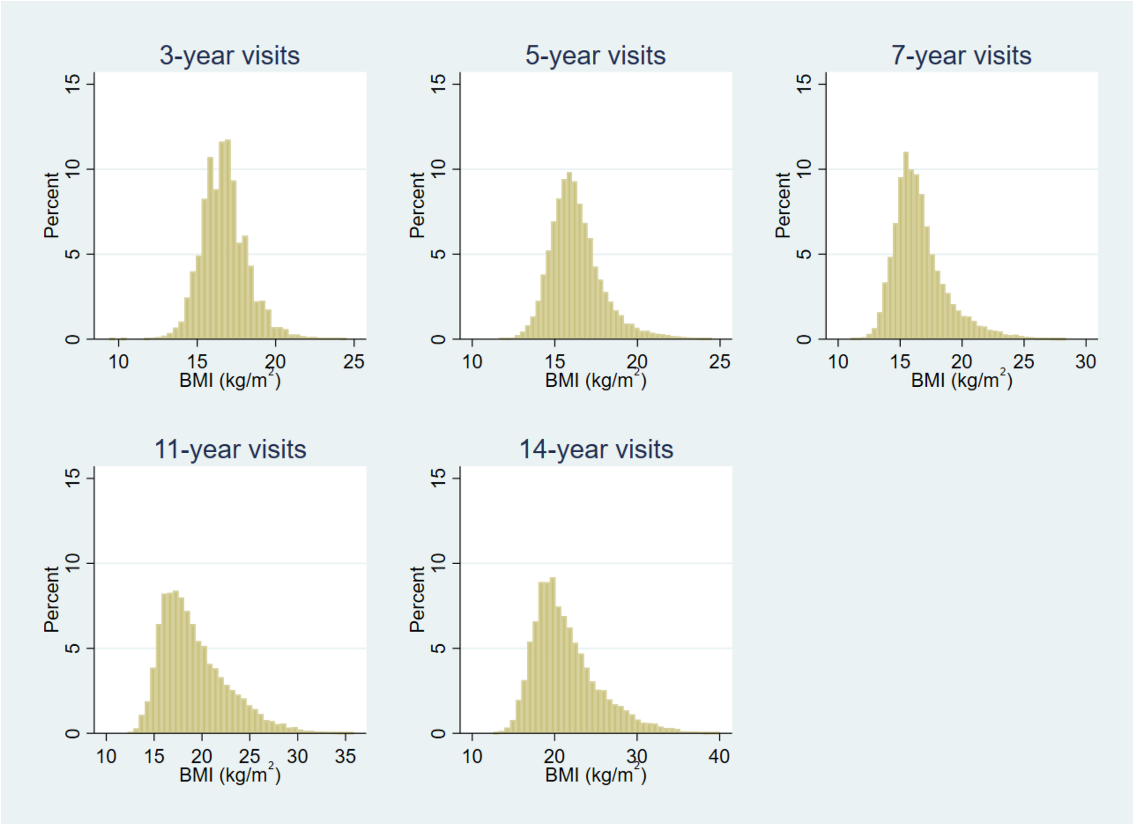

Figure S2: Distribution of observed BMI (kg/m^2) data by sweep
*BMI = Body mass index

Appendix II: Supplementary materials for Chapter 4

Table S1: Height difference (cm) with 95% confidence interval between White and each minority ethnic subgroup at each sweep*

	3 years	5 years	7 years	11 years	14 years
	diff [95% CI]	diff [95% CI]	diff [95% CI]	diff [95% CI]	diff [95% CI]
Boys					
White	ref	ref	ref	ref	ref
Indian	0.6 [0.0, 1.1]	0.8 [0.1, 1.4]	0.6 [0.0, 1.1]	1.4 [0.4, 2.4]	-0.1 [-1.4, 1.2]
Pakistani	0.6 [0.2, 1.0]	1.0 [0.5, 1.5]	0.6 [0.2, 1.0]	0.3 [-0.5, 1.0]	-0.9 [-1.9, 0.1]
Bangladeshi	-0.1 [-0.8, 0.6]	0.6 [-0.2, 1.4]	-0.1 [-0.8, 0.6]	-0.5 [-1.6, 0.7]	-0.8 [-2.3, 0.7]
Black Caribbean	1.3 [0.5, 2.2]	1.8 [0.8, 2.8]	1.3 [0.5, 2.2]	2.4 [0.8, 4.0]	1.2 [-0.9, 3.3]
Black African	2.8 [2.1, 3.4]	3.9 [3.1, 4.6]	2.8 [2.1, 3.4]	4.3 [3.1, 5.4]	2.9 [1.3, 4.6]
Girls					
White	ref	ref	ref	ref	ref
Indian	0.4 [-0.2, 0.9]	0.3 [-0.4, 1.0]	0.4 [-0.2, 0.9]	0.3 [-0.8, 1.4]	-3.2 [-4.2, -2.2]
Pakistani	0.6 [0.2, 1.0]	0.3 [-0.2, 0.8]	0.6 [0.2, 1.0]	-0.5 [-1.3, 0.3]	-2.9 [-3.6, -2.2]
Bangladeshi	0.3 [-0.4, 0.9]	0.2 [-0.6, 0.9]	0.3 [-0.4, 0.9]	-1.4 [-2.6, -0.3]	-5.9 [-6.9, -4.9]
Black Caribbean	2.4 [1.5, 3.3]	3.3 [2.3, 4.3]	2.4 [1.5, 3.3]	5.5 [3.8, 7.2]	2.0 [0.3, 3.7]
Black African	3.9 [3.2, 4.6]	4.3 [3.5, 5.0]	3.9 [3.2, 4.6]	5.9 [4.5, 7.2]	2.3 [1.2, 3.5]

*Based on unweighted linear regression models, adjusting for the actual age at measurements. White group was used as the reference group. Diff: estimated difference.

Table S2: Summary of level-1 residuals from unadjusted mixed effect fractional polynomial models, by ethnicity and sex group

		Level-1 residuals (observed-estimated*), cm					
		Boys			Girls		
Age	Ethnicity	n †	Mean	SD	n †	Mean	SD
3y visits	White	5,838	0.04	0.98	5,691	0.00	1.07
	South Asian	571	-0.03	0.92	531	-0.04	1.05
	Black African/Caribbean	199	-0.02	0.99	169	-0.04	1.13
5y visits	White	6,152	-0.12	1.12	5,859	-0.08	1.14
	South Asian	576	0.07	1.06	552	0.13	1.13
	Black African/Caribbean	212	0.02	1.05	199	0.18	1.12
7y visits	White	5,603	0.14	0.94	5,421	0.13	1.21
	South Asian	504	-0.05	1.07	506	-0.14	1.31
	Black African/Caribbean	191	0.01	0.93	172	-0.25	1.47
11y visits	White	5,263	-0.06	1.17	5,151	-0.08	1.20
	South Asian	537	-0.01	1.30	517	0.04	1.28
	Black African/Caribbean	181	-0.02	1.17	167	0.12	1.34
14y visits	White	4,469	0.03	0.66	4,430	0.04	0.86
	South Asian	488	0.01	0.65	486	-0.01	0.94
	Black African/Caribbean	151	0.01	0.64	149	-0.04	0.89

*Height was predicted based on subject-specific growth trajectories.
†Number of observations available.

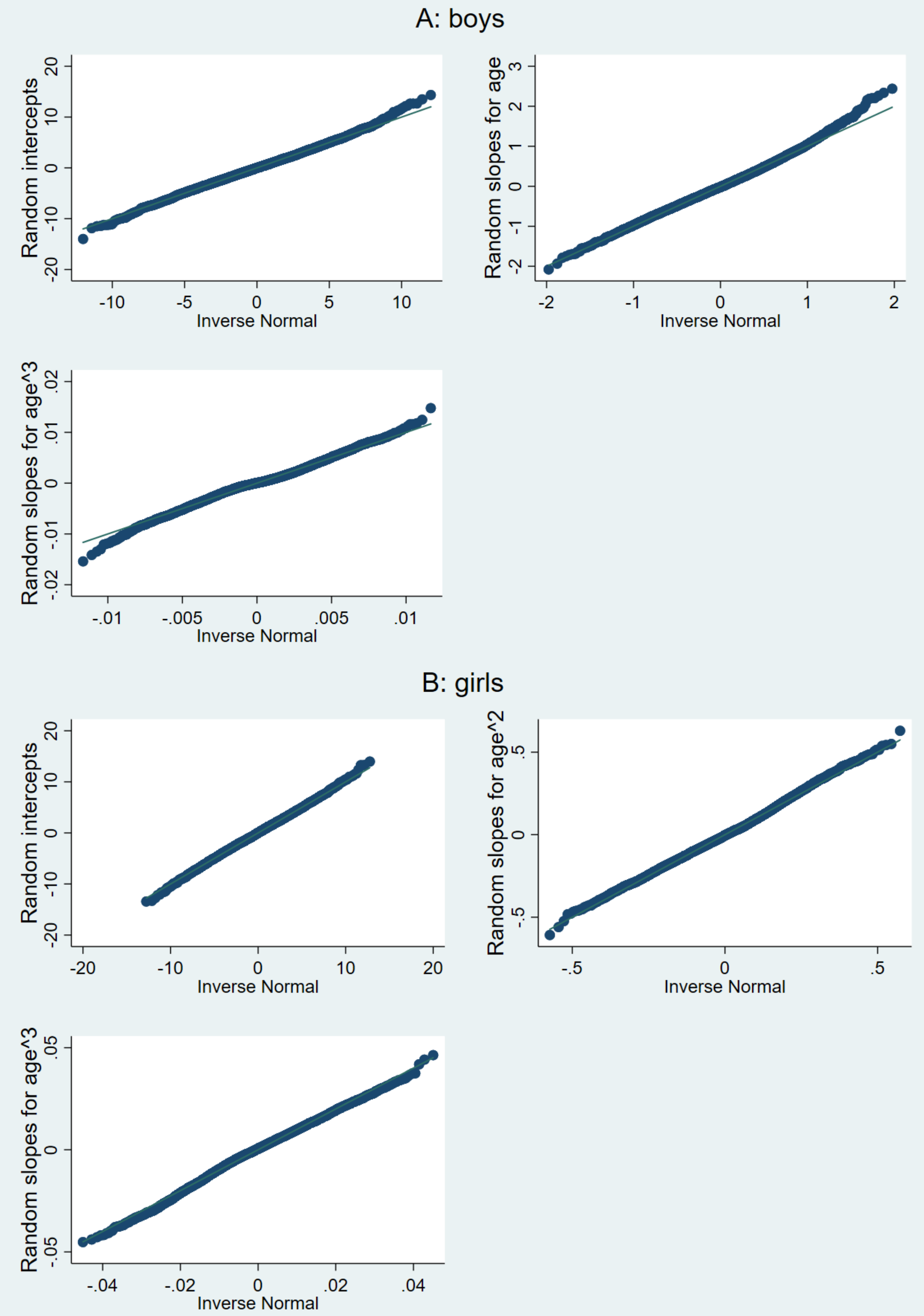

Figure S3: Q-Q (quantile-quantile) plots of random intercepts and random coefficients for age terms

Estimated from unadjusted mixed-effects fractional polynomial models. In boys, random effects were allowed for intercept, age and age^2. In girls, random effects were allowed for intercept, age^2 and age^3.

Table S3: Overview of puberty measures by ethnic group

	Boys				Girls			
	White	South Asian	Black African-Caribbean	*p*†	White	South Asian	Black African-Caribbean	*p*†
Stage of voice change at 11-year visit				0.002				
Has not started, n(%)	4,864(87%)	525(84%)	167(78%)		n/a	n/a	n/a	
Has barely started, n(%)	560(10%)	77(12%)	33(15%)		n/a	n/a	n/a	
Has definitely started, n(%)	167(3%)	23(4%)	13(6%)		n/a	n/a	n/a	
PDS score at 14-year visit‡, mean(SD)	2.57(0.51)	2.56(0.56)	2.48(0.44)	0.12	3.09(0.47)	3.01(0.45)	3.15(0.43)	<0.001
Menarcheal age (year), mean(SD)	n/a	n/a	n/a		12.1(1.08)	11.9(1.12)	11.7(1.19)	<0.001

*Cell values are unweighted n(%) or mean(SD).

†ANOVA was used for continuous puberty variables and chi-squared tests for categorical variables.

‡PDS: Pubertal Development Scale, on a scale from 1 and 4, higher PDS score indicates more advanced pubertal development stage. It was derived based on the methods provided in Petersen AC et al 2. At 11-year visits, parents were asked to rate their child's pubertal development in one of following three categories – 'has definitely not started', 'has barely started' or 'has definitely started'. At 14-year visits, children were asked to rate their own pubertal development in one of the following four categories - 'has definitely not started', 'has barely started', 'has definitely started', or 'seems to have completed'. There were five gender-specific questions. In boys, these included growth spurt, body hair, skin changes, voice change and facial hair. In girls, these included growth spurt, breast development, body hair, skin changes and menarche. For menarche, only two response options were given (yes/no).The following scoring system was used to assign scores to response options for puberty measures - has not started (score 1), has barely started (score 2), has definitely started (score 3). For onset of menarche, it was score 1 for 'no' and 4 for 'yes'. The PDS score was calculated as the mean score of all five puberty measures. Individuals who had item non-response for three or more puberty measures were excluded.

[2] Petersen, A.C., et al., *A self-report measure of pubertal status: Reliability, validity, and initial norms.* Journal of Youth and Adolescence, 1988. **17**(2): p. 117-133.

Table S4: Estimated difference in mean height (cm) with 95% CI between White and minority ethnic groups, from sensitivity analysis using maximum available sample for each model*

	Boys				Girls			
	Model1 (*n*=8267)	Model2 (*n*=7943)	Model3 (*n*=7939)	Model 4 (*n*=7928)	Model1 (*n*=7871)	Model2 (*n*=7527)	Model3 (*n*=7521)	Model 4 (*n*=7515)
				South Asian vs. White				
3	0.6 (0.3, 0.9)	0.6 (0.2, 0.9)	1.3 (1.0, 1.6)	1.4 (1.0, 1.7)	0.6 (0.3, 1.0)	0.5 (0.2, 0.9)	1.3 (1.0, 1.6)	1.5 (1.1, 1.8)
5	0.5 (0.1, 0.8)	0.4 (0.0, 0.7)	1.1 (0.8, 1.5)	1.2 (0.8, 1.5)	0.0 (-0.3, 0.3)	-0.1 (-0.5, 0.2)	0.6 (0.3, 1.0)	0.8 (0.4, 1.2)
7	0.5 (0.1, 0.9)	0.4 (0.0, 0.8)	1.1 (0.7, 1.5)	1.2 (0.8, 1.6)	0.0 (-0.4, 0.4)	-0.1 (-0.6, 0.3)	0.7 (0.2, 1.1)	0.8 (0.4, 1.2)
9	0.5 (0.0, 0.9)	0.5 (0.0, 0.9)	1.2 (0.7, 1.7)	1.3 (0.8, 1.7)	0.0 (-0.5, 0.5)	-0.1 (-0.7, 0.4)	0.6 (0.1, 1.2)	0.8 (0.3, 1.3)
11	0.4 (-0.1, 0.9)	0.4 (-0.2, 0.9)	1.1 (0.6, 1.7)	1.2 (0.7, 1.7)	-0.5 (-1.1, 0.0)	-0.6 (-1.2, 0.0)	0.1 (-0.4, 0.7)	0.3 (-0.3, 0.9)
14	-0.6 (-1.2, 0.0)	-0.6 (-1.3, 0.0)	0.1 (-0.6, 0.8)	0.2 (-0.5, 0.9)	-3.1 (-3.6, -2.6)	-3.2 (-3.7, -2.6)	-2.4 (-2.9, -1.9)	-2.2 (-2.8, -1.7)
				Black African-Caribbean vs. White				
3	2.2 (1.8, 2.7)	2.2 (1.7, 2.7)	2.5 (2.0, 3.0)	2.6 (2.1, 3.0)	3.3 (2.8, 3.9)	3.1 (2.5, 3.7)	3.4 (2.9, 4.0)	3.6 (3.1, 4.2)
5	3.1 (2.5, 3.6)	3.1 (2.5, 3.6)	3.4 (2.8, 3.9)	3.4 (2.9, 3.9)	3.6 (3.1, 4.2)	3.4 (2.8, 3.9)	3.7 (3.2, 4.3)	3.9 (3.4, 4.4)
7	3.6 (3.0, 4.3)	3.7 (3.0, 4.3)	3.9 (3.3, 4.6)	4.0 (3.4, 4.6)	4.6 (4.0, 5.3)	4.4 (3.7, 5.1)	4.7 (4.1, 5.4)	4.9 (4.2, 5.6)
9	3.9 (3.2, 4.6)	3.9 (3.1, 4.6)	4.2 (3.5, 4.9)	4.2 (3.5, 5.0)	5.5 (4.7, 6.3)	5.3 (4.5, 6.2)	5.6 (4.8, 6.4)	5.8 (5.0, 6.6)
11	3.8 (3.0, 4.6)	3.8 (2.9, 4.6)	4.1 (3.2, 4.9)	4.1 (3.3, 4.9)	5.5 (4.6, 6.4)	5.4 (4.5, 6.3)	5.7 (4.8, 6.6)	5.9 (4.9, 6.8)
14	2.8 (1.7, 3.8)	3.0 (1.9, 4.0)	3.2 (2.2, 4.3)	3.3 (2.2, 4.4)	2.5 (1.7, 3.3)	2.4 (1.5, 3.2)	2.7 (1.8, 3.5)	2.9 (2.0, 3.7)

**n* indicates the number of children included in the model. Diff: estimated difference in mean height; CI: confidence interval.

Model 1: unadjusted model.

Model 2: model 1 + adjusted for prenatal factors (maternal age, smoking during pregnancy, birth order).

Model 3: model 2 + adjusted for birthweight.

Model 4: model 3 + adjusted for family SECs (maternal education, family income).

Table S5: Estimated difference in mean height (cm) with 95% CI between White and minority ethnic groups, from unadjusted model and models adjusted for puberty measures*

	Boys			Girls		
	(1) Unadjusted (*n*=7,918)	(2) + voice change (*n*=6,183)	(3) + PDS (*n*=4,853)	(1) Unadjusted (*n*=7,508)	(2) + menarcheal age (*n*=4,564)	(3) + PDS (*n*=4,821)
	SA-White					
3	0.5 (0.2, 0.8)	0.6 (0.2, 0.9)	0.5 (0.2, 0.9)	0.5 (0.2, 0.9)	0.3 (-0.1, 0.7)	0.5 (0.1, 0.9)
5	0.4 (0.0, 0.7)	0.4 (0.0, 0.8)	0.4 (0.0, 0.8)	-0.1 (-0.5, 0.2)	-0.4 (-0.8, 0.0)	-0.2 (-0.6, 0.2)
7	0.4 (0.0, 0.8)	0.4 (0.0, 0.9)	0.4 (-0.1, 0.9)	-0.1 (-0.5, 0.3)	-0.6 (-1.1, -0.1)	-0.1 (-0.6, 0.4)
9	0.4 (0.0, 0.9)	0.5 (0.0, 1.0)	0.5 (-0.1, 1.0)	-0.1 (-0.6, 0.4)	-0.9 (-1.4, -0.3)	0.0 (-0.5, 0.6)
11	0.4 (-0.2, 0.9)	0.4 (-0.2, 1.0)	0.4 (-0.2, 1.0)	-0.6 (-1.2, 0.0)	-1.5 (-2.1, -0.8)	-0.4 (-1.0, 0.3)
14	-0.6 (-1.3, 0.1)	-0.5 (-1.3, 0.2)	-0.5 (-1.2, 0.2)	-3.2 (-3.7, -2.6)	-3.5 (-4.1, -2.9)	-3.0 (-3.5, -2.4)
	Black-White					
3	2.2 (1.7, 2.7)	2.2 (1.6, 2.8)	2.3 (1.7, 3.0)	3.2 (2.6, 3.8)	3.2 (2.5, 3.9)	3.3 (2.6, 4.0)
5	3.1 (2.6, 3.7)	3.0 (2.3, 3.6)	3.2 (2.5, 3.9)	3.5 (2.9, 4.0)	3.5 (2.8, 4.2)	3.5 (2.8, 4.2)
7	3.7 (3.1, 4.4)	3.5 (2.7, 4.2)	3.7 (2.9, 4.6)	4.5 (3.8, 5.2)	4.2 (3.4, 5.0)	4.5 (3.7, 5.3)
9	4.0 (3.2, 4.7)	3.6 (2.8, 4.5)	4.0 (3.0, 4.9)	5.4 (4.6, 6.3)	4.8 (3.8, 5.7)	5.4 (4.5, 6.4)
11	3.8 (3.0, 4.7)	3.5 (2.5, 4.4)	3.9 (2.9, 5.0)	5.5 (4.5, 6.4)	4.7 (3.7, 5.8)	5.5 (4.5, 6.6)
14	3.1 (2.0, 4.2)	2.7 (1.5, 3.9)	3.4 (2.2, 4.6)	2.5 (1.6, 3.3)	2.4 (1.4, 3.4)	2.5 (1.5, 3.5)

*n indicates the number of children included in the model. PDS: pubertal development score, on a scale from 1 and 4, higher PDS indicates more advanced pubertal development stage.

(1) Unadjusted mixed effects fractional polynomial model as presented in the main analysis;

(2) Adjusted for voice change and interaction between voice change and age terms (in boys); menarcheal age and interaction between menarcheal age and age terms (in girls);

(3) Adjusted for PDS score at 14 years.

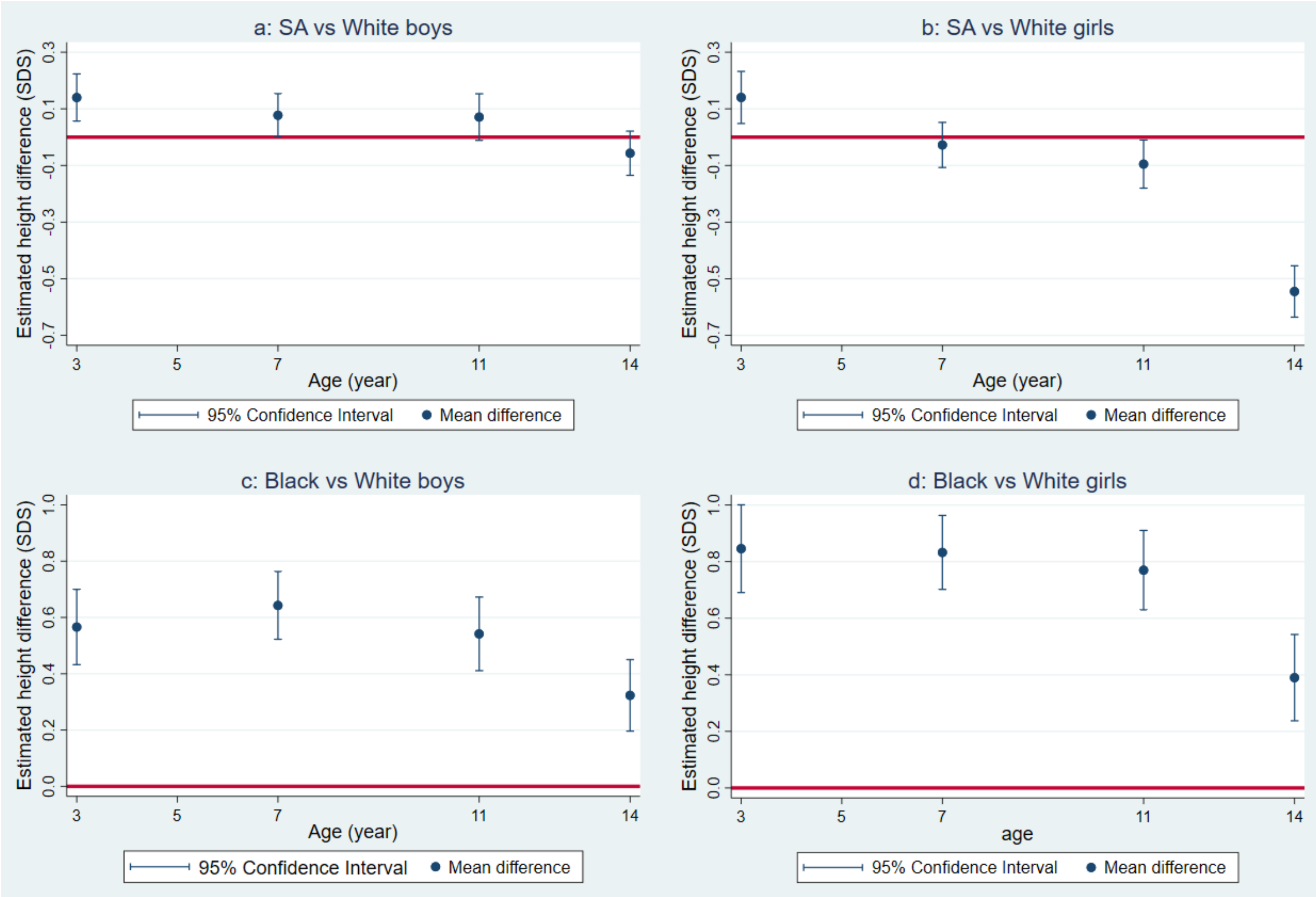

Figure S4: Estimated ethnic differences in height Standard Deviation Scores (SDS) with 95% confidence interval, based on unadjusted mixed effects fractional polynomial models

SDS were standardised internally. Reference line (y=0) indicates no height difference between ethnic groups. SA: South Asian. Black: Black African-Caribbean.

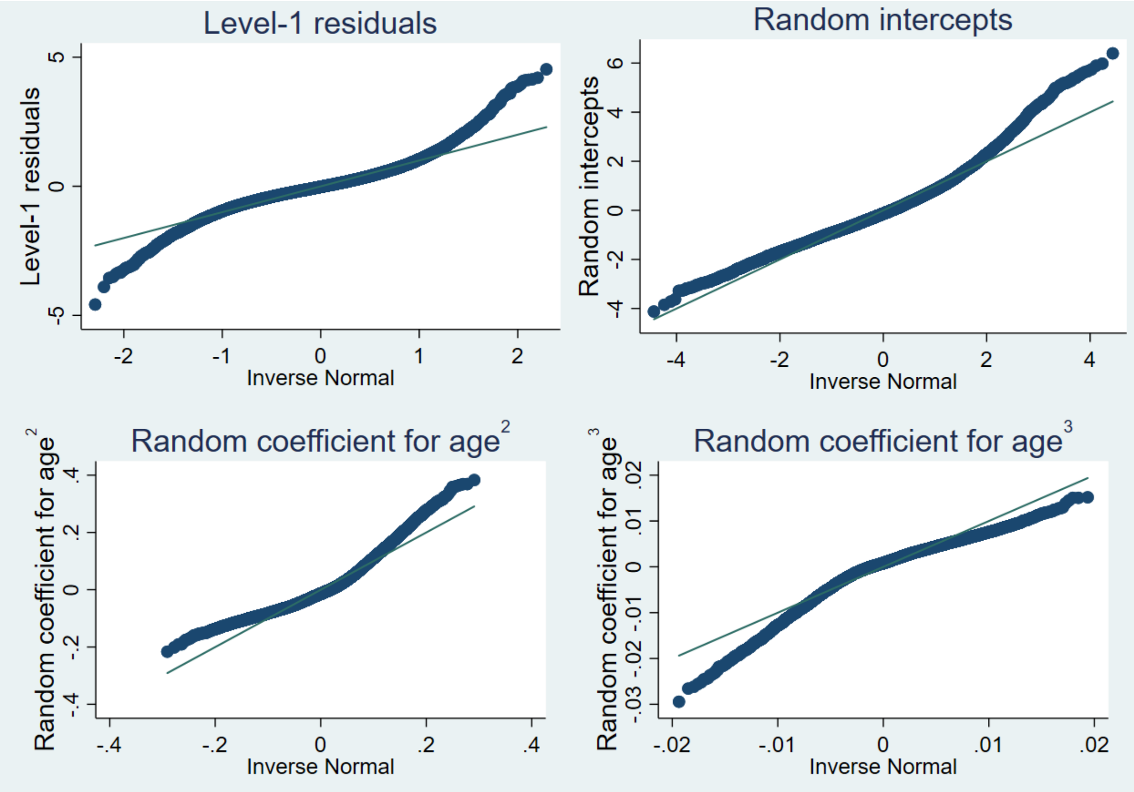

Figure S5: Q-Q (quantile-quantile) plots of level-1 residuals and random effects
Estimated from unadjusted mixed-effects fractional polynomial models.

Table S6: Comparison of distributions of the observed and imputed data

	Observed	Imputed	Completed
Maternal pre-pregnancy BMI	*n*=14168	*n*=1828	*n*=15996
Thin	5%	5%	5%
Healthy	65%	65%	65%
Overweight	20%	21%	21%
Obese	9%	9%	9%
Maternal smoking during pregnancy	*n*=15704	*n*=292	*n*=15996
No	77%	66%	76%
Yes	23%	34%	24%
Duration of exclusive breastfeeding	*n*=15450	*n*=546	*n*=15996
None	34%	40%	34%
Less than 4 months	63%	58%	63%
4 months or longer	3%	2%	3%
Early introduction to solid foods	*n*=15454	*n*=542	*n*=15996
No	65%	66%	65%
Yes	35%	35%	35%

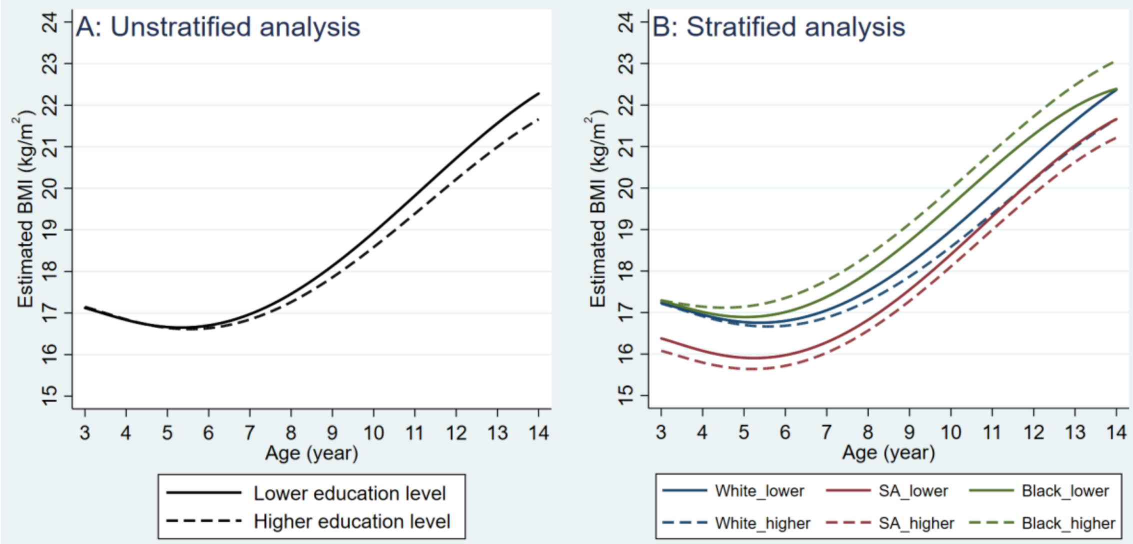

Figure S6: Estimated BMI trajectories between 3 and 14 years by <u>maternal education</u>, from unstratified (model 1) and stratified (model 2) mixed effects fractional polynomial models.

Models were adjusted for sex. The solid (—) lines represent 'higher' maternal groups education (GCSE grades A*-C & above) while the dashed (– –) lines represent 'lower' education groups (GCSE grades D-G & below). SA: South Asian; Black: Black African-Caribbean; not: not in poverty. In panel B, each colour represents one ethnic group.

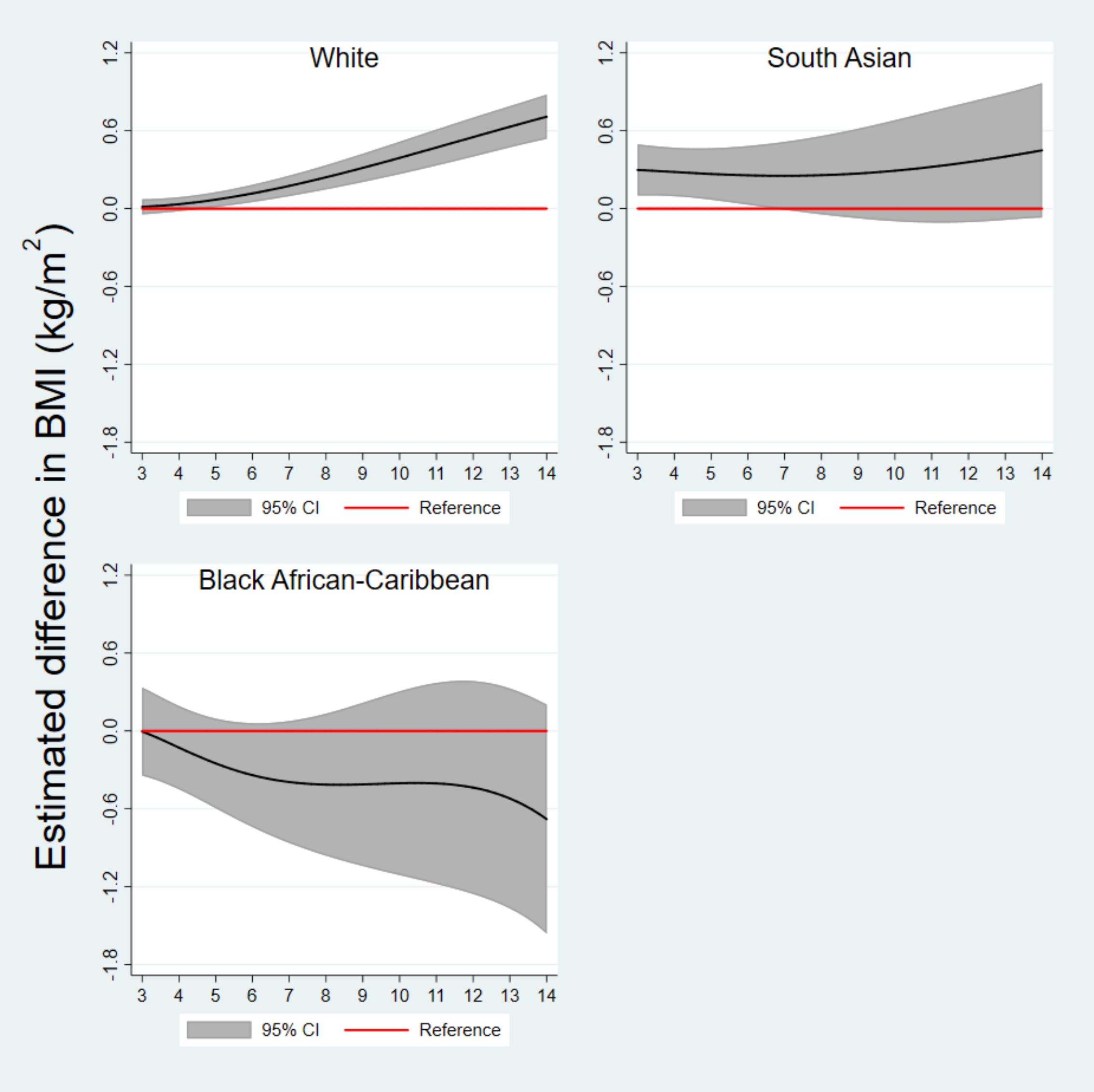

Figure S7: Estimated mean BMI differences with 95% confidence intervals from 3 to 14 years between lower and higher maternal education groups, based on mixed effects fractional polynomial models.

Models were adjusted for sex. Higher maternal education group (i.e. GCSE grades A*-C & above) was the reference group.

Table S7: Comparison of estimated income differences in mean BMI (kg/m^2) with 95% confidence intervals between main analysis and sensitivity analysis using family income quintiles, based on mixed effects fractional polynomial models

	White				**South Asian**				**Black African-Caribbean**			
	Main analysis*		Sensitivity analysis†		main analysis*		sensitivity analysis†		Main analysis*		Sensitivity analysis†	
Age	diff	95% CI	diff	95% CI	diff	95% CI	diff	95% CI	diff	95% CI	diff	95% CI
3	0.05	(0.00, 0.11)	0.10	(0.03, 0.17)	0.30	(0.10, 0.49)	0.62	(0.30, 0.94)	-0.11	(-0.44, 0.21)	-0.49	(-0.98, 0.00)
4	0.07	(0.02, 0.12)	0.14	(0.07, 0.20)	0.24	(0.05, 0.42)	0.54	(0.23, 0.84)	-0.23	(-0.54, 0.08)	-0.58	(-1.04, -0.12)
5	0.10	(0.05, 0.16)	0.20	(0.13, 0.27)	0.19	(0.00, 0.39)	0.49	(0.17, 0.81)	-0.37	(-0.71, -0.04)	-0.69	(-1.18, -0.20)
6	0.14	(0.08, 0.21)	0.30	(0.21, 0.38)	0.18	(-0.04, 0.40)	0.50	(0.14, 0.87)	-0.51	(-0.89, -0.13)	-0.81	(-1.38, -0.24)
7	0.19	(0.12, 0.27)	0.41	(0.31, 0.51)	0.21	(-0.05, 0.46)	0.59	(0.17, 1.01)	-0.63	(-1.08, -0.18)	-0.92	(-1.59, -0.25)
8	0.25	(0.16, 0.34)	0.55	(0.43, 0.66)	0.26	(-0.03, 0.56)	0.73	(0.24, 1.22)	-0.72	(-1.25, -0.20)	-1.03	(-1.81, -0.25)
9	0.32	(0.22, 0.42)	0.69	(0.56, 0.83)	0.35	(0.01, 0.68)	0.93	(0.37, 1.48)	-0.79	(-1.40, -0.19)	-1.13	(-2.03, -0.23)
10	0.39	(0.28, 0.51)	0.84	(0.69, 1.00)	0.45	(0.06, 0.83)	1.15	(0.52, 1.78)	-0.84	(-1.52, -0.17)	-1.22	(-2.24, -0.21)
11	0.48	(0.34, 0.61)	1.00	(0.83, 1.17)	0.55	(0.13, 0.97)	1.38	(0.69, 2.08)	-0.88	(-1.62, -0.14)	-1.32	(-2.42, -0.21)
12	0.56	(0.42, 0.70)	1.16	(0.97, 1.34)	0.65	(0.19, 1.10)	1.61	(0.86, 2.35)	-0.90	(-1.69, -0.12)	-1.41	(-2.58, -0.25)
13	0.65	(0.50, 0.80)	1.31	(1.11, 1.51)	0.72	(0.25, 1.20)	1.80	(1.01, 2.59)	-0.93	(-1.74, -0.12)	-1.52	(-2.72, -0.32)
14	0.75	(0.59, 0.91)	1.45	(1.24, 1.66)	0.77	(0.26, 1.27)	1.93	(1.10, 2.77)	-0.95	(-1.79, -0.11)	-1.63	(-2.87, -0.39)

*****In the main analysis, estimates are mean BMI differences (95%CI) between poverty and non-poverty (reference) groups.

†In the sensitivity analysis, estimates are mean BMI differences (95%CI) between lowest and highest (reference) income quintile groups.

Models were adjusted for sex. Diff: estimated mean BMI difference in cm. CI: confidence interval.

Table S8: Estimated mean BMI differences (kg/m^2) with 95% confidence intervals between maternal education groups ('lower' vs. 'higher' group) from unadjusted and adjusted mixed effects models

	Model 2: unadjusted		**Model 3:** model 2 + maternal BMI & smoking		**Model 4:** model 3 + infant feeding	
Age	**Diff***	**95% CI**	**Diff***	**95% CI**	**Diff***	**95% CI**
			White			
3	0.01	(-0.04, 0.07)	-0.03	(-0.09, 0.03)	0.20	(-0.02, 0.41)
4	0.03	(-0.02, 0.09)	-0.01	(-0.06, 0.05)	0.19	(-0.01, 0.39)
5	0.07	(0.01, 0.13)	0.03	(-0.03, 0.09)	0.19	(-0.02, 0.40)
6	0.12	(0.05, 0.18)	0.08	(0.01, 0.14)	0.20	(-0.05, 0.44)
7	0.18	(0.10, 0.25)	0.13	(0.05, 0.21)	0.20	(-0.08, 0.49)
8	0.24	(0.15, 0.33)	0.20	(0.11, 0.29)	0.21	(-0.12, 0.55)
9	0.31	(0.21, 0.42)	0.27	(0.16, 0.38)	0.23	(-0.16, 0.62)
10	0.39	(0.27, 0.52)	0.35	(0.23, 0.47)	0.25	(-0.20, 0.70)
11	0.47	(0.33, 0.61)	0.43	(0.29, 0.57)	0.28	(-0.22, 0.78)
12	0.55	(0.40, 0.70)	0.51	(0.36, 0.66)	0.31	(-0.23, 0.85)
13	0.63	(0.47, 0.79)	0.59	(0.43, 0.75)	0.35	(-0.23, 0.93)
14	0.71	(0.54, 0.88)	0.66	(0.49, 0.83)	0.39	(-0.23, 1.01)
			South Asian			
3	0.30	(0.10, 0.50)	0.27	(0.07, 0.46)	0.02	(-0.29, 0.32)
4	0.28	(0.10, 0.47)	0.25	(0.07, 0.44)	0.05	(-0.24, 0.33)
5	0.27	(0.07, 0.47)	0.24	(0.04, 0.43)	0.05	(-0.25, 0.36)
6	0.26	(0.03, 0.48)	0.23	(0.01, 0.45)	0.04	(-0.31, 0.38)
7	0.25	(-0.01, 0.51)	0.23	(-0.03, 0.48)	-0.01	(-0.41, 0.39)
8	0.26	(-0.04, 0.56)	0.23	(-0.07, 0.53)	-0.07	(-0.53, 0.39)
9	0.27	(-0.07, 0.62)	0.24	(-0.10, 0.58)	-0.14	(-0.67, 0.38)
10	0.29	(-0.10, 0.68)	0.26	(-0.12, 0.65)	-0.22	(-0.82, 0.37)
11	0.32	(-0.11, 0.75)	0.29	(-0.13, 0.72)	-0.29	(-0.95, 0.36)
12	0.36	(-0.10, 0.82)	0.33	(-0.13, 0.79)	-0.35	(-1.05, 0.36)
13	0.40	(-0.09, 0.89)	0.37	(-0.11, 0.85)	-0.37	(-1.12, 0.37)
14	0.45	(-0.07, 0.97)	0.42	(-0.09, 0.93)	-0.35	(-1.14, 0.44)
			Black African-Caribbean			
3	-0.01	(-0.34, 0.33)	-0.01	(-0.35, 0.32)	0.11	(-0.51, 0.73)
4	-0.13	(-0.45, 0.19)	-0.13	(-0.45, 0.18)	0.10	(-0.48, 0.68)
5	-0.25	(-0.60, 0.10)	-0.25	(-0.59, 0.09)	0.10	(-0.52, 0.72)
6	-0.34	(-0.74, 0.06)	-0.34	(-0.73, 0.05)	0.11	(-0.62, 0.83)
7	-0.39	(-0.86, 0.08)	-0.39	(-0.85, 0.07)	0.12	(-0.73, 0.97)
8	-0.41	(-0.96, 0.13)	-0.41	(-0.95, 0.13)	0.14	(-0.85, 1.14)
9	-0.41	(-1.04, 0.22)	-0.41	(-1.03, 0.21)	0.16	(-1.00, 1.31)
10	-0.40	(-1.11, 0.31)	-0.40	(-1.10, 0.29)	0.15	(-1.15, 1.45)
11	-0.40	(-1.18, 0.37)	-0.41	(-1.17, 0.36)	0.13	(-1.30, 1.55)
12	-0.44	(-1.26, 0.38)	-0.44	(-1.25, 0.37)	0.06	(-1.45, 1.58)
13	-0.52	(-1.37, 0.33)	-0.53	(-1.36, 0.31)	-0.05	(-1.60, 1.51)
14	-0.68	(-1.56, 0.20)	-0.68	(-1.56, 0.19)	-0.21	(-1.82, 1.40)

***estimated mean BMI difference in kg/m^2. CI: confidence interval. Model 2 included sex, maternal education, age terms, and interaction between maternal education and all age terms. Analysis was stratified by ethnic group (i.e. models were fitted for each ethnic group separately). Model 3: model 2 + maternal pre-pregnancy BMI and smoking during pregnancy. Model 4: model 3 + exclusive breastfeeding and early introduction to solid foods.

Table S9: Estimated mean BMI differences (kg/m^2) with 95% confidence intervals (CIs) between poverty and non-poverty (reference) groups for Black African-Caribbean children, from unadjusted mixed effects fractional polynomial model and the model adjusted for height

	Poverty vs. Non-poverty group			
	Unadjusted model		Adjusted for height	
Age	diff	95% CI	diff	95% CI
3	-0.11	(-0.44, 0.21)	-0.11	(-0.44, 0.21)
4	-0.23	(-0.54, 0.08)	-0.23	(-0.54, 0.08)
5	-0.37	(-0.71, -0.04)	-0.37	(-0.71, -0.04)
6	-0.51	(-0.89, -0.13)	-0.51	(-0.90, -0.13)
7	-0.63	(-1.08, -0.18)	-0.63	(-1.08, -0.18)
8	-0.72	(-1.25, -0.20)	-0.72	(-1.25, -0.20)
9	-0.79	(-1.40, -0.19)	-0.80	(-1.40, -0.19)
10	-0.84	(-1.52, -0.17)	-0.85	(-1.53, -0.17)
11	-0.88	(-1.62, -0.14)	-0.88	(-1.63, -0.14)
12	-0.90	(-1.69, -0.12)	-0.91	(-1.69, -0.12)
13	-0.93	(-1.74, -0.12)	-0.93	(-1.74, -0.12)
14	-0.95	(-1.79, -0.11)	-0.96	(-1.80, -0.12)

Appendix IV: Supplementary materials for Chapter 6

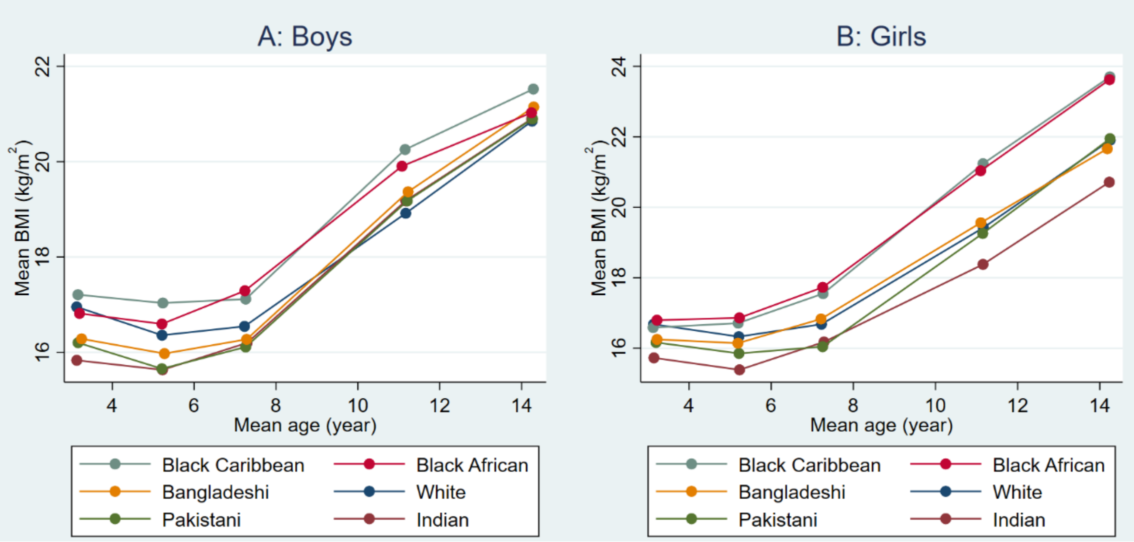

Figure S8: Observed mean age and BMI at each follow-up visit across six ethnic group, by sex

Table S10: Ethnic differences in observed mean BMI (kg/m^2) at each sweep by sex

	Boys						Girls					
	White	Indian	Pakistani	Bangladeshi	Black Caribbean	Black African	White	Indian	Pakistani	Bangladeshi	Black Caribbean	Black African
3 years												
Mean(SD)	16.8(1.5)	15.8(1.5)	16.2(1.7)	16.3(2.2)	16.9(1.9)	16.8(1.7)	16.7(1.5)	15.7(1.6)	16.2(1.7)	16.3(2.3)	16.6(1.9)	16.8(1.9)
Regression coefficient*												
b	(ref)	-1.12	-0.74	-0.67	0.26	-0.17	(ref)	-0.95	-0.50	-0.38	-0.10	0.13
p	(ref)	<0.001	<0.001	<0.001	0.10	0.17	(ref)	<0.001	<0.001	0.01	0.60	0.39
5 years												
Mean(SD)	16.4(1.5)	15.6(1.9)	15.7(1.8)	16.0(2.0)	17.0(2.2)	16.6(1.9)	16.3(1.6)	15.4(1.6)	15.9(1.9)	16.2(2.2)	16.7(2.0)	16.9(1.9)
Regression coefficient*												
b	(ref)	-0.73	-0.70	-0.39	0.66	0.21	(ref)	-0.94	-0.47	-0.14	0.38	0.53
p	(ref)	<0.001	<0.001	<0.01	0.00	0.09	(ref)	<0.001	<0.001	0.33	0.05	<0.001
7 years												
Mean(SD)	16.5(2.0)	16.2(2.6)	16.1(2.7)	16.3(2.5)	17.1(2.6)	17.3(2.5)	16.7(2.2)	16.2(2.4)	16.0(2.4)	16.9(3.1)	17.5(2.5)	17.7(2.7)
Regression coefficient*												
b	(ref)	-0.38	-0.46	-0.32	0.55	0.70	(ref)	-0.54	-0.65	0.21	0.85	0.99
p	(ref)	0.02	<0.001	0.12	0.02	<0.001	(ref)	<0.01	<0.001	0.29	<0.01	<0.001
11 years												
Mean(SD)	18.9(3.3)	19.2(3.8)	19.2(4.0)	19.4(4.0)	20.3(4.4)	19.8(3.7)	19.4(3.5)	18.4(3.4)	19.3(4.0)	19.7(3.9)	21.2(4.4)	21.0(4.3)
Regression coefficient*												
b	(ref)	0.26	0.23	0.42	1.34	0.98	(ref)	-1.04	-0.15	0.28	1.82	1.60
p	(ref)	0.32	0.25	0.16	<0.01	<0.01	(ref)	<0.001	0.47	0.35	<0.001	<0.001
14 years												
Mean(SD)	20.9(3.8)	20.9(4.5)	20.9(4.6)	21.1(4.7)	21.5(3.9)	21.0(3.6)	21.9(3.9)	20.7(3.8)	21.9(4.7)	21.7(4.4)	23.7(4.2)	23.6(4.4)
Regression coefficient*												
b	(ref)	0.05	0.06	0.28	0.66	0.15	(ref)	-1.17	0.02	-0.18	1.80	1.68
p	(ref)	0.87	0.80	0.44	0.19	0.70	(ref)	<0.001	0.92	0.61	<0.01	<0.001

*Based on linear regression, adjusting for age at the BMI measurement. b: coefficient (i.e. difference relative to the White group). Ref: reference group. SD: standard deviation.

Table S11: Estimated BMI differences in cm with 95% confidence intervals (CIs) for models adjusted for family SECs, maternal smoking and infant feeding*

	South Asian vs. White		Black African-Caribbean vs. White		
	(A) Unadjusted model	(B) Adjusted for family SECs	(C) Unadjusted model	(D) Adjusted for maternal smoking	(E) Adjusted for infant feeding
Age	diff(95% CI)	diff(95% CI)	diff(95% CI)	diff(95% CI)	diff(95% CI)
Boys					
3	-0.79(-0.90, -0.67)	-0.80(-0.92, -0.67)	0.02(-0.17, 0.21)	0.06(-0.12, 0.25)	0.08(-0.11, 0.26)
4	-0.76(-0.86, -0.65)	-0.77(-0.88, -0.66)	0.14(-0.04, 0.31)	0.19(0.02, 0.36)	0.20(0.03, 0.37)
5	-0.68(-0.79, -0.57)	-0.69(-0.81, -0.58)	0.30(0.12, 0.48)	0.36(0.18, 0.54)	0.38(0.20, 0.56)
6	-0.56(-0.69, -0.43)	-0.58(-0.72, -0.45)	0.48(0.27, 0.68)	0.54(0.34, 0.75)	0.58(0.37, 0.79)
7	-0.41(-0.56, -0.26)	-0.45(-0.60, -0.29)	0.65(0.41, 0.89)	0.72(0.48, 0.97)	0.77(0.53, 1.02)
8	-0.24(-0.42, -0.07)	-0.30(-0.48, -0.11)	0.80(0.52, 1.08)	0.88(0.60, 1.17)	0.95(0.66, 1.24)
9	-0.07(-0.28, 0.13)	-0.15(-0.37, 0.06)	0.91(0.58, 1.24)	1.00(0.67, 1.34)	1.08(0.75, 1.42)
10	0.08(-0.16, 0.31)	-0.03(-0.28, 0.21)	0.97(0.59, 1.35)	1.07(0.69, 1.45)	1.17(0.79, 1.56)
11	0.19(-0.07, 0.45)	0.05(-0.22, 0.32)	0.97(0.55, 1.40)	1.08(0.66, 1.51)	1.20(0.77, 1.62)
12	0.25(-0.03, 0.53)	0.07(-0.22, 0.37)	0.90(0.45, 1.36)	1.02(0.56, 1.48)	1.14(0.68, 1.61)
13	0.24(-0.06, 0.53)	0.02(-0.30, 0.33)	0.76(0.27, 1.24)	0.88(0.39, 1.37)	1.01(0.51, 1.50)
14	0.13(-0.19, 0.44)	-0.13(-0.46, 0.20)	0.52(0.00, 1.04)	0.64(0.12, 1.17)	0.78(0.25, 1.31)
Girls					
3	-0.58(-0.71, -0.46)	-0.63(-0.75, -0.50)	0.03(-0.18, 0.24)	0.05(-0.17, 0.26)	0.07(-0.14, 0.29)
4	-0.59(-0.70, -0.47)	-0.64(-0.76, -0.52)	0.15(-0.05, 0.34)	0.17(-0.03, 0.36)	0.20(0.00, 0.39)
5	-0.58(-0.70, -0.46)	-0.64(-0.77, -0.51)	0.32(0.12, 0.52)	0.35(0.15, 0.56)	0.39(0.19, 0.60)
6	-0.55(-0.69, -0.41)	-0.63(-0.78, -0.49)	0.53(0.30, 0.77)	0.58(0.34, 0.81)	0.63(0.39, 0.86)
7	-0.52(-0.68, -0.35)	-0.61(-0.79, -0.44)	0.76(0.49, 1.04)	0.82(0.55, 1.10)	0.88(0.60, 1.16)
8	-0.47(-0.66, -0.28)	-0.59(-0.79, -0.39)	0.99(0.66, 1.31)	1.07(0.74, 1.39)	1.13(0.80, 1.46)
9	-0.43(-0.65, -0.20)	-0.57(-0.80, -0.33)	1.20(0.82, 1.57)	1.29(0.92, 1.67)	1.36(0.99, 1.74)
10	-0.39(-0.64, -0.13)	-0.55(-0.82, -0.29)	1.37(0.95, 1.80)	1.49(1.06, 1.91)	1.56(1.13, 1.99)
11	-0.36(-0.63, -0.08)	-0.55(-0.84, -0.26)	1.50(1.03, 1.97)	1.63(1.16, 2.10)	1.71(1.24, 2.19)
12	-0.35(-0.64, -0.05)	-0.58(-0.89, -0.26)	1.57(1.06, 2.07)	1.71(1.20, 2.22)	1.80(1.29, 2.31)
13	-0.37(-0.68, -0.05)	-0.63(-0.96, -0.31)	1.56(1.02, 2.09)	1.72(1.18, 2.25)	1.81(1.27, 2.34)
14	-0.42(-0.75, -0.09)	-0.73(-1.08, -0.38)	1.46(0.89, 2.03)	1.63(1.06, 2.20)	1.73(1.16, 2.29)

*Estimates are differences (diff) with 95% confidence interval (95% CI) between minority ethnic group and the White group from unadjusted and adjusted mixed effects fractional polynomial models, which were fitted for boys and girls separately. Family SECs: family socio-economic circumstances (i.e. family income and maternal education).

Columns A and C were estimated from the same unadjusted models, which included age terms, ethnicity (i.e. White, South Asian and Black African-Caribbean), and interaction between ethnicity and all age terms. Column B was estimated from models adjusted for family SECs and interaction between family SECs and all age terms ($p<0.001$ for overall effects in both boys and girls). Column D was based on models adjusted for maternal smoking and interaction between maternal smoking and all age terms ($p<0.001$ for overall effects in both boys and girls). Column E was based on models adjusted for breastfeeding, early introduction to solid foods and interaction between them and all age terms ($p<0.001$ for overall effects in both boys and girls).

Table S12: Differences in key variables between participants with and without missing data in maternal BMI and infant weight gain variables*

	Maternal pre-pregnancy BMI			Infant weight gain		
Key variables	Not missing (n=14,163)	Missing (n=1,831)	*p*†	Not missing (n=13,443)	Missing (n=2,551)	*p*†
Male, n(%)	7251 (51%)	933 (51%)	0.85	6805 (51%)	1379 (54%)	<0.01
Ethnicity, n(%)			<0.01			<0.01
White	12602 (89%)	1220 (67%)		11791 (88%)	2031 (80%)	
South Asian	1180 (8%)	427 (23%)		1256 (9%)	351 (14%)	
Black African-Caribbean	381 (3%)	184 (10%)		396 (3%)	169 (7%)	
Family income quintiles, n(%)			<0.01			<0.01
Highest quintile	2476 (17%)	170 (9%)		2361 (18%)	285 (11%)	
Fourth quintile	2702 (19%)	183 (10%)		2551 (19%)	334 (13%)	
Third quintile	2801 (20%)	260 (14%)		2635 (20%)	426 (17%)	
Second quintile	3048 (22%)	500 (27%)		2941 (22%)	607 (24%)	
Lowest quintile	3136 (22%)	718 (39%)		2955 (22%)	899 (35%)	
Maternal highest academic qualification, n(%)			<0.01			<0.01
Higher education diploma or degree	3661 (26%)	297 (16%)		3504 (26%)	454 (18%)	
A-level	1399 (10%)	122 (7%)		1310 (10%)	211 (8%)	
GCSE grades A*-C	4907 (35%)	497 (27%)		4597 (34%)	807 (32%)	
GCSE grades D-G	1495 (11%)	233 (13%)		1425 (11%)	303 (12%)	
Others	323 (2%)	111 (6%)		328 (2%)	106 (4%)	
None of these	2378 (17%)	571 (31%)		2279 (17%)	670 (26%)	
Infant weight gain (SDS)	-0.04 (1.16)	0.08 (1.29)	<0.01	--	--	--
Maternal pre-pregnancy BMI (kg/m^2)	--	--	--	23.8 (4.5)	23.5 (4.3)	<0.01
Height at 3 years (cm)						
Boys	96.4 (4.1)	96.8 (4.2)	0.03	96.5 (4.1)	99.5 (6.0)	0.03
Girls	95.3 (4.0)	95.7 (4.4)	<0.01	95.3 (4.1)	96.1 (3.4)	0.63
Height at 14 years (cm)						
Boys	166.8 (8.6)	166.8 (8.4)	0.86	166.8 (8.6)	167.1 (8.8)	0.37
Girls	161.2 (6.3)	160.6 (6.9)	0.04	161.2 (6.4)	160.5 (6.4)	<0.01

* Cell values are mean (SD), unless otherwise stated. SD: standard deviation. SDS: standard deviation score.

† Differences were tested using t-tests for continuous variables and chi-squared for categorical variables.

Table S13: Correlation coefficients between maternal BMI/infant weight gain and other variables included in the imputation model*

	Maternal pre-pregnancy BMI				**Infant weight gain**			
	(A) Missing pattern		(B) Values when observed		(C) Missing pattern		(D) Values when observed	
Variables	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Child's sex (female)	0.002	1.00	0.001	1.00	-0.025	0.00	-0.002	1.00
Child's birthweight	-0.033	0.00	0.126	<0.01	-0.023	0.18	-0.588	<0.01
Family income quintiles (1: poorest quintile to 5: highest quintile)	-0.148	0.00	0.000	1.00	-0.122	<0.01	-0.059	<0.01
Maternal education, grouped (1: lowest to 5: highest)	-0.140	0.00	-0.001	1.00	-0.108	0.00	-0.062	<0.01
Maternal smoking during pregnancy, grouped (1: none to 4: 20+ cigarettes/day)	-0.031	0.01	-0.050	<0.01	0.035	0.00	0.114	<0.01
Maternal age at childbirth	-0.065	0.00	0.133	<0.01	-0.101	0.00	-0.034	<0.01
Duration of exclusive breastfeeding, grouped (1: none to 3: 4+ months)	-0.035	0.00	-0.007	1.00	-0.050	0.00	-0.030	0.03
Ethnicity (1 'White'; 2 'South Asian'; 3 'Black')	0.205	0.00	0.025	0.18	0.094	0.00	0.129	<0.01
Early introduction to solid food	-0.035	0.00	0.041	<0.01	-0.017	1.00	-0.032	0.01

*Cell values are pairwise correlation coefficients (*r*) and Bonferroni-adjusted significance level (*p*). The proportion of missing data in the analysis sample was high in maternal pre-pregnancy BMI (11%) and infant weight gain (16%), and low in other variables (i.e. maternal smoking 2% and birthweight 0.2%). Therefore the correlation coefficients between maternal BMI/infant weight gain and other variables included in the imputation model are provided here.

Columns A and C display the correlation between each factor and missingness of maternal BMI/infant weight gain. A positive coefficient in these columns indicate a positive association and vice versa. Columns B and D display the correlation between each factor and values of maternal BMI/infant weight gain when observed. A positive correlation coefficient indicates that participants with a higher value in this factor were more likely to have missing value in maternal BMI/ infant weight gain.

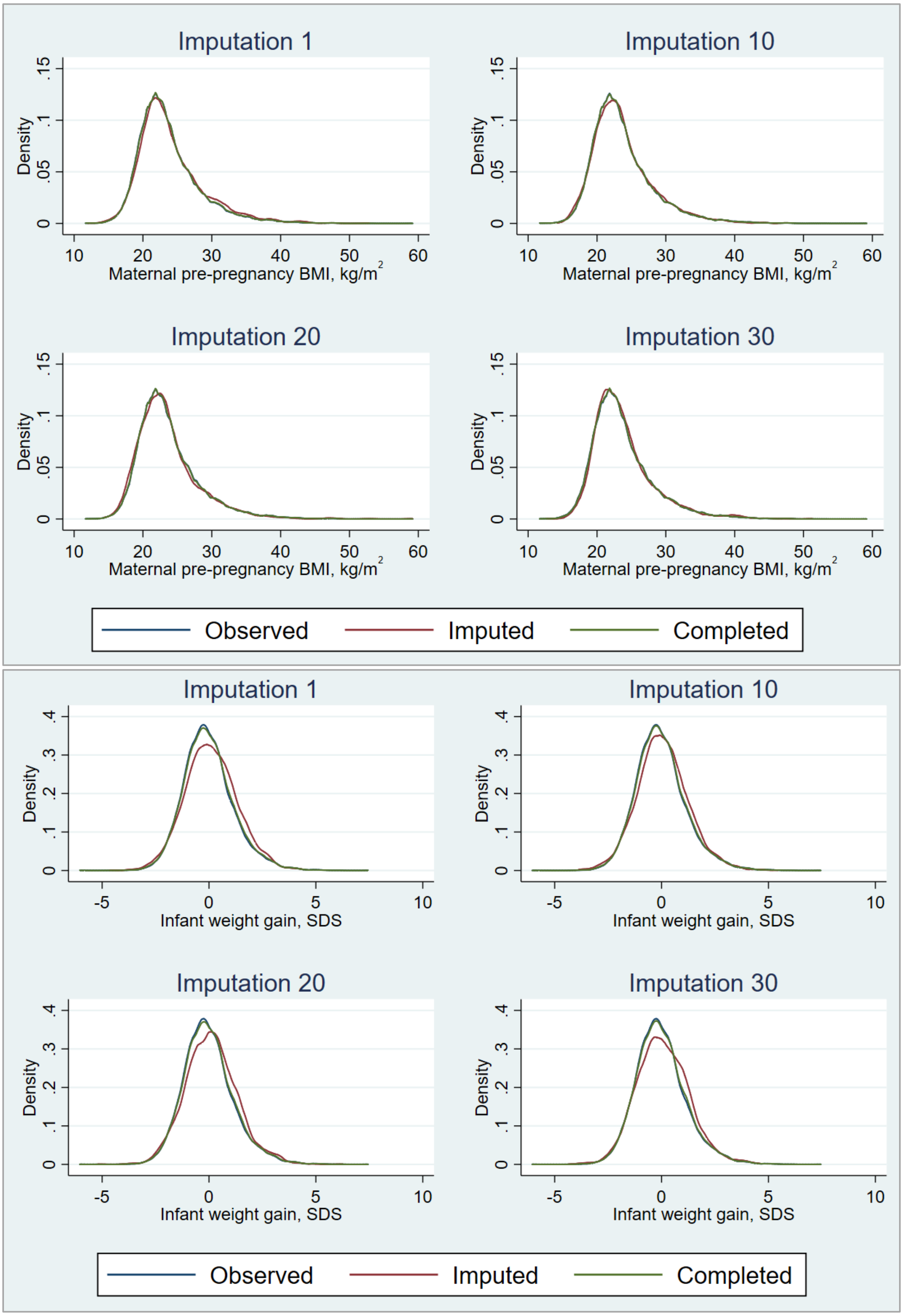

Figure S9: Comparison of density distributions of the observed and imputed data for maternal pre-pregnancy BMI and infant weight gain variables (at imputation = 1, 10, 20, 30)

*Upper panel for maternal pre-pregnancy BMI (kg/m^2) and lower panel for infant weight gain (SDS).

Table S14: Relative risk ratio (RRR) of overweight and obesity at each age by ethnic group, from unadjusted multinomial logistic regression*

	3 years		5 years		7 years		11 years		14 years	
Boys	**RRR (95% CI)**	***p***	**RRR (95% CI)**	***p***	**RRR (95% CI)**	***p***	**RRR (95% CI)**	***p***	**RRR (95% CI)**	***p***
Overweight†	0.25(0.24, 0.27)	<0.01	0.18(0.16, 0.19)	<0.01	0.16(0.15, 0.17)	<0.01	0.26(0.23, 0.28)	<0.01	0.25(0.23, 0.28)	<0.01
White	Ref		Ref		Ref		Ref		Ref	
South Asian‡	0.52(0.40, 0.68)	<0.01	0.83(0.61, 1.12)	0.21	1.18(0.88, 1.59)	0.26	1.68(1.33, 2.13)	<0.01	1.58(1.04, 2.40)	0.03
Black African-Caribbean‡	1.11(0.75, 1.64)	0.61	1.47(1.01, 2.14)	0.04	1.83(1.27, 2.62)	<0.01	1.80(1.31, 2.47)	<0.01	1.71(0.97, 3.01)	0.06
Obesity†	0.05(0.05, 0.06)	<0.01	0.05(0.04, 0.06)	<0.01	0.05(0.04, 0.06)	<0.01	0.07(0.06, 0.08)	<0.01	0.10(0.09, 0.12)	<0.01
White	Ref		Ref		Ref		Ref		Ref	
South Asian‡	1.06(0.66, 1.70)	0.80	2.00(1.31, 3.05)	<0.01	2.38(1.58, 3.58)	<0.01	2.04(1.44, 2.90)	<0.01	1.79(1.20, 2.67)	<0.01
Black African-Caribbean‡	2.81(1.54, 5.12)	<0.01	3.88(2.12, 7.08)	<0.01	2.20(1.06, 4.59)	0.03	3.12(1.73, 5.62)	<0.01	0.84(0.33, 2.12)	0.71
Girls										
Overweight†	0.26(0.24, 0.28)	<0.01	0.24(0.22, 0.26)	<0.01	0.22(0.21, 0.24)	<0.01	0.35(0.33, 0.39)	<0.01	0.30(0.27, 0.33)	<0.01
White	Ref		Ref		Ref		Ref		Ref	
South Asian‡	0.63(0.48, 0.84)	<0.01	0.77(0.57, 1.04)	0.09	1.29(0.96, 1.74)	0.09	1.06(0.86, 1.31)	0.58	1.04(0.78, 1.39)	0.77
Black African-Caribbean‡	1.07(0.67, 1.72)	0.78	1.99(1.41, 2.81)	<0.01	2.32(1.35, 4.00)	<0.01	1.83(1.35, 2.48)	<0.01	2.12(1.50, 3.00)	<0.01
Obesity†	0.07(0.06, 0.08)	<0.01	0.07(0.06, 0.08)	<0.01	0.07(0.07, 0.08)	<0.01	0.09(0.08, 0.11)	<0.01	0.11(0.09, 0.13)	<0.01
White	Ref		Ref		Ref		Ref		Ref	
South Asian‡	1.31(0.86, 1.99)	0.21	1.12(0.75, 1.67)	0.57	1.59(1.07, 2.37)	0.02	1.22(0.82, 1.81)	0.32	1.48(1.03, 2.13)	0.03
Black African-Caribbean‡	2.77(1.92, 4.00)	<0.01	2.58(1.67, 3.98)	<0.01	3.49(2.39, 5.10)	<0.01	3.02(2.03, 4.48)	<0.01	1.54(0.94, 2.54)	0.09

* CI: confidence interval. Ref: reference group. 'Overweight' group does not include 'obesity'. Analysis is weighted to take into account disproportional sampling design and attrition at each sweep.

† Estimates in row are the overall risks of 'overweight' (vs. 'healthy') when the predictor in the models is evaluated at zero (i.e. White).

‡ RRR indicates how the risk ratio (risk of the outcome vs. healthy BMI group) changes with ethnicity. An RRR > 1 indicates that the risk of the outcome is higher in the minority ethnic group than in the White group, and an RRR < 1 indicates that the risk of the outcome is lower in the minority ethnic group.

Table S15: Estimated BMI differences in cm with 95% confidence interval (CI) between South Asian and White groups at each age, from unadjusted and adjusted mixed effects fractional polynomial models

Age	Model 1	Model 2	Model 3	Model 4	Model 5
	Diff(95% CI)	Diff(95% CI)	Diff(95% CI)	Diff(95% CI)	Diff(95% CI)
Boys					
3	-0.79(-0.90, -0.67)	-0.79(-0.91, -0.68)	-0.71(-0.84, -0.58)	-0.53(-0.64, -0.42)	-0.51(-0.62, -0.40)
4	-0.75(-0.86, -0.65)	-0.76(-0.86, -0.66)	-0.68(-0.79, -0.56)	-0.48(-0.58, -0.38)	-0.46(-0.56, -0.36)
5	-0.67(-0.78, -0.56)	-0.68(-0.79, -0.57)	-0.58(-0.70, -0.47)	-0.37(-0.47, -0.27)	-0.34(-0.44, -0.24)
6	-0.55(-0.67, -0.42)	-0.55(-0.68, -0.43)	-0.43(-0.55, -0.31)	-0.20(-0.32, -0.09)	-0.17(-0.29, -0.06)
7	-0.39(-0.54, -0.24)	-0.40(-0.55, -0.25)	-0.25(-0.37, -0.12)	0.00(-0.14, 0.13)	0.04(-0.10, 0.17)
8	-0.22(-0.40, -0.05)	-0.23(-0.40, -0.05)	-0.03(-0.17, 0.10)	0.22(0.06, 0.38)	0.27(0.11, 0.43)
9	-0.06(-0.26, 0.15)	-0.06(-0.27, 0.14)	0.18(0.03, 0.33)	0.44(0.25, 0.62)	0.50(0.31, 0.69)
10	0.09(-0.14, 0.32)	0.09(-0.15, 0.32)	0.38(0.21, 0.55)	0.63(0.42, 0.85)	0.71(0.49, 0.93)
11	0.20(-0.06, 0.46)	0.20(-0.06, 0.45)	0.54(0.34, 0.74)	0.79(0.55, 1.03)	0.88(0.63, 1.13)
12	0.25(-0.03, 0.53)	0.25(-0.03, 0.53)	0.63(0.40, 0.86)	0.88(0.61, 1.15)	0.98(0.71, 1.25)
13	0.23(-0.07, 0.53)	0.23(-0.07, 0.53)	0.64(0.38, 0.91)	0.88(0.60, 1.16)	0.99(0.71, 1.28)
14	0.11(-0.21, 0.43)	0.12(-0.20, 0.43)	0.55(0.23, 0.86)	0.78(0.48, 1.08)	0.89(0.59, 1.19)
Girls					
3	-0.58(-0.70, -0.46)	-0.60(-0.72, -0.47)	-0.55(-0.70, -0.41)	-0.37(-0.50, -0.24)	-0.37(-0.50, -0.23)
4	-0.59(-0.70, -0.47)	-0.59(-0.71, -0.48)	-0.52(-0.64, -0.39)	-0.35(-0.46, -0.23)	-0.34(-0.45, -0.22)
5	-0.58(-0.70, -0.46)	-0.58(-0.70, -0.46)	-0.46(-0.58, -0.33)	-0.30(-0.41, -0.18)	-0.28(-0.39, -0.17)
6	-0.55(-0.69, -0.41)	-0.55(-0.69, -0.41)	-0.38(-0.51, -0.25)	-0.22(-0.34, -0.10)	-0.20(-0.32, -0.08)
7	-0.52(-0.68, -0.35)	-0.51(-0.67, -0.35)	-0.29(-0.42, -0.15)	-0.13(-0.26, 0.00)	-0.10(-0.23, 0.03)
8	-0.47(-0.66, -0.28)	-0.47(-0.66, -0.28)	-0.19(-0.33, -0.04)	-0.03(-0.17, 0.11)	0.00(-0.13, 0.14)
9	-0.43(-0.65, -0.21)	-0.42(-0.64, -0.20)	-0.08(-0.24, 0.08)	0.07(-0.08, 0.22)	0.11(-0.04, 0.26)
10	-0.39(-0.64, -0.14)	-0.38(-0.63, -0.13)	0.02(-0.17, 0.20)	0.16(-0.01, 0.34)	0.21(0.04, 0.39)
11	-0.36(-0.63, -0.08)	-0.35(-0.62, -0.07)	0.11(-0.10, 0.32)	0.25(0.04, 0.45)	0.30(0.09, 0.51)
12	-0.35(-0.64, -0.05)	-0.33(-0.62, -0.04)	0.19(-0.05, 0.43)	0.30(0.06, 0.54)	0.36(0.12, 0.60)
13	-0.37(-0.67, -0.06)	-0.33(-0.64, -0.03)	0.25(-0.03, 0.53)	0.33(0.05, 0.60)	0.40(0.12, 0.67)
14	-0.42(-0.75, -0.09)	-0.36(-0.69, -0.04)	0.29(-0.03, 0.62)	0.32(0.00, 0.64)	0.39(0.07, 0.71)

*Diff: estimated difference in mean BMI between South Asian and White (reference) groups. Model 1: unadjusted model; model 2: model 1 adjusted for child's height; model 3: model 2 further adjusted for maternal smoking and pre-pregnancy BMI; model 4: model 3 further adjusted for birthweight and infant weight gain; model 5: model 4 further adjusted for breastfeeding and early introduction to solid foods. All covariates were included as both main effects and their interaction with all age terms.

Table S16: Estimated BMI differences in cm with 95% confidence interval (CIs) between Black African-Caribbean and White groups at each age, from unadjusted and adjusted mixed effects fractional polynomial models

Age	Model 1	Model 2	Model 3	Model 4	Model 5
	Diff(95% CI)	Diff(95% CI)	Diff(95% CI)	Diff(95% CI)	Diff(95% CI)
Boys					
3	0.03(-0.15, 0.21)	0.01(-0.17, 0.20)	0.00(-0.19, 0.18)	-0.18(-0.39, 0.03)	-0.08(-0.28, 0.12)
4	0.15(-0.02, 0.32)	0.13(-0.04, 0.30)	0.12(-0.05, 0.29)	-0.08(-0.27, 0.10)	-0.06(-0.22, 0.11)
5	0.32(0.14, 0.49)	0.29(0.12, 0.47)	0.29(0.11, 0.47)	0.05(-0.13, 0.23)	0.00(-0.17, 0.16)
6	0.49(0.29, 0.70)	0.47(0.27, 0.67)	0.47(0.27, 0.68)	0.19(0.00, 0.39)	0.07(-0.11, 0.25)
7	0.66(0.43, 0.90)	0.64(0.40, 0.87)	0.64(0.40, 0.88)	0.32(0.12, 0.53)	0.14(-0.05, 0.34)
8	0.81(0.53, 1.09)	0.78(0.50, 1.06)	0.78(0.50, 1.06)	0.43(0.21, 0.65)	0.21(0.00, 0.42)
9	0.92(0.59, 1.24)	0.89(0.56, 1.21)	0.88(0.55, 1.20)	0.49(0.25, 0.74)	0.25(0.01, 0.49)
10	0.97(0.60, 1.35)	0.95(0.57, 1.32)	0.92(0.55, 1.30)	0.51(0.22, 0.79)	0.25(-0.03, 0.52)
11	0.97(0.55, 1.39)	0.94(0.53, 1.36)	0.90(0.48, 1.32)	0.45(0.12, 0.79)	0.19(-0.14, 0.51)
12	0.89(0.44, 1.35)	0.87(0.42, 1.32)	0.81(0.35, 1.26)	0.33(-0.05, 0.71)	0.04(-0.34, 0.43)
13	0.74(0.26, 1.22)	0.71(0.23, 1.20)	0.63(0.15, 1.12)	0.12(-0.32, 0.56)	-0.19(-0.63, 0.25)
14	0.49(-0.02, 1.01)	0.47(-0.04, 0.99)	0.37(-0.15, 0.89)	-0.18(-0.70, 0.34)	-0.54(-1.06, -0.02)
Girls					
3	0.03(-0.17, 0.24)	-0.01(-0.22, 0.20)	-0.05(-0.26, 0.16)	-0.33(-0.58, -0.09)	-0.18(-0.41, 0.04)
4	0.15(-0.04, 0.34)	0.10(-0.09, 0.29)	0.06(-0.13, 0.25)	-0.24(-0.46, -0.03)	-0.20(-0.39, -0.01)
5	0.32(0.12, 0.52)	0.27(0.07, 0.47)	0.22(0.02, 0.42)	-0.11(-0.32, 0.10)	-0.18(-0.37, 0.00)
6	0.53(0.30, 0.77)	0.48(0.25, 0.71)	0.42(0.19, 0.65)	0.04(-0.18, 0.27)	-0.13(-0.33, 0.07)
7	0.76(0.49, 1.04)	0.70(0.43, 0.97)	0.63(0.35, 0.90)	0.20(-0.03, 0.44)	-0.04(-0.26, 0.17)
8	0.99(0.67, 1.31)	0.92(0.60, 1.24)	0.83(0.51, 1.15)	0.35(0.10, 0.60)	0.06(-0.18, 0.29)
9	1.20(0.82, 1.57)	1.13(0.75, 1.50)	1.01(0.64, 1.39)	0.47(0.20, 0.75)	0.15(-0.11, 0.41)
10	1.37(0.95, 1.80)	1.30(0.88, 1.72)	1.16(0.73, 1.59)	0.57(0.25, 0.89)	0.23(-0.07, 0.53)
11	1.50(1.03, 1.97)	1.43(0.96, 1.89)	1.26(0.79, 1.73)	0.62(0.25, 0.99)	0.26(-0.09, 0.62)
12	1.57(1.06, 2.07)	1.50(1.00, 2.00)	1.30(0.80, 1.81)	0.62(0.20, 1.05)	0.24(-0.18, 0.66)
13	1.56(1.03, 2.09)	1.51(0.98, 2.03)	1.27(0.74, 1.80)	0.56(0.07, 1.05)	0.13(-0.35, 0.61)
14	1.46(0.90, 2.02)	1.43(0.87, 1.99)	1.15(0.59, 1.72)	0.44(-0.14, 1.01)	-0.09(-0.65, 0.48)

*Diff: estimated difference in mean BMI between Black African-Caribbean and White groups with the White group as the reference. Model 1: unadjusted model; model 2: model 1 adjusted for child's height; model 3: model 2 further adjusted for family income and maternal education; model 4: model 3 further adjusted for maternal BMI; model 5: model 4 further adjusted for birthweight and infant weight gain. All covariates were included as both main effects and their interaction with all age terms.

Table S17: Estimated odds ratios (ORs) of overweight with 95% confidence intervals (CIs) by sex, from unadjusted logistic regression

	3 years	5 years	7 years	11 years	14 years
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Boys	(n=13413)	(n=13688)	(n=12420)	(n=11866)	(n=10270)
White	Ref	Ref	Ref	Ref	Ref
SA	0.62(0.49, 0.78)	1.08(0.84, 1.39)	1.47(1.16, 1.86)	1.76(1.43, 2.17)	1.64(1.18, 2.28)
Black	1.41(0.96, 2.07)	1.99(1.34, 2.96)	1.92(1.33, 2.77)	2.09(1.50, 2.90)	1.46(0.87, 2.45)
Girls	(n=13594)	(n=13825)	(n=12507)	(n=11796)	(n=10214)
White	Ref	Ref	Ref	Ref	Ref
SA	0.77(0.61, 0.97)	0.85(0.67, 1.09)	1.37(1.07, 1.75)	1.10(0.88, 1.36)	1.16(0.90, 1.49)
Black	1.41(0.99, 2.02)	2.13(1.59, 2.84)	2.61(1.73, 3.94)	2.07(1.56, 2.75)	1.97(1.39, 2.78)

*Overweight was defined using IOTF references and included obesity. Models were weighted to take into account disproportional sampling design and attrition. SA: South Asian; Black: Black African-Caribbean. Ref: reference group.

Table S18: Ethnic differences in the relationship between BMI (kg/m^2) and waist circumference (cm) at 5 and 7 years, based on linear regression models

	Waist (cm)			
	5 years		7 years	
	b	**95%CI**	b	95%CI
Boys	*n*=7032		*n*=6749	
Intercept	49.36	[49.23,49.48]	49.38	[49.25,49.51]
Ethnicity				
White	ref	--	ref	--
South Asian	-0.74	[-1.04,-0.43]	-0.79	[-1.12,-0.46]
Black	-0.66	[-1.25,-0.07]	-0.37	[-1.06,0.32]
BMI	1.97	[1.93,2.02]	1.92	[1.88,1.97]
BMI*Ethnicity				
White	ref		ref	
South Asian	0.36	[0.24,0.48]	0.42	[0.29,0.55]
Black	-0.03	[-0.21,0.14]	0.19	[-0.01,0.39]
Age (centred)	1.66	[1.42,1.91]	1.46	[1.19,1.74]
Girls	*n*=6371		*n*=6231	
Intercept	51.52	[51.40,51.65]	51.36	[51.22,51.49]
Ethnicity				
White	ref	--	ref	--
South Asian	-0.19	[-0.54,0.15]	-0.03	[-0.39,0.34]
Black	-1.02	[-1.69,-0.36]	0.58	[-0.24,1.39]
BMI	2.23	[2.19,2.27]	2.17	[2.13,2.20]
BMI*Ethnicity				
White	ref	--	ref	--
South Asian	0.30	[0.19,0.41]	0.18	[0.08,0.29]
Black	0.16	[-0.01,0.32]	-0.14	[-0.32,0.05]
Age (centred)	1.33	[1.04,1.63]	1.20	[0.88,1.52]

*b: coefficient estimate. CI: confidence interval. Estimates were based on regression of waist on age, BMI, ethnicity and ethnicity*BMI. Age was centred at mean and BMI was centred at 14 kg/m^2, therefore the coefficients for ethnicity reflect ethnic differences in waist circumference when age equals to the mean value and BMI equals to 14 kg/m^2. Analysis was repeated for 5 years and 7 years separately.

Table S19: Ethnic differences in the relationship between BMI (kg/m^2) and body fat (%) at 7, 11 and 14 years, based on quadratic regression models

	Boys						Girls					
	7 years		11 years		14 years		7 years		11 years		14 years	
N	5683		5390		5381		5138		4387		4372	
Intercept	15.7	[15.52,15.92]	15.9	[15.69,16.05]	9.9	[9.52,10.26]	12.2	[12.00,12.48]	4.7	[3.85,5.45]	10.2	[9.79,10.53]
Ethnicity												
White	ref	--	ref	--	ref	--	ref	--	ref	--	ref	--
South Asian	0.95	[0.37,1.54]	1.47	[0.96,1.97]	2.05	[0.92,3.18]	2.03	[1.30,2.75]	2.27	[-0.10,4.64]	2.73	[1.68,3.77]
Black African-Caribbean	1.64	[0.51,2.77]	0.46	[-0.63,1.55]	3.11	[1.05,5.17]	-0.37	[-2.01,1.28]	4.67	[0.71,8.63]	3.69	[1.41,5.97]
BMI	1.24	[1.09,1.39]	2.34	[2.21,2.48]	1.93	[1.79,2.08]	2.60	[2.51,2.70]	1.65	[1.43,1.86]	2.61	[2.52,2.71]
Ethnicity*BMI												
White	ref	--	ref	--	ref	--	ref	--	ref	--	ref	--
South Asian	0.79	[0.32,1.26]	0.48	[0.08,0.89]	0.22	[-0.22,0.67]	0.03	[-0.25,0.31]	-0.04	[-0.70,0.62]	-0.19	[-0.46,0.08]
Black African-Caribbean	-0.63	[-1.40,0.14]	0.16	[-0.57,0.90]	-0.98	[-1.76,-0.20]	0.31	[-0.27,0.90]	-1.29	[-2.37,-0.22]	-0.58	[-1.12,-0.03]
BMI^2	0.10	[0.08,0.13]	-0.01	[-0.03,0.01]	0.01	[-0.00,0.02]	-0.05	[-0.05,-0.04]	0.01	[-0.01,0.02]	-0.05	[-0.06,-0.04]
Ethnicity*BMI^2												
White	ref	--	ref	--	ref	--	ref	--	ref	--	ref	--
South Asian	-0.09	[-0.16,-0.01]	-0.08	[-0.15,-0.02]	0.00	[-0.03,0.04]	-0.02	[-0.04,0.01]	0.02	[-0.02,0.06]	0.00	[-0.02,0.02]
Black African-Caribbean	0.08	[-0.03,0.19]	-0.02	[-0.13,0.08]	0.07	[0.01,0.13]	-0.03	[-0.07,0.02]	0.08	[0.01,0.14]	0.02	[-0.01,0.05]
Age (centred)	0.13	[-0.12,0.37]	0.22	[-0.01,0.44]	-2.09	[-2.35,-1.82]	-1.53	[-1.69,-1.36]	-2.00	[-2.33,-1.66]	-0.58	[-0.72,-0.43]

*b: coefficient estimate. CI: confidence interval. Estimates were based on regression of body fat on age, BMI, BMI^2, ethnicity and interaction between ethnicity and both BMI terms. Age was centred at mean and BMI was centred at 14 kg/m^2, therefore the coefficients for ethnicity reflect ethnic differences in body fat when age equals to the mean value and BMI equals to 14 kg/m^2. Analysis was repeated for 7, 11, and 14 years separately.

Table S20: Estimated ethnic differences in waist circumference SDS, body fat SDS and body mass index (BMI) SDS with 95% confidence interval from weighted linear regression models

			Unadjusted		
	Age	N	White	South Asian	Black African-Caribbean
Boys					
Waist SDS	5	7043	ref	-0.45 (-0.61, -0.30)	0.07 (-0.17, 0.32)
	7	6417	ref	-0.19 (-0.33, -0.05)	0.17 (-0.03, 0.38)
Body fat SDS	7	6344	ref	0.20 (0.11, 0.29)	0.35 (0.18, 0.53)
	11	5969	ref	0.71 (0.58, 0.84)	0.60 (0.30, 0.90)
	14	5067	ref	0.89 (0.65, 1.13)	0.29 (-0.42, 1.00)
BMI SDS	5	7106	ref	-0.52 (-0.65, -0.40)	0.24 (0.02, 0.46)
	7	6413	ref	-0.34 (-0.46, -0.21)	0.24 (0.05, 0.43)
	11	6071	ref	0.05 (-0.07, 0.17)	0.38 (0.14, 0.63)
	14	5186	ref	-0.02 (-0.19, 0.16)	-0.04 (-0.45, 0.37)
Girls					
Waist SDS	5	6770	ref	0.07 (-0.17, 0.32)	0.27 (0.10, 0.43)
	7	6251	ref	0.17 (-0.03, 0.38)	0.50 (0.32, 0.68)
Body fat SDS	7	6155	ref	0.35 (0.18, 0.53)	0.61 (0.36, 0.87)
	11	5850	ref	0.60 (0.30, 0.90)	0.64 (0.45, 0.84)
	14	4971	ref	0.29 (-0.42, 1.00)	0.58 (0.38, 0.77)
BMI SDS	5	6808	ref	-0.34 (-0.45, -0.24)	0.32 (0.16, 0.48)
	7	6267	ref	-0.23 (-0.35, -0.10)	0.39 (0.20, 0.58)
	11	5913	ref	-0.09 (-0.21, 0.04)	0.46 (0.26, 0.67)
	14	5034	ref	-0.12 (-0.25, 0.02)	0.43 (0.22, 0.64)

*ref: reference group. Estimates are based linear regression of each adiposity outcome on age at the measurement and ethnicity. Analysis was weighted with sampling and attrition weights.

Appendix V: Supplementary materials for Chapter 7

Table S21: Comparison of participant characteristics between the included eligible sample (i.e. analysis sample) and the excluded eligible sample

	Analysis sample (*n*=10 711)		**Excluded sample (*n*= 895)**		***p-value*†**
Continuous variables	*n*	Mean (SD)	*n*	Mean(SD)	*p*
Maternal pre-pregnancy BMI, kg/m^2	10711	23.7 (4.4)	16	25.7 (6.0)	0.21
BMI (5-year visit), kg/m2	10079	16.3 (1.6)	813	16.3 (1.8)	0.89
BMI (7-year visit), kg/m^2	9277	16.6 (2.1)	744	16.7 (2.4)	0.15
BMI (11-year visit), kg/m^2	8722	19.1 (3.4)	692	19.5 (3.7)	<0.01
BMI (14-year visit), kg/m^2	7556	21.3 (3.9)	617	21.9 (4.4)	<0.01
Categorical variables	*n*	%	*n*	%	*p*
Rapid weight gain	10,711		895		0.06
Yes		42.4%		45.6%	
Birthweight for gestational age	10,711		895		<0.01
SGA		8.8%		12.6%	
AGA		81.3%		77.8%	
LGA		10.0%		9.6%	
Maternal smoking in pregnancy	10,711		887		0.05
Yes (>0 cigarette/day)		22.5%		19.6%	
Duration of exclusive breastfeeding	10,711		895		<0.01
None		30.8%		36.9%	
0 – 4 months		65.6%		60.7%	
4 months or longer		3.6%		2.5%	
Early introduction to solid foods	10,711		893		<0.01
Yes (<4 months)		36.3%		30.6%	
Mother's highest academic qualifications	10,711		881		<0.01
Diploma or degree		28.0%		17.4%	
A-level		10.4%		6.9%	
GCSE grades A*-C		34.2%		28.2%	
GCSE grades D-G		10.2%		12.4%	
Others		2.3%		5.2%	
None		14.8%		30.0%	
Family income quintiles	10,711		895		<0.01
Lowest quintile		19.5%		37.2%	
Second quintile		21.1%		27.6%	
Third quintile		19.9%		14.0%	
Fourth quintile		20.5%		11.2%	
Highest quintile		19.0%		10.1%	
Ethnicity	10,711		895		<0.01
White		86.9%		64.7%	
South Asian		7.0%		22.8%	
Black		2.0%		8.0%	
Others		4.1%		4.5%	

* Values are unweighted mean (SD), unless otherwise stated. RWG: rapid weight gain; SGA/AGA/LGA: small-/appropriate-/large-for-gestational age.

† *P*-value for the differences between groups. Welch's t-tests were used for continuous variables, due to unequal variances between groups. Chi-squared tests were used for categorical variables.

Table S22: Comparison of deviance between first-, second- and third-order fractional polynomial models for BMI between 5 and 14 years

Model	d.f.*	Powers	Deviance	Deviance difference†	*P*‡
Boys					
Linear	1	1	85168	738	<0.001
First-order	2	2	84772	342	<0.001
Second-order	4	0.5 0.5	84464	34	<0.001
Third-order	6	1 2 2	84430	--	--
Girls					
Linear	1	1	87336	1014	<0.001
First-order	2	2	86578	256	<0.001
Second-order	4	0 1	86332	10	0.006
Third-order	6	1 2 2	--	--	--

* Degrees of freedom, including the number of fractional polynomial powers and coefficients estimated. † The deviance difference compares the fit with that of the best fitting third-order model (i.e. model with powers 1 2 2). ‡ P value for the deviance difference between each model and the best fitting third-order model with a x^2 distribution.

Table S23: Estimated mean BMI difference at each age between RWG and non-RWG (reference) groups, from sensitivity analysis using an alternative RWG variable derived using UK 1990 growth references

	Model 1		**Model 2**		**Model 3 (stratified analysis)**					
	Unadjusted		Adjusted		SGA		AGA		LGA	
age	diff	95%CI	diff	95%CI	diff	95%CI	diff	95%CI	diff	95%CI
Boys										
5	0.8	(0.8, 1.0)	0.8	(0.8, 0.9)	1.0	(0.5, 1.2)	0.9	(0.9, 1.1)	1.7	(0.9, 1.8)
6	1.0	(1.0, 1.2)	1.0	(1.0, 1.2)	1.4	(0.8, 1.5)	1.1	(1.1, 1.3)	2.3	(1.3, 2.1)
7	1.1	(1.1, 1.3)	1.1	(1.1, 1.3)	1.5	(0.9, 1.7)	1.2	(1.2, 1.4)	2.7	(1.4, 2.5)
8	1.2	(1.2, 1.4)	1.2	(1.2, 1.4)	1.4	(0.9, 1.8)	1.3	(1.3, 1.5)	2.9	(1.5, 2.7)
9	1.2	(1.2, 1.5)	1.2	(1.2, 1.5)	1.4	(0.8, 1.9)	1.4	(1.3, 1.6)	3.1	(1.6, 2.9)
10	1.3	(1.3, 1.6)	1.3	(1.3, 1.6)	1.3	(0.8, 1.9)	1.5	(1.4, 1.7)	3.2	(1.6, 3.1)
11	1.3	(1.3, 1.6)	1.3	(1.3, 1.6)	1.1	(0.7, 1.9)	1.5	(1.4, 1.8)	3.3	(1.7, 3.3)
12	1.3	(1.3, 1.7)	1.3	(1.3, 1.7)	1.0	(0.6, 2.0)	1.6	(1.5, 1.8)	3.4	(1.7, 3.5)
13	1.3	(1.3, 1.7)	1.4	(1.3, 1.7)	0.9	(0.5, 2.0)	1.6	(1.5, 1.9)	3.5	(1.7, 3.6)
14	1.4	(1.3, 1.7)	1.4	(1.3, 1.7)	0.7	(0.4, 2.0)	1.7	(1.5, 2.0)	3.5	(1.7, 3.8)
Girls										
5	0.9	(0.9, 1.1)	0.9	(0.9, 1.1)	1.4	(0.8, 1.5)	1.1	(1.1, 1.3)	3.0	(1.6, 2.7)
6	1.1	(1.2, 1.3)	1.1	(1.2, 1.4)	1.5	(1.0, 1.7)	1.4	(1.3, 1.5)	3.6	(2.0, 3.0)
7	1.2	(1.3, 1.5)	1.2	(1.3, 1.5)	1.6	(1.1, 1.9)	1.5	(1.5, 1.7)	4.1	(2.2, 3.4)
8	1.3	(1.4, 1.6)	1.3	(1.4, 1.7)	1.8	(1.2, 2.1)	1.6	(1.6, 1.9)	4.5	(2.4, 3.8)
9	1.4	(1.5, 1.8)	1.4	(1.5, 1.8)	1.9	(1.3, 2.3)	1.7	(1.7, 2.0)	4.9	(2.5, 4.1)
10	1.5	(1.6, 1.9)	1.5	(1.6, 1.9)	2.1	(1.4, 2.5)	1.8	(1.7, 2.1)	5.2	(2.7, 4.4)
11	1.6	(1.6, 2.0)	1.6	(1.6, 2.0)	2.2	(1.5, 2.7)	1.8	(1.8, 2.2)	5.6	(2.8, 4.7)
12	1.6	(1.7, 2.1)	1.7	(1.7, 2.1)	2.4	(1.6, 2.9)	1.9	(1.8, 2.3)	5.9	(2.9, 5.0)
13	1.7	(1.7, 2.2)	1.7	(1.8, 2.2)	2.5	(1.6, 3.1)	2.0	(1.9, 2.4)	6.2	(3.0, 5.4)
14	1.8	(1.8, 2.2)	1.8	(1.8, 2.3)	2.7	(1.7, 3.3)	2.0	(1.9, 2.4)	6.5	(3.1, 5.7)

*Values are estimated mean BMI differences with 95% confidence interval (CI) in kg/m^2, from mixed effects fractional polynomial models. RWG: rapid weight gain was defined as a change in weight z-scores greater than 0.67 SDS (UK 1990 growth references). SGA/AGA/LGA: small/appropriate/large for gestational age. Model 1 is the unadjusted model. Model 2 adjusted for maternal pre-pregnancy BMI, maternal smoking during pregnancy, duration of exclusive breastfeeding, early introduction of solid foods and ethnicity. Model 3 is model 2 stratified by birthweight group.

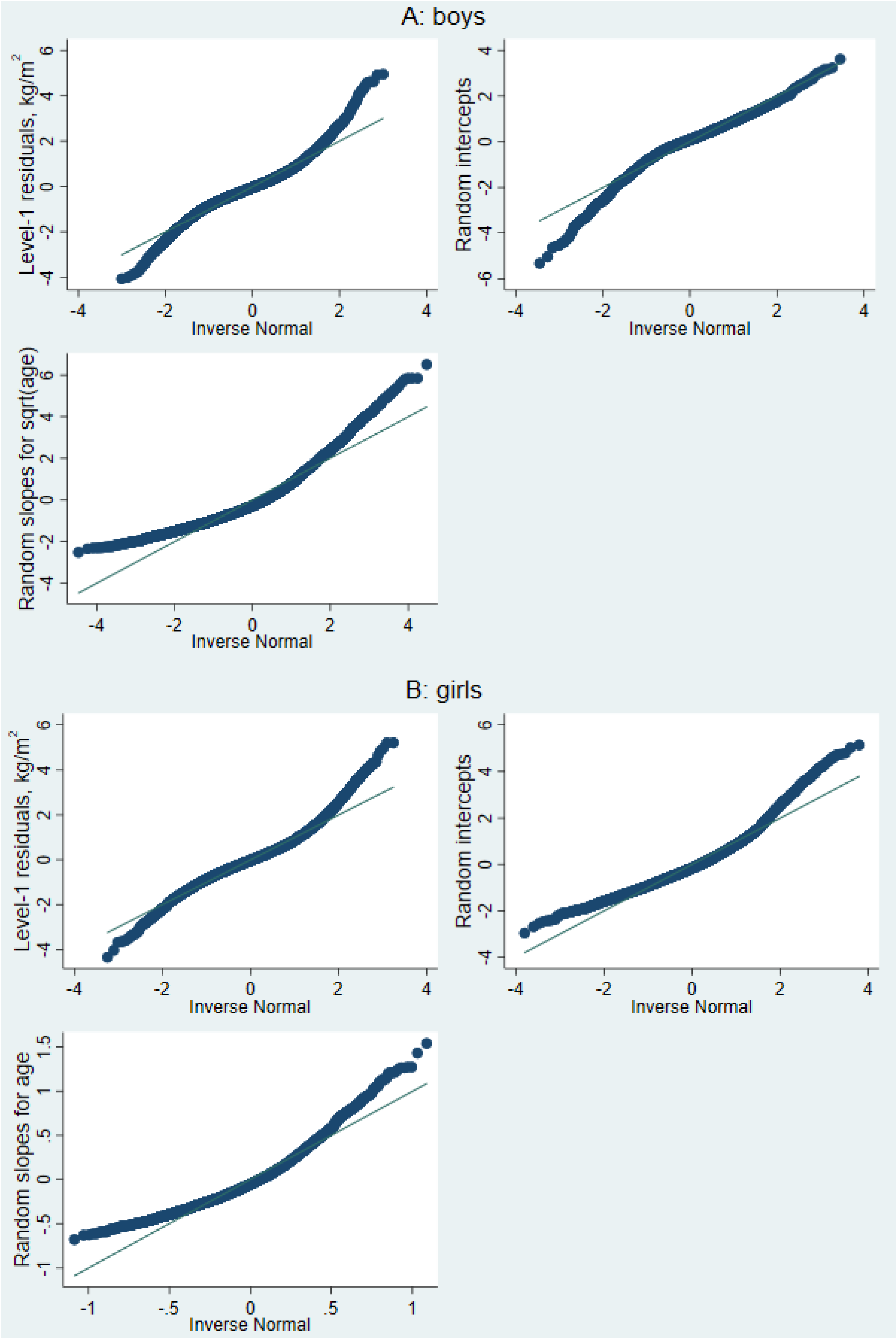

Figure S10: Q-Q (quantile-quantile) plots of level-1 residuals, level-2 random intercepts and random coefficients for age terms from second-order fractional polynomial models for BMI between 5 and 14 years

Estimated from mixed-effects fractional polynomial models. In boys, random effects were allowed for intercept and $\sqrt{age}$. In girls, random effects were allowed for intercept and age.

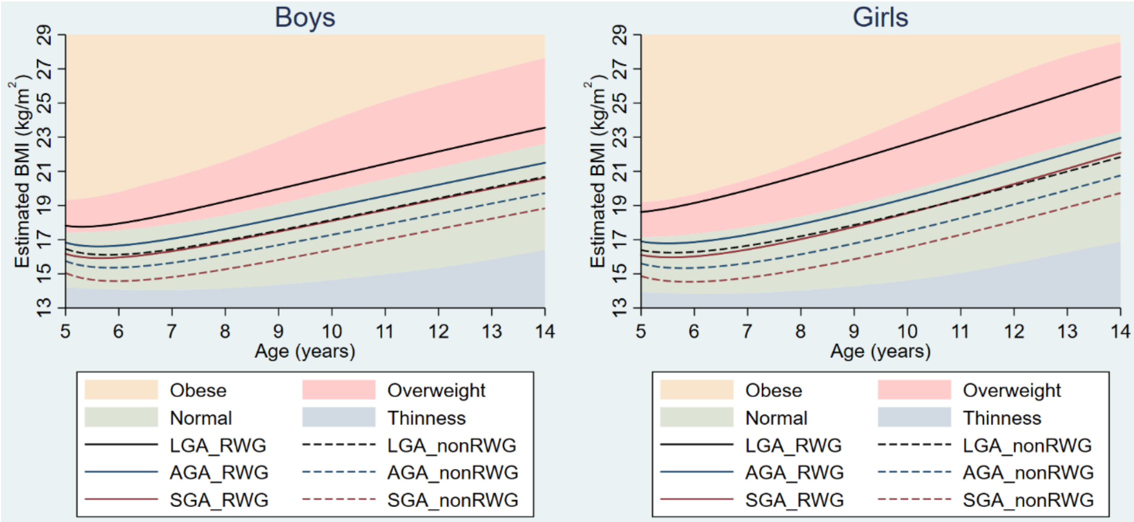

Figure S11: BMI trajectories (5-14 years) by RWG and birthweight groups, mapped onto IOTF BMI reference bands from sensitivity analysis using alternative birthweight for gestational age variable

Estimated from mixed effects fractional polynomial models, adjusted for maternal pre-pregnancy BMI, maternal smoking during pregnancy, duration of exclusive breastfeeding, early introduction of solid foods and ethnicity. RWG: rapid weight gain; IOTF: International Obesity Task Force.