Body mass index and use of healthcare services in children: analyses from the Born in Bradford cohort study

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Abstract

The prevalence of childhood obesity in the UK is among the highest in Europe, but it is not well-known how childhood obesity affects the health of children from different ethnic backgrounds and what burden it carries for healthcare systems in childhood. South Asian people in the UK are shown to have a higher risk of obesity-associated diseases and their patterns of healthcare utilisation vary from that of White British people mostly due to different health-seeking behaviours and barriers to healthcare access. In this thesis, I explored the utilisation of primary and secondary healthcare services and associated healthcare costs by children's weight status in a multi-ethnic birth cohort and investigated potential effect modification by ethnicity.

I conducted a systematic-review and meta-analysis of the association between children's weight status and healthcare utilisation. This informed analyses of the Born in Bradford (BiB) cohort with linked primary and secondary healthcare data, which enabled analyses of healthcare utilisation and costs by children's weight status and ethnicity using negative binomial regression models.

The prevalence of obesity was 10.1% in Pakistani children and 9.9% in White British children, the two main ethnic groups in the BiB cohort. In the cohort analyses: obese children had significantly higher rates and costs of primary care consultations, primary care prescriptions and A&E visits, when compared to normal weight children. There was no effect modification by ethnicity, however independent of weight status, Pakistani children had significantly higher rates and costs compared to White British children across all measures of healthcare utilisation.

This thesis suggests that childhood obesity results in higher utilisation and costs of primary and secondary healthcare services during primary school years, indicative of higher clinical need and poor health in obese children compared to normal weight children. The findings highlight the importance of implementing effective childhood obesity interventions and prevention strategies that are tailored to the specific needs of a multi-ethnic population.

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Author's declaration

I declare that this thesis is a presentation of my original work, and I am the sole author.

This work has not previously been presented for an award at this, or any other, University.

All sources are acknowledged as references.

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2. Conference abstracts

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Chapter 1 Introduction

1.1 Obesity

Obesity is defined as a disease with excess accumulation of fat leading to an increased risk of adverse health outcomes in an individual (World Health Organization., 2018). More than 250 years ago, Dr Malcolm Flemyng described obesity as a disease stating, "corpulency, when in extraordinary degree, may be reckoned as a disease, and hath a tendency to shorten life, by paving a way to dangerous distempers" (Flemyng, 1760). During most of the last century and into the 21st century, the question of whether or not obesity should be identified as a disease process has sparked much debate and disagreement among scientists and researchers. It has been argued that obesity is not a disease but a consequence of an individual's behaviour and identifying it as a disease would take the responsibility away from an individual (Church, 2014). For the large part, this debate has been due to lack of research and available evidence into the complex and multi-factorial causal mechanisms of obesity. In 1997, the World Health Organization (WHO) and the International Obesity task force described obesity as a serious disease that was incompletely understood (World Health Organization, 1998). Over time, research has provided a deeper understanding in to the genetic, metabolic, environmental, and behavioural factors that result in obesity which are also discussed in detail later in this chapter. These developments have resulted in a number of worldwide professional health organizations recognizing obesity as a complex chronic disease (Scottish Intercollegiate Guidelines Network, 2010, Kyle et al., 2016). Most recently, the World Obesity Federation has described obesity as a "chronic, relapsing, progressive disease process" (Bray et al., 2017). This universal recognition of obesity as a serious chronic disease is expected to result in stakeholders taking it more seriously with increased funding going into future research

and interventions aimed at reducing the increasing prevalence of overweight and obesity worldwide.

1.2 Identification of Overweight and Obesity

Body Mass Index (BMI) is the recommended and most widely used anthropometric index to identify and classify individuals as underweight, normal weight, overweight and obese (World Health Organization, 2018a). BMI is calculated by dividing the weight of an individual in kilogram (kg) with the square of their height in meters (m^2).

BMI = (kg/m^2)

For adults 20 years and older, BMI is interpreted using weight status categories that are fixed for both men and women (World Health Organization, 2018b) (Table 1.1).

Table 1.1 *Identification of weight status in adults*

BMI	**Weight Status**
Below 18.5	Underweight
18.5 – 24.9	Normal or Healthy Weight
25.0 – 29.9	Overweight
30.0 – 34.9	Obesity class I
35.0-39.9	Obesity class II
Above 40	Obesity class III

The method to measure BMI in children is similar to that of adults (kg/m^2), however, the interpretation of BMI is different. In children, the height, weight and adiposity changes with age and differs by sex (National Obesity Observatory, 2011), therefore BMI in children is classified by using thresholds taking into account the age and sex of a child. These thresholds are calculated from a reference population by weighing and measuring the variation in BMI by age and sex in a large sample of children. An individual child of a particular sex and age can be compared to the mean BMI for that age and sex in the reference population and the extent of variation from the reference value can be

calculated. International Obesity Task Force (IOTF) thresholds are widely used, particularly to make global comparisons of overweight and obesity in children (National Obesity Observatory, 2011). Age and sex-specific cut-off points are extrapolated from the adult BMI cut-offs of 25 kg/m^2 and 30 kg/m^2 for overweight and obesity, respectively (Cole et al., 2000). The WHO has developed two separate growth references for children aged 0-5 years and 5-19 years. The WHO recommends use of standard deviation (SD) spacing to identify thresholds for overweight and obesity (World Health Organization, 2006).

- Underweight: <-2 SD
- Normal Weight: ≥-2 SD and <+1 SD
- Overweight: between +1 SD and <+2 SD
- Obesity: ≥+2 SD

In the United Kingdom (UK), the UK90 growth reference curves based on a sample of British children are used to identify overweight and obesity in children aged four years and over (Cole et al., 1995). These UK90 reference curves identify weight category of a child of specific sex and age based upon reference population centiles (Dinsdale et al., 2011). As an example, the interpretation of an obese boy of a specific age would be if his BMI falls at or above the 95th percentile for his age (Table 1.2). For children aged 0-4 years, the WHO growth reference curves are recommended for use in the UK with the interpretation similar to what is shown in table 1.2 (Dinsdale et al., 2011).

Table 1.2 *Identification of weight status in children and adolescents*

Weight Status Category	**Percentile Range**
Underweight	Less than the 5th percentile
Normal or Healthy Weight	5th percentile to less than the 85th percentile
Overweight	85th to less than the 95th percentile
Obese	Equal to or greater than the 95th percentile

BMI is used as a screening and not a diagnostic tool to identify excess body fat (CDC, 2019). In other words, BMI is not a direct measure of body fat level as the weight component of the equation includes the muscle, water and bone weight of an individual, and can therefore be considered as a proxy for measures of body fat (Adab et al., 2018). BMI has been found to correlate with body fat levels measured through direct methods, however questions have been raised around the use of BMI as a tool to accurately predict body fat levels, particularly for individuals belonging to different sex or ethnic groups (Purnell, 2018). This critique of BMI is explored in detail later on in this chapter.

1.3 Obesity: a global epidemic

Obesity, which is often declared as a pandemic, has almost tripled since 1975 (Swinburn et al., 2019). According to recent estimates in 2016, more than 1.9 billion adults were overweight globally, with 650 million being obese (World Health Organization., 2018). This steep increase in obesity has been observed across the globe, with a report in 2015 estimating that obesity has doubled in 73 countries since 1980 (GBD Obesity Collaborators, 2017). If the current unabated rise of overweight and obesity continues, the future predictions do not present a very hopeful picture. As shown in figure 1.1 , if the current

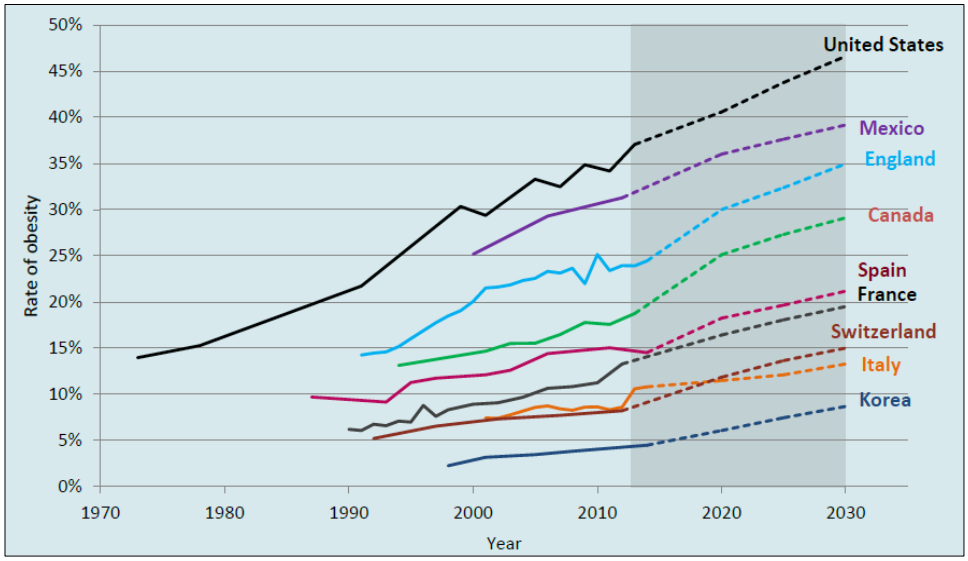

Figure 1.1 *Future trends in obesity prevalence up to 2030 (OECD, 2017)*

trend continues, the rate of obesity would almost double by 2030 compared to rates in 2010.

The rise of obesity in children and adolescents has been an even greater concern. The WHO has declared childhood obesity as one of the biggest public health problems of the present time which is putting future generations at a potential risk of unwanted health conditions (World Health Organization., 2018). In 2016, 41 million children under the age of 5 years and over 340 million children and adolescents aged 5-19 years were overweight or obese globally. This represents an alarming increase from 4% in 1975 to 18% in 2016. If the current trends continue, the total number of obese and overweight children are predicted to rise up to 70 million by 2025 (World Health Organization., 2017b). Additionally, once only considered a problem of developed countries, obesity rates have also seen a steep rise in developing and low-income countries. In the WHO African region alone, the number of overweight and obese children increased from 4 million in 1975 to 9 million in 2016 (World Health Organization., 2017a). This is of great concern, as the health systems in low-income countries have to bear the burden of undernutrition and associated morbidity alongside the rising burden of overweight and obesity (World Health Organization., 2018).

1.3.1 Obesity in the United Kingdom

In a recent report by the Organisation for Economic Co-operation and Development (OECD), the United Kingdom (UK) is the 2nd most obese country in the European region with a reported adult obesity rate of around 26% in 2016 (OECD, 2017). The most recent National Health Service (NHS) national statistics data reports that 28% of the adults in England were obese in 2019 (NHS Digital, 2020a). Childhood overweight and obesity is also of serious public health concern in the UK, and in 2019 the government released its latest plan to tackle the growing problem (HM Government, 2019a).

The trends for childhood obesity have been quite similar to adults, where the prevalence of 9.9% in 2020 for children aged 4-5 years has seen no drop from 9.8% in 2010. The trend is more concerning for prevalence at age 10-11 years with an increase in obesity from 17.5% in 2010 to 21.0% in 2020 (NHS Digital, 2020d). Additionally, obesity and overweight are consistently reported to be more prevalent in Black, Asian and other ethnic minority groups in the UK (Public Health England, 2019a). Moreover, a strong relationship between deprivation and obesity is observed with children living in the most deprived areas being twice as likely to be obese compared to children in the least deprived areas (NHS Digital, 2020d). This role of ethnicity and deprivation in the context of childhood obesity is explained in further detail later on in this chapter.

1.4 What determines obesity?

Before talking about the factors that determine the weight status of an individual, it is important to briefly explain the factors that determine the health of a population. An understanding of the determinants of population health provides a better appreciation of the complex network of factors that affect weight status of an individual in a population. Years of epidemiological research and evidence building has led to an understanding of what determines the health of a population. Over time, an understanding has emerged that health of a population is determined by a complex interwoven web of multiple factors. These factors not only include individual, biological and behavioural factors, but also a broader range of economic, social, and environmental factors. This relatively modern holistic approach reflects a social understanding of the determinants of health and is often referred to as 'Social determinants of Health' approach or a 'socio-ecological' model of determinants of health. In contrast to a biomedical approach to health, this understanding of wider 'social determinants' of health has gained emergence in the health literature of recent decades, particularly around the start of 1980s. The WHO's strategy for 'Health for

All By The Year 2000' was published in 1982 (World Health Organization, 1982) and it was followed by the WHO's Ottawa charter in 1986. Both these strategies adopted principles of equal access to healthcare for all the members of the society (World Health Organization, 1986). Since then, many socio-ecological models of health determinants have been published, with all showing an appreciation and understanding of environmental and social factors, and the interactions between them (Hamilton and Bhatti, 1996, Hancock, 1993, Evans et al., 1994). A widely used example is a model proposed by Dahlgren and Whitehead (Dahlgren and Whitehead, 1993) (Figure 1.2). This model illustrates the complex interactions between various factors that determine an individual's health. The immediate determinants of an individual's health status are biological and behavioural factors, some of which are influenced by social networks, which are further influenced by broader socio-economic, cultural, and environmental conditions. Moreover, social and economic policies have an influence on social determinants of health. The WHO defines social determinants of health as: 'the conditions in which people are born, grow, live, work and age' (World Health Organization., 2020) . These social determinants are responsible for health inequalities, which can be defined as disparities in the health status and unequal

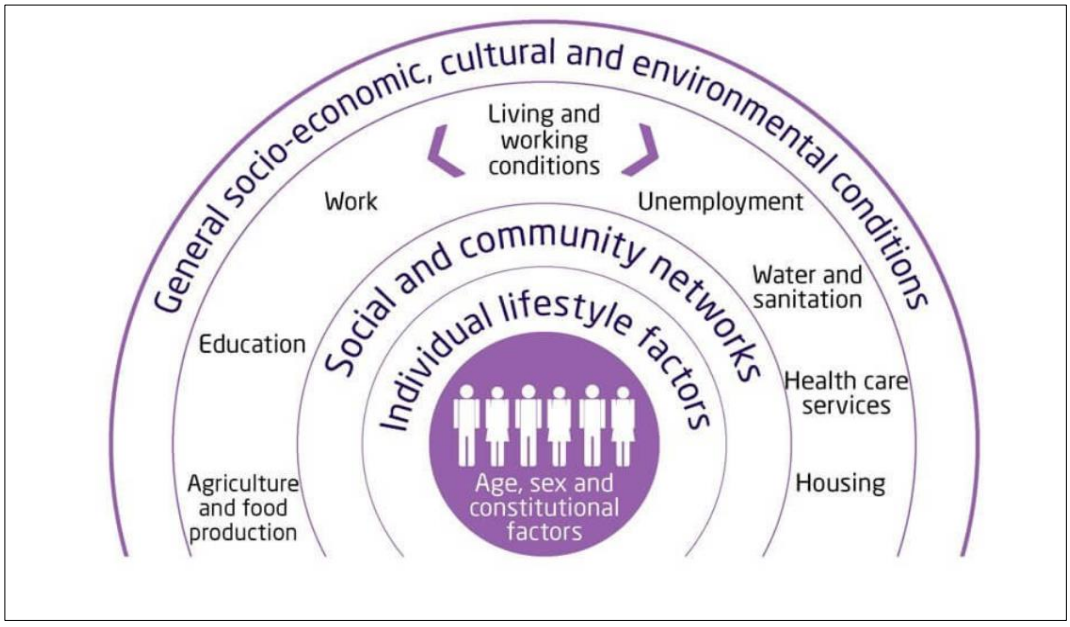

Figure 1.2 *Dahlgren and Whitehead's model of determinants of health (source: Dahlgren and Whitehead, 1993)*

distribution of determinants of health between people belonging to different groups (World Health Organization., 2020). Extensive research has shown that people who are most affected by social inequalities, such as people with low socio-economic status or living in a deprived area, are more likely to have relatively poor health status (Stringhini et al., 2017). The concept of health inequality due to social inequality is further explained later in this section in the context of childhood obesity.

The fundamental cause of obesity and excess fat accumulation is the energy imbalance where an individual's energy intake exceeds the amount of energy used through daily activities and exercise (World Health Organization., 2018). Therefore, in theory, prevention or treatment of obesity should involve neutralizing this energy imbalance by eating healthy and being physically active. For many years, individual behaviours such as excessive food intake and decreased physical activity were the focus of research on determinants of obesity. However, today obesity is better understood as a consequence of complex interactions between behavioural, environmental, social, metabolic and genetic factors (Burgoine et al., 2017, Ang et al., 2013, Albuquerque et al., 2017). An illustration of this complex interaction is the 'ecological model' introduced by Egger and Swinburn (Egger and Swinburn, 1997) (Figure 1.3). This model depicts that an individual's environment and biology drive its behaviour, and the accumulation of excess fat is mediated by their energy expenditure. Central to this ecological model and a socio-ecological approach to obesity is the concept of an 'obesogenic environment'. This concept is based on the notion, backed by research, that certain types of environments influence individuals to consume more food and be less physically active, leading to excess accumulation of fat (Lakerveld et al., 2018, Brug et al., 2006). For example, research has shown that people who live in areas with increased access to fast food outlets have increased odds of being overweight and

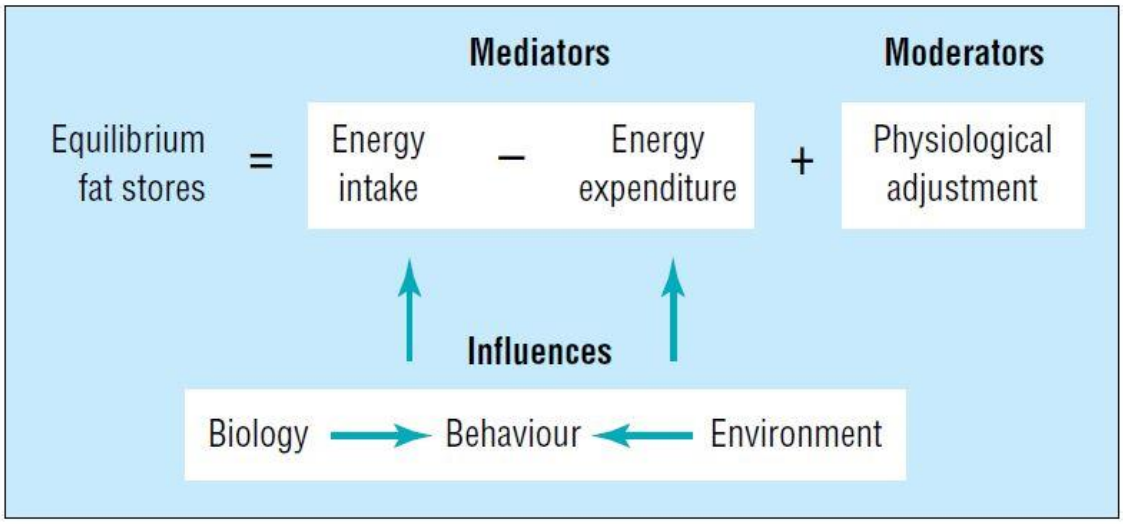

Figure 1.3 *Egger and Swinburn's 'ecological model' for obesity (source: Egger and Swinburn, 1997)*

obese (Burgoine et al., 2016, Chee Cheong et al., 2019, Public Health England, 2014). Additionally, the proportion of obesity is found to be lower in environments that promote physical activity (Saelens et al., 2012), while it is higher in environments that do not promote physical activity or do not have access to green spaces (Townshend and Lake, 2017). Implicit in the socio-ecological approach to obesity is the health inequality due to unequal distribution of social determinants of health. Extensive literature has shown that for both adults and children, the prevalence of obesity is higher in individuals with low socioeconomic status (SES). People with low SES experience this inequality as a consequence of their inability to buy healthy foods, and their lack of awareness about nutrition. A similar association between material deprivation and obesity has also been widely reported. Extensive literature reports that individuals living in a deprived area are more likely to be overweight or obese (Kinra et al., 2000, Conrad and Capewell, 2012, Noonan and Fairclough, 2018). A more recent example of this is the trend of childhood obesity in England in the last decade. As previously mentioned, the prevalence of obesity at age 4/5 years was 9.8% in 2010 and 9.9% in 2020, however the disparity gap between the least deprived and most deprived areas has increased by 1.8 percentage points (Public Health England, 2019a). This is due to prevalence of obesity remaining similar in most

deprived areas but falling in the least deprived areas (Figure 1.4 & Figure 1.5). At age 10/11 years, the increase in gap is even steeper, increasing to 4.8 percentage points higher in 2020 than in 2010. This is due to an increase in prevalence in most deprived areas but remaining similar in least deprived areas (Figure 1.4 & Figure 1.5).

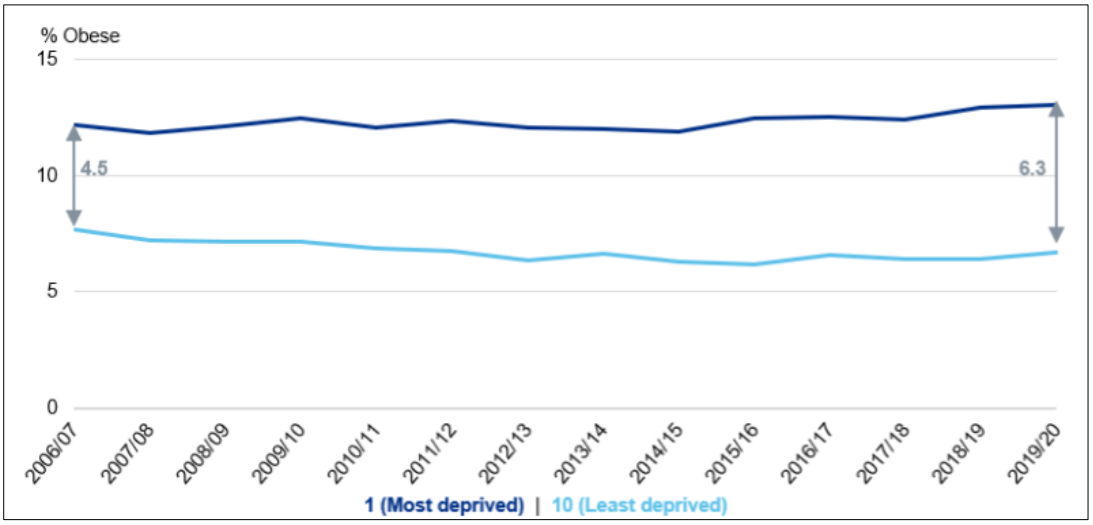

Figure 1.4 *Trend of childhood obesity prevalence In the UK at age 4/5 years from 2006/07 to 2017/18 by deprivation*

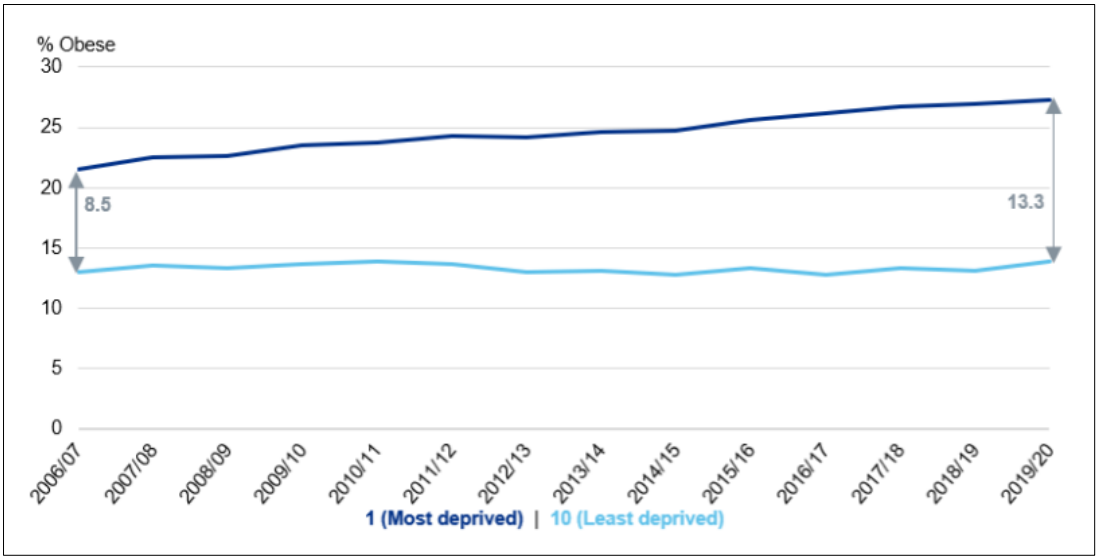

Figure 1.5 *Trend of childhood obesity prevalence in the UK at age 10/11 years from 2006/07 to 2017/18 by deprivation*

As mentioned earlier, obesity not only results from environmental and behavioural factors, but is a consequence of complex interactions between multiple factors. For example, two people of a similar age being exposed to a same environment could have different levels of fat accumulation. This suggests that individuals might have different levels of susceptibility

to weight gain. Research has shown this difference to be in part a result of the genetic and neuro-metabolic profile of an individual. Body fatness or adiposity has been found to be among the most heritable human traits (Farooqi and O'Rahilly, 2007). A meta-analysis has shown that 47% to 80% of the inter-individual variation in BMI can be explained through genetic factors (Elks et al., 2012). Additionally, there is a suggestion that the BMI of children who are adopted, corresponds more with their biological parents than with their adoptive parents (Stunkard et al., 1986). However, it is still not understood how genes influence the mechanisms of energy imbalance. As mentioned above, the World Obesity Federation has desribed obesity as a chronic, progressive and relapsing disease (Bray et al., 2017). Research has shown a role of neuro-metabolic mechanisms in regulation of body weight. Various hormones have been found to have a role in energy regulation after food intake. Briefly summarising, there are two hormones that play a significant role in energy homeostasis; leptin and ghrelin. Leptin is a hormone that promotes satiety while ghrelin promotes hunger (Klok et al., 2007). Obese individuals, or individuals with genetic precedent to be obese, have been found to have lower leptin and higher ghrelin levels, resulting in difficulties in controlling behaviours of excessive food intake, leading to progression of obesity overtime (Zheng et al., 2009). Additionally, leptin and ghrelin levels are found to be low and high, respectively in obese individuals who underwent a period of intentional weightloss (Greenway, 2015). These changes make it difficult for such individuals to maintain the lost weight and not gain it back, resulting in the relapsing nature of obesity.

It is difficult to explain the rapid increase in obesity prevalence based on one or two of the above mentioned factors. None of these can individually determine an individual's anatomy, physiology and behaviour. Therefore, it is the complex interaction between these factors at different stages in life, that can result in weight gain.

1.5 Obesity and undesirable health effects

One of the main reasons why overweight and obesity are identified as a serious global public health problem and are a major focus of medical research is the strong association of excessive fat accummulation or adiposity with an increased risk of morbidity and mortality. An increase in BMI above the normal threshold in adults (>25 kg/m^2) has been shown to be a significant predictor for development of various diseases such as cardiovascular diseases, Type 2 diabetes and cancer (Hubert et al., 1983, Parikh et al., 2003, DeFronzo et al., 2015). In 2015, a higher than normal BMI was associated with 4 million deaths that were 7.1% of deaths from all causes worldwide (GBD Obesity Collaborators, 2017). Of these 4 million deaths in overweight and obese people, 2.7 million deaths were attributable to cardiovascular diseases while 0.6 million were due to diabetes. Additionally, the rate of global deaths attributable to higher than normal BMI increased by 28.3% from 1990 to 2015, with 53.7 deaths per 100,000 population in 2015 (GBD Obesity Collaborators, 2017). In a recent analysis from the UK, overweight and obesity were reported to be responsible for 5.5 % of all deaths. A J-shaped association was observed between BMI and all-cause mortality (Figure 1.6), with the lowest mortality being at 25 kg/m^2 (Bhaskaran et al., 2018). Additionally, the authors reported a strong association of high BMI with mortality

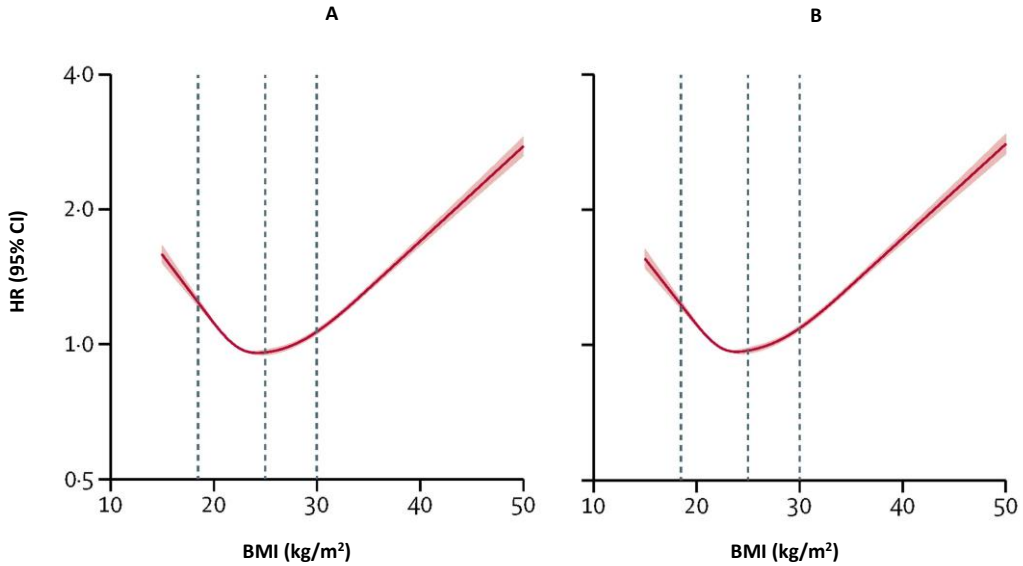

Figure 1.6 *A) All-cause mortality B) Non-Communicable disease mortality Source: (Bhaskaran et al., 2018)*

due to cancer, diabetes, cardiovascular and respiratory diseases. In addition to mortality and morbidity, a higher than normal BMI is also associated with decreased quality of life and is estimated to result in the reduction of disease free years by 40-75 years in 2015 (Nyberg et al., 2018).

1.5.1 Health effects of childhood obesity

Childhood obesity has been of importance to public health as it is a significant predictor of obesity in adulthood (Singh et al., 2008). Individuals who are overweight and obese in childhood are significantly more likely to be overweight and obese in later life (Singh et al., 2008, Simmonds et al., 2015). This tracking of obesity from childhood into adulthood is associated with an increased burden of morbidity and mortality related with various associated diseases. More recently, the focus has shifted towards the association of excessive fat accumulation in children with an increased risk of undesirable health outcomes during childhood and adolescense. For example, the increasing prevalence of childhood obesity has led to an increase in the incidence of previously unusual metabolic imbalances at this age, and a rise in associated health conditions (Chen et al., 2012, Abbasi et al., 2017, Messiah et al., 2019, Singer and Lumeng, 2017). Obesity has been found to be associated with increased insulin resistance, glycemia markers, and increased blood pressure in children, conditions that act as precursors to the development of various cardio-metabolic diseases (Nightingale et al., 2013, Falkner, 2018, Adams et al., 2008). In the UK, a recent analysis by Diabetes UK reported a high prevalence of Type 2 diabetes in young people under the age of 25, with approximately 7,000 individuals treated in 2016/2017 (Iacobucci, 2018). Additionally, obesity in children is associated with an increased risk of mental health problems such as depression and lower self-esteem (Franklin et al., 2006, Pulgarón, 2013). Weight bias and stigma towards obese individuals due to the common perception of obesity being a consequence of personal behaviour and

lack of will power are identified as main causes of these psychological problems in obese children (Palad et al., 2019).

1.5.2 Role of adiposity

Excess accumulation of fat or adiposity has been found to be the main driver behind obesity associated high risk of morbidity (Bray et al., 2017). The pathophysiological pathways through which adiposity could cause the commonly associated diseases are shown in figure 1.7. For the sake of a clear explanation, the complex interactions of these pathophysiological factors on the causal pathways are not shown (Figure 1.7). Owing to this important role of adiposity in the development of associated diseases, it is of utmost importance to accurately identify fat levels in individuals. BMI is the screening tool that is most widely used as a proxy for the measure of body fatness, as weight and height are relatively easy and less expensive to measure at healthcare facilities compared to direct methods of body fat measurement. Although BMI correlates with percentage of body fat, concerns have been raised about its accuracy in ethnically diverse populations, as ethnicity is reported to independently influence the relationship between BMI and body fat (Purnell, 2018, Jackson et al., 2009). For example, research has shown that for a given BMI for age, body fat levels vary between individuals belonging to different ethnic groups (Eyre et al., 2017, McConnell-Nzunga et al., 2018).

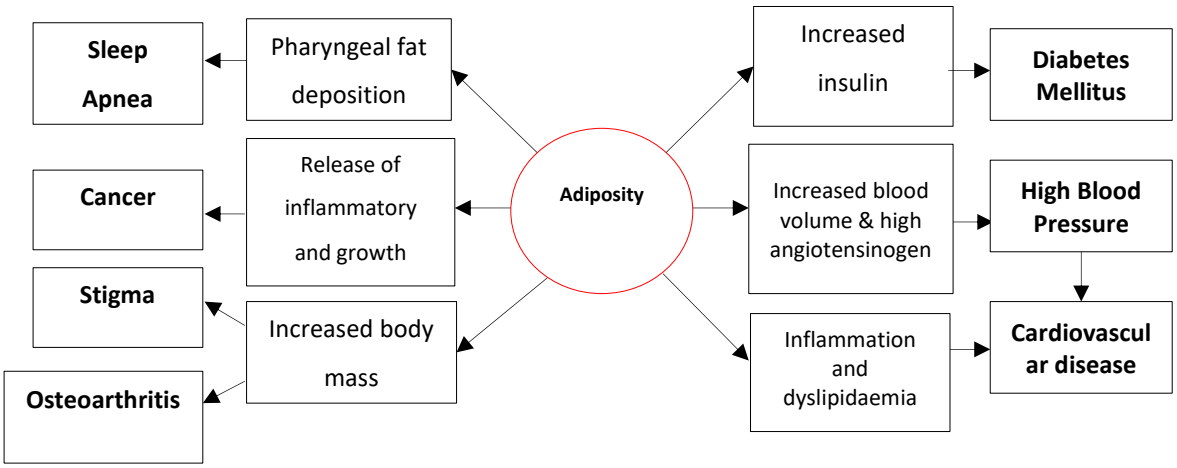

Figure 1.7 *Pathophysiological pathways involved with the development of diseases associated with obesity*

1.6 Ethnicity, overweight and obesity

Disparities in the prevalence of overweight and obesity have been reported between ethnic groups in the UK and in various countries around the world (Rossen and Talih, 2014, Rossen, 2014, Public Health England, 2019a). According to the most recent estimates by Public Health England (PHE), children of Asian origin have a higher prevalence of obesity in England than White British children (Public Health England, 2019a). In 2018/19, the prevalence of obesity (including severe obesity) in Pakistani children at age 10-11 years was 26.6%, compared to 18.1% in White British children. Similar trends are observed for Indian Bangladeshi and children of Black ethnicity (Figure 1.8). In the reception school year (age 4-5 years), the prevalence was higher in Pakistani (10.9%) and Bangladeshi (12.1%) children but was lower in Indian children (7.5%) compared to White British children. An assumption is made in the literature that this disparity can be explained by the association of ethnicity with deprivation and other determinants of obesity (Zilanawala et al., 2015, Powell-Wiley et al., 2014, Public Health England, 2019a). In England, an analysis done on the census data in 2011 showed that people belonging to South Asian origin, particularly Pakistani and Bangladeshi ethnicity were more likely to live in deprived neighbourhoods (Jivraj and Khan, 2013). 32% of the Pakistani and 40% of the Bangladeshi people were living in 10% most deprived neighbourhoods compared to 8.5% White British and 8.3% Indian people (HM Government, 2019b).

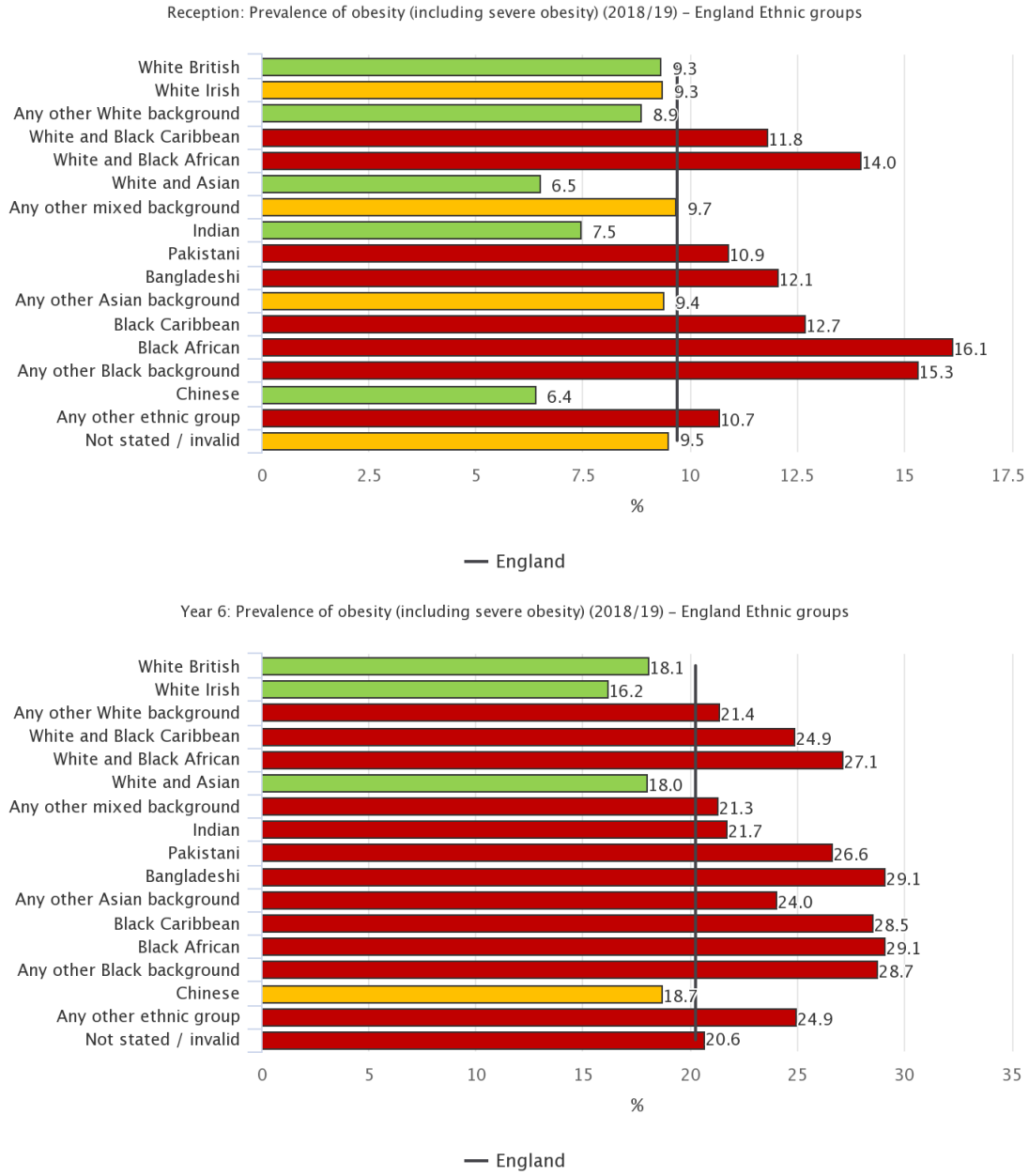

Figure 1.8 *Prevalence of obesity (including severe obesity) in children by ethnicity in 2018/19. a) Reception year b) Year 6*

Most recently, PHE reported results of an analysis of differences in childhood obesity by ethnic groups adjusted/stratified by deprivation status (Public Health England, 2019a). They used White British as a reference category to compare the prevalence of obesity with Asian and Black ethnic children. They aggregated Pakistani, Indian, and Bangladeshi children into an Asian category, and Caribbean and African children in Black category. In reception year boys, prevalence was lower for Asian children in the most deprived quintile

and the least deprived quintile and only slightly higher in other quintiles (Figure 1.9). In reception year Asian girls, the prevalence of obesity was lower in all deprivation quintiles (Figure 1.9). For Asian children, the prevalence of obesity in school year 6 boys (age 10-11 years) was much higher in all 5 deprivation quintiles (Figure 1.10). In year 6 girls, the prevalence was only slightly higher and was 1.1% lower in the most deprived quintile (Figure 1.10). For Black children, the prevalence of obesity was much higher than White children for both sexes and school years, and across all deprivation quintiles. These estimates are for the combined Asian category for children; therefore, care should be taken when interpreting these results in the context of individual South Asian ethnic group. These results could be different for Pakistani, Bangladeshi, and Indian ethnic children, as differences in the prevalence of obesity between each South Asian category has also been reported and mentioned earlier. Additionally, as previously mentioned, the proportion of Pakistani and Bangladeshi children living in deprived areas is much higher than Indian children. Nevertheless, higher prevalence of obesity for year 6 Asian boys in all deprivation quintiles reflects the role of interactions between socio-cultural factors in determining obesity. Various studies have explored the role of cultural differences in understanding the difference of obesity prevalence between ethnic groups. Studies have reported that adults and children from ethnic minority background (Pakistani, Bangladeshi, Black etc.) are more likely to have obesogenic lifestyles. Falconer et al. (2014) reported that South Asian and Black children were three times more likely to have an obesogenic lifestyle compared to White British children. A lack of knowledge on the importance of healthy lifestyle on long-term health, the inability to afford healthy foods, fear of racial discrimination, and religious values in Muslim households have been reported as barriers to a healthier lifestyle (Lucas et al., 2013, Khunti et al., 2007, Trigwell et al., 2015, Patel et al., 2017).

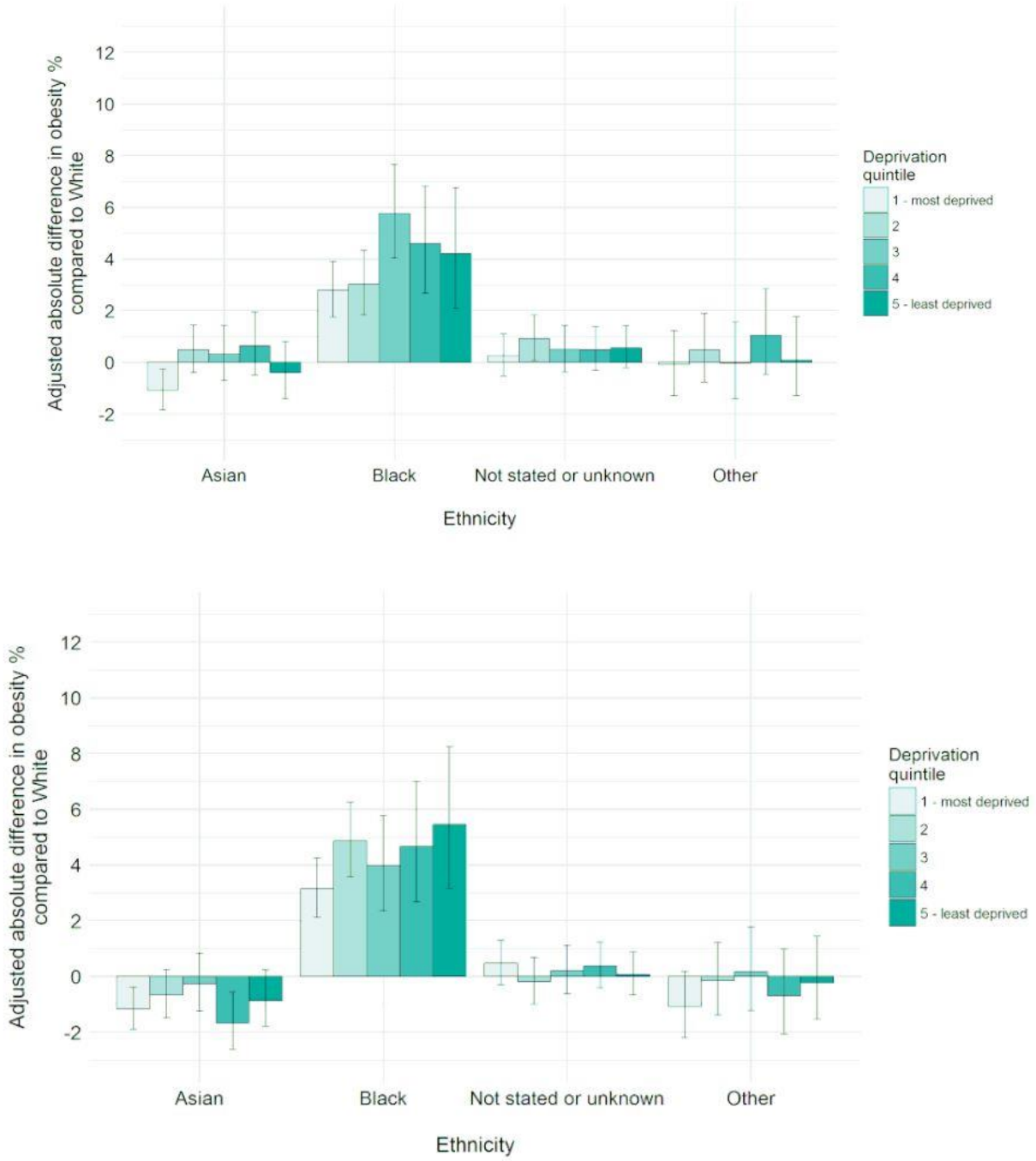

Figure 1.9 *Difference in obesity prevalence by ethnicity and deprivation quintile a) Reception boys b) Reception girls (source: Public Health England, 2019)*

These disparities in overweight and obesity across ethnic groups become more significant when the heterogeneity in risks of associated cardio-metabolic diseases between ethnic groups is taken into consideration. South Asians and other minority ethnic groups have consistently been reported to have a much higher risk of Type-2 diabetes and

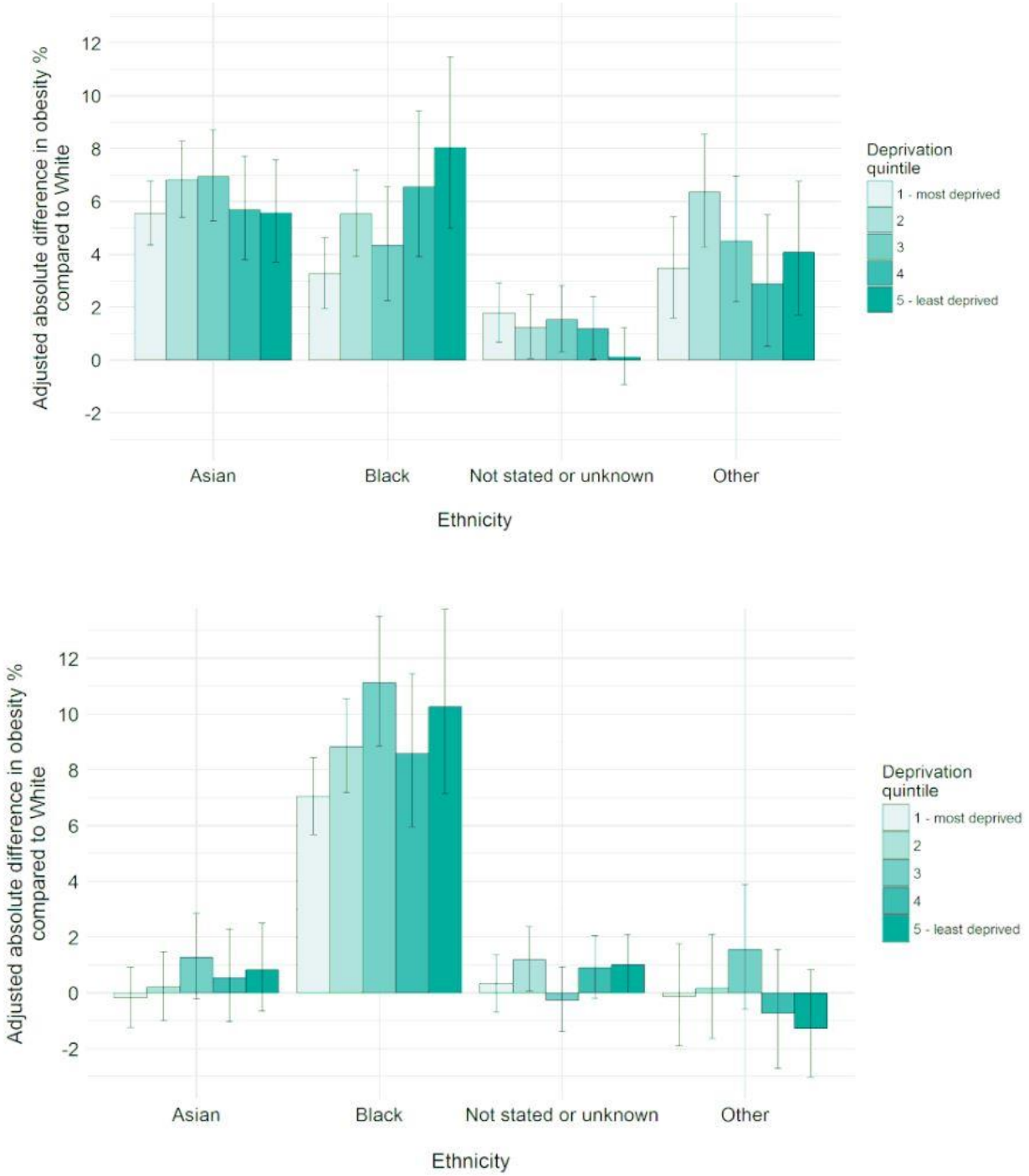

Figure 1.10 *Difference in obesity prevalence by ethnicity and deprivation quintile a) Year 6 boys b) Year 6 girls (source: Public Health England, 2019)*

cardiovascular diseases (Liu et al., 2009, Ehtisham et al., 2004). In the UK, studies have found South Asian adults to have an approximately threefold higher risk of Type-2 diabetes (Ntuk et al., 2014). Moreover, these differences not only exist during adulthood, but the emergence of ethnic differences in Type-2 diabetes precursors and higher risk of cardio-metabolic disease has been observed during childhood, in as early as the first decade of life

(Whincup et al., 2002, Whincup et al., 2010). Differences in body composition and, cultural and environmental factors have been identified as potential reasons to explain this higher prevalence of obesity and risk of associated diseases in minority ethnic groups (Whincup et al., 2010, Ehtisham et al., 2005). A higher body fat percentage in South Asians for a given BMI compared to White British people is significantly associated with increased metabolic risk of Type-2 diabetes (Whincup et al., 2010). It has been reported that South Asian populations carry an equivalent risk of cardio-metabolic diseases at a much lower BMI value compared to White European populations, with a substantial proportion of these South Asians having high risk even below the BMI of 25 kg/m^2 (Ntuk et al., 2014).

Physiologically, adiposity is the main driver behind associated morbidity (section 1.5.2), therefore it is important to have an accurate measure of body fat levels, particularly in ethnic populations such as South Asians. As mentioned earlier, BMI has been found to underestimate body fat estimates in South Asian populations. The accuracy of BMI as a proxy of body fat in ethnic adults has been debated many a times in the academic literature as these are derived largely from a population of European origin (Onis et al., 2007, WHO Expert Consultation, 2004). A WHO expert panel in 2004 acknowledged that BMI underestimates body fat and subsequent risk of cardio-metabolic diseases in Asian populations. However, the panel ruled out the use of ethnicity-specific values to define weight status due of lack of data to indicate one clear BMI cut-off for all Asian populations, and they proposed methods for countries to make their own decisions about the definitions of BMI based on associated risk of diseases in their respective populations (WHO Expert Consultation, 2004). However, they did recommend the use of "Public Health Action Points" (23 kg/m^2 for increased risk and 27.5 kg.m^2 for high risk) for health professionals to intervene to help Asian adults manage their weight. In the UK, the National Institute for

Health and Care Excellence (NICE) recommends the use of these "Public Health Action Points" in South Asian adults to reduce risk of associated diseases (NICE, 2019).

More recently, work has been done in the UK by Hudda et al. (2017) to derive ethnicity-specific BMI values for British South Asian children. Sex stratified BMI adjustments were derived, ensuring that adjusted BMI values are associated with fat-mass in the same way as in White British children. They found standard BMI values underestimated fat mass in British South Asian children and calculated sex-specific BMI adjustments of +1.12 kg/m^2 for boys and +1.07 kg/m^2 for girls at all age and body fatness levels. Moreover, application of these ethnicity-specific BMI values to a population of children involved in 2013 National child Measurement Programme (NCMP) resulted in significantly higher prevalence of overweight and obesity in South Asian children (Hudda et al., 2018). The accuracy of these ethnicity-specific BMI values in predicting associated cardio-metabolic risk has not yet been assessed. However, it can be assumed from these findings that the use of standard BMI values for British South Asian children not only underestimates the prevalence of overweight and obesity in the population studied, but could also potentially underestimate the burden on the healthcare system resulting from increased morbidity and associated healthcare utilisation.

1.7 Overview of the policies to tackle obesity in England

The first obesity related policy document was released in England by the National Audit Office in 2001 (Bourn, 2001). Prior to that, a plan for tackling obesity was released by the government in 1999 as part of the "Saving lives: our healthier nation" strategy (Secretary of State for Health, 1999). Since then, the government has increasingly acknowledged obesity as a national public health problem due to the burden it poses and is predicted to pose on the health of people and the healthcare system. Throughout the early 2000s, various annual reports and updated strategy plans to tackle obesity were released (The

Health Commitee, 2004, Department of Health, 2005, Department of Health, 2002). In 2004, the UK government took a specific focus on childhood obesity for the first time, and a national Public Service Agreement (PSA) was announced to "halt the year by year progress of obesity in children by the year 2010" (Department of Health, 2004). This was followed by a strategic plan to tackle childhood obesity in 2006 (National Audit Office, 2006). For the most part in the early 2000s, the policy strategies on tackling obesity were focused on the role of individual responsibility and individual decisions in bringing about change to lifestyle and behaviour. These policies were criticized for ignoring the complex role of economic, social and environmental factors in determining the behaviour of individuals and the lack of plan to prioritize the responsibility of the government and private sector in bringing about change to these socio-ecological factors (Evans, 2006, Musingarimi, 2009, Jebb et al., 2013, Ulijaszek and McLennan, 2016).

A report titled "Tackling Obesities – Future choices" was released by the government's Foresight project in 2007 (Butland et al., 2007). This report attempted to reframe obesity as a problem determined by complex factors that go beyond individual responsibility. This was followed by the release of "Healthy Lives, Healthy People: a call to action on obesity in England" report in 2011 (Department of Health, 2011a) and the government's policy to tackle obesity for 2010-2015 (Department of Health, 2015). These reports acknowledged the responsibility of the government to implement interventions and regulations that facilitate and empower individuals in making healthy choices. As part of the 2010-2015 policy, it was stated that the government plans to involve local authorities, and private food and marketing industries to give people advice, guidance, and to improve food labelling so that people can make healthier choices. The government stressed that an "individual's freedom of choice is their top priority, and that they will favour interventions that won't

compel any individual but will only equip them to make healthier choices" (Bettenhausen et al., 2015).

The main policy intervention that was implemented by the government as a result of its foresight project was Change4life (Mitchell et al., 2011). It is a social marketing campaign, that was established in 2009 to support individuals and families in making healthier and informed decisions about food and physical activity. It was initially planned for 3 years but is still ongoing in 2021 and is mainly focused on families with children under the age of 11 years. This programme echoed the government's message regarding enabling individuals to make healthier choices. Additionally, in 2011, the government developed a Public Health Responsibility Deal (Department of Health, 2011b). This deal relied on a list of voluntary pledges with the food industry. For example, voluntary pledges for on food nutritional labelling and caloric reduction were developed (Department of Health, 2011a). The government policies during this time were continually criticized for being overly reliant on individual responsibility and behaviour change (Vallgårda and Medicine, 2015, Jebb et al., 2013, Ulijaszek and McLennan, 2016). The criticism was also directed at the voluntary role of the food industry, as evidence suggests that such voluntary approaches and individual self-regulation often fail to reflect into successful strategies that improve public health (Sacks et al., 2013, Moodie et al., 2013, Hawkes, 2005, Sharma et al., 2010, British Medical Association, 2017). This evidence was supported by the continued failure of government policies to halt the unabated growth of childhood obesity.

Recent strategic plans to tackle childhood obesity were released by the government in 2016 (HM Government, 2016) with an updated "chapter 2" released in 2018 (HM Government, 2018) and a "chapter 3" released in 2020 (HM Government, 2019a). These plans took on a holistic approach to childhood obesity and proposed actions to tackle different socio-ecological factors contributing to it. In the 2016 action plan, government introduced a Soft

Drinks Industry Levy (SDIL) on sugary soft drinks to incentivize reduction of sugar in drinks (HM Revenues and Customs, 2016). This was phrased in the plan as a "first major step towards tackling childhood obesity" (HM Government, 2018). Initial evaluation of SDIL showed that it was successful in stimulating the industry to reformulate their products and decrease sugar contents in soft drinks subject to levy, with a decrease of 28.8% in sugar content of these drinks from 2015 to 2018 (Public Health England, 2019c). Based on the evidence from PHE to take action on the excess caloric and sugar consumption in UK children (Public Health England, 2015), the government also introduced a sugar reduction programme to challenge food industry and retailers to voluntarily decrease the sugar content in their foods, also setting a challenge of 20% sugar reduction by 2020 (HM Government, 2016). Additionally, the government stated that, in light of the recent evidence of excess sugar consumption, they will work closely with PHE to update the School Food Standards introduced in 2015. In chapter 2 of the plan released in 2018, the government has set it as a national ambition to "halve childhood obesity and significantly reduce the gap in obesity between children from the most deprived areas by 2030" (HM Government, 2018). The report also introduced a plan to extend SDIL to sugary milk drinks, an action that is also recommended as an essential in the most recent independent report on obesity by the UK's Chief Medical Officer (Davies et al., 2019). In addition to the sugar reduction, the government has also introduced a caloric reduction programme, with an aim to challenge the food and drink industry to voluntarily reduce calories in food eaten by children by 20% by 2024 (HM Government, 2018).

These recent action plans of the government have been praised for acknowledging the role and responsibility of food and marketing industries to create a positive shift in the environment in which children live. A criticism has been the lack of statutory regulations on the food industry to reduce sugar and caloric content and reducing the pricing of healthy

food products (Mytton et al., 2019, Knai et al., 2016, Knai et al., 2018). The success of this new holistic approach adopted in this recent action plan in terms of reduction of overall prevalence of childhood obesity and meeting the national ambition is yet to be evaluated.

1.8 Obesity and healthcare utilisation

As mentioned earlier, the effects of overweight and obesity on an individual and society are profound, with associated high mortality and substantial loss of life-years (Grover et al., 2015). However, focusing on the outcome of mortality or years of life lost underestimates the overall burden that overweight and obesity impose on an individual, a society and a healthcare system. The health burden of obesity is due in large part to the morbidity and loss of healthy life-years resulting from associated diseases (Wang et al., 2011). Therefore, in order to completely assess the burden of excess bodyweight on a society and healthcare system, it is essential to quantify this burden through analyses of healthcare utilisation (also termed as healthcare use in this thesis) at primary and secondary care level with associated health-care costs in overweight and obese individuals. In 2017, obesity and associated medical conditions resulted in 30% higher medical costs worldwide (GBD Obesity Collaborators, 2017). In the UK, a recent report by the Department of Health & Social Care estimated that obesity and its associated conditions cost the NHS £6.1 billion annually with an estimation of costs to wider scoiety at £27 billion (Department of Health & Social Care, 2020a). Additionally, obesity is reported to be one of the top three social burdens in the world and is only second to smoking in the UK (McKinsey Global Institute, 2014). On an individual level, various studies have quantified the healthcare utilisation and associated costs in overweight and obese individuals with all of them reporting an increased utilisation of healthcare services in excess weight individuals (Finkelstein et al., 2014, Wang et al., 2008, Tucker et al., 2006). In England, over one million hospital admissions in 2019 were directly or indirectly associated with obesity (NHS Digital,

2021). In a recent analysis, it was reported that a reduction of only 1% in obesity prevalence would add 3 million and 16 million Quality Adjusted Life years (QALYs) in the UK and the USA, respectively (Wang et al., 2011). An important point to consider is that the majority of such studies quantify healthcare utilisation in obese individuals by assuming that they will start accruing this obesity-related healthcare burden at or after a certain age during adulthood, thereby ignoring the obesity assoicated morbidity and loss of disease-free years during childhood (John et al., 2010).

1.8.1 What determines healthcare utilisation?

It could be inferred that increase in obesity related morbidity during childhood is associated with an increased need for clinical services, which would then result in higher healthcare use in obese children. However, clinical need is not the only factor that determines the use of healthcare services. Much like the complex interplay of multiple factors in determining health of an individual, healthcare utilisation is also determined by a myriad of factors and clinical need is only one part of this bigger equation (Aday and Andersen, 2005). Models of healthcare utilisation provide insight into defining these deterministic factors and specify the relationship between them. To my knowledge, there are no obesity-specific models available that theorise a framework of multiple factors that determine healthcare utilisation in obese individuals.

Existing theoretical models of healthcare utilisation can be used as a foundation to build a theoretical framework to explain variation in use of healthcare services by weight status of individuals. The most widely used theoretical model to explain the influence of multiple factors on access to and use of healthcare services is the behavioural model of healthcare utilisation (Andersen, 1995, Andersen and Davidson, 2007). This model explains healthcare utilisation as a function of four broad factors: 1) Environment (availability of healthcare services, ease of excess to healthcare services) 2) Population characteristic (predisposing

characteristics such as cultural and ethnic beliefs and norms; characteristics that enable access to healthcare such as socioeconomic status; emergence of ill-health and an individual's assessment of their clinical need) 3) Health behaviour (personal health behaviour such as lifestyle, smoking, exercise, diet etc) 4) Outcomes (patient satisfaction of the care provided; improvement in health status). For equitable access to and use of healthcare services based on clinical need, an individual should have a predisposition to using healthcare, accompanied by the presence of factors that enable them access to the services. A predisposition to using healthcare services is based on demographic and social factors and the health beliefs of an individual. These behaviours of healthcare use are enabled by resources at the individual (income) and environmental (availability of healthcare services) levels.

It could be assumed that the relatively higher prevalence of obesity in the UK South Asian children would result in a higher clinical need, which would then translate into an increased healthcare use burden. However, to the best of my knowledge there is no literature evidence as of yet to back such an assumption. Additionally, as mentioned above, clinical need paints only part of the deterministic picture of healthcare utilisation. Evidence shows differences in perceptions, beliefs, and attitudes of people from different ethnic and cultural backgrounds towards health in general and obesity in particular, with people belonging to South Asian culture less likely to consider obesity as a condition that could seriously affect their health and the health of their children (Caprio et al., 2008, Lucas et al., 2013, Patel et al., 2017). Such beliefs could play an important role in determining attitudes towards health service uptake and subsequent healthcare utilisation in overweight and obese individuals. Based on the healthcare model, other factors that could determine differences in healthcare use among different ethnic groups are the enabling (facilitators) and disabling (barriers) characteristics of the healthcare system, and the

variation in patient satisfaction regarding the care received. Although this area of research is relatively less explored, there is some evidence from the UK and internationally that shows variations in the patterns of healthcare service use between people from different ethnicities, immigrants and people living in socio-economically deprived areas (Kossarova et al., 2017, Katikireddi et al., 2018). It is to be noted that these groups are not mutually exclusive, and I've previously mentioned that ethnic minority groups in the UK are more likely to be living in deprived areas than the White British people (Ministry of Housing Communities and Local Government, 2020). The factors that drive this variation have been reported to be barriers to access to primary healthcare services, poor performance of these services and dissatisfaction with the services provided (Cowling et al., 2013a).

1.9 Healthcare utilisation and childhood obesity: focus of this research

The focus of this thesis is on healthcare utilisation by obese children during childhood. As mentioned previously, recent research has reported a rise in the prevalence of previously unusual obesity-associated conditions such as Type-2 diabetes and metabolic syndrome during childhood (Abbasi et al., 2017, Messiah et al., 2019). This unusual rise has been attributed to the rise in prevalence of obesity in children. However, it could be argued that looking at the risk of obesity associated diseases during childhood would underestimate the burden of childhood obesity on the health of obese children, and its burden on the healthcare system. The reason being that research have shown that excess adiposity is associated with physiological and metabolic changes in the body (Nightingale et al., 2013, Singer and Lumeng, 2017, Weiss and Caprio, 2005), and a prolonged exposure to these changes mediates a progression towards development of serious obesity-associated cardiometabolic diseases such as Type-2 diabetes, and cardiovascular disease (Barrett et al., 2020). Therefore, due to their progressive nature, quantification of health burden of childhood obesity through the perspective of these obesity-associated diseases does not

consider the immediate adverse health experienced by obese children due to physio-metabolic changes occurring in their bodies before the point of clinical diagnosis of a disease is reached.

As previously mentioned in this chapter, healthcare utilisation is informed by clinical need (Andersen and Davidson, 2007). In this thesis I focus on the utilisation of primary and secondary healthcare services by obese children as an indicator of ill-health and clinical need arising as a consequence of obesity. However, as discussed earlier, healthcare utilisation behaviour is determined by many factors in addition to clinical need (Andersen and Davidson, 2007). It is known through evidence that proportion of obesity is higher in children from ethnic minority groups in the UK (Public Health England, 2019a). Additionally, research has shown that people of South Asian ethnicity are more adipose for a given BMI (Hudda et al., 2017) and carry a disproportionately higher risk of developing obesity associated diseases compared to White British people (Ntuk et al., 2014, Whincup et al., 2010). Therefore, an argument could be made that ethnicity would have an impact on healthcare utilisation with obese children from the South Asian background experiencing greater ill-health and a greater clinical need resulting in an increased frequency of healthcare use. However, when exploring healthcare utilisation in the context of ethnicity, consideration should be given to the potential impact of socioeconomic status. Evidence shows that people from ethnic minority groups in the UK are more likely you live in deprived neighbourhoods (Ministry of Housing Communities and Local Government, 2020). As mentioned in the preceding section, variation in patterns of healthcare utilisation has been identified in literature with people from ethnic minority groups and people living in deprived neighbourhoods.

Therefore, quantification of primary and secondary healthcare utilisation in a multi-ethnic population will not only highlight the burden of morbidity and decreased quality of life in

obese children but will also potentially inform and trigger policy action and will facilitate implementation of prevention and treatment programmes tailored to the specific needs of an ethnically diverse UK population.

1.10 Thesis aims and objectives

There are two primary aims of this thesis: first, to critically review the existing literature on healthcare utilisation in overweight and obese children, and identify gaps and avenues for further research. Second, through a prospective secondary data analyses of the Born in Bradford (BiB) cohort, to explore the primary and secondary healthcare utilisation and costs in overweight and obese White British and Pakistani origin children all born and growing up in the same UK city.

The second aim will be achieved by meeting the following two objectives:

1. To quantify the healthcare burden of childhood obesity through analysis of rates and costs of primary and secondary healthcare use.
2. To explore the impact of ethnicity on the association between childhood obesity and primary and secondary healthcare use.

1.11 Thesis structure

The overall thesis takes the form of eight chapters. Following the introductory chapter, the second chapter of the thesis is a systematic review and meta-analysis of the literature on healthcare utilisation in obese and overweight children. The third chapter provides a detailed explanation of the methodology and analytical approaches used in this thesis. Chapter four describes the BiB cohort data, giving the participant characteristics and distributions of the variables used in the main analyses. Chapters five to seven provide results of the analysis of primary healthcare use, secondary healthcare use and healthcare

costs, respectively. The final chapter summarises, discusses and concludes these findings, with a focus on interpretation and implications for health policy and practice.

Chapter 2 A systematic review and meta-analysis of the association between childhood obesity and healthcare utilisation

This chapter reports the findings of the systematic review and meta-analysis of studies that have quantified the relationship between childhood overweight and obesity with healthcare utilisation during childhood. The work that comprises this chapter has been published in BMJ Open (Hasan et al., 2020) (appendix A1.1).

In chapter one, I discussed the burden of morbidity associated with obesity and its association with increased healthcare use. I also outlined the lack of research on this association during childhood and presented the rationale for investigating the use of healthcare services during childhood in children who are overweight and obese.

This systematic review acknowledges the scarcity of research in this field for children and brings together the available global evidence to guide the research questions of this thesis by recommending research on the existing research gaps. To the best of my knowledge, this is the first systematic review and meta-analysis with the aim of summarising and quantifying the literature on differences in healthcare use between children of different weight status.

2.1 Objectives

2.1.1 Primary Objective

- To describe the association of overweight and obesity with healthcare utilisation during childhood and adolescence in a systematic way

2.1.2 Secondary objectives

- To identify the obesity associated conditions that may explain the association of overweight or obesity in children with increased healthcare use

- To assess the impact of participant characteristics such as gender, ethnicity, and socioeconomic status on the above-mentioned association
- To describe the association of overweight and obesity with costs of healthcare use

2.2 Methods

This review is reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) recommendations to ensure systematic reporting of findings. (Moher et al., 2009). A review protocol was established *a priori* in accordance with the PRISMA–P guidelines and was registered with PROSPERO (Reg no. CRD42018091752)

2.2.1 Study eligibility

Titles and abstracts of the studies were exported from the databases using the bibliographic software Endnote (Hupe, 2019).

2.2.1.1 Participants

Participants up to the age of 19 years with known BMI status. The decision for the inclusion of children or adolescents up to the age of 19 years was made based upon the WHO's definition of a child and adolescent (World Health Organization, 2013).

2.2.1.2 Outcomes

There were two outcomes of interest in this review:

1. Primary healthcare use
2. Secondary healthcare use

2.2.1.3 Inclusion and exclusion criteria

Potentially relevant titles and abstracts were screened for initial assessment of eligibility using the following inclusion criteria:

- Observational studies assessing the impact of overweight or obesity on healthcare utilisation in children or adolescents
- Studies published in the English language
- Studies report at least one outcome measure of primary or secondary healthcare utilisation

The exclusion criteria were:

- Studies reporting the association for underweight children only
- Studies that included participants over 19 years of age
- Studies that included participants both less than and greater than 19 years of age but did not stratify the results by age groups
- Review articles

Additionally, instead of restricting the inclusion criteria to studies using predefined standard Body Mass Index (BMI) cut-offs for childhood overweight (sex- and age-specific BMI ≥ 85th centile and < 95th centile) and obesity (sex-and age-specific BMI ≥ 95th centile)(Dinsdale et al., 2011, Centre for Disease Control and Prevention, 2019), the decision was made to include the study-specific definitions with the aim of assessing the effect of varying BMI cut-offs on the association of overweight or obesity with healthcare utilisation.

2.2.2 Literature search

A systematic literature search was performed in five electronic databases (PubMed, Medline, EMBASE, Web of Science and CINAHL) from inception to July 2018. To keep the findings of the review up to date with the current literature, an update of database searches was conducted in May 2020. This search update covered the full data range from inception to May 2020, and records found in the previous search were removed based on the methods described by Bramer and Bain (2017). The search strategy focused on studies

reporting association between weight status and healthcare utilisation in children. Only studies published in English were considered for inclusion. The searches were conducted by assembling terms that could relate to the three main components of the review: "children or adolescents", "obesity or overweight" and "healthcare utilisation". These terms were comprised of keywords, text terms or medical subject headings appropriate for each literature database. A copy of the searches conducted to identify studies is given in the appendix A1.2. I also searched the reference lists of screened publications to look for additional articles. A forward and backward reference search for all the studies meeting the inclusion criteria was carried out to identify any other relevant studies. Research reported in grey literature was not searched. Conference abstracts and review articles were not eligible for inclusion. However, reference lists of screened review articles were checked for potentially relevant studies.

2.2.3 Study selection

Titles and abstracts of records retrieved through literature search up to July 2018 were screened by me (first reviewer) with a random sample of 10% of these studies screened by a second reviewer. Studies were then full text screened by the first reviewer to assess their eligibility for inclusion in the review. A random sample of 10% of these full-text studies was also screened by the second reviewer. The level of agreement between the two reviewers at each stage was assessed by Cohen's kappa score. The score was classified as follows: <0.20 indicated a poor agreement; 0.21-0.40 a fair agreement; 0.41-0.60 a moderate agreement; 0.61-0.80 a good agreement; 0.81-1.00 a very good agreement (Altman, 1990). All disagreements were resolved through discussion between the two reviewers and by consulting a third reviewer if required.

Additional records retrieved from the search update in May 2020 were screened for title, abstract and full text by the first reviewer.

2.2.4 Data extraction

A customized pre-designed data extraction form was designed to extract data from the included studies. The principal outcomes that were extracted from each study were the measures of effect size between weight status and healthcare utilisation. The following information was also extracted from each study: first author's surname, year of publication, study design, country, sample size, age-range, time frame, sex of participants, definition of exposure (obesity/overweight), methods of measuring exposure. A sample of completed data extraction form is given in appendix A1.3. Data for each study were extracted by the first reviewer and was also reviewed by a second reviewer. Any discrepancies were discussed and resolved through consensus between the two reviewers.

2.2.5 Assessment of study quality

The Quality Assessment tool for Observational Cohort and Cross-sectional studies by the National Heart and Lung Institute (NHLBI) was used to assess the quality and risk of bias of each included study (National Heart and Lung Institute, 2014). This assessment tool rates study quality along 14 criteria (Table 2.2), with three possible outcomes for each question: 'Yes', 'No' and 'Cannot determine/Not reported/Not applicable". For a response of 'Yes', a score of one was assigned against the criteria, whereas a score of zero was assigned for any answer other than 'Yes'. Each study was then rated good, fair, or poor based on a score ranging from 0 to 14; where a 'good' study was considered to have the least risk of bias, 'fair' was susceptible to some bias and 'poor' indicated a high risk of bias.

2.2.6 Narrative synthesis

Due to the diverse nature of healthcare utilisation outcomes, measures of effect and lack of appropriate or sufficient data in the majority of studies to statistically analyse these effect size measurements, a decision was made to summarise the findings of the included studies narratively. A narrative synthesis was developed to explain the impact of weight

status on all the reported measures of health service use in different studies: emergency department visits, outpatient visits, General Practitioner (GP) visits, hospital admissions and hospital length of stay (LOS). Additionally, potential sources of heterogeneity across studies were explored.

2.2.7 Statistical analysis

A meta-analysis was undertaken by pooling the evidence from studies that reported enough and appropriate data on respective measures of healthcare utilisation. Rate ratios (RRs) with 95% confidence intervals (CI) were the most used summary statistic to measure the effect of association between weight status and health service use. The 'meta' command in Stata version 16.1 (StataCorp, 2019) was used to generate meta-analysis for rate ratios (RRs) of healthcare utilisation in obese and overweight children, using normal weight children as a reference. Studies that reported RRs with corresponding measures of precision [(95% Confidence Intervals (CIs) or Standard Errors (SEs)] were included in the meta-analysis. Additionally, studies with appropriate raw data to compute crude RRs were eligible for inclusion in the meta-analysis. Meta-analysis uses effect sizes in a metric that makes them closest to normally distributed, therefore before undertaking the analysis in Stata, rate ratios were log transformed and corresponding standard errors were computed from effect sizes and 95% CIs using the Comprehensive Meta-Analysis software version 3 (Borenstein, 2013). Afterwards, a random-effects meta-analysis with Hartung-Knapp-Sidik-Jonkman (HKSJ) method was carried out (Hartung and Knapp, 2001, Sidik et al., 2006). The error rates for this method have consistently been shown to be more robust than the more commonly used DerSimonian and Laird method, particularly when there are small number of studies in the meta-analysis (IntHout et al., 2014).

2.2.8 Publication bias

Publication bias was assessed using funnel plots, however due to the number of studies included in the analysis being less than 10, statistical tests for funnel plot asymmetry were not performed (Sterne et al., 2011). Heterogeneity among studies was assessed using the I^2 statistic. Based on the interpretation provided in the Cochrane's Handbook for Systematic Reviews, heterogeneity in this review is considered substantial if $I^2 > 50\%$ (Higgins, 2011).

2.3 Results

This section presents the results of the narrative synthesis and meta-analysis.

2.3.1 Study selection

A PRISMA flow diagram for study selection is shown in figure 2.1. The search of electronic databases up to July 2018 identified 36,077 records. After removal of duplicates, 18,966 studies were screened by titles and abstracts. A random sample of 1900 studies (10%) was also reviewed by the second reviewer. The level of agreement between reviewers at this stage was reflected by a Cohen's kappa score of 0.86. Full texts of 578 studies were screened by the first reviewer with a random sample of 60 studies (10%) also reviewed by the second reviewer. The Cohen's kappa score for level of agreement at this stage was 0.67, which indicated a good agreement. Twenty-six articles were eligible for inclusion at this stage.

The search update in May 2020 identified 8,504 additional articles, of which 4 were eligible for inclusion. Three additional articles were identified through searching the reference lists of screened systematic reviews. Overall, 33 studies were eligible for inclusion. All these studies were included in the narrative synthesis, but only six were included in the meta-analysis based on the criteria mentioned in section 2.2.7.

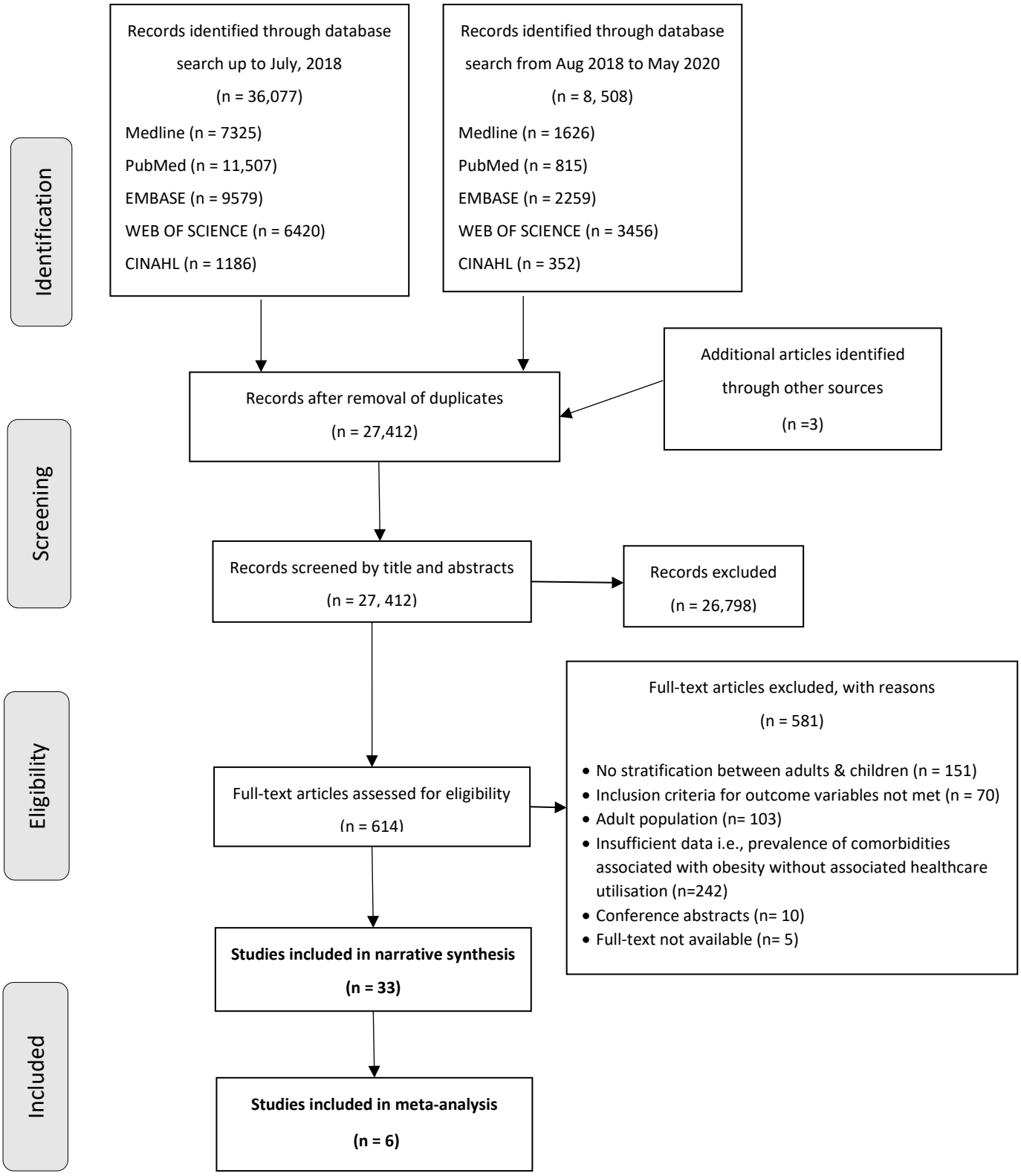

Figure 2.1 *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) study selection diagram*

2.3.2 Study characteristics

The basic characteristics of included studies are summarised in table 2.1. The majority of these studies (n = 20) were conducted in the USA. Twenty-three of the included studies were cohort studies. Nine of the remaining studies used cross-sectional methods, while one study was a case-control study (Table 2.1). Multiple studies reported data from two surveys/cohorts. The Medical Expenditure Panel Survey (MEPS) is reported in five studies (Monheit et al., 2009, Skinner et al., 2008, Trasande and Chatterjee, 2009, Turer et al., 2013, Wright and Prosser, 2014) and the German Interview and Examination Survey for Children and Adolescents (KiGGS) is reported in two studies (Wenig et al., 2011, Wenig, 2012). As studies from the same survey/cohort reported data for different years or different outcome measures, decision was made to analyse the data for each individual study, and not at the level of the survey/cohort. None of the six studies included in the meta-analysis use data from the same source.

Table 2.1 summarises the measures of healthcare utilisation reported across the included studies. The most commonly reported outcome measures were emergency department (ED) visits (n=10) (Estabrooks and Shetterly, 2007, Hampl et al., 2007, Hering et al., 2009, Janicke et al., 2010, Lynch et al., 2015, Trasande and Chatterjee, 2009, Turer et al., 2013, Wright and Prosser, 2014, Wyrick et al., 2013, Kovalerchik et al., 2020) and outpatient (n=11) visits (including primary care and specialty visits) (Wright and Prosser, 2014, Wenig, 2012, Turer et al., 2013, Trasande and Chatterjee, 2009, Lynch et al., 2015, Janicke et al., 2010, Hering et al., 2009, Hampl et al., 2007, Estabrooks and Shetterly, 2007, Kovalerchik et al., 2020, Ortiz-Pinto et al., 2020). Seven studies reported on healthcare use associated with respiratory diseases (Lynch et al., 2015, Buescher et al., 2008, Woolford et al., 2007, Carroll et al., 2006, Ortiz-Pinto et al., 2020, Kelly et al., 2019, Griffiths et al., 2019), two reported on musculoskeletal conditions (van Leeuwen et al., 2018, Ortiz-Pinto et al., 2020)

and two on conditions concerning mental health (Estabrooks and Shetterly, 2007, Ortiz-Pinto et al., 2020). The rest of the studies analysed the overall healthcare use in children with no reporting on reasons for utilisation. The studies represented children between 1 to 19 years of age. Table 2.1 shows that seven studies calculated BMI from anthropometric measurements (height and weight) based on self- or parent-reported data (Breitfelder et al., 2011, Monheit et al., 2009, Trasande and Chatterjee, 2009, Trasande et al., 2009, Turer et al., 2013, Wright and Prosser, 2014). In all other studies, heights and weights were either measured as part of the study or recorded from the health facility records. Two studies reported data on weight only and used weight/age (W/A) ratio to define obesity or overweight (Fleming-Dutra et al., 2013, Bechere Fernandes et al., 2014). Additionally, different variables were adjusted for in the multivariable analysis in respective studies. These variables are listed in table 2.1.

2.3.3 Study quality

The response for each study against the criteria in NHLBI's quality assessment tool to critically appraise the internal validity is shown in table 2.2. Fourteen studies scored a "good" rating, sixteen had a "fair" rating, while three had a "poor" rating (Table 2.2). The studies included in the meta-analysis were either of "good" or "fair" quality; therefore, weighting based on quality assessment was not done in the meta-analysis. However, quality assessment was used to weigh the strength of evidence during narrative synthesis.

Table 2.1 *Basic characteristics of included studies*

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Adams, 2008[a]	USA	4,263	Cross-sectional	14-19 years	Physical assessment measurement	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Primary care referrals Dental referrals	Not reported
Bechere Fernandes et al, 2014	Brazil	91	Retrospective cohort	1-10 years	Hospital based measurements	Weight/age ratio (W/A) for 1-3 years: Excess weight W/A ≥2 z-scores, normal weight as interval from -2 to +2 z scores. Age 3-10: excess weight BMI ≥1 z-score, normal weight BMI -2 to +1 z-score	Length of stay in the hospital	Age and sex

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Bertoldi, 2010	Brazil	4,452	Prospective cohort	11-12 years	Measurement by researchers	Not given	Medicine uptake in 15 days prior to interview	Skin color, sex, socioeconomic status, pregnancy complication, ICU admission, nutrition status, sedentary lifestyle, and use of sedatives by mothers
Bettenhausen, 2015[a]	USA	518	Cross-sectional	5-17 years	Hospital based measurement	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Inpatient length of stay Readmission rates	Age, sex, race, and insurance
Bianchi-Hayes, 2015[a]	USA	17,444	Retrospective cohort study	2-18 years (NHANES)	Measured by trained health technicians	Overweight BMI ≥ 85th and < 95th percentile. Obese BMI ≥ 95th percentile	Total healthcare visits Total no. of hospitalisations Mental health visits	Age, sex, ethnicity, health insurance status, household income, presence of asthma or diabetes, and the educational status of the head of household.

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Breitfelder et al., 2011	Germany	3,508	Cross-sectional	9-12 years (GINI and LISA)	Measured or self-reported	Overweight: BMI > 90th to 97th percentile. Obese > 97th percentile	Expenditure associated with physician, therapist and inpatient rehabilitation visits	Sex, region, parental education and income
Buescher et al., 2008[a]	USA	30,528	Cross-sectional	12-18 years	Clinical measurements	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Well-child visits Respiratory related health visits Total expenditure	Sex and ethnicity
Carroll et al., 2006[a]	USA	219	Retrospective cohort	2-18 years	Not given	Overweight BMI ≥ 85th and < 95th percentile. Obese BMI ≥ 95th percentile	Duration of total ICU and hospital length of stay	Age, severe persistent asthma, admission modified pulmonary index score
Dilley et al., 2007[a]	USA	1,216	Retrospective cohort	≥ 2 years	Medical record	Overweight ≥ 95th percentile. At risk for overweight: BMI of 85th to 94th percentile	No. of visits to private practice or public health clinics	Age, race, BMI percentile, insurance status, parental education, and household tobacco use

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Doherty et al., 2017	Ireland	5,924	Prospective cohort	13 years (GUI)	Measurement by health professionals	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	GP visits Inpatient stay	Child characteristics: gender birthweight, gestation age and citizenship. Mother's characteristics: Age, health status, education status, marital status, and depression score. Household characteristics: Income, location, and health insurance status
Estabrooks and Shetterly, 2007[*a]	USA	8,282	Prospective cohort	3-17 years	Hospital medical record	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Primary care (outpatient) visits ED visits No. of hospitalisations	Sex, age and disease status

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Fleming-Dutra et al., 2013[a]	USA	32,966	Retrospective cohort	2-18 years	Hospital Medical record	Overweight > 95th percentile sex=specific weight for age. Normal weight ≤ 95% sex-specific weight for age.	Billed charges for child's visit Hospitalisation rate ED length of stay in hours	Race, age, sex, insurance, and acuity
Griffiths et al., 2018	United Kingdom	3,269	Prospective cohort	5-14 years	Measured by trained interviewers	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥ 95th percentile	Hospital admission	Sex, mode of delivery, preterm, long standing illness, disability, maternal BMI
Hampl et al., 2007[*a]	USA	8,404	Retrospective cohort	5-18 years	Measured by clinical nursing staff	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Primary care visits ED visits Laboratory use	Age, sex, race and insurance status

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Hering et al., 2009	Israel	Cases: 363 Controls: 382	Retrospective case control	4-18 years	Clinical measurement	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	ED visits Primary care clinic visits Hospital admissions	Control group matched for age and gender
Janicke et al., 2010[*a]	USA	2,00	Retrospective cohort	7-15 years	Measured by a trained researcher	Overweight: BMI z-score ≥1 and < 2. Obese: BMI z-score ≥ 2	ED visits Acute care claims Outpatient and medical claims	Age, sex, ethnicity, insurance status
Kelly et al., 2019	United Kingdom	9,443	Prospective cohort	4-5 years	Measured by trained school nurses	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥ 95th percentile	GP appointments GP prescriptions	Sex, maternal age, gestational age, means tested benefits, Index of Multiple deprivation (2010)
Kovalerchik et al., 2020[*a]	USA	30,352	Retrospective cohort	3-17 years	Hospital based measurements	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Emergency Department visits Outpatient visits	age, age^2, sex, race/ethnicity, and insurance status.

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Kuhle et al., 2011[*]	Canada	4,380	Prospective cohort	10-11 years	Measured by research assistants	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	GP visits Specialist referrals Total Healthcare costs	Sex, income, education status and geographic region
Lynch et al., 2015[*a]	USA	19,528	Retrospective cohort	2-18 years	Hospital medical record	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Outpatient visits ED visits No. of hospitalisations	Sex, age and socioeconomic status
Monheit et al., 2009[a]	USA	6,738	Retrospective cohort	12-19 years (MEPS)	Parent- and self-directed	At risk for overweight BMI ≥85th and < 95th percentile. Overweight BMI ≥ 95th percentile	Overall health expenditure	Age, race, region, parental education attainment, and parental smoking
Ortiz Pinto et al., 2019	Spain	1,857	Prospective cohort	4-6 years	Measured by pediatricians	Overweight: BMI z-score ≥1 and ≤ 2. Obese: BMI z-score >+2	Primary care visits Drug Prescriptions Hospital admissions	Sex, age in months, mother's education, breast feeding duration, family purchasing power

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Skinner et al., 2008[a]	USA	Not given	Cross-sectional	6-17 years (MEPS)	Physical examination in NHANES. Parent reported in MEPS	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Healthcare expenditure	Year, sex, race, poverty and insurance status.
Trasande and Chatterjee, 2009[a]	USA	19,613	Prospective cohort	6-19 years (MEPS)	Parent- and self-reported	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Outpatient visits ED visits Healthcare expenditure	Race, gender, insurance status and family income.
Trasande et al., 2009[a]	USA	Not given	Prospective cohort	2-19 years	Parent- and self-reported	Based on ICD-9 diagnostic codes	Obesity associated hospitalisations	Age, sex, ethnicity, expected primary payer, hospital location, hospital teaching status, and median household income.

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Turer et al., 2013[a]	USA	17,224	Cross-sectional	10-17 years (MEPS)	Parent- and self-reported	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Hospital based outpatient, or clinic visit Specialist visits ED visits Outpatient prescriptions	Gender, age, race, insurance status, and poverty status
van Leeuwen et al., 2018	Netherlands	617	Prospective cohort	2-18 years (DOERAK)	Measured by GP or research assistant	Overweight: BMI z-score ≥1 and < 2. Obese: BMI z-score ≥ 2	No. and type of musculoskeletal consultation Total no. of consultations	Age, gender, socioeconomic status and marital status.
Wake et al., 2010	Australia	923	Prospective cohort	5-19 years	Measured by trained field workers	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Healthcare visits	Sex, age and SEIFA disadvantage index
Wenig et al., 2011	Germany	14,592	Retrospective cohort	3-17 years (KiGGS)	Measured through physical examination	Overweight: BMI > 90th to 97th percentile. Obese > 97th percentile	No. of pharmaceuticals taken in the last 7 days	Age, sex, socioeconomic status and migrant status

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Wenig, 2012	Germany	14,277	Cross-sectional	3-17 years (KiGGS)	Measured through physical examination	Overweight: BMI > 90th to 97th percentile. Obese > 97th percentile	Physician visits	Sex, age, BMI group, socioeconomic stats, town size, and east or west Germany variable.
Woolford et al., 2007[a]	USA	7,77,274	Cross-sectional	2-18 years	Hospital based measurements	Obesity was defined based on ICD-9-CM codes. (Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile)	Length of stay Total charges	Sex, race, region and hospital type
Wright and Prosser, 2014[a]	USA	23,727	Cross-sectional	6-17 years (MEPS)	Parent- and self-reported	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	ED visits Outpatient visits Prescription of drugs	Age, BMI class, sex, ethnicity, census region, poverty status, insurance status and survey year,

First author, Year	Country	No. of participants	Study Design	Age in years (Cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of Healthcare utilisation	Covariates
Wyrick et al., 2013[a]	USA	1,746	Prospective cohort	2-18 years	Hospital based measurements	Overweight BMI ≥85th and < 95th percentile. Obese BMI ≥ 95th percentile	Admissions from ED	Age and sex

[*] **Studies included in the meta-analysis**

[a] **Studies using Centre for Disease control (CDC) criterion to define obesity**

Table 2.2 *Assessment of study quality*

Study	Criteria														Rating
	Research Question or Objective clearly stated	Study population clearly defined	Participation rate of eligible persons at least 50%	Groups recruited from the same population with uniform eligibility criteria	Sample Size Justification	Exposure assessed prior to the outcome	Sufficient timeframe to see an effect	Different levels of exposure of interest (categorical/continuous)	Exposure variables clearly defined or not. Were the tools used for measurement were accurate	Repeated exposure assessment	Outcome measures clearly defined and measured	Blinding of the outcome assessors	Loss to follow-up 20% or less	Statistical analysis (measurement and adjustment of confounding variables)	
Adams, 2008	1	0	0	1	0	0	0	1	0	0	1	0	0	0	**Poor**
Bechere Fernandes et al, 2014	1	1	0	1	1	1	1	1	1	0	1	0	0	1	**Good**
Bertoldi, 2010	1	0	0	1	0	1	1	0	1	0	0	0	0	1	**Poor**
Bettenhausen, 2015	1	1	0	1	0	1	1	1	1	0	1	0	0	1	**Fair**
Bianchi-Hayes, 2015	1	1	0	1	0	1	1	1	1	0	1	0	0	1	**Fair**
Breitfelder et al., 2011	1	1	0	1	0	0	0	1	1	0	0	0	0	1	**Fair**
Buescher et al., 2008	1	1	0	1	0	1	1	1	1	0	1	0	0	1	**Fair**
Carroll et al., 2006	1	1	0	1	0	1	1	1	0	0	1	0	0	1	**Fair**
Dilley et al., 2007	1	0	0	1	0	1	1	1	0	0	0	0	0	1	**Poor**

Doherty et al., 2017	1	1	0	1	0	1	1	1	1	1	1	0	0	1	**Good**
Estabrooks and Shetterly, 2007*	1	1	0	1	0	1	1	1	1	1	1	0	0	1	**Good**
Fleming-Dutra et al., 2013	1	1	0	0	1	1	1	1	0	0	1	0	0	1	**Fair**
Griffiths et al., 2018	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**Good**
Hampl et al., 2007*	1	1	0	1	0	1	1	1	1	0	1	0	1	1	**Good**
Hering et al., 2009	1	1	0	1	0	1	1	1	1	0	1	0	0	1	**Fair**
Janicke et al., 2010*	1	1	0	1	0	0	0	1	1	0	1	0	0	1	**Fair**
Kelly et al., 2019	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**Good**
Kovalerchik et al., 2020*	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**Good**
Kuhle et al., 2011*	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**Good**
Lynch et al., 2015*	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**Good**
Monheit et al., 2009	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**1**	**1**	**0**	**0**	**0**	**0**	**1**	**Fair**
Ortiz-Pinto et al., 2019	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**Good**
Skinner et al., 2008	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**0**	**0**	**1**	**0**	**0**	**1**	**Fair**

Trasande and Chatterjee, 2009	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**Fair**
Trasande et al., 2009	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**0**	**0**	**0**	**1**	**0**	**0**	**1**	**Fair**
Turer et al., 2013	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**0**	**1**	**Fair**
van Leeuwen et al., 2018	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**Good**
Wake et al., 2010	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**0**	**1**	**1**	**Good**
Wenig et al., 2011	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**Fair**
Wenig, 2012	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**0**	**0**	**0**	**1**	**Fair**
Woolford et al., 2007	**1**	**1**	**0**	**1**	**0**	**0**	**1**	**1**	**0**	**0**	**1**	**0**	**0**	**1**	**Fair**
Wright and Prosser, 2014	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**0**	**0**	**1**	**Good**
Wyrick et al., 2013	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**0**	**1**	**0**	**1**	**1**	**Good**

'1' = 'Yes', '0' = No/cannot determine/not recorded. Rating = Poor: score ≤ 6, Fair: score 7 – 9, Good: score ≥ 10.
***Studies included in the meta-analysis**

2.3.4 Narrative synthesis and Meta-analysis

Findings from all included studies were synthesized narratively for each outcome measure of healthcare utilisation. A subgroup synthesis was done by dividing studies based on BMI cut-offs, ethnicity and method of anthropometric measurement.

Six studies were included in the meta-analysis (Estabrooks and Shetterly, 2007, Hampl et al., 2007, Janicke et al., 2010, Kuhle et al., 2011, Lynch et al., 2015, Kovalerchik et al., 2020). All of these studies were cohort studies (Table 2.1). All six studies reported an association between weight status and outpatient visits and were included in the meta-analysis for outcome measure of outpatient visits. Five of these six studies also reported on association of weight status with ED visits and were therefore included in a separate meta-analysis for outcome measure of ED visits (Estabrooks and Shetterly, 2007, Hampl et al., 2007, Janicke et al., 2010, Lynch et al., 2015, Kovalerchik et al., 2020). Additionally, five of these (Estabrooks and Shetterly, 2007, Hampl et al., 2007, Kuhle et al., 2011, Lynch et al., 2015, Kovalerchik et al., 2020) used a similar definition to define obesity (age and sex specific BMI ≥ 95th percentile) while one study (Janicke et al., 2010) defined it as age and sex specific BMI z-score ≥ 2, which also corresponds to BMI ≥ 95th percentile (Dinsdale et al., 2011). Moreover, five studies included in the meta-analysis for ED visits were conducted in the USA. The sixth study, which was only part of analysis for outpatient visits was conducted in Canada. For one study (Hampl et al., 2007) the appropriate effect sizes with corresponding standard errors were calculated using the available raw data. One study assessed healthcare use over one-year and three-year periods. A decision was made to include data for one-year period due to larger sample size, as many participants were lost to follow-up by the end of three-year period (Estabrooks and Shetterly, 2007). Due to a small number of studies eligible for inclusion in the meta-analysis and limited to no data available on key covariates, it was not possible to perform a subgroup analysis.

2.3.4.1 Emergency department visits

Ten studies reported ED visits as an outcome measure for healthcare utilisation (Lynch et al., 2015, Trasande and Chatterjee, 2009, Turer et al., 2013, Janicke et al., 2010, Hampl et al., 2007, Estabrooks and Shetterly, 2007, Hering et al., 2009, Wright and Prosser, 2014, Fleming-Dutra et al., 2013, Kovalerchik et al., 2020). In both obese and overweight children compared to normal weight children, the general direction of association was an increase in visits; however, variability in the strength and direction of association was reported. For obese children compared to normal weight children, five studies reported a significant increase in ED visits (Lynch et al., 2015, Trasande and Chatterjee, 2009, Turer et al., 2013, Janicke et al., 2010, Kovalerchik et al., 2020). Three studies reported a non-significant increase in ED visits (Hampl et al., 2007, Hering et al., 2009, Estabrooks and Shetterly, 2007). Additionally, one study reported a non-significant decrease of ED visits in 6-11 years old obese children, while for obese children aged 12-17 years, a significant increase in visits was reported (Wright and Prosser, 2014). For overweight children, four studies reported a significant increase in ED visits compared to normal weight children (Lynch et al., 2015, Trasande and Chatterjee, 2009, Turer et al., 2013, Kovalerchik et al., 2020). Two studies reported a non-significant increase (Hampl et al., 2007, Wright and Prosser, 2014) and two studies reported a non-significant decrease (Estabrooks and Shetterly, 2007, Janicke et al., 2010).

In the five studies included in the meta-analysis for ED visits, obese children were significantly more likely to visit emergency departments compared to normal weight children (Figure 2.2).

The associated effect size (RR) was 1.34 (95% CI: 1.07-1.68). The effect size for overweight versus healthy weight was RR= 1.11 (95% CI: 0.92-1.33) (Figure 2.3). The I^2 statistic showed substantial between-study heterogeneity for obese versus normal weight (I^2 = 94.3 %, P < 0.01) and overweight versus normal weight (I^2 = 92.5 %, P < 0.01). Appendix A1.4 shows forest plots for ED visits in obese children compared to normal weight children calculated using the pre-specified adjusted RRs reported by individual studies

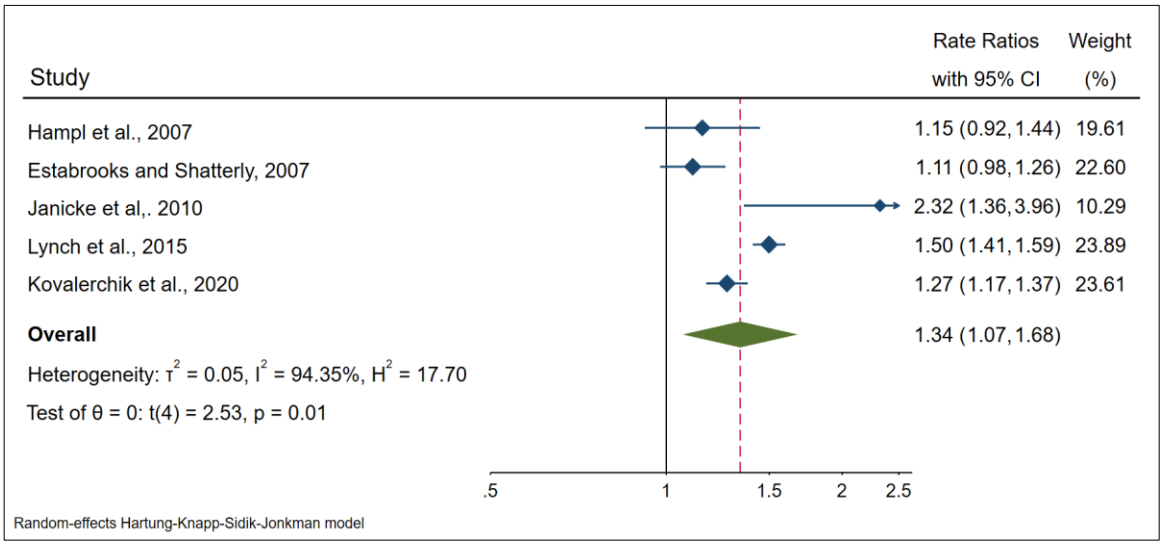

Figure 2.2 *Forest plot for unadjusted effect sizes (Rate ratios with 95% Cis) for ED visits in obese children*

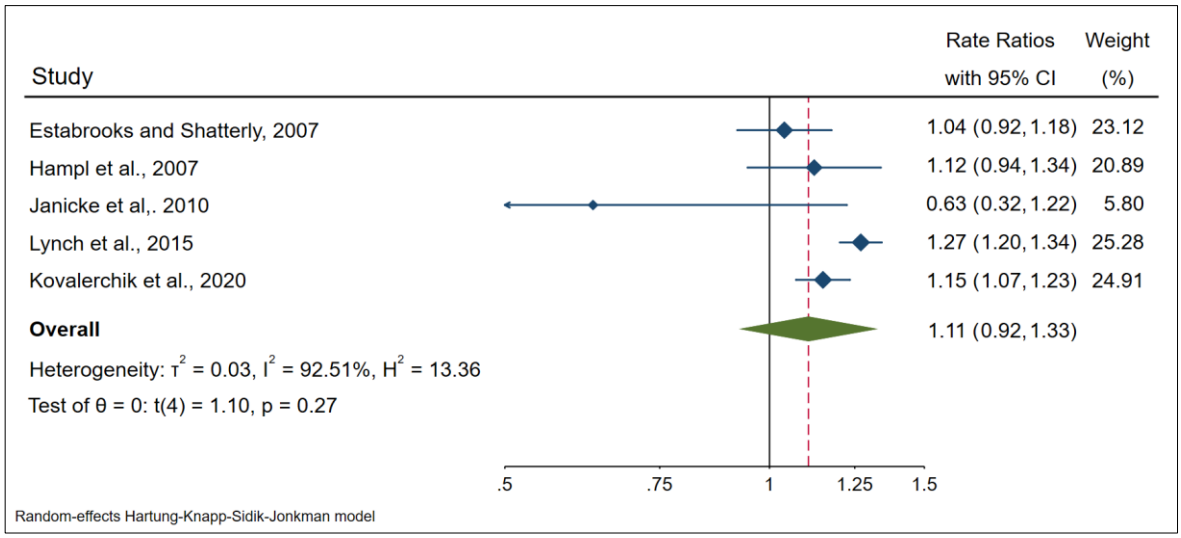

Figure 2.3 *Forest plot for unadjusted effect sizes (Rate ratios with 95% Cis) for ED visits in overweight children*

On visual inspection of funnel plot asymmetry, there is a possibility of publication bias, with a small sized study reporting high RRs for obese children (Figure 2.4). A statistical test for publication bias was not performed due to small number of studies (n < 10).

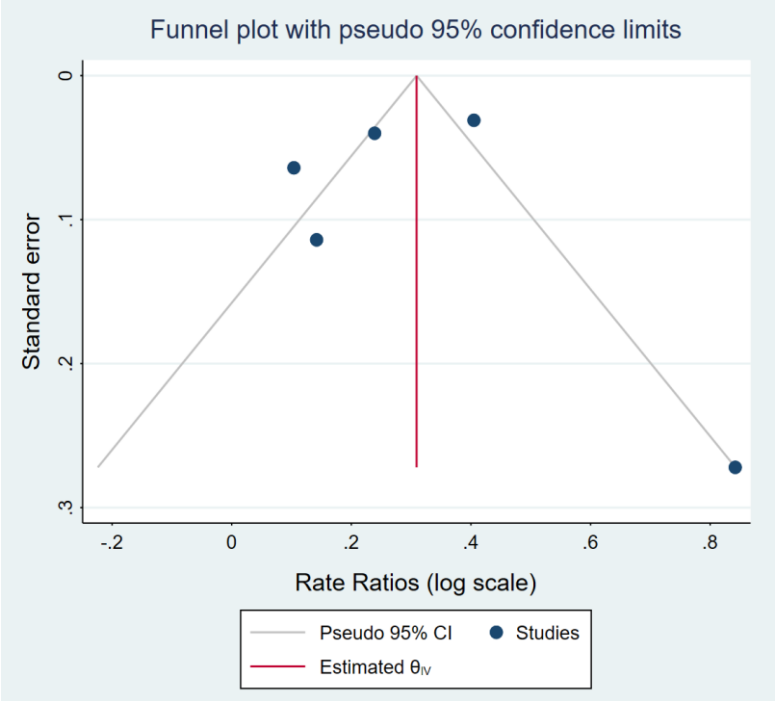

Figure 2.4 *Funnel plot with pseudo 95% confidence limits for rate ratios in obese children for ED visits compared to normal weight children. The y-axis is the standard error of log rate ratio.*

2.3.4.2 Outpatient visits

Eleven studies reported outpatient visits as a measure of healthcare utilisation (Hering et al., 2009, Trasande and Chatterjee, 2009, Turer et al., 2013, Wenig, 2012, Wright and Prosser, 2014, Estabrooks and Shetterly, 2007, Hampl et al., 2007, Janicke et al., 2010, Lynch et al., 2015, Kovalerchik et al., 2020, Ortiz-Pinto et al., 2020). In obese children compared to normal weight children, the general direction of association was an increase in visits, however variability in the strength of association was reported. Seven studies reported a significant increase in outpatient visits for obese children (Lynch et al., 2015, Hering et al., 2009, Trasande and Chatterjee, 2009, Turer et al., 2013, Estabrooks and

Shetterly, 2007, Janicke et al., 2010, Kovalerchik et al., 2020), while four studies reported a non-significant increase (Hampl et al., 2007, Wenig, 2012, Wright and Prosser, 2014, Ortiz-Pinto et al., 2020). For overweight children compared to normal weight children, three studies reported a significant increase in outpatient visits (Estabrooks and Shetterly, 2007, Lynch et al., 2015, Kovalerchik et al., 2020). Five studies reported a non-significant increase (Trasande and Chatterjee, 2009, Turer et al., 2013, Hampl et al., 2007, Wenig, 2012, Wright and Prosser, 2014) while two studies reported a non-significant decrease in outpatient visits (Janicke et al., 2010, Ortiz-Pinto et al., 2020).

Pooled unadjusted RRs for obese versus normal weight and overweight versus normal weight were 1.11 (95% CI: 1.02-1.20) and 1.02 (95% CI: 0.98-1.08), respectively (Figure 2.5 and Figure 2.6). Significant between study heterogeneity was observed for both obese vs normal weight children (I^2 = 87.6%, P < 0.01) and overweight vs normal weight children (I^2 = 73 %, P < 0.01). Appendix A1.5 shows forest plots for outpatient visits in obese children compared to normal weight children calculated using the pre-specified adjusted RRs reported by individual studies.

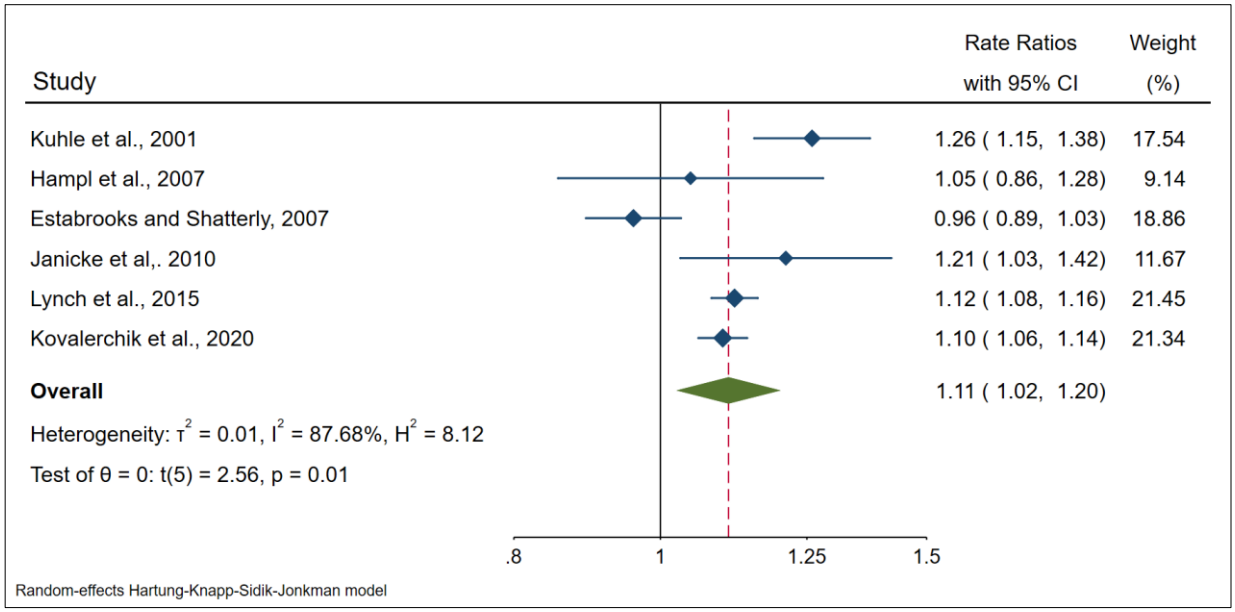

Figure 2.5 *Forest plot for unadjusted effect sizes (Rate ratios with 95% Cis) for outpatient visits in obese children*

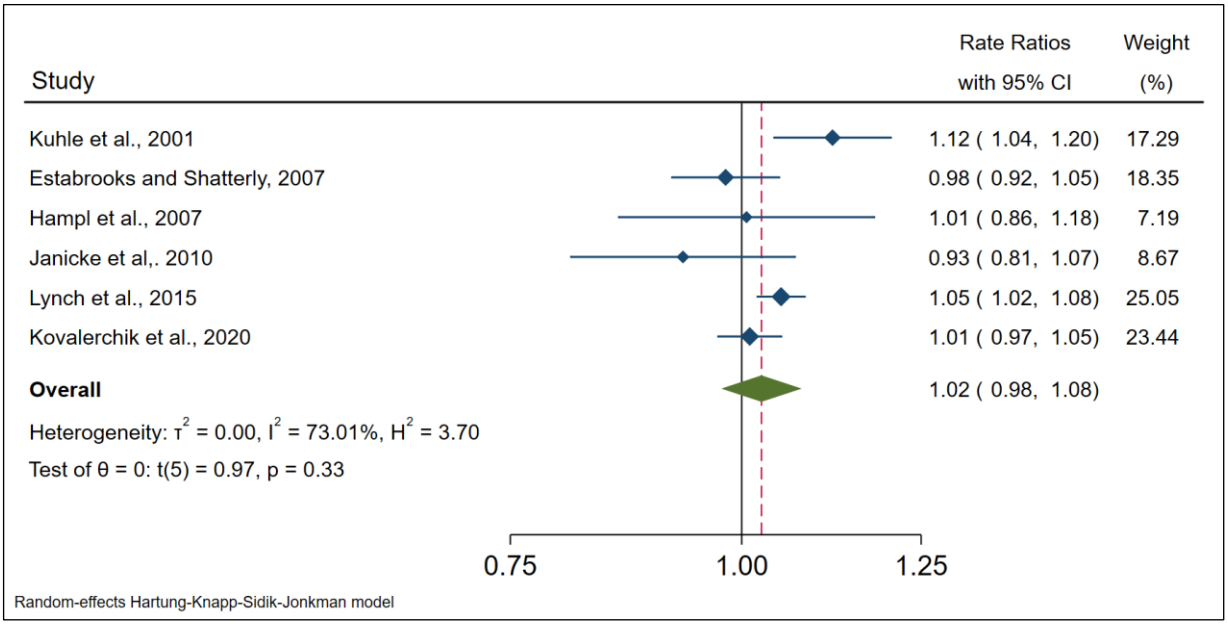

Figure 2.6 *Forest plot for unadjusted effect sizes (Rate ratios with 95% Cis) for outpatient visits in overweight children*

Visual inspection of funnel plot asymmetry for outpatient visits in obese children suggests publication bias (Figure 2.7). Statistical tests to assess publication bias were not performed due to the small number of studies (n < 10).

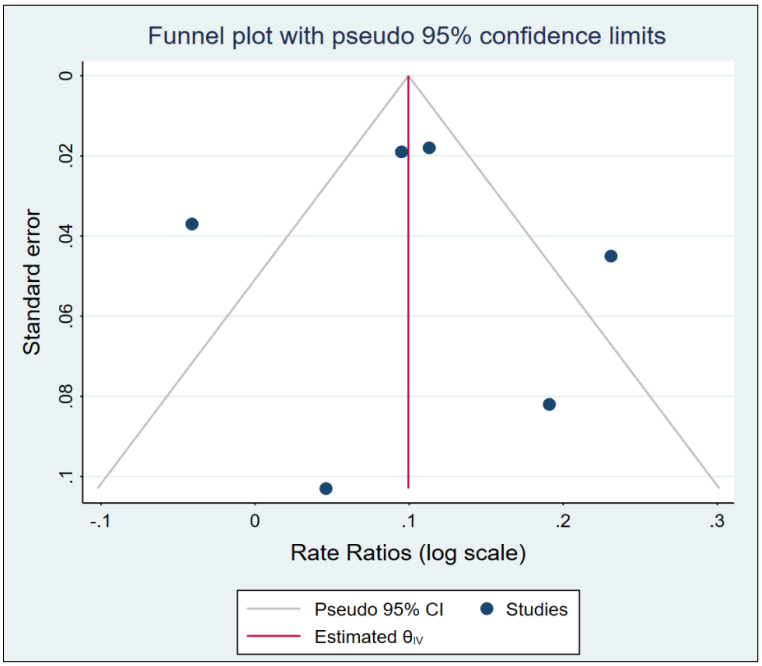

Figure 2.7: *Funnel plot with pseudo 95% confidence limits for rate ratios in obese children for outpatient visits compared to normal weight children. The y-axis is the standard error of log rate ratio.*

2.3.4.3 Hospital admissions and length of stay

Seven studies reported hospital admissions as a measure of healthcare use (Bianchi-Hayes et al., 2015, Estabrooks and Shetterly, 2007, Hering et al., 2009, Lynch et al., 2015, Wyrick et al., 2013, Ortiz-Pinto et al., 2020, Griffiths et al., 2019). One study reported a significant increase (Hering et al., 2009) while two studies reported a non-significant increase (Estabrooks and Shetterly, 2007, Griffiths et al., 2019) in hospital admissions for obese children compared to normal weight children. Two studies reported a non-significant decrease in admissions (Bianchi-Hayes et al., 2015, Ortiz-Pinto et al., 2020). Additionally, one study reported that 14.5% of obese or overweight children were admitted, compared to 16.5% normal weight children (Wyrick et al., 2013). For overweight children, one study reported a significant decrease (Bianchi-Hayes et al., 2015) while one reported a non-significant decrease (Estabrooks and Shetterly, 2007) in admissions compared to normal weight children.

Hospital LOS was reported as a measure of healthcare utilisation by six studies (Trasande and Chatterjee, 2009, Bechere Fernandes et al., 2014, Bettenhausen et al., 2015, Fleming-Dutra et al., 2013, Woolford et al., 2007, Carroll et al., 2006). Four studies found a significant increase in LOS for obese children compared to normal weight (Bechere Fernandes et al., 2014, Trasande and Chatterjee, 2009, Woolford et al., 2007, Carroll et al., 2006). One study reported a slight significant decrease in LOS for obese children (Bettenhausen et al., 2015), while one study reported no association between obese and normal weight children (Fleming-Dutra et al., 2013).

2.3.4.4 GP visits

Three studies reported GP visits as a measure for healthcare utilisation (Doherty et al., 2017, Kuhle et al., 2011, Kelly et al., 2019). All three studies reported a significant increase in GP visits for overweight and obese children, compared to their normal-weight peers.

2.3.4.5 Associated costs of healthcare

Fourteen of the included studies estimated costs of healthcare utilisation by BMI status. A summary of the results of cost-analysis by each study is given in appendix A1.6**.** Most of these studies (n=10) were from the USA and used Medicaid insurance claims data to analyse costs. The remaining studies were from Germany (n = 2), the United Kingdom (n=1) and Canada (n=1).

Three studies analysed costs associated with primary care services (Janicke et al., 2010, Kelly et al., 2019, Wenig, 2012); two studies analysed costs for hospital admissions (Trasande and Chatterjee, 2009, Woolford et al., 2007); one study analysed costs associated with ED visits (Fleming-Dutra et al., 2013) ; one for primary care prescriptions (Breitfelder et al., 2011), while the remainder (n=7) of the studies presented an aggregate analysis of primary and secondary healthcare costs (Breitfelder et al., 2011, Buescher et al., 2008, Hampl et al., 2007, Kuhle et al., 2011, Monheit et al., 2009, Trasande and Chatterjee, 2009, Wright and Prosser, 2014). The expenditure associated with obese children for any measure of healthcare use reported in these studies was higher compared to normal weight children. Additionally, underweight children were also estimated to have a higher expenditure compared to normal weight children. The association for overweight children was mixed, with some studies reporting a positive association, and some a negative association (Appendix A1.6).

2.3.4.6 Associated medical conditions

Five studies reported on the effect of asthma or acute respiratory disorders on healthcare utilisation in obese children (Buescher et al., 2008, Carroll et al., 2006, Lynch et al., 2015, Woolford et al., 2007, Kelly et al., 2019). Of these studies, four reported that obese children significantly incurred increased healthcare use for asthma compared to normal weight children (Buescher et al., 2008, Carroll et al., 2006, Woolford et al., 2007, Kelly et al., 2019).

Additionally, two studies found that other acute respiratory conditions are also significantly associated with increased healthcare use in obese children (Buescher et al., 2008, Lynch et al., 2015). Furthermore, two studies reported a non-significant increase for respiratory conditions in obese children (Woolford et al., 2007, Ortiz-Pinto et al., 2020).

Two studies reported that obese children are at a significantly greater risk of seeking healthcare for mental health problems compared to normal weight children (Estabrooks and Shetterly, 2007, Ortiz-Pinto et al., 2020). The risk for overweight children was also reported to be higher but non-significant. Two studies reported a non-significant increase in visits for musculoskeletal problems in obese children compared to normal weight children (van Leeuwen et al., 2018, Ortiz-Pinto et al., 2020).

2.3.4.7 BMI cut-offs

Table 2.1 shows that twenty of the included studies used the Centre for Disease Control or the International Obesity task force cut-off points to classify children into weight categories. However, some studies used the term "overweight" in place of obese for ≥ 95% percentile, while using the term "at-risk of overweight (AROW)" in place of overweight for children with BMI percentiles ≥ 85% and ≤ 95%. During the analysis, I adjusted for these differences in terminologies.

Two studies used the weight for age BMI z-score classification (Janicke et al., 2010, Bechere Fernandes et al., 2014). The effect size reported by these two studies for obese children was significant and much stronger than the studies not using this criterion. Three studies using data from German survey KiGGs and GINI and LISA cohorts used the country-specific BMI cut-off values with obesity defined as > 97th percentile (Wenig, 2012, Breitfelder et al., 2011) . It was not possible to formally establish a comparison based on BMI cut-off criteria due to the small number of studies using respective BMI cut-offs, and the use of different outcome measures across these studies.

2.3.4.8 Ethnicity

Two studies reported the effect of ethnicity on the association of weight status with healthcare utilisation (Dilley et al., 2007, Monheit et al., 2009). Both these studies were from the USA. They reported a decrease in healthcare utilisation in Black overweight or obese children compared to White overweight or obese children. Additionally, one study also reported decreased healthcare use in obese Asian or Hispanic children compared to White obese children (Monheit et al., 2009).

2.3.4.9 Anthropometric measurements

Seven studies recorded the height and weight by self- or parental reporting without validation (Breitfelder et al., 2011, Monheit et al., 2009, Trasande and Chatterjee, 2009, Turer et al., 2013, Wright and Prosser, 2014, Skinner et al., 2008). Five of these studies used data from the MEPS survey in the USA. Variability in the direction and strength of association between weight status and healthcare use was observed across these studies. This heterogeneity could be subject to reporting bias due to self- or parent-reporting, however, not enough data was available to formally assess this.

2.4 Discussion

This systematic review and meta-analysis has demonstrated an association between excess weight and increased healthcare use in children. Thirty-three studies were included in the review, of which six had appropriate data to be included in the meta-analysis. Attesting to the diverse nature of health services and the variability in their provision in different countries, the studies used multiple outcome measures to define healthcare utilisation. Commonly examined outcome measures were outpatient visits, ED visits, hospital admissions, and hospital length of stay. Studies included in the meta-analysis reported an increased rate of healthcare utilisation in obese children compared to normal weight children. A significant unadjusted positive association of obesity with increased outpatient

and ED visits was observed in the meta-analysis. The results of the narrative synthesis supported these findings and indicated that obese children are much more likely to have higher healthcare utilisation for all the reported outcome measures. However, variability in the direction and strength of association was observed across studies, with a few studies reporting a negative or no association.

A vast body of research and associated systematic reviews exist which have analysed not only the burden of adult obesity on healthcare systems but also the incremental health burden of childhood obesity during adulthood (Reilly and Kelly, 2011, Wang et al., 2006, Wang et al., 2011). Such studies have indicated repeatedly that obesity is significantly related to a greater risk of morbidity in adult life and associated increase in healthcare utilisation. This review builds on this knowledge and suggests that much like adult life, obesity during childhood results in an increased burden of morbidity on healthcare services. These findings can be explained in the light of recent clinical research reporting an increasing prevalence of obesity-related conditions in childhood that were more commonly associated with adulthood in the past (Pulgarón, 2013, Abbasi et al., 2017).

This leads my discussion into one of the secondary objectives of the review; to analyse the most common obesity associated health conditions that are contributing to an increase in healthcare utilisation in children with obesity. Most of the included studies did not attempt to ascertain the reason for increased healthcare utilisation. Two studies included in the review analysed the rate of mental health related visits in obese children, with both reporting an increased risk. These findings support the previous evidence that has shown obesity to be a strong risk factor for stigmatization and development of low self-esteem and other mental health issues in children (Strauss et al., 2003, Franklin et al., 2006). The role of obesity in increasing the risk of asthma in children is well-founded (Visness et al., 2010). Five studies in the review supported the previous evidence and reported that

obesity leads to increased health service utilisation in not only asthmatic children, but also in children with other respiratory diseases.

Regional variation in rates of healthcare utilisation is well reported in literature (Cheung and Gray, 2013, Finkelstein et al., 2016, Godøy and Huitfeldt, 2020). When studies conducted in different regions or countries with different population characteristics and healthcare systems are systematically reviewed and analysed together, regional variation in healthcare utilisation may result in between study heterogeneity. Evidence suggests that this regional variation is in part driven by population-specific factors such as ethnicity, socioeconomic status, health status, cultural beliefs and preferences (Finkelstein et al., 2016). The prevalence of childhood obesity varies between different regions and countries. It is also well reported that within a population the prevalence of obesity varies between children of different ethnic origins (World Health Organization., 2017a, Caprio et al., 2008, NHS Digital, 2018). Additionally, evidence shows an inverse relationship between the prevalence of obesity and low socioeconomic status (Shrewsbury and Wardle, 2008, NHS Digital, 2018). The extent to which this variability in prevalence translates into variability in associated morbidity and healthcare use is not known. There is evidence that healthcare seeking behavior and health care uptake varies across ethnic groups and socioeconomic classes (Coker et al., 2009, Fischer et al., 2017, Amre et al., 2002, Kangovi et al., 2013). Most of this evidence suggest that people belonging to Black, South Asian and other minority ethnic groups are at a disadvantage in accessing health services (Szczepura, 2005, Scheppers et al., 2006). Additionally, cultural beliefs and perceptions towards health status in general and weight status in particular may contribute to ethnic disparities in healthcare utilisation (Kocken et al., 2012, Peña et al., 2012). None of the studies included in the review analysed the impact of socioeconomic status while only two studies analysed the impact of ethnicity. They reported a significantly lower use of health services in obese children of

Black, Asian and other ethnic minority groups compared to White children. To what extent this lower use is a result of disadvantage in access to healthcare services and what results from differences in prevalence and in levels of morbidity remains unclear. Additionally, both of these studies were from the USA, which has specific health insurance programs for children (Pediatrics, 2014, Dubay and Kenney, 2009). Therefore, care should be taken in generalizing these findings to other countries with different healthcare systems. In the light of these two studies and previous research evidence, it can be inferred that ethnicity and socio-economic status could be sources of between-study heterogeneity reported in this review; however, as the studies did not report the ethnic and socioeconomic characteristics of the populations studied, it was not possible to explore this further. Evidence also suggests that in addition to population-specific factors, regional variation in healthcare is in part due to differences in region-specific factors such as access to health services, healthcare resources, health policies and physician beliefs (Finkelstein et al., 2016, Godøy and Huitfeldt, 2020). For example, some percentage of the between-study heterogeneity reported in this review may be attributable to regional variations in physician beliefs towards excess weight or barriers and facilitators to healthcare access. However, exploring the extent of heterogeneity due to region-specific variables was beyond the scope of this review.

2.4.1 Strengths and limitations

This review has a number of strengths. First, to my knowledge this is the first systematic review and meta-analysis of the utilisation of healthcare services in obese and overweight children. Second, I have used a comprehensive search strategy, with publications not restricted by region or year of publication which resulted in the inclusion of 33 studies reporting outcome measures from primary and secondary healthcare. Additionally, a

protocol was developed and registered *a priori,* and methodological guidelines were followed on conducting and reporting a review.

A limitation of this review was the restriction of studies to the English language reports only. A limitation of the meta-analysis was the inclusion of only six studies which meant I was unable to include all the outcomes described in the review. Additionally, there was uncertainty over the weighted effect sizes due to between study heterogeneity in methods and outcomes.

There were some further limitations in terms of the characteristics of the included studies. First, the majority of the studies were from the USA, with the remainder being from eight first-world countries, therefore limiting the extent to which the findings may be generalized beyond certain national contexts due to differences in healthcare services and systems. Secondly, there was poor reporting of data for key study characteristics. For example, none of the studies included in the meta-analysis reported the use of healthcare services stratified by sex. Therefore, it was not possible to run a subset analysis and adjust for covariates in a meta-regression to formally analyse sources of between study heterogeneity.

2.5 Chapter summary

In summary, this systematic review has shown that overweight and obesity in children is positively associated with increased utilisation of ED and outpatient healthcare services during childhood. This finding remained in the meta-analysis albeit with potential heterogeneity between studies. The reported evidence for inpatient health service use is mixed. The studies included in the review are limited to only a few developed countries, therefore it is difficult to generalise these findings to other countries due to differences in healthcare systems and delivery of health services. The substantial between-study

heterogeneity reported in the review might be due to these differences across countries, however it was not possible to formally analyse this due to insufficient data. The review has identified areas of research where gaps exist. Particularly, further research is required in understanding the dynamics of obesity-associated health conditions that may drive increased healthcare utilisation in children. Additionally, the driving factors behind the varying effect of ethnicities and socio-economic status on association of obesity with healthcare utilisation are yet to be explored. Such evidence is necessary for the development of policies for clinical practice and research, and for their implementation in a way that while being cost-effective, can successfully target the therapeutic needs of obese and overweight children from different ethnic and socio-economic backgrounds.

Chapter 3 Methods

This chapter describes the analytical methodology for this thesis using the Born in Bradford (BiB) cohort study.

3.1 Introduction

To investigate the relationship between BMI status (used interchangeably with "weight status" in this thesis) and use of healthcare services in children and to investigate the impact of ethnicity on this relationship, I designed and undertook three separate studies using the BiB cohort study with linked primary and secondary healthcare records.

I compared underweight, overweight, and obese children to the reference category of normal weight children to answer the following research questions:

1. Is BMI status in children at age 4/5 years associated with variation in the use of primary healthcare services?
2. Is BMI status in children at age 4/5 years associated with variation in the use of secondary healthcare services?
3. Does the association between BMI status at age 4/5 years and subsequent primary and secondary healthcare service use vary by ethnicity?
4. Do costs associated with primary and secondary healthcare resource use vary by BMI status and/or ethnicity in children?

The proceeding sections in this chapter explain in detail the methods used to answer these research questions. This begins with an introduction to the data source - the BiB cohort study. Afterwards, the exposure variable is introduced, and the criteria used for the selection of the analysis cohort is explained. Later, the outcome variables of healthcare use are introduced, and a theoretical framework is laid out for the selection of covariates. The

chapter ends with a detailed explanation of statistical methods used to model the outcomes to answer each research question.

3.2 The Born in Bradford study

The source of data used to answer the research questions in this thesis is the Born in Bradford (BiB) cohort study. BiB is a prospective multi-ethnic birth cohort based in the city of Bradford, United Kingdom. Bradford, a city in West Yorkshire, is unique in terms of its high ethnic diversity, with almost 20% of the population being South Asian, particularly of Pakistani origin (Public Health England, 2019b). Bradford scores far below national average on most health indicators in comparison to other English cities (Public Health England, 2019b). The BiB study was established in response to the issue of adverse health outcomes in the children of the city. The study aims, as mentioned by Raynor (2008) are as follows:

- To describe and compare health and ill-health within a largely bi-ethnic population.
- To identify modifiable causal pathways promoting wellbeing or contributing to ill-health.
- To develop a model for integrating research into routine data systems within the National Health Service in England, and potentially health care systems in other countries.
- To build and strengthen local research capacity.

The BiB study recruited women during pregnancy and is following them and their children through childhood and into adolescence. Women were recruited at the maternity unit of the Bradford Royal Infirmary at 26-28 weeks gestation, as they attended the antenatal clinic for an oral glucose tolerance test (OGTT). The OGTT is a test that is performed at 26-28 weeks of gestation to screen for gestational diabetes but can be performed as indications arise. In Bradford, the OGTT is routinely offered to all pregnant women at 26-28 weeks

gestation as the population is considered to be at high risk. Therefore, all pregnant women attending the maternity unit from March 2007 to December 2010 were offered participation in the BiB study. Women who gave an informed consent to participate completed an interviewer administered questionnaire and had their height and weight measured. To facilitate data collection from women who were non-English speakers, interviews were administered in a range of South Asian languages (including Mirpuri, Urdu, Bengali and Punjabi). The last round of recruitment was done by 24th December 2010 and the last BiB child was born on 2nd June 2011. Each mother was assigned a unique identification number (MotherID) and each child born to these mothers was also given a unique identification number (ChildID). Ethical approval for the data collection and subsequent use of data for research purposes was granted by the Bradford National Health Service Research Ethics Committee (ref 06/Q1202/48). More than 80% of the women who were offered participation took up the offer to participate and completed the questionnaire. The full BiB cohort recruited 12, 453 women comprising 13, 776 pregnancies over the four years (Wright et al., 2012).

Data collection for the BiB study comprised of questionnaires administered to parents at recruitment, and linkage and abstraction of data from routine clinical records and additional research measurements and biochemical specimens from BiB parents and children. Figure 3.1 reports the data collected at various time points in the BiB study. At recruitment, in addition to mother's height, weight and OGTT results, data was collected on a range of sociodemographic variables as part of the recruitment questionnaire. Mainly, women reported on ethnicity, ancestry, wellbeing, smoking status, alcohol intake, education, their income, partner's income, means-tested benefits status, their employment status, and partner's employment status. At birth, data on birthweight, sex,

gestational age, and neonatal head circumference is collected routinely in Bradford for all children within 24 hours of birth.

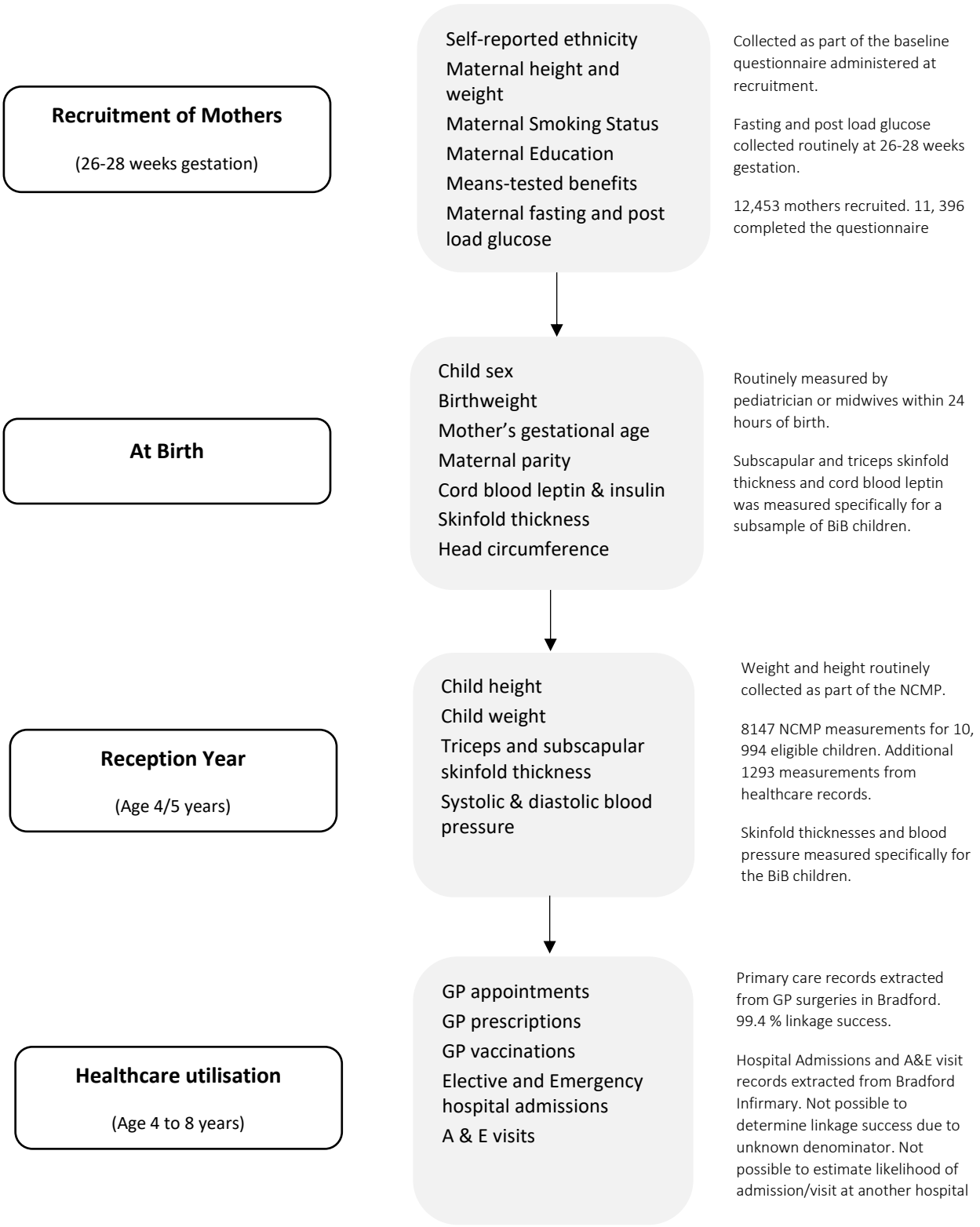

Figure 3.1 *Collection of different variables at different timepoints in the BiB study*

This data was abstracted for children enrolled in the BiB study from their routine clinical records. Additionally, mid upper arm and abdominal circumference, subscapular and triceps thickness were measured by a paediatrician or attending midwife and trained research administrators (usually within 24 hours of births but could be up to 72 hours) specifically from BiB children.

As discussed in chapter 1, the overarching aim of this thesis is to explore the association of BMI status in BiB children at age 4/5 years with subsequent healthcare use up to the age of 8 years. At age 4/5 years, height and weight measurements for BiB children were abstracted from the National Child Measurement Programme (NCMP). For this project, BiB children eligible to start school by the academic year 2014/2015 were considered for inclusion. For BiB children with missing NCMP height and/or weight measurement, height and weight measurements were extracted from their primary health care records. A complete explanation of the NCMP measurements, data linkage for BiB children and definitions used for these measures as part of this thesis are explained in section 3.3 of this chapter**.**

Primary and secondary healthcare data for BiB children from the age of 4 years to the age of 8 years was extracted by linking to their healthcare records using NHS number, surname, sex, and date of birth. Details of the linkage process and definitions for each measure of healthcare use analysed in this thesis are given in section 3.6 of this chapter.

3.2.1 Data access

My application to access the BiB data was approved in two stages. The initial application was approved on 14th January 2019 and a collaboration agreement was signed by both parties. As part of ethical consideration by the BiB executive, it was pointed out that I will require a research passport from the University of York (UoY) to access the linked healthcare data for BiB children. After acquisition of a research passport, I submitted an

updated application to use the data in March 2019, which was immediately accepted by the BiB executive without a requirement to sign another BiB collaboration agreement. Any additional ethical approval to carry out the study was not required from the University of York, and this was confirmed in writing by the Department of Health Sciences' Research Governance committee (appendix A2.1).

I was given access to the BiB data in three stages. I initially received access to data from mothers' baseline questionnaires and child growth measures in March 2019. This was followed by access to the primary and secondary healthcare data for BiB children in September 2019. An update to the healthcare data for BiB children was received by the BiB team in 2020. I was given access to the update of primary healthcare records in July 2020, while the access to the updated secondary healthcare records was given in September 2020.

3.2.2 Data management

The BiB collaboration agreement states that any use of data, including for research and publication will be done in a way to ensure that the study participants remain unidentifiable. Therefore, the BiB data team only shares pseudo-anonymised data with researchers, where each study participant is identified through a unique identification number to preserve anonymity. However, there was still a risk of participants becoming re-identifiable and sensitive information being accessed by a third party due to their primary and secondary healthcare records being accessible. Therefore, to ensure participant anonymity and to prevent a risk of access to data by any third party, a necessary best practice guidance was specified by the BiB executive and duly followed by me over the course of this study. This included:

- The baseline questionnaire data and child growth data will be transferred via digital secure transmission of encrypted data to the University of York (UoY)

server, and this will only be accessed by the investigator (me) through a UoY passport protected system.

- The primary and secondary healthcare records of children will not be transferred to the UoY servers. These records will be stored on a secure network at the Bradford Institute for Health Research (BIHR) and will only be accessed by the investigator onsite.
- The investigator will only be given access to the healthcare data at the UoY server under certain conditions:
    - The data has been formatted to remove any participant identifiable information from the health records. For example, I was only given access to this data at UoY on the condition that the data only had counts of consultations for each participant and all the other variables with information recorded against each consultation were dropped.
    - The BiB data team will approve the format of each healthcare dataset before securely transferring it to UoY server through online encrypted data transfer.

3.3 The exposure variable

The exposure variable that informs the analyses carried out in this thesis is a BiB child's BMI status at age 4/5 years. This is defined as a child being classified into either underweight, normal weight, overweight, or obese category based upon their BMI using the UK90 reference curves (Cole et al., 1995). As mentioned previously, the height and weight measurements for BiB children were extracted from the measurements taken as part of the NCMP (section 3.2). NCMP is a nationally mandated programme where height and weight of children in reception year (age 4/5 years) and year 6 (age 10/11 years) are measured in state-maintained schools of England (NHS Digital, 2019d). Parents of eligible

children are sent an “opt-out” form if they want to opt-out of the programme. One measurement for height and weight is recorded by NCMP trained school nurse teams for each child. Weight is recorded in kilograms (kg) with the use of class III digital scales. Height is measured in centimetres with a correctly assembled stand on height measure that shows height in centimeters and millimetres. Figure 3.2 shows a timeline of data collection for BiB children. The overall nationwide NCMP participation rates of eligible children increased from 93.8% in school year 2012/13 and 2013/14 to 96% in 2014/15. In Bradford, the participation rates for these school years were 88%, 85% and 88%, respectively (NHS Digital, 2019f). For BiB children who had no NCMP record at reception year, the earliest available height and weight measurements at age 4/5 years were extracted from linked primary healthcare records (13.7%).

Using these height and weight measurements, the BMI for each child was derived as weight (kg) /height $(m)^2$. Classifying children or adolescents (aged <19 years) into weight categories is complicated by the fact that height and body composition are continually changing. The proportion of fat to lean mass varies with sex, age, and physical maturity, making it problematic to define physiological norms as in adults. Consequently, BMI adjusted for age and sex, expressed as centile or standard deviation scores (z-scores) of a BMI distribution in a reference population is the most commonly used measure to define weight categories in children. For the purpose of this PhD project, these age and sex standardized BMI z-scores (zBMI) were derived for BiB children in relation to the UK90 reference population (Cole et al., 1995) using the *zanthro* command in Stata (Vidmar et al., 2013). Here, a zBMI of zero is equivalent to the mean of UK90 reference population. A positive value indicates a zBMI more than the UK90 mean, and a negative value indicates a zBMI below the UK90 mean. Using these sex and age specific BMI z-scores, BiB children were classified as underweight, normal weight, overweight and obese using population monitoring cut-offs

of ≤ 2nd centile (zBMI – 2.054) for underweight, 2nd to 84th centile for normal weight, ≥85th centile (zBMI of +1.036) for overweight and ≥95th centile (zBMI of +1.645) for obese.

3.3.1 Ethnicity-specific BMI values

As mentioned in the introductory chapter of this thesis, ethnic differences in Type-2 diabetes precursors and higher risk of cardio-vascular disease have been observed during childhood, in as early as the first decade of life. People from minority ethnic groups are found to be at a higher risk of developing these conditions (Whincup et al., 2002, Whincup et al., 2010). Differences in body composition, cultural and environmental factors have been identified as potential reasons to explain this higher prevalence of obesity and risk of associated diseases in minority ethnic groups (Whincup et al., 2010, Ehtisham et al., 2005). Higher fat percentage in South Asians for a given BMI is reported to be significantly associated with an increased metabolic risk of Type-2 diabetes (Bray et al., 2017). Physiologically, adiposity is suggested to be the main driver behind obesity associated morbidity, therefore it is important to have an accurate measure of body fat levels, particularly in ethnic populations such as South Asians.

As explained in detail in Chapter 1, more recently, work has been done in the UK by Hudda et al. (2017) to derive ethnicity-specific BMI values for British South Asian children. Sex stratified ethnicity-specific BMI values were derived, ensuring that these ethnicity-specific values were associated with fat-mass in a same way as in White British children. They found standard BMI values to underestimate fat mass in British South Asian (SA) children and calculated sex-specific BMI adjustments of +1.12 kg/m^2 for SA boys and +1.07 kg/m^2 for SA girls at all age and body fatness levels.

As part of this project, these ethnicity-specific BMI values were applied to BMI measures of children of Pakistani origin in the BiB cohort and children were re-categorized into weight categories based upon the re-calculated BMI z-scores. Sensitivity analysis was carried out

comparing the proportion of Pakistani children in each weight category derived with ethnicity-specific BMI values against the proportion of children in each weight category with conventional BMI cut-offs. After application of these ethnicity-specific BMI values, additional analyses were carried out to explore the distributions of covariates in each weight category, and to analyse the magnitude of association with the outcome variables of interest.

3.4 Study participants

Children were included in the study if they had height and weight measurements recorded at age 4/5 years, either through NCMP or primary healthcare records and were participating in the BiB study.

3.5 Study period

To investigate the impact of BMI status at age 4/5 years on healthcare use in the subsequent years of life, a five-year study period was used. The point of exposure for each child was the date on which his/her height and weight measurements were recorded. A timeline with different data collection points for BiB children is presented in figure 3.2. The first child entered the study in the school year 2011/2012, while the last school year of NCMP measurements was 2014/15.

3.5.1 Person-years

A child contributed years (person-years) to the study from the date of exposure to the age of 8 years (107 months) or the date of withdrawal or death, whichever was earlier. The decision to include a five-year period up to the age of 8 years was primarily based on the availability of BiB healthcare data up to this age for all children.

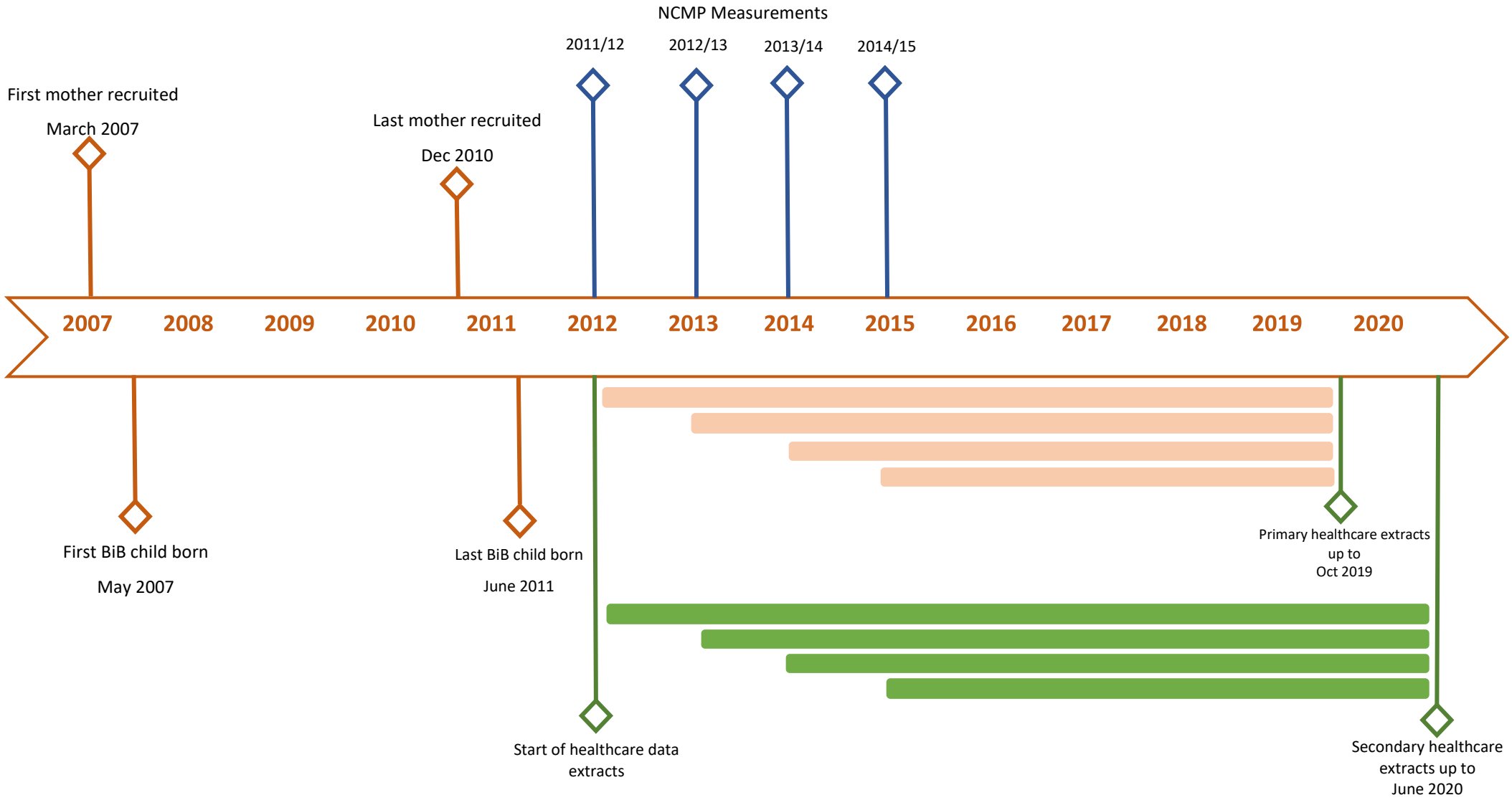

Figure 3.2 *Timeline of data collection for BiB children*

3.6 Outcome variables

The outcome variables informing analyses to answer the research questions (section 3.1) in this project are explained in this section.

3.6.1 Healthcare service use

The primary outcome of interest in my project is healthcare service use. As discussed in the systematic review of the relevant literature in Chapter 2, different measures are used to define healthcare use as an outcome. As part of this thesis, outcome variables of healthcare use are divided into two broad categories of primary and secondary healthcare. Within each of these categories, different outcome measures were used to analyse healthcare use. These measures are explained in detail in the proceeding sections.

3.6.1.1 Primary Healthcare use

Primary healthcare services provide a first point of contact in the healthcare system in the UK. These include general practices (GP), community pharmacies, dental and optometry services. In the BiB study, primary care data was linked from participating general practices in Bradford. Data records were extracted by the Born in Bradford data analysis team from SystmOne (Young, 2010), which is an electronic record system used by all general practices in Bradford to record GP events along with clinical codes, staff member role, and prescriptions associated with each event. These records were extracted for each BiB child by matching the NHS number, gender, surname and date of birth. The linkage rate was very high, with 99.4% of the BiB children being matched to their primary care records. In the initial phase, the BiB team extracted records up to the date of 9th August 2017, which corresponds to the age of about 10 years for the oldest BiB child. I received an extract of this initial primary care dataset in August 2019. In the 2nd phase, the BiB team extracted primary care records for all BiB children up to October 3rd 2019. I received an extract of this data in July 2020, and the analyses reported in this thesis are based on this updated extract.

In the extract that I received access to, data was available on healthcare use measures of primary care consultations and prescriptions. I created a separate dataset for each of these measures. For the sake of simplicity, I will describe these measures as primary care consultations and primary care prescriptions throughout this thesis.

For each primary care consultation, the child's unique identification number, age in years and months, staff member role and CTV3 Read code was recorded. Read codes are used to record/identify clinical terminologies associated with each appointment (NHS Digital, 2020f). They are not only used to code clinical diagnosis associated with each appointment, but also encode multiple information about patients including: ethnicity and religion; clinical symptoms; laboratory test results; therapeutic or surgical procedures; and variety of administrative tasks (NHS Digital, 2020d). Various terms were used to record the attending staff member's role/designation with each appointment. I broadly classified these terms into four staff role categories: General Practitioners (GPs), nurse practitioners, healthcare assistants/practitioners, and administrative staff. Additionally, each primary care consultation was either recorded as clinical or administrative. As explained in the previous chapters, healthcare use associated with overweight and obesity results from high morbidity associated with excess weight and excess adiposity. Therefore, a decision was made to not include the administrative appointments and to only analyse appointments coded as clinical when the corresponding staff member role was coded as general practitioner or nurse practitioner. The rationale behind only including clinical consultations with a general practitioner or nurse was twofold. First, I am interested in morbidity associated with excess adiposity, therefore such consultations are recorded as clinical. Secondly, at a general practice, only doctors and nurse practitioners have the responsibility to clinically diagnose and prescribe medications to patients. I performed two separate analyses to model primary care utilisation in this thesis; one for only the clinical

consultations with a doctor termed as ‘GP doctor consultations’; the second for GP doctor and nurse clinical consultations combined, which are termed as ‘primary care consultations’.

In the primary care prescriptions dataset, each prescription was coded using the British National Formulary (BNF) classification. BNF is a pharmaceutical reference book that contains information on prescribing medicines, along with details and classification of medicines used in the National Health Service (NHS) (Royal Pharmaceutical Society of Great Britain, 2009). BNF codes a drug into a chapter based on the therapeutic indications for use in different body systems. For example, aspirin is coded in two chapters based on its use as an antiplatelet (BNF chapter 2) and as an analgesic (BNF chapter 4). Using the chapter and section codes of the BNF classification, I removed the non-drug items such as vitamin/mineral supplements, and wound management products such as dressings, plasters etc (pseudo BNF chapters 18, 19 & 20 to 23) from the analysis. Additionally, I also dropped the prescription items related to vaccination or immunisation (BNF chapter 14).

For each BiB child, I created a total count of consultations per year from the date of his/her height and weight measurement up to the age of 107 months (unless he/she withdrew earlier) or the end of extract, whichever was earlier. These counts were created after removing the events that were coded as “did not attend” through identifying the relevant read codes. I created two separate datasets, one with counts for GP doctor consultations (clinical coded appointments with a doctor) for each child & the other with a count for all primary care consultations (clinical coded doctor or nurse consultations combined together). For primary care prescriptions, I created a dataset with counts of total number of drug prescriptions per year per child in a similar way. Additionally, to assess the likelihood of a primary care consultation, I categorised each child into either of these two

categories: atleast one consultation during the study period, no consultation during the study period.

There was no information available in the datasets to identify if a child was not matched to his/her primary care record. Therefore, if a child had no appointment in the above mentioned period, there was no way to ascertain whether it was due to inability to link to primary care records or whether it was due to child having no appointment during this time. However, due to a high match rate (99.6%), it was assumed that a child with no record had no appointment during this period.

3.6.1.2 Secondary healthcare use

Secondary healthcare records for hospital admissions and Accidents and Emergency (A&E) visits were extracted for BiB children only from the Bradford Royal Infirmary electronic patient records. This extraction was done by the BiB data analysis team through matching children's NHS numbers. The extraction of records was done up to July 2020. I received the latest build of these datasets in September 2020. The structure of these datasets was based on the Hospital Episode Statistics (HES) database (NHS Digital, 2019b). HES is a database of all admissions, A&E visits, and outpatient appointments at NHS hospitals in England. Each hospital record in HES contains clinical, administrative, geographical, and general patient information (NHS Digital, 2019f). There was no specific data dictionary available for BiB healthcare data. A complete list of what information was available for BiB health records can be accessed through the online HES data dictionaries for Admitted Patient Care (APC) & A&E visits (NHS Digital, 2020c, NHS Digital, 2020b).

Admitted Patient Care (APC) is the term used for hospital admissions in the HES database. In this thesis, I use the terms APC and hospital admissions interchangeably. A list of variables that I was given access to for BiB children's admission records is given in appendix A2.2**.** At this stage, it is important to make a distinction between an admission spell and an

episode. A hospital admission spell encompasses the total time a patient is under-treatment, from admission to discharge. An admission episode is the duration of care under a consultant during an admission spell (NHS Digital, 2019f). Therefore, if a patient is transferred to a different department and consultant, a new admission episode record is generated within the same admission spell. Sometimes an admission spell could contain episodes of care in different NHS providers (organizations), however since the data for BiB children is extracted only from the Bradford Royal Infirmary, all spells were single provider spells.

In this thesis, I performed the analyses of APC use at the level of admission spells. Information on episodes within a spell was used to allocate costs to each spell for analysis of healthcare costs. This costing method is explained in detail in section 3.6.2.2 later in this chapter**.** For each child, I created a total count of admission spells per year from the date of height and weight measurements to the age of 107 months, or date of withdrawal or the end date of extract, whichever was earlier. Additionally, I categorised children into two categories based on whether they had at least one admission or not. For each admission spell in the dataset, I created a variable for length of stay (LoS) in bed days at the hospital using the duration of stay recorded against each episode within a spell. Using this variable of LoS, I created counts of total LoS for children with at least one admission during the study period. Additionally, using the information available on admission method (ADMIMETH, appendix A2.2) and patient classification (CLASSPAT, appendix A2.2), I categorized each spell as elective, emergency, or day case. In a day case spell, if a child was allotted a bed to undergo a procedure and was discharged on the same day, an LoS of one was recorded. For A&E records, a list of variables that I was given access to is shown in appendix 2.2. For each BiB child, I created counts of A&E visits per year from the date of exposure to the end of study period.

As mentioned above, the data for secondary healthcare use was extracted only from the Bradford Royal Infirmary's electronic patient records. It was not possible to estimate the likelihood of a hospital admission and A&E visit occurring at another hospital. Therefore, it was not possible to ascertain from the available information whether children with no records went to another hospital, the data was not linked, or they had no admissions or A&E visits during the study period. This issue with data being only available from the Bradford Royal Infirmary with no information on admissions to any other hospital could lead to an underestimation of real count of hospital admissions and A&E visits, particularly for children who were more sick and required care from healthcare services that were only available in other nearby tertiary care hospitals. However, considering the high match rate for hospital admissions for children and their mothers (99.1%), it was assumed that children with no record had no events during the study period. Therefore, while creating counts, children with no admission and A&E record were treated as if they had zero secondary healthcare use during the study period.

3.6.2 Healthcare costs

The secondary outcomes of interest in my project are the costs associated with use of primary and secondary healthcare services. As described in the preceding section, the main measures of healthcare utilisation in this thesis are:

- Primary care consultations
- Hospital admission spells
- A&E visits

In this section, the methods used to calculate costs associated with each of these measures are described.

3.6.2.1 Primary care costs

Primary care costs were calculated for each consultation based on the annual unit cost figures reported by the Personal Social Service Research Unit (PSSRU) (Curtis and Burns, 2019). PSSRU, which is a part of the Department of Health and Social Care has published annual unit cost figures for community-based healthcare since 1992. PSSRU describes a unit cost as "total expenditure incurred to produce one unit of output" (Curtis and Burns, 2016). For community-based healthcare, PSSRU reports this unit cost as cost of one hour or one minute of a nurse or General Practitioner's (GP) time (Curtis and Burns, 2019). Costs associated with consultations are then calculated by multiplying the amount of time recorded against each consultation by unit cost figures.

As part of the BiB primary healthcare data access, I was not given access to information on the date and year for each consultation, with the BiB data team citing the reason of preserving the anonymity and confidentiality of the data behind this decision. As a result, it was not possible for me to ascertain in what year a particular consultation took place to assign it the relevant annual unit cost. Additionally, the amount of time recorded against each consultation was not available. Therefore, to work around these issues, I took the following approach to assign cost to each consultation.

- I had to decide on which year's release of PSSRU cost figures to use to assign costs to consultations. The first consultation in the cohort took place in 2013, while the data was extracted up to October 2019. I decided to use the latest release (2019/20) of cost figures. The rationale behind this decision was based on the aim of the study. As the aim was to predict annual costs per child in each BMI category, using the latest cost figures would provide annual predictions that are representative of current economic climate and are up to date with the current primary care practice guidelines.

- I then extracted average consultation length (in minutes) by consultation type (surgery, clinic, telephone, or home-visit) from PSSRU unit costs data. Average unit cost for each consultation type was then calculated based on the average consultation length of a particular consultation type and average unit cost (appendix A2.3)**.** These average consultation costs per type were then assigned to the consultations in the dataset by consultation type.
- PSSRU also reports an annual estimate of average prescription cost associated with a GP consultation (Curtis and Burns, 2019). This average prescription cost was also added to each GP consultation cost in the data (appendix A2.3).

The average unit cost for GP consultations in 2019/20 was £255 per hour. The GP consultations on average lasted for 9.22 minutes for surgery consultations, 17.2 minutes for clinic consultations, 23.4 minutes for home visits and 7.1 minutes for telephone consultations. The average unit costs for each consultation type using the above-mentioned methods are shown in appendix A2.3. The average prescription cost associated with a GP consultation in 2019/20 was £30.9. Additionally, the average unit cost for a consultation with a nurse at a GP surgery was £42 per hour. Average consultation length for practice nurses was 15.5 minutes. The average unit cost per consultation with a nurse was calculated to be £10.9 (appendix A2.3).

3.6.2.2 Hospital Admissions

In England, costs associated with secondary healthcare service use are calculated using the average unit costs of providing each service. These unit costs are published as NHS improvement reference costs and are updated annually based on national tariffs (NHS Improvement, 2018). For admitted patient care (APC), cost associated with an admission spell is based on the primary and secondary diagnoses and procedures recorded against a spell. Diagnoses are recorded using the ICD-10 codes, while procedures, interventions and

operations are recorded using the OPCS-4 coding system (NHS Digital, 2019e). There are more than 26,000 codes currently that are used to describe diagnoses and interventions, therefore setting a tariff against, and costing by every combination of diagnoses and intervention would be extremely complex (NHS Digital, 2019c). So, to set a tariff at a workable and clinically meaningful level, a methodology has been developed to cluster these diagnoses and interventions into common groups called Health Resource Groups (HRGs), with each group identified by a code (NHS Digital, 2019f).

HRGs are defined as consistent units of currency for admission spells that are clinically similar and use common levels of healthcare resources (NHS Digital, 2019f). HRGs were first introduced in 1991 and have been used to cost clinical activity since 1997. Since their inception, HRGs have gone multiple version updates to keep them up to date with advancements in clinical practice. The current version of HRGs in use is the HRG4+ (NHS Digital, 2019f). Like the NHS reference tariff costs, HRG4+ are year specific and are updated annually. For example, number of HRGs in the 2019/20 HRG4+ iteration increased to 2,832 from 2,782 in the 2018/19 iteration. These annual updates involve addition of new HRGs based on new combinations of ICD-10 and OPCS-4 codes, ensuring "greater granularity" in their classification with improved identification of resource use (NHS Digital, 2019f).

Therefore, the first step in costing APC data is derivation of HRGs for each admission spell in a dataset. This is done using a "Grouper" software (NHS Digital, 2019f). Grouper is released by NHS Casemix office and gets an annual update in accordance with the HRG4+ update. The APC dataset is uploaded as an input file and the grouper employs an algorithm to cluster ICD-10 and OPCS-4 codes with similar resource use to identify HRGs for each admission spell. However, grouper requires information on additional variables to be recorded against each spell to identify an HRG for a spell (NHS Digital, 2019a). These additional mandatory variables include but are not limited to patient demographics (sex,

age), number of consultant episodes in a spell and number of bed days. As part of the BiB APC dataset, I requested access to all the mandatory variables required to create HRGs (Appendix A2.2)**.** As mentioned previously, the BiB healthcare datasets did not contain information on the date and year of patient activity. Therefore, after I created an input file with all the mandatory information to upload in the grouper, I had to decide on which years HRG grouping algorithm to use. I decided to use the 2018/19 reference costs grouper. The rationale behind this decision was that these HRGs were the latest release and were most consistent with the current clinical practice (NHS Digital, 2019f). Additionally, this latest release had maximum number of HRGs released to date. With the most recent update of BiB APC data being extracted up to July 2020, using these groupers ensured that the highest percentage of spells in the dataset were grouped. To ensure consistency, I used the latest edition (2018/19, published in January 2020) of reference costs so that maximum number of spells could be costed (NHS, 2020).

Costs were then calculated for each admission spell after merging the APC dataset with derived HRGs to the NHS reference cost dataset. The cost of a spell with a particular HRG depends on the type of admission. For example, resource use of a day case of gallbladder removal (cholecystectomy) would be different from resource use of an emergency cholecystectomy. Using the information recorded on admission method and patient classification (Appendix A2.2), I categorized admission spells in to five types; elective, non-elective short stay (less than two days), non-elective long stay, day case and others. In addition to the admission type, costs associated with an admission spell can vary based on the following characteristics of a spell:

- *Excess bed days:* Each HRG has a maximum expected length of stay (trim point) based on the admission type (elective and non-elective long stay). Any stay in the hospital beyond this trim point is referred to as excess bed days and accrue

additional costs (NHS Digital, 2019g). Therefore, if a spell in the BiB dataset had excess bed days associated with it, I calculated this additional cost by multiplying the number of excess bed days with the cost per excess bed day for the admission type and HRG associated with the spell. These costs were then added to the overall cost of the spell.

- *Unbundled HRG:* Unbundled HRG is used to identify activity and costs that do not reflect the primary reason for a patient admission and treatment, and therefore are "unbundled" from the spell (core) HRG (NHS Digital, 2019f). Unbundled HRG reflects elements of patient care pathway that are not included in the core HRG and are therefore generated in addition to the core HRG for a spell. Currently, unbundled HRGs are generated for the following elements of care:
    a. Chemotherapy
    b. Radiotherapy
    c. Diagnostic imaging and Nuclear Medicine
    d. Rehabilitation
    e. Renal Dialysis for Acute Kidney Injury
    f. Critical Care
    g. Specialist Palliative Care
    h. High-Cost Drugs

If none of these elements are part of a spell, then no unbundled HRG is generated. In the BiB APC dataset, if a spell had an unbundled HRG, reference cost for it was added to the total spell cost.

A summary of the steps carried out in costing the BiB APC data is shown in figure 3.3.

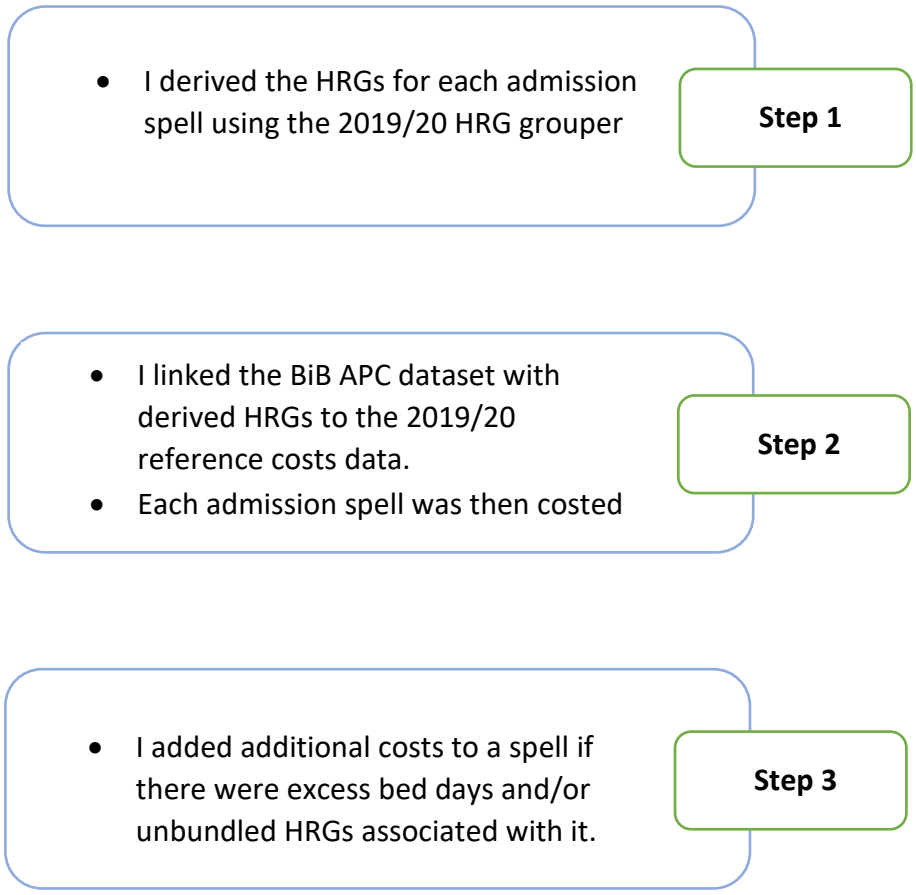

Figure 3.3 *Overview of the costing methodology*

3.6.2.3 Accidents and Emergency

Similar to APC, costs are calculated for A&E use after derivation of HRGs for each visit in the dataset using the grouper software. However, in case of A&E visits, the process is not as complex and information required is not as extensive (appendix A2.2) (NHS Digital, 2019f). To identify an HRG for a visit, the grouper uses information on the patient sex, A&E diagnoses, and A&E investigations recorded against each visit.

After derivation of HRGs and linkage with the NHS reference cost data, cost for each visit varies depending on the type of emergency department (consultant-led emergency department; consultant-led mono-specialty service; other Minor injury departments; and NHS walk-in centers) and whether the patient was admitted or not. For costing the BiB A&E

data, I used the 2018/19 HRG grouper and 2018/19 reference costs based on the rationale explained in the preceding section (section 3.6.2.2).

3.7 Covariates of interest

The covariates of interest included in the studies of this thesis are described in this section with a rationale for their inclusion. Additionally, I also explain the methods used to measure and define these variables.

3.7.1 Theoretical model

In a longitudinal observational study like BiB, the magnitude of association between an exposure and outcome could be confounded, modified, or moderated by a range of other variables called the covariates. For example, relationship between obesity and cardio-metabolic diseases is likely to be modified by ethnicity as people of South Asian origin are reported to be at a higher risk of developing such conditions (Whincup et al., 2010, Liu et al., 2009). Therefore, based on a careful consideration of literature on BMI status, healthcare use and the BiB cohort, I identified a set of covariates to be included in the studies.

Figure 3.4 illustrates a model that theorises the relationship of covariates available in the BiB dataset with the exposure and outcome variables using a Directed Acyclic Graph (DAG). This DAG depicts the plausible pathways of relationship of covariates to exposure and outcomes:

- *Confounder* is causally related to both the exposure and outcome independently.
- *Mediator* is on the causal pathway from exposure to outcome and accounts for the relationship between the exposure and the outcome.
- *Moderator* is a variable that modifies the strength of association between the exposure and the outcome.

To specify the statistical models accurately, I only included the covariates in statistical analyses with a known theorised relationship to the outcome, while also being careful to mitigate the risk of overfitting the data through inclusion of too many covariates. These covariates can broadly be classified into three categories: child characteristics; maternal characteristics; socio-economic status measures.

3.7.2 Child characteristics

In this section the child characteristics included as covariates in the analytic studies are described.

3.7.2.1 Child sex

Sex for each child was collected from the linked routine hospital data collected at birth. The prevalence of underweight, overweight and obesity is different between boys and girls (Shah et al., 2020). According to the most recent estimates in England, prevalence of obesity in boys at reception year was 10.1 % while it was 9.7 % in girls (NHS Digital, 2020e). This difference became larger at year 6 with 23.6% boys being obese compared to 18.4% obese girls. Similar trends were observed for underweight prevalence.

Differences in health profile by sex has also been reported in the literature (Piccini et al., 2018, Khera et al., 2014). These differences in health profiles of boys and girls have been shown to translate into different patterns of healthcare use by both sexes. These different patterns of healthcare use have been reported as consequences of not only differences in biology, but also differences in cultural and societal norms surrounding the health of boys and girls (Khera et al., 2014). Since child sex is related to both the exposure and outcomes of this project, it is adjusted for in the analyses to control for its confounding effect.

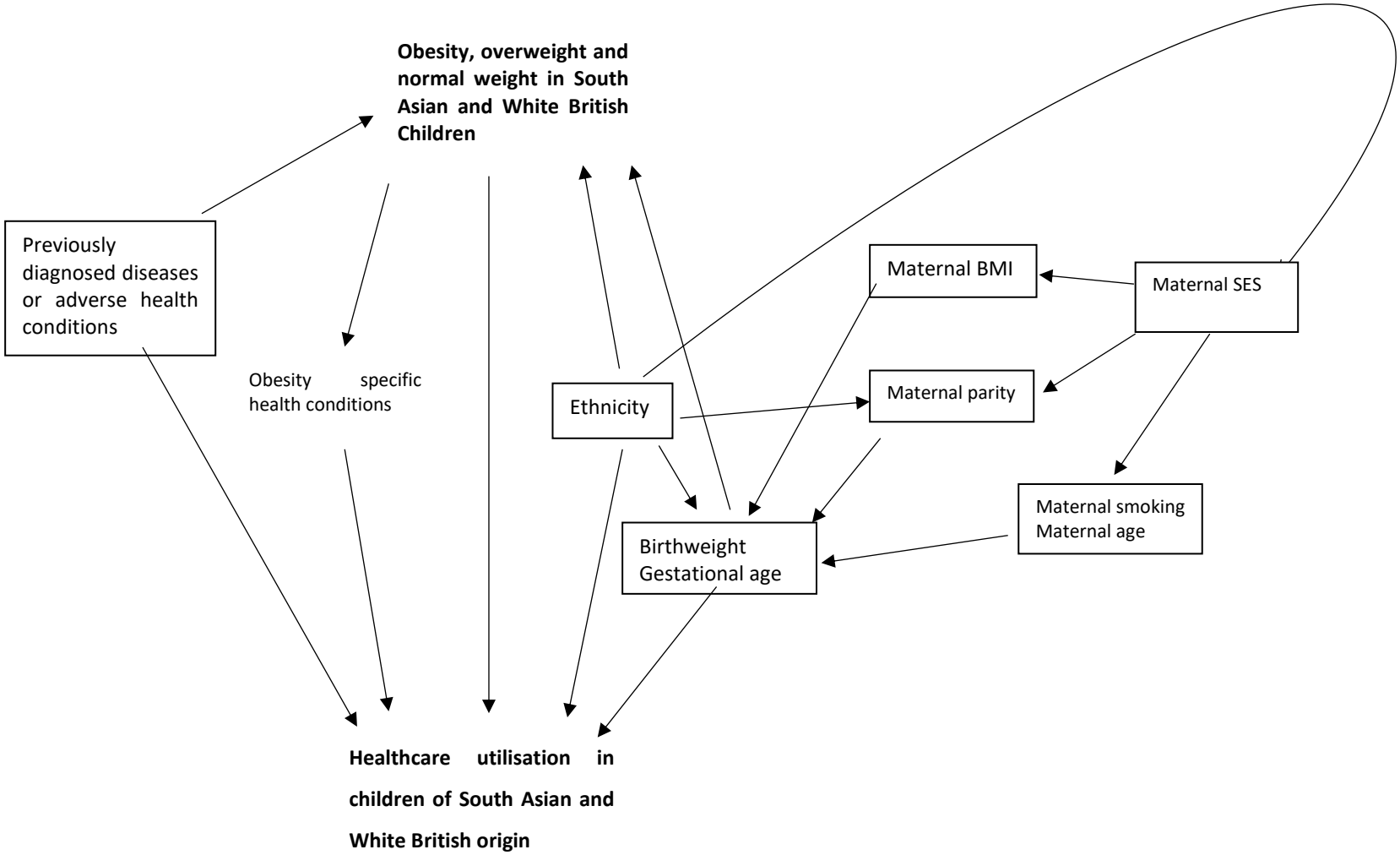

Figure 3.4 *DAG representing the exposure variable of weight category (obese, overweight and normal weight), outcome variable of healthcare utilisation. Variables that could potentially confound the association between exposure and outcome are shown in respective boxes.*

3.7.2.2 Ethnicity

Ethnicity for each child was assigned from the self-reported ethnicity by mothers at their recruitment questionnaire interview. Classification of ethnicity was based on the categories defined by the UK Office of National Statistics (Office for National Statistics, 2003). The UK Office of National Statistics (ONS) has five main categories for ethnicities: 'White', 'Mixed/Multiple ethnic groups', 'Asian/Asian British', 'Black/Africa/Caribbean/Black British', and 'Other ethnic group'. Each of these categories are further divided into subcategories. At the recruitment interview, women were asked to choose a group from the ONS list that best described their background. For example, women with Pakistani background had to choose the category 10 (Asian/British Asian subcategory). Women who chose category 1 (White subcategory labeled as English/Welsh/Scottish/Northern Irish/British) were defined as White British. A mother's ethnicity was assigned to each child born to that mother. Children for whom there was no mother questionnaire or ethnicity was missing from the questionnaire, data on ethnicity was extracted by the BiB team from the primary health care records using their NHS numbers. As ethnicity at recruitment was self-reported by mothers, questions could arise about the reliability of these assessments, particularly in the case of a father being not of the same ethnicity. Therefore, additional information that was collected from mothers on their, their partner's and their parent's country of birth was used to assess reliability. All women who reported themselves as Pakistani were confirmed to have a South Asian (Pakistani, Indian or Bangladeshi) origin. However, no such confirmation could be done for children whose ethnicities were extracted from primary health care records.

For the main analyses in this thesis, I have classified ethnicity into three categories: 1. White British 2. Pakistani 3. Others. The category "Others" included 'White Irish', White-Other', 'White & Black Caribbean', White & Black African', 'White & Indian' White & Asian', 'Mixed-

Other', 'Black-Caribbean', 'Black-African', 'Black-Other', 'Asian-Indian', Asian-Bangladeshi', 'Asian-Other', 'Chinese', 'Japanese', 'Filipino' and 'Other'. In reporting of descriptive statistics after application of ethnicity-specific BMI values for South Asian children (section 3.3.1), ethnicity was classified into five categories with two additional categories of Bangladeshi and Indian children. As discussed in detail in the introduction chapter, the prevalence of underweight, overweight and obesity at reception and year 6 is different for different ethnic groups, with British South Asian children reporting higher prevalence in all categories compared to White British children (Public Health England, 2019a). South Asians have consistently been reported to have a higher risk of developing obesity-associated diseases such as Type-2 diabetes and other cardio-metabolic diseases (Ntuk et al., 2014, Whincup et al., 2010).

Additionally, evidence shows variation in patterns of healthcare service use between different ethnic groups. As morbidity and healthcare use are directly related, ethnicity is theorised to have a causal relationship with healthcare use. Therefore, ethnicity is adjusted for in the analyses.

3.7.2.3 Birthweight

Weight at birth is routinely measured and recorded by midwives for all children born at the Bradford Royal Infirmary. For BiB children, birthweight was recorded at birth using SECA digital scales and was extracted from linked clinical records using the unique NHS number for each child.

A child's birthweight has been reported to be a significant predictor of their health during childhood. A recent study carried out on BiB children reported small size at birth to be significantly associated with increased primary and secondary healthcare use (West et al., 2018). Additionally, a study reported low birthweight to be a significant risk factor for developmental delay in children at age of 5 years (Karimi et al., 2011). Birthweight has also

reported to be positively correlated with childhood BMI status, with children with higher birthweight having greater odds of being overweight or obese during childhood and in later life (Rugholm et al., 2005, Evensen et al., 2017). These and other such research evidence justify the use of child's birthweight as a continuous covariate in the analyses carried as part of this thesis. Additionally, I used this continuous birthweight variable to generate a categorical variable with two categories: 'Low birthweight' & 'Normal birthweight'. These categories were based upon the WHO's clinical definitions (WHO, 2014) for low birthweight (< 2500gm) and normal birthweight (≥2500 gm). These categories were defined to descriptively assess the distribution of normal and low birthweight (LBW) children in each ethnicity and BMI category.

3.7.2.4 Gestational age

Gestational age (to the last completed week) is routinely recorded at the time of each birth. For BiB children, data on gestational age was extracted from linked clinical records using the unique NHS number for mothers. Gestational age is used to classify children as preterm or not preterm. The WHO defines a child born before 37th gestational week as a preterm child with further sub-categories of preterm birth based on gestational age (World Health Organization, 2018c): extremely preterm (<28 weeks); very preterm (28 to 32 weeks); moderate to late preterm (32 – 37 weeks).

Research has shown that being born preterm is associated with adverse developmental and health problems during childhood with it being the leading cause of death in children under the age of 5 years (Chawanpaiboon et al., 2019). Additionally, a recent meta-analysis reported that small for gestational age is significantly associated with childhood asthma risk (Sonnenschein-van der Voort et al., 2014). Being born preterm also has a significant positive relation with being a low birth weight infant (Blencowe et al., 2013). Therefore, as ill-health is related with healthcare use, being preterm has a direct association with the

outcome of healthcare use. In addition to this direct effect, the effect of gestational age on exposure (BMI status) and outcome is also mediated through child birthweight. Due to this association between birthweight and gestational age, both were included as continuous covariates in analyses to adjust for the effect of one while predicting the variability in outcome based on the other.

To calculate the proportion of children categorised as preterm for each category of sex, ethnicity and BMI, a categorical variable was generated from gestational age. The three WHO subcategories for preterm birth were combined to create two categories: 'preterm', and 'not preterm'.

3.7.3 Maternal characteristics

This section describes the variables on maternal characteristics included as covariates in the analyses in this thesis.

3.7.3.1 Maternal age

Information on maternal age at birth was recorded at the recruitment interview. The age range of mothers at childbirth was from ≤20 to ≥40 (West et al., 2013).

In the relevant literature, mothers' age at birth has been shown to have a U-shaped relationship with indicators of child health. Children of mothers of very young (age <20) and advanced age (>35) are shown to be at a greater risk of adverse child health outcomes such as stunted growth, mortality, and anemia (Finlay et al., 2011, Fall et al., 2015). Additionally, very young and advanced maternal ages are also significantly associated with low birth weight in children and higher risk of being preterm (Kozuki et al., 2013, Restrepo‐Méndez et al., 2015). This association of maternal age with low birth weight and preterm birth puts it on a causal pathway to BMI status and to healthcare use, therefore confounding the association of exposure and outcome.

3.7.3.2 Maternal BMI

Heights of mothers were extracted from the weight and height measurements done at recruitment (26-28 weeks gestation) using digital scales and a Leicester height measure. Weights of mothers were abstracted from their antenatal records, which were measured at median 12 weeks gestation (Interquartile range 11-14). Maternal BMI was then derived using these height and weight measurements (kg/m^2). Mothers were categorized into weight categories based upon the BMI thresholds of underweight < 18.5, normal weight 18.5-24.9, overweight 25.0-29.9, and obese ≥ 30.0 (World Health Organization, 2018a).

A recent study for BiB children that analysed the association of maternal exposures with child adiposity at age 4/5 years found maternal BMI to be a significant predictor of adiposity in children (West et al., 2018). Additonally, a recent meta-analysis reported that children of mothers who were obese before pregnancy had 264% higher odds of being obese during childhood (Heslehurst et al., 2019).

3.7.4 Socio-economic status

Socio-economic status (SES) during childhood is reported to be associated with the BMI status of children. The recent NCMP end-year report showed that children from deprived areas have more than double the prevalence of obesity than those living in the least deprived areas (NHS Digital, 2020d). Additionally, in most western countries, prevalence of overweight is higher among children from less affluent families, while the opposite effect has been seen in developing countries (Due et al., 2009, Wang and Lim, 2012). In either case, an association between SES and child BMI status exists and has frequently been reported in literature. Childhood SES is inversely associated with health outcomes. Research has shown that children from a lower SES have a lower health status with an increased risk of adverse health effects such as respiratory illness, LBW, and high childhood mortality (Wolfe, 2015, Chen, 2004, Wickham et al., 2016). As ill-health is related to

healthcare use, SES status of children could potentially modify the strength of association between exposure (BMI status) and outcomes in the studies performed as part of this thesis.

As an individual's health is determined through complex interactions between various individual, social and environmental factors (Albuquerque et al., 2017), adjusting for a single measure for SES may not encompass the overall impact of SES on health of the children. Therefore, I decided to adjust for multiple SES variables that not only account for the effect of SES at an individual level, but also at a general socio-economic or area level.

3.7.4.1 Means-tested benefits

Means-tested benefits are type of public benefits in England that are available to people who can demonstrate that their income and capital savings are below a specified limit. Means-tested benefit is adjusted for as an individual level SES measure in this project. Means-tested benefits were recorded as a binary variable, with mothers reporting whether they were in receipt of benefits or not at the recruitment questionnaire.

3.7.4.2 Index of Multiple Deprivation

As part of the analyses in this thesis, I used the Index of Multiple Deprivation (IMD) as an area-level measure of SES for each child based on the 2015 IMDs. IMD combines information from seven different domains of deprivation (Income, Employment, Education, Health, Crime, Housing and Environment) to produce an overall measure of relative deprivation (Department for Communities and Local Government, 2015). This deprivation is measured at a level of clearly defined small areas in England. These small areas are called Lower Super Output Areas (LSOAs). LSOAs are designed to be of comparable size, with an average of about 1500 residents per LSOA. Each LSOA is uniquely identified with an LSOA code. In 2015, England had 32,844 LSOAs (Smith et al., 2015). Based upon deprivation score, IMD 2015 ranked each LSOA in England from 1 (most deprived) to 32,844 (least

deprived). This relative ranking of LSOAs is also done at district levels to produce relative IMD scores for LSOAs within each district (District of Bradford in this project).

In the BiB dataset, data on a child's postcode and LSOA was already available. Using the data available online for IMD 2015 (https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015), I matched data for each LSOA in the BiB dataset using the unique LSOA code. Using the ranking of LSOAs within the Bradford district, I created ten categories (deciles) of IMD, from most deprived (1st category) to least deprived (10th category). To account for the very small number of observations in certain IMD decile categories in the BiB data, I collapsed these to produce five categories, with the 20% most deprived LSOAs within Bradford in the first category to 20% least deprived LSOAs in the fifth category.

3.8 Statistical Analyses

I performed all the analyses using Stata/SE software version 16 (StataCorp, 2019). This section is divided in to three subsections:

1. Descriptive statistics – description of general characteristics of the BiB cohort by exposure (BMI status) and ethnicity.
2. Statistical analyses of healthcare use – bi- and multi-variable regression to model healthcare use to identify the association between exposure and the outcomes, exploring the impact of ethnicity and other covariates.
3. Statistical analysis of healthcare costs – Regression models to predict healthcare costs by BMI status and exploring the impact of ethnicity.

3.8.1 Analysis cohort

As previously mentioned in section 3.4, children with height and weight measurements at age 4/5 years were included in the analyses in this thesis and constitute the analysis cohort.

Children in this analysis cohort who were withdrawn from primary and secondary healthcare linkage before the date of their height and weight measurements were not part of the regression analyses of healthcare use and costs. However, descriptive statistics for these children are described in this thesis.

3.8.2 Descriptive statistics

I carried out descriptive analyses to describe the study population and distribution of outcomes and covariates by BMI status and ethnicity. The following analyses were performed:

- Description of the cohort based on inclusion (analysis cohort) and exclusion.
- Prevalence estimates of underweight, normal weight, overweight and obese children in the analysis cohort. Prevalence in each BMI category was also reported by ethnicity and sex.
- Distribution of covariates by exposure
- Comparison of Pakistani and White British children on covariates of interest
- Distribution of outcome variables by exposure (BMI categories) and ethnicity.

Normally distributed continuous variables were described using means and 95% confidence intervals, while medians were used as a summary statistic for non-normally distributed data. Categorical variables were described using frequencies and proportions.

Independent two sample t-tests were performed to calculate mean differences for normally distributed continuous variables between BMI (reference; normal weight) and ethnicity categories (reference: White British). Outputs were presented as mean differences with 95% confidence intervals (CIs). Significance level was defined at $p < 0.05$. Nonparametric Mann-Whitney U tests were performed to assess differences between not normally distributed continuous variables. For categorical variables, chi-squared tests were

performed to examine associations and differences in percentages. Chi-square tests for trend were performed for ordinal categorical variables. z-tests for proportions were also carried out to analyse the difference in proportions of overweight/obese children between ethnic groups.

3.8.2.1 Prevalence estimate

Prevalence estimates of children in each BMI category were estimated for the whole analysis cohort. Prevalence was also reported by ethnicity and sex.

3.8.2.2 Missing data

Percentage of missing data for each covariate was reported by BMI categories.

3.8.3 Statistical analyses of healthcare use

Separate analyses were performed to model all outcome measures of primary and secondary healthcare use (section 3.6).

3.8.3.1 Univariate Negative Binomial Regression

Univariate negative binomial regression models were performed for each outcome measure of healthcare use separately, using BMI status as a predictor variable. Negative binomial regression was performed instead of Poisson regression as the assumption of equidispersion (mean of outcome is equal to variance) was expected to not be met. This decision was confirmed using dispersion parameter *alpha* being significantly different from zero. Unadjusted (univariate) incidence rate ratios (IRRs) were calculated comparing the rates between BMI categories (reference category: normal weight). Additional univariate models were run separately for predictor variables of sex (reference: male) and ethnicity (reference: White British). The time under exposure (person-year, section 3.5.1) for each child was incorporated in these models to account for different lengths of time each child remained in the study.

3.8.3.2 Multivariable Negative Binomial Regression

Multivariable negative binomial regression models were run to examine the association between child BMI status at age 4/5 years and outcomes of healthcare use. A separate model was run for each measure of healthcare use. The analyses were adjusted for covariates of child sex, birthweight, gestational age, ethnicity, maternal age, maternal BMI, means tested benefits and IMD. Multicollinearity among these predictor variables was quantified using a Variance Inflation Factor (VIF). The assumption of linearity was assessed by plotting scatter plots of a predictor variable on the log of outcome counts with a line for linear fit, a line for quadratic fit and lowess smoothing. Birthweight, gestational age, maternal age and maternal BMI were included as continuous variables in the analyses. Ethnicity was included as a categorical variable with 3 categories (White British, Pakistani, Other) with White British as the reference group. Being male was the reference category for the effects of sex.

These multivariable analyses were carried out in two stages. Initially, a complete case analysis was done for each outcome measure, therefore children with missing data on any of the covariates were not included in the analysis. Afterwards, analyses were carried out after imputing missing values for covariates using multiple imputation, a complete explanation of which is given later in section 3.8.4**.**

3.8.3.3 Zero-inflation

As mentioned earlier, denominator for secondary healthcare use is unknown in the cohort. It is not possible to know whether children with zero A&E visits and zero admissions actually did not use healthcare services during the period of interest (actual zeros) or they did but at a provider other than the Bradford Royal Infirmary. This leads to excessive zeros in the dataset. To account for this, I also performed zero-inflated negative binomial regression (zinb) models to predict counts of secondary healthcare use. A zinb model has two

components; a negative binomial component that predicts counts for a list of predictors, and a logistic component that predicts the probability of being an actual zero based upon the covariates in the logit model (a child who never visited an A&E unit during the time period). I used IMD categories to predict the probability of being an actual zero in the logistic part of the model. It predicted the change in probability of being an actual zero with one unit increase in the IMD. A decision to report the predictions of a standard negative binomial model or zinb was based on the results of Akaike and Bayesian Information Criterion (AIC and BIC) and the Vuoung test. The model with the lowest AIC/BIC was the better fit.

3.8.3.4 Multivariable logistic regression

Separate multivariable logistic regression models were run to predict the probability of at least one primary care consultation, atleast one hospital admission, and atleast one A&E visit in children based on the values of exposure and covariates. The outcome variable in each model of respective measure of healthcare use was a binary variable with two categories: children with atleast one healthcare event and children with no healthcare event.

3.8.3.5 Cluster-robust standard errors

An assumption that underlies the Poisson or negative binomial process is the independence of events – the probability of one event occurring is independent of the probability of another. However, this assumption is not satisfied in longitudinal studies such as BiB, where events for each child are interdependent. To relax this assumption of independence, I specified cluster-robust standard errors in the models using child identification number as the cluster variable. This specified that the events are independent between clusters but not within.

3.8.3.6 Interactions

Interactions between BMI and all other covariates were tested for statistical significance by applying likelihood ratio tests. Additionally, interactions between ethnicity and other covariates were also tested for statistical significance using the likelihood ratio test. The analyses were stratified accordingly.

3.8.3.7 Assessment of influential observations

Influential observations are observations that have a large effect on the estimated effect sizes obtained after running a regression model. The effect of such observations is determined by examining the change in the estimated regression effect size that occurs when the observations are removed from the analysis. Assessment of influential observations as part of the analysis in this thesis was done by estimating the Cook's distance, Pearson standardized and deviance residuals and plotting them against the predicted values of the outcomes. The decision on influence of an observation and whether it should be kept in the analysis was made after observing the change in the regression coefficients after removal of such an observation.

3.8.4 Multiple Imputation

Missing data are unavoidable in epidemiological and health research. Missing data can present certain challenges in analysing multivariable datasets. Missing data in a statistical analysis can lead to biased parameter estimates depending upon the type of missing data, the percentage of missing data, and the mechanism by which the data are missing (Sterne et al., 2009). Additionally, in a multivariable statistical analysis, missing data may result in loss of power and/or efficiency of the analysis as subjects with missing data on variables of interest are removed from an analysis (Sterne et al., 2009). Various statistical methods have been developed to deal with the problem of missing data, however selection of an appropriate method depends upon an understanding of the type or mechanism of

missingness. Missing data are usually classified in to three types. For a variable, data is said to be missing completely at random (MCAR) when the probability of missing is equal for all subjects in the data and it does not depend on the values of other variables or unobserved values of the variable itself (Pedersen et al., 2017). A variable is said to be missing at random (MAR) if the missingness in the variable can be predicted by other observed variables in the dataset. When missingness in a variable depends upon the unobserved (missing) values of the variable itself, the data is said to be missing not at random (MNAR) (Pedersen et al., 2017). An understanding of missing data mechanism for a variable in a dataset is important for the selection of an appropriate method to deal with missingness. For example, when the data are MCAR, doing a complete case analysis (list wise deletion), where a subject with missing data on any analytic variable is removed from the analysis, will not result in biased results (Pedersen et al., 2017). However, doing a complete case analysis for data that are either MAR or MNAR may give biased parameter estimates (Pedersen et al., 2017). Other methods to deal with missing data include mean imputation, missing indicator method, single value imputation, and multiple imputation. Multiple imputation underlies the assumption that the data are at least MAR, and therefore can also be used if the data are MCAR (White and Carlin, 2010). In the analysis carried out in this thesis, I use multiple imputation to deal with missing data with the underlying assumption that the data are MAR.

Multiple imputation is a three-stage process. In the first stage, it uses a Bayesian approach to estimate *m* different data sets of plausible values for the missing data drawn from its posterior predictive distribution conditional on the observed data (Azur et al., 2011). Multiple imputed datasets (m>1) are created. Within each imputed dataset, the missing values for a variable *y* are replaced by the imputed values using an imputation model. This imputation model is a regression model of *y* on a set of variables with complete data,

among individuals with observed values of *y.* In the second stage, the association of interest (regression coefficients) along with its standard error (within-imputation variation) is estimated using the complete-data analytic model within each imputed dataset *m*. These analyses in *m* datasets give different results as multiple imputation incorporates the uncertainty about the missing data during stage one by creating different plausible imputations in each *m* dataset (between-imputation variation). In stage three, the aim is to provide unbiased and valid estimate of association of interest based on information from each imputed data set. Therefore, measures of association from each imputed dataset are combined by Rubin's rule, which calculates the corresponding standard error accounting for both within- and between-imputation variations (Sterne et al., 2009, White et al., 2011).

When developing the imputation model for variables with missing data during stage one, it is important to assess its compatibility with the analytic model (stage two) to avoid bias in the analysis model. It means that the imputation model should at least contain all the variables (including outcome) that are in the analytic model (Bartlett et al., 2015). The variables should also follow the same form (e.g., continuous, or categorical) and any interactions or transformations that are part of the analytic model should also be part of the imputation model. Therefore, as part of the analyses carried out in this thesis, compatibility was assured by running separate multiple imputations for each outcome, and if the analysis model for a particular outcome had an interaction term, it was included in the imputation model.

3.8.4.1 Patterns of missing data

The choice of an imputation method depends upon the patterns of missingness in the data. Generally, pattern of missingness is classified as either monotone or non-monotone missing. A monotone pattern arises when the variables can be ordered such that, for each subject, if data for one variable is missing, it is also missing for other variables (Van Buuren,

2007). Pattern of missingness was determined using the "*misstable pattern"* and *"misstable nest"* commands in Stata version 16 (StataCorp, 2019). As the pattern of missingness was non-monotone and missing values for different type of variables (e.g., continuous, and categorical) were needed to be imputed, multiple imputation by chained equation (MICE) method was used in this thesis to impute missing values.

3.8.4.2 Multiple Imputation by Chained Equations

Multiple Imputation by Chained Equations (MICE) is a method to impute missing variables by specifying separate imputation models for each variable with missing values, using the variable's conditional distribution (Azur et al., 2011, Nightingale et al., 2011). Therefore, MICE can handle different variable types as each variable is imputed using its specific model (e.g., linear model for a continuous missing variable or a logistic model for a categorical missing variable). MICE is a cyclic process, where each cycle consists of a chain of specified regressions, one for each missing variable with missing values (stage one). This process is repeated for a specified number of cycles to produce a single imputed data set. This procedure is repeated *m* times to produce *m* imputed data sets (Sterne et al., 2009, Nightingale et al., 2011). MICE was run using the *"mi impute chained"* command in Stata version 16. The number of cycles to run in one imputation was kept at Stata standard (n = 10) and the stability or convergence of an imputation model was assessed by visualizing trace plots. A linear regression model was used to impute continuous missing variables, while logistic, multinomial logistic and ordered logistic models were run to impute binary, unordered, and ordered categorical variables, respectively. A MICE model assumes normal distribution to impute a continuous variable (Nightingale et al., 2011). In case of a non-normal distribution of a variable with missing data, Predictive Mean Matching (PMM) method was used to impute (Nightingale et al., 2011). For a variable *x* with missing values, PMM imputes using a suitable observed value (*k)* of *x. k* was specified as 10 in the

imputation model based upon the recommendations by Morris et al. (2014), meaning that one of the 10 suitable observed values of *x* will be chosen at random to impute the missing value of *x.* The decision of how many imputations to run was taken based upon the recommendations by Nightingale et al. (2011). They suggest running a number of imputations that are equal to or exceed overall percentage of missing data in the dataset.

Auxiliary variables are variables that are either predictors of the incomplete variable of interest or are predictors of missingness of the incomplete variables. Auxiliary variables are not part of the analytic model and are added to the imputation model as they make the assumption of MAR more plausible and can improve the imputations by reducing the standard error of the estimates for the analysis model (Johnson et al., 2011, Enders, 2010). Identification of potential auxiliary variables was done by examining their correlation with incomplete variables. If a variable was well correlated ($r > 0.4$), it was included in the imputation model (Enders, 2010). Auxiliary variables were additionally identified by creating a binary variable that identified missingness for each incomplete variable. Using logistic regression, these identifier variables were regressed on potential auxiliary variables to assess if they significantly predict missingness in the incomplete variables.

3.8.4.3 Checking the imputation model

Imputation models were checked by comparing the distributions of the observed data with the imputed data in each imputed data set. Boxplots and dot plots were used to visualize these distributions for continuous variables. Additionally, summary statistics were tabulated for observed and imputed data for categorical and continuous variables.

Diagnostic plots were produced, and a goodness of fit assessment was done for imputation models. Additionally, diagnostic plots and goodness of fit assessment was done for each analytic model in imputed data sets.

3.8.5 Statistical Analysis of Healthcare costs

The aim of analysing healthcare costs was to predict mean annual costs per child within each BMI category for each measure of healthcare cost (Primary care, hospital admission and A&E visits), adjusting for various characteristics (covariates).

3.8.5.1 Descriptive statistics

I performed descriptive analyses of primary and secondary healthcare costs to describe the distribution of costs within each BMI category. Additionally, I also described the distribution of costs within each BMI category by ethnic groups. The distribution of costs was checked using the skewness, kurtosis and Shapiro-Wilk tests of normality in Stata 16 (StataCorp, 2019). I did not perform t-tests to study between group mean differences in costs as healthcare costs are expected to have a positive (right-tailed) skew due to high probability of zero-costs – more on this in the following section.

3.8.5.2 Regression analyses for healthcare costs

A separate regression model was carried out for primary care, hospital admissions and A&E cost data. Additional models were also run to predict costs by ethnicity for each of these measures of healthcare costs separately.

Selection of an appropriate analytic strategy to model healthcare costs is a complex process, with different models being currently employed in the health economics literature (Dunn et al., 2003, Gregori et al., 2011, Mihaylova et al., 2011). The commonly used models in literature to model healthcare costs, particularly for routinely collected observational data are ordinary least square (OLS) linear regression model, log transformed linear regression and Generalized Linear Models (GLM) with gamma errors (Han et al., 2019, Kent et al., 2017, Pagano et al., 2015, Korda et al., 2015). In literature, it is recommended to select a model over another based on the specific study aims and the distribution of the

outcomes. In my project, the main aspects to consider while selecting an appropriate model to predict costs were:

- *Right (positive skew) tailed distribution:* Healthcare costs are expected to have a gamma distribution, with a positive (right-tailed) skew due to non-negative data and a higher proportion of population accruing zero or low costs (Pagano et al., 2015, Mihaylova et al., 2011). Therefore, the assumption of normality of the outcome and residuals that underlies the OLS regression is not satisfied in such cases, and the model misfits the data (Kirkwood and Sterne, 2010). A solution to this problem could be to log-transform the cost data.
- *Zero-costs:* Log-transformation of costs to approximate normal distribution to satisfy assumption for OLS regression could work in theory, however this is complicated with the presence of zero-costs, as log of zero is not defined. It has been suggested in literature to add a constant to all zero-values (for example: 0 + 1) before log-transformation (Gregori et al., 2011, Pagano et al., 2015). This solves the issue of zero-costs but could bias the relationship between covariates and outcome. The distribution of log-transformed highly positively skewed data would do a poor job at normal distribution approximation. Secondly, the aim of the study was to predict mean costs on a normal scale, not a transformed scale. Therefore, a log-linear model will require back-transformation of mean predicted costs with methods that could potentially introduce further bias in the results.
- *Person*-years *and clustering*: As mentioned previously, the aim of modelling costs was to predict annual mean costs per child within each BMI category. To achieve this in the BiB dataset, a modelling strategy that takes into account the varying time that each child (person-years) contributed to the study needed to be identified. Additionally, the identified model should also account for the lack of

independence (clustering) between costs of a given child over the years the child remains in the study.

Given the above-mentioned aspects that needed to be accounted for in identifying an appropriate multivariable model, I predicted mean annual costs per child using a multivariable GLM model with a log link function and gamma distribution. All models were run in Stata version 16 (StataCorp, 2019). Separate models were carried out for each measure of healthcare costs i.e., primary healthcare, APC and A&E costs. GLM models with gamma distribution are frequently used to model routinely collected healthcare costs and are shown to perform well in the presence of positive skew and zero-costs (Pagano et al., 2015). Use of the log-link function within the GLM framework ensured that the costs were modelled on a transformed scale, while the final output is given in annual mean costs on the original scale with gamma errors. Cluster-robust standard errors were specified in each model to account for the potential lack of independence between costs (including zero-costs) for a given child across years of study. Adjustment for the time a child contributes to the study (person-years) was done by specification of an offset in the models. For each measure of healthcare costs, I derived estimates of mean annual costs per child within each BMI category. I also derived estimates of absolute mean differences in costs for each BMI category with normal weight as a reference. Additionally, I derived estimates of costs within each BMI category separately for each ethnic group. All the models were adjusted for child sex, IMDs, means tested benefits, mother's age at birth, gestational age, birthweight, and mother's BMI.

In health economics literature, a two-part model is often employed to model costs in the presence of excess zeros (Mihaylova et al., 2011, Dunn et al., 2003). The first part models the probability of incurring any costs for any combination of covariates and exposure variable. The dependent variable in this model has two categories, one with participants

with zero-costs, the other with participants with positive costs. The second part of the two-part model estimates mean annual costs only for participants that incurred any cost. Annual mean costs per participant are then predicted by multiplying the probability of incurring any cost in the first part with estimated mean costs from the second part. These two-part models are employed and recommended in studies where the aim is to understand, evaluate and assess performance of a given healthcare system (Pagano et al., 2015, Dunn et al., 2003).

In the BiB cohort, excess-zeros were present in the secondary healthcare cost data (APC & A&E costs). However, as the aim of analysis was to evaluate the impact of individual covariates and predict annual mean costs per child within each BMI category, a single equation GLM model was selected due to ease of interpretation and evidence of better performance based on metrics of BIC and Root Mean Squared Errors (RMSE). Additionally, as mentioned previously (section 3.6.1.2)**,** the secondary healthcare data for BiB children was only collected from the Bradford Royal Infirmary. There was no way to know whether these zero-costs were due to no healthcare use or because children accessed a different healthcare provider. Therefore, running a two-part model could potentially have introduced hidden bias in the predictions.

Chapter 4 Descriptive statistics of the Born in Bradford analysis cohort

This chapter presents the descriptive statistics for the BiB children by exposure (BMI status) and ethnicity.

4.1 Overview

The chapter starts with selection of the analysis cohort used in the subsequent regression analyses, as outlined in Chapter 3 (section 3.4; section 3.8.1). This is followed by prevalence estimates of underweight, normal weight, overweight and obese children in the analysis cohort by sex and by ethnicity.

The rest of the chapter provides description of key covariates in the analysis cohort by exposure and by ethnicity. The chapter ends with the description of the missing data on the key covariates.

4.2 Analysis cohort

Selection of the analysis cohort was based on the criteria mentioned in Chapter 3 (section 3.8.1). Of the 10,995 children eligible to start school by the year 2014/2015, 9,440 had anthropometric measurements (height and weight) at age 4/5 years from either the NCMP records or primary care records (Figure 4.1). Forty-one of these children were withdrawn from linkage of their healthcare records before the date of their anthropometric measurements and were therefore not included in the analysis cohort. There were two children who died during the study period (after their anthropometric measurements). Although death during the study period was not a criterion for exclusion to prevent selection bias and preserve generalisability to the Bradford population, these two children were excluded from the study due to contradiction in their death record between primary

care and secondary health records (recorded as died in one record and alive in the other record). As the data was pseudo-anonymised, it was not possible to confirm whether these two children were alive or not and were therefore excluded from the study.

1

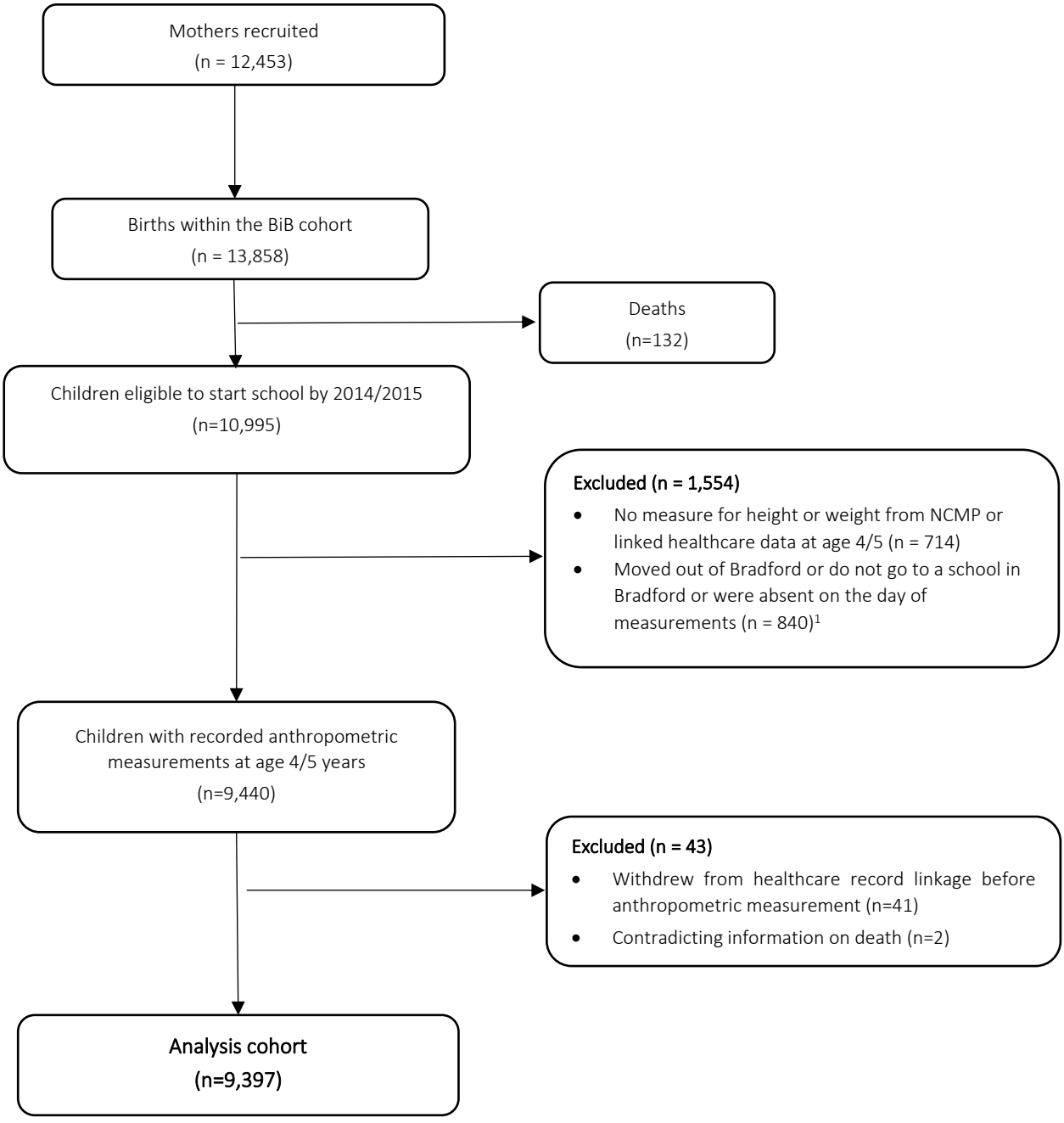

Figure 4.1 *Flow chart for selection of analysis cohort*

[1] No data on baseline characteristics were available for the 840 excluded children who moved out of Bradford, or did not go to a school in Bradford or were absent on the day of height and weight measurements

Table 4.1 *Comparison of analysis cohort and excluded children on key covariates*

Characteristics	Analysis cohort (n=9,397)	Not in the analysis cohort (n = 757)	p-value[1]
Child Sex			0.79
Boys	4, 831 (51.4%)	393 (51.9%)	
Girls	4, 566 (48.6%)	364 (48.5%)	
Ethnicity			0.03
White British	3,469 (36.9%)	243 (32.1%)	
Pakistani	4,346 (46.2%)	381 (50.3%)	
Others	1,323 (14.0%)	104 (13.7%)	
Missing	259 (2.7%)	29 (3.8%)	
Gestational age			0.67
Term	8,646 (92.0%)	704 (93.0%)	
Preterm	576 (6.1%)	50 (6.6%)	
Missing	175 (1.8%)	3 (0.4%)	
Birthweight			0.71
Normal Birthweight	8,426 (89.6%)	676 (89.3%)	
Low birthweight	796 (8.4%)	67 (8.8%)	
Missing	175 (1.8%)	14 (1.8%)	
IMD categories			<0.01
1st (most deprived)	3,138 (33.4%)	292 (38.5%)	
2nd	2,823 (30.0%)	222 (29.3%)	
3rd	1,999 (21.3%)	160 (21.1%)	
4th	1,026 (10.9%)	65 (8.6%)	
5th (least deprived)	320 (3.4%)	10 (1.3%)	
Missing	91 (0.9%)	8 (1.0%)	
Means tested benefits			0.25
In receipt	3,497 (37.2%)	280 (36.1%)	
Not in receipt	4,449 (47.3%)	323 (42.6%)	
Missing	1,451 (15.4%)	154 (20.3%)	

Percentages are given by columns
[1]P-value for a chi-square test, excluding the missing values

Table 4.1 provides a comparison of the analysis cohort with BiB children not included in the study on important characteristics. The two groups had similar distribution of most characteristics apart from ethnicity and IMDs. The proportion of Pakistani children in the excluded group was higher and the proportion of children living in the most deprived areas of Bradford was also higher in the excluded group.

In this analysis cohort, 8,109 children had their height and weight measurements recorded as part of the NCMP, while 1,288 children had their measurements extracted from primary care records. Table 4.2 gives the distribution of BMI by these two measurement sources. The first primary care measurement was recorded on 13 June 2011 while the latest was recorded on 25 Nov 2014. For NCMP, first measurement was recorded on 28 September 2011, while the latest was on 21 May 2015.

Table 4.2 *Distribution of BMI in the analysis cohort by measurement source*

Characteristics	Whole analysis cohort (9,397)	NCMP (8,109)	Primary care (1,288)	p-value[1] (χ2)
Mean BMI z-score (s.d.)	0.19 (± 1.13)	0.20 (±1.10)	0.18 (±1.27)	
BMI status, n (column %)				<0.01 (15.3)
Underweight	189 (2.0%)	148 (1.8%)	41 (3.1%)	
Normal weight	7,244 (77.1%)	6,282 (77.4%)	962 (74.7%)	
Overweight	1,028 (10.9%)	892 (11.0%)	136 (10.5%)	
Obese	936 (9.9%)	787 (9.7%)	149 (11.5%)	

Percentages are given by columns

[1]p-value associated with the chi-squared test; χ2 provides value for Pearson chi-squared between NCMP and primary care group

4.3. Characteristics by exposure

This section presents the description of key characteristics (covariates) by BMI categories. These characteristics are presented in subsections as child characteristics, maternal characteristics, and socio-economic status. Text summaries follow the tabular description of these characteristics to highlight key findings.

4.3.1. Child characteristics

Table 4.3 presents the proportion of children in each BMI category. These proportions are also presented by child sex. Overall, number of obese children in the analysis cohort was 936 (9.9%), while there were 189 (2.0%) underweight and 1,028 (10.9%) overweight children. The proportion of underweight and obesity was slightly higher in boys, while higher proportion of girls was normal weight and overweight (Table 4.3, Figure 4.2)

Table 4.3 *Proportion in each BMI category by child sex*

Characteristics	n	Underweight	Normal Weight	Overweight	Obese	p-value[1] (χ2)
Overall (%)	9,397	189 (2.1%)	7,244 (77.1%)	1,028 (10.9%)	936 (9.9%)	
Child sex						0.03 (8.89)
Boys (%)	4,831	116 (2.4%)	3,706 (76.7%)	516 (10.6%)	493 (10.2%)	
Girls (%)	4,566	73 (1.6%)	3,538 (77.5%)	512 (11.2%)	443 (9.7%)	

*proportions are given by rows

[1]p-value associated with the chi-squared test; χ2 provides value for Pearson chi-squared

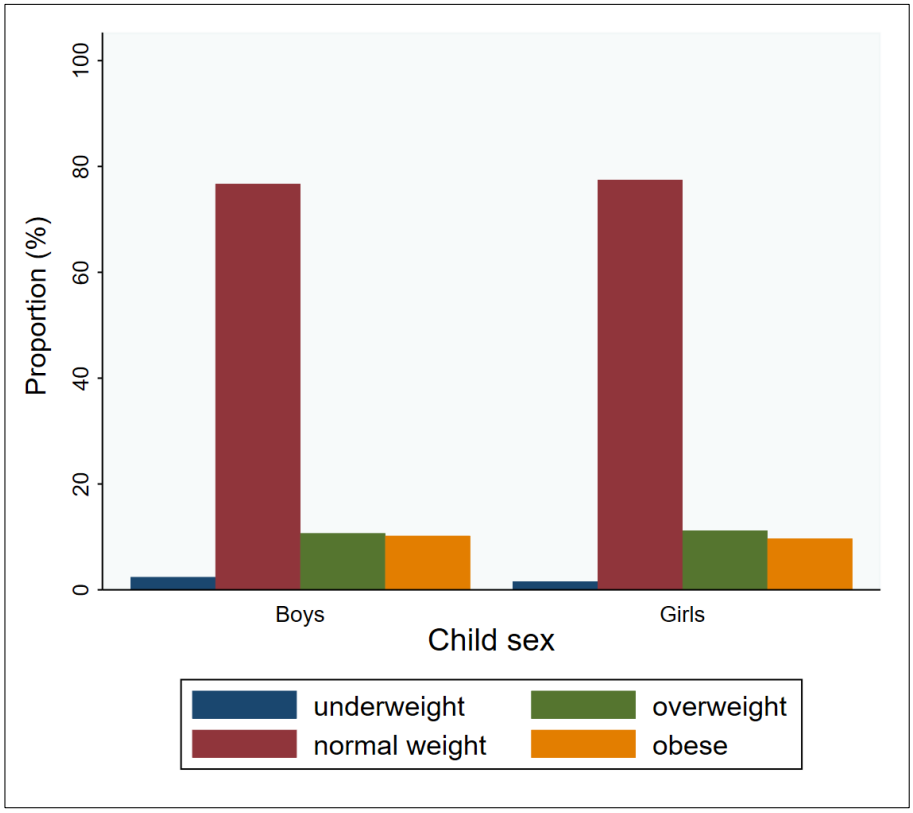

Figure 4.2 *Proportions in each BMI category by child sex*

Table 4.4 presents a description of child characteristics by BMI status. Both birthweight (Shapiro-wilk: $p < 0.01$) and gestational age (Shapiro-wilk: $p < 0.01$) were not normally distributed (appendix A3.1), therefore the associated p-values of test of difference are presented after performing Mann-Whitney tests. Underweight children on average had a lower birthweight, while the birthweight in overweight and obese children was higher compared to normal weight children. Additionally, in the children born with low birthweight (<2500gm), the proportion of underweight at age 4/5 years was higher (5.7%) compared to the proportion of underweight in children born with normal birthweight (1.6%). Similar distribution was observed by gestational age. Among preterm children, 4.5% were underweight, while 1.8% of the non-preterm children were underweight.

Table 4.4 *Child characteristics by BMI status**

Characteristics	Underweight	Normal Weight	Overweight	Obese	p-value[1] (χ2)
Mean Birthweight (gm)[2] (s.d.)	2749.38 (±607.12)	3170.85 (±544.88)	3375.15 (±546.83)	3344.81 (±579.78)	
Test of difference, range (p-value)[3]	860-3,960 (<0.01)	660-5,260 (reference)	880-5,180 (<0.01)	840-5,360 (<0.01)	
Mean gestational age[2] (s.d.)	38.37 (±2.28)	39.06 (±1.80)	39.23 (±1.76)	39.14 (±1.82)	
Test of difference, range (p-value)[3]	28-42 (<0.01)	25-44 (reference)	26-44 (<0.01)	27-42 (0.18)	
Child ethnicity n (row %)					<0.01 (90.6)
White British (3,469)	20 (0.5%)	2,646 (76.2%)	457 (13.1%)	346 (9.9%)	
Pakistani (4,346)	133 (3.0%)	3,368 (77.5%)	403 (9.2%)	442 (10.1%)	
Other (1,323)	34 (2.5%)	1,037 (78.3%)	138 (10.4%)	114 (8.6%)	
Missing (259)	2 (0.7%)	193 (74.5%)	30 (11.5%)	34 (13.1%)	
Child birthweight[2] n (row %)					<0.01 (89.8)
Low birthweight (796)	46 (5.7%)	646 (81.1%)	49 (6.1%)	55 (6.9%)	
Normal birthweight (8,426)	140 (1.6%)	6,454 (76.6%)	960 (11.3%)	872 (10.3%)	
Missing (175)	3 (1.7%)	144 (82.3%)	19 (10.8%)	9 (5.1%)	
Gestational age[2] n (row %)					<0.01 (22.3)
Preterm (576)	26 (4.5%)	444 (77.0%)	49 (8.5%)	57 (9.9%)	
Not preterm (8,646)	160 (1.8%)	6,656 (76.9%)	960 (11.1%)	870 (10.0%)	
Missing (175)	3 (1.7%)	144 (82.2%)	19 (10.8%)	9 (5.1%)	

*Percentages are given by rows

[1]p-values of chi-square tests, excluding the missing values; value of Pearson chi-square is in the bracket

[2]Birthweight in grams; Gestational age in weeks; Low birthweight (<2500gm); preterm (<37 weeks)

[3]Mann-Whitney U test. Separate tests of difference from normal weight by underweight, overweight and obese groups. Significant difference: $p \leq 0.05$

4.3.2. Maternal characteristics

Maternal BMI and maternal age were not normally distributed, therefore Mann-Whitney tests of difference were performed (appendix A3.1). The mothers of overweight and obese

children had a much higher mean BMI compared to the mothers of normal weight children (Table 4.5).

The mothers of underweight children had slightly higher mean age at birth compared to normal weight children. The age-distribution of mothers of normal weight, overweight and obese children was quite similar (Table 4.5).

Table 4.5 *Maternal characteristics by exposure*

Characteristics	Underweight	Normal Weight	Overweight	Obese
Maternal BMI, mean (s.d.)	23.32 (±5.63)	25.53 (±5.33)	27.77 (±6.09)	29.02 (±6.53)
Test of difference, median (range, p-value)[1]	22.57 (14.7-56.8, <0.01)	24.58 (15.0-55.7, reference)	26.60 (17.2-55.7, <0.01)	27.97 (16.1-56.9, <0.01)
Maternal age, mean (s.d.)	28.10 (±5.18)	27.28 (±5.55)	27.17 (±5.82)	27.36 (±5.69)
Test of difference, median (range, p-value)[1]	28 (17-42, 0.02)	27 (15-49, reference)	26 (15-44, 0.25)	27 (15-44,0.73)

[1] Mann-Whitney U test. Separate tests of difference from normal weight by underweight, overweight and obese groups. Significant difference: $p \leq 0.05$

4.3.3 Socio-economic status

A trend was observed in the prevalence of obesity by deprivation, with children living in the deprived areas having a high proportion of obesity, while children living in the least deprived area having the lowest proportion of obesity (Table 4.6, Figure 4.3). The prevalence of underweight and overweight was also lowest among children living in the 20% least deprived area, while the prevalence of normal weight was the highest (Table 4.6).

Table 4.6 *Socio-economic status by BMI status*

Characteristics	Underweight	Normal Weight	Overweight	Obese	p-value[1] (χ2)
IMD categories* n (row %)					<0.01 (40.0)
1st (most deprived) (3,138)	68 (2.1%)	2,376 (75.7%)	343 (10.9%)	351 (11.2%)	
2nd (2,823)	66 (2.3%)	2,163 (76.6%)	297 (10.5%)	297 (10.5%)	
3rd (1,999)	39 (1.9%)	1,581 (79.1%)	203 (10.1%)	176 (8.8%)	
4th (1,026)	13 (1.2%)	787 (76.7%)	143 (13.9%)	83 (8.1%)	
5th (least deprived) (320)	2 (0.6%)	270 (84.3%)	29 (9.0%)	19 (5.9%)	
Missing (91)	1 (1.1%)	67 (73.6%)	13 (14.3%)	10 (10.1%)	
Means tested benefits* n (row %)					0.95 (0.31)
In receipt (3,497)	73 (2.1%)	2,677 (76.5%)	389 (11.1%)	358 (10.2%)	
Not in receipt (4,449)	91 (2.0%)	3,426 (77.0%)	492 (11.0%)	440 (9.9%)	
Missing (1,451)	25 (1.7%)	1,141 (78.6%)	147 (10.1%)	138 (9.5%)	

*Percentages are given by rows

[1]p-values of chi-square tests, excluding the missing values; value of Pearson chi-square is in the bracket

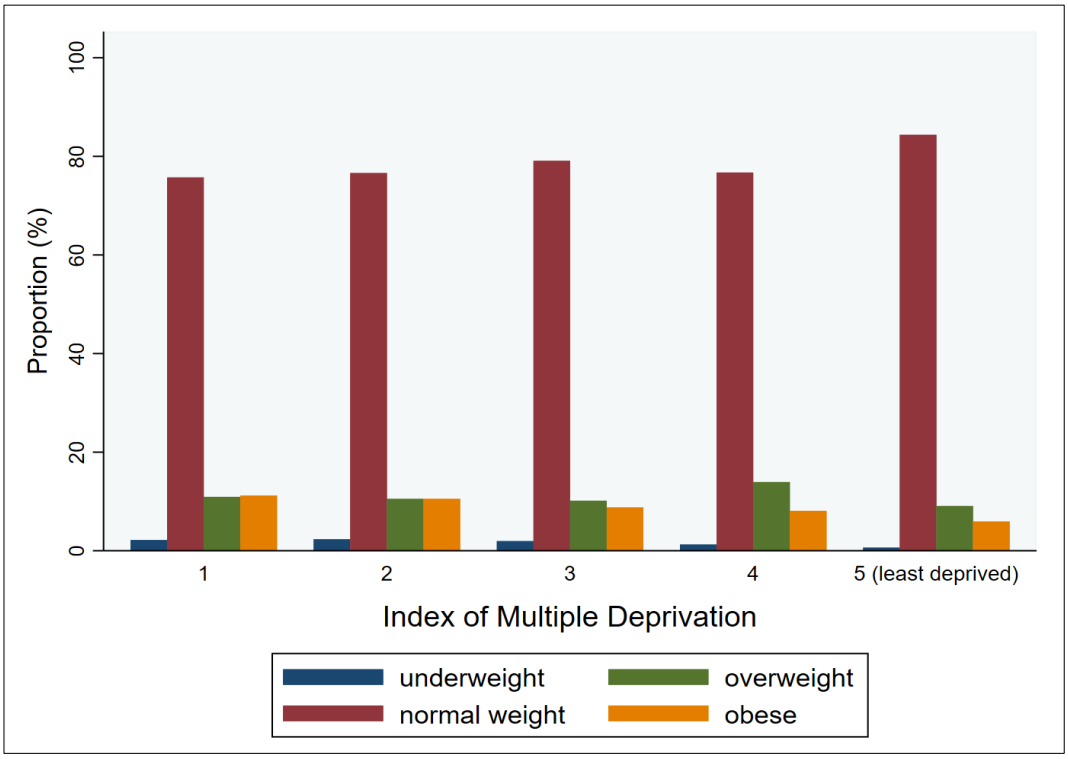

Figure 4.3 *Proportions by BMI status in each IMD category*

4.4. Characteristics by ethnicity

In this section, description of the child, maternal and socio-economic covariates is presented by ethnic groups.

4.4.1. Child characteristics

There were 3,496 White British and 4,346 Pakistani children in the analysis cohort. The proportion of underweight, normal weight, overweight and obese children by ethnic groups is given in table 4.7. Prevalence of underweight was higher in Pakistani children (3.0%) compared to White British children (0.5%). There was only a slight difference in the prevalence of obesity between the two groups, with Pakistani children having a slightly higher proportion of obese children (Table 4.7).

Table 4.8 presents the description of child characteristics by ethnicity. Pakistani children on average had a lower birthweight compared to White British children and children in the Other category. Additionally, a higher proportion of Pakistani children were born with low birthweight (10.0%) compared to White British children (6.6%). The proportion of Pakistani children born preterm (5.8 %) was lower than White British children (6.4%), however the difference was not significant ($p = 0.10$).

Table 4.7 *Proportion of children in each BMI category by ethnicity*

Characteristics	n	Underweight (%)	Normal Weight (%)	Overweight (%)	Obese (%)	p-value[1] (χ2)
White British						0.97 (0.23)
Overall	3,469	20 (0.5%)	2,646 (76.2%)	457 (13.1%)	346 (9.9%)	
Boys	1,754	11 (0.6%)	1,334 (76.0%)	232 (13.2%)	177 (10.1%)	
Girls	1,715	9 (0.5%)	1,312 (76.5%)	225 (13.1%)	169 (9.8%)	
Pakistani						0.04 (8.13)
Overall	4,346	133 (3.0%)	3,368 (77.5%)	403 (9.2%)	442 (10.1%)	
Boys	2,224	84 (3.7%)	1,716 (77.1%)	200 (8.9%)	224 (10.0%)	
Girls	2,122	49 (2.3%)	1,652 (77.8%)	203 (9.5%)	218 (10.2%)	
Others						0.36 (3.16)
Overall	1,323	34 (2.5%)	1,037 (78.3%)	138 (10.4%)	114 (8.6%)	
Boys	707	20 (2.8%)	551 (77.9%)	68 (9.6%)	68 (9.6%)	
Girls	616	14 (2.2%)	486 (78.9%)	70 (11.3%)	46 (7.4%)	

*Percentages are given by rows

[1]p-values of chi-square tests by sex, excluding the missing values; value of Pearson chi-square is in the bracket

Table 4.8 *Description of child characteristics by ethnicity*

Characteristics	White British (3,469)	Pakistani (4,346)	Others (1,323)	p-value[1] (χ2)
Mean Birthweight[2] (s.d.)	3320.15 (±569)	3120.25 (±534)	3155 (±558)	
Test of difference, range (p-value)[3]	800-5,260 (reference)	660-5,140 (<0.01)	760-5,360 (<0.01)	
Mean gestational age[2] (s.d.)	39.18 (±1.85)	39.01 (±1.78)	38.98 (±1.82)	
Test of difference, range (p-value)[3]	27-44 (reference)	25-43 (<0.01)	26-44 (<0.01)	
Mean BMI z-score	0.40 (±0.97)	0.06 (±1.21)	0.08 (±1.15)	
Mean difference[4] (p-value)	0.00	0.34 (<0.01)	0.31 (<0.01)	
Child Sex (column %)				0.20 (3.2)
Girls	1,715 (49.4%)	2,122 (48.8%)	616 (46.5%)	
Boys	1,754 (51.5%)	2,224 (51.1%)	707 (53.4%)	
Child BMI (column %)				<0.01 (99.67)
Underweight	20 (0.5%)	133 (3.0%)	34 (2.5%)	
Normal weight	2,646 (76.2%)	3,368 (77.5%)	1,037 (78.3%)	
Overweight	457 (13.1%)	403 (9.2%)	138 (10.4%)	
Obese	346 (9.9%)	442 (10.1%)	114 (8.6%)	
Child birthweight (column %)				<0.01 (29.23)
Low birthweight	226 (6.6%)	432 (10.0%)	124 (9.5%)	
Normal birthweight	3,166 (93.3%)	3,852 (89.9%)	1,170 (90.4%)	
Gestational age (column %)				0.10 (4.58)
Preterm (576)	218 (6.4%)	249 (5.8%)	96 (7.4%)	
Not preterm (8,646)	3,174 (93.5%)	4,035 (94.1%)	1,198 (92.5%)	

*Percentages are given by columns

[1]p-values of chi-square tests , excluding the missing values; value of Pearson chi-square is in the bracket

[2]Birthweight in grams; Gestational age in weeks

[3] Mann-Whitney U test. Separate tests of difference from White British for Pakistani and others. Significant difference: $p \leq 0.05$

[4]ttests of difference.

4.4.1.1. Ethnicity-specific BMI values

Table 4.9 reports the proportion of Pakistani children in each BMI category after application of ethnicity-specific BMI values. The proportion of underweight children reduced to only 0.2%, while the proportion of normal weight children also reduced (60.3%). On the other end, the proportion of overweight and obese children increased to 19.5% and 19.9%, respectively (Table 4.9). Figure 4.4 shows a graphical comparison of proportions before and after application of the ethnicity-specific values.

Table 4.9 *Proportions by BMI categories in Pakistani children after ethnicity-specific BMI values*

Characteristic	After ethnicity-specific BMI values[1,2]				
	Underweight	Normal Weight	Overweight	Obese	p-value[3] (χ2)
Overall prevalence (n = 4,346)	11 (0.2%)	2,621 (60.3%)	848 (19.5%)	866 (19.9%)	0.09 (6.2)
Boys (n = 2,224)	7 (0.3%)	1,309 (58.8%)	441 (19.8%)	467 (21.0%)	
Girls (n = 2,122)	4 (0.1%)	1,312 (61.8%)	407 (19.1%)	399 (18.8%)	

[1]Underweight < 2nd percentile, Healthy ≥2nd to 84th percentile, Overweight 85th to 94th percentile, Obese ≥ 95th percentile

[2]Pakistani boys: +1.12 kg/m2, Pakistani girls: 1.07 kg/m2

[3]p-values of chi-square tests by sex, excluding the missing values; value of Pearson chi-square is in the bracket

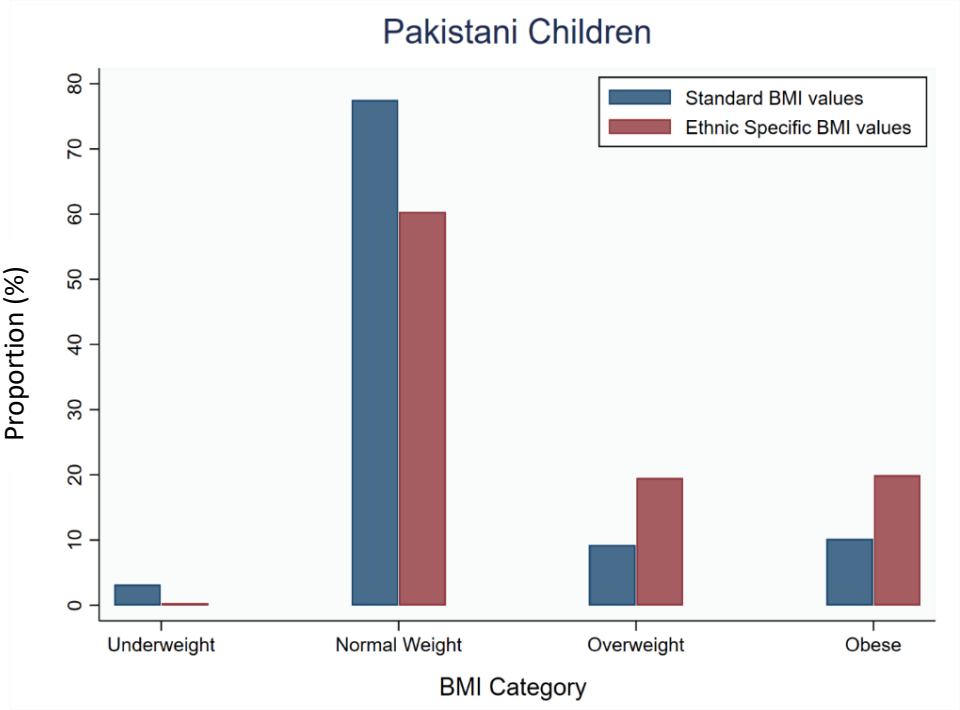

Figure 4.4 *Proportions by BMI status in Pakistani children after ethnicity-specific BMI values*

4.4.2. Maternal characteristics

Mothers of White British children had a higher mean BMI compared to Pakistani children and children of the other ethnicities (Table 4.10). The mean age at birth was higher in Pakistani women.

Table 4.10 *Maternal characteristics by ethnicity*

Characteristics	White British (3,469)	Pakistani (4,346)	Others (1,323)
Maternal BMI, mean (s.d.)	26.87 (±6.01)	25.65 (±5.45)	25.38 (±5.33)
Test of difference, range (p-value)[1]	15.38-56.99 (reference)	14.77-55.77 (<0.01)	15.62-48.88 (<0.01)
Maternal age, mean (s.d.)	26.67 (±6.08)	27.62 (±5.16)	27.86 (±5.41)
Test of difference, range (p-value)[1]	15-45 (reference)	16-49 (<0.01)	15-44 (<0.01)

[1] Mann-Whitney U test. Separate tests of difference from White British for Pakistani and others. Significant difference: $p \leq 0.05$

4.4.3. Socio-economic status

Overall, most children were residents in the lower 60% of the areas by deprivation (Table 4.11). Among the children living in the 20% most deprived areas, the proportion of Pakistani children was significantly much higher (53.1%) compared to White British children (29.1%). If we look at the children living in the 20% least deprived areas, most of them were White British (87.3%) with very few Pakistani children (6.6%). Figure 4.5 gives a graphical representation of these distributions.

Among the children whose parents were in receipt of means tested benefits, higher proportion was made up of Pakistani children (54.5%). Among those whose parents were not in receipt, the proportion of Pakistani (41.9%) and White British children (42.5%) was almost similar.

Table 4.11 *Socio-economic status by ethnicity*

Characteristics	White British (3,469)	Pakistani (4,346)	Others (1,323)	p-value[1] (χ2)
IMD categories* (row %)				<0.01 (1.3e+03)
1st (most deprived)	889 (29.1%)	1,619 (53.1%)	539 (17.6%)	
2nd	724 (26.1%)	1,691 (61.1%)	349 (12.6%)	
3rd	783 (40.3%)	873 (44.9%)	287 (14.7%)	
4th	752 (75.5%)	126 (12.6%)	117 (11.7%)	
5th (least deprived)	263 (87.3%)	20 (6.6%)	18 (5.9%)	
Missing	58 (65.9%)	17 (19.3%)	13 (14.7%)	
Means tested benefits* (row %)				<0.01 (130.8)
In receipt	1,212 (34.6%)	1,909 (54.5%)	376 (10.7%)	
Not in receipt	1,894 (42.5%)	1,864 (41.9%)	691 (15.5%)	
Missing	363 (30.4%)	573 (48.0%)	256 (21.4%)	

*Percentages are given by rows
[1]p-values of chi-squared tests, excluding the missing values

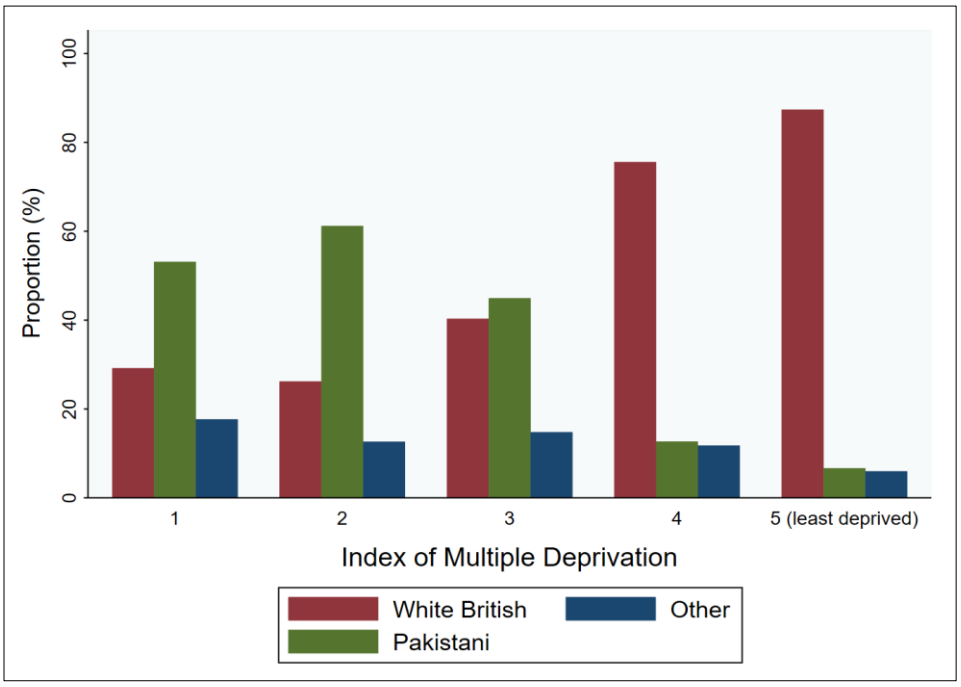

Figure 4.5 *Proportion of each ethnic group in each IMD category*

4.5. Missing data

Using the guidelines recommended by Sterne et al. (2009) , this section reports the methods applied in the stage one of MICE, while results of the analytic models are reported later in the relevant primary and secondary healthcare analysis chapters. Table 4.12 shows the proportion of missing data in the analysis cohort, along with the proportions of missing data in incomplete covariates of interest.

Table 4.12 *Missing data on covariates*

Characteristics	Missing (%)	Not missing (%)
Total	2,053 (22%)	7,344 (78%)
Ethnicity	259 (2.7%)	9,138 (97.2%)
Birthweight	175 (1.8%)	9,222 (98.1%)
Index of Multiple Deprivation	91 (0.9%)	9,306 (99.0%)
Gestational Age	175 (1.8%)	9,222 (98.1%)
Mother's BMI	1,966 (20.9%)	7,431 (79.0%)
Means Tested Benefit	1,451 (15.4%)	7,946 (84.5%)

Percentages are given by rows
BMI: Body Mass Index

Overall, 22% of the subjects in the analysis cohort had missing data on variables of interest. As reported in the methods chapter (section 3.7)**,** child sex, birthweight, ethnicity, IMD, mean tested benefits, gestational age, maternal BMI and maternal age were included as covariates in the full analytic model for each outcome of primary and secondary healthcare use. Among these variables, data was missing for ethnicity, birthweight, IMD, gestational

age, mean tested benefits and mother's BMI. The pattern of missingness was non-monotone (appendix A3.2). Appropriate imputation models were specified for each of these incomplete variables and MICE was run separately for each outcome of interest. Twenty imputations were run to impute missing data. The above-mentioned covariates with complete data were also included in the MICE procedures as predictors for each specified imputation model. The distribution of birthweight, maternal BMI and maternal age was not normal (appendix A3.1). PMM with *k =10* was found to be adequate for their imputation. Appendix A3.3 shows a comparison of the distribution of imputed variables for the observed and each imputed data sets for each outcome of interest. The binary categorical variable mean tested benefits was imputed using a logistic regression model. Ethnicity and IMD were imputed using multinomial logistic and ordinal logistic models, respectively.

Appendix A3.4 reports that missingness in means tested benefits and maternal BMI was significantly associated with ethnicity and pre-pregnancy diabetes. Logistic regression analysis of the missingness identifiers for means tested benefits and maternal BMI reported significantly higher odds of missingness in mothers with pre-pregnancy diabetes (appendix A3.4). Therefore, pre-pregnancy diabetes was included as an auxiliary variable in the MICE. These variables make the MAR assumption in the MICE plausible. Trace plots to assess stability and convergence of imputation models are shown in appendix A3.5. No clear pattern was observed, and therefore 10 cycles were considered adequate.

4.6. Chapter summary

In this chapter, I have described characteristics of the analysis cohort by their BMI status and ethnicity. The ethnic and socio-economic distribution of children by BMI status varied as expected. Expected differences in the birthweight of children by BMI status were also

observed. Additionally, ethnic groups also varied in their distribution of socio-economic status with a higher proportion of Pakistani children living in the deprived areas. Application of ethnicity-specific BMI values resulted in a much higher proportion of Pakistani children being categorised as overweight and obese.

The next three chapters present the results of univariable and multivariable analyses of primary healthcare use, secondary healthcare use and healthcare costs, respectively.

Chapter 5 Analyses of the relationship between BMI status and Primary healthcare use

This chapter presents the results of the analyses of primary healthcare use in BiB children.

5.1 Introduction

In this chapter, I present the results of the negative binomial regression analyses of the univariable (unadjusted) and multivariable (adjusted) relationships between the exposure (BMI status) and outcome measures of primary healthcare use. Additionally, I present the results of the negative binomial regression analyses of the above-mentioned relationships by ethnic groups. Alongside the tabular presentation of results, summaries are provided highlighting the key findings from the analyses. Graphical representation of the results is presented where it aids the interpretation of results. As discussed in chapter 3 (section 3.6.1.1), three measures of primary healthcare use were modelled separately as outcomes:

1. Primary care consultations
2. GP doctor consultations
3. Primary care prescriptions

Figure 5.1 gives a detailed breakdown of all primary care events by event type (clinical or administrative) and staff member role. Of the 9,397 children in the analysis cohort (chapter 4, section 4.2), 9,304 children had at least one event during the study period. In total, there were 64,567 clinical consultations with doctors or nurses during the study period. These are termed as “Primary care consultations” when presenting results. Out of these “Primary care consultations” 48, 476 were with a doctor. These clinical doctor consultations were also separately analysed and are termed as “GP doctor consultations”. The events where staff role is classified as “Other” (Figure 5.1) were instances when a staff member other than a doctor or a nurse took the appointment. Examples of such events were bookings

over the phone with the administrative staff, or when a child was seen by a healthcare assistant to review a prescription or a test report. As already rationalised in chapter 3 (section 3.6.1.1), appointments that were attended by a doctor or a nurse but were coded as administrative were not included in the analyses. In the BiB dataset, these events were usually when a child visited to receive and review results for a urine or a blood test.

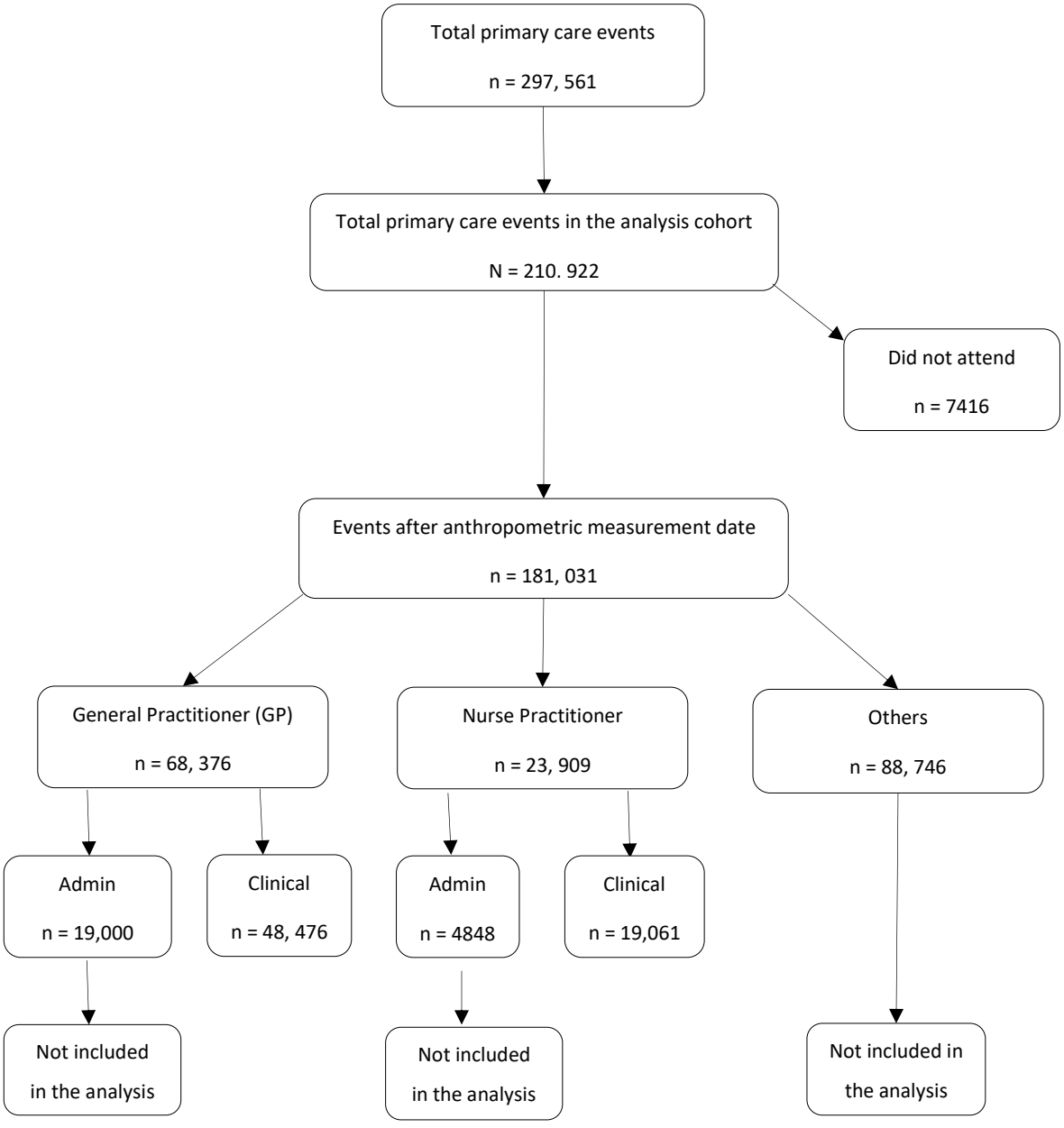

Figure 5.1 *Breakdown of primary care events (up to 3rd October 2019) by event type and staff member roles*

5.2 Descriptive statistics

Table 5.1 reports the distribution of each measure of primary care use by BMI status. Histograms of each outcome measure by BMI categories are given in appendix A4.1**.** All outcome variables were positively (right-tailed) skewed and not normally distributed (Shapiro-wilk test: $p < 0.01$). Therefore, nonparametric Mann-Whitney U tests of difference were undertaken to assess the differences in these count outcomes for underweight, overweight, and obese children compared to normal weight children.

Table 5.1 also reports the means and variances of the counts of outcome variables. None of the outcomes were equidispersed, and therefore negative binomial regression models were used for the univariable and multivariable analyses.

Table 5.1 *Distribution of primary healthcare outcomes by BMI status*

Primary healthcare outcome	Normal weight (7,244)	Underweight (189)	p-value[1]	Overweight (1,028)	p-value[1]	Obese (936)	p-value[1]
Primary care consultations							
Mean (variance)	6.99 (58.69)	9.70 (94.78)		7.16 (63.07)		8.24 (72.19)	
Median (range)	4 (2-8)	6 (2-12)	<0.01	4 (2-9)	0.34	5 (2-10)	< 0.01
GP doctor consultations							
Mean (variance)	5.02 (38.24)	6.85 (56.95)		5.14 (44.24)		5.89 (46.59)	
Median (range)	3 (1-6)	4 (1-9)	<0.01	3 (1-6)	0.93	4 (1-7)	<0.01
Primary care prescriptions							
Mean (variance)	11.55 (303.73)	14.91 (403.08)		11.91 (299.06)		14.03 (390.15)	
Median (range)	7 (2-18)	11 (3-26)	<0.01	7 (3-19)	0.14	10 (3-25)	< 0.01

[1]p-values associated with Mann-Whitney U tests of difference

5.3 Results of statistical analyses

This section presents the results of negative binomial regression models for each outcome of primary care use. As mentioned in Chapter 4 (section 4.5), the number of children with no missing information on covariates (complete cases) was 7,344. Therefore, results of complete case multivariable models and multiple imputed models are presented. All multivariable models were adjusted for ethnicity, birthweight, child sex, maternal age, maternal BMI, gestational age, Index of Multiple Deprivation (IMD) and means-tested benefits. Variance inflation factors (VIF) for all the continuous variables did not detect any multicollinearity among them (appendix A4.2). No significant interactions were observed between the predictor variables, and therefore no interaction terms were included in the adjusted analyses. For analysis of primary care consultations, one observation was found to be influential (appendix A4.3) and had an impact on the significance of regression coefficients. Therefore, analysis was performed after dropping this observation.

5.3.1 Primary care consultations

Table 5.2 presents the predicted rates per 1000 person-years for primary care consultations in each exposure category, along with the incidence rate ratios (IRRs) using normal weight as reference. There was evidence from both unadjusted and adjusted models that being underweight or obese had an influence on the frequency of primary care consultations in children (Table 5.2, Table 5.3). The strength of associations was higher in the unadjusted model and was only slightly attenuated in the adjusted model (Table 5.2, Figure 5.2).

Table 5.3 presents a complete output of the multivariable regression model before (complete case model) and after imputation of missing covariates. Goodness of fit and assessment of linearity assumptions for the complete case model are given in appendix A4.4**.** The goodness of fit diagnostics for the multiple imputed model are given in appendix A4.5. The adjusted rate of consultations in obese children was 1.19 (95% CI: 1.10 – 1.28)

times that of normal weight children ($p < 0.01$). The rate in underweight children was 1.25 times (95% CI: 1.07 – 1.46) that of normal weight children ($p < 0.01$). For overweight children, there was non-significant evidence of a higher rate of consultations. Results of a logistic regression model to assess probability of accessing primary healthcare services by BMI status is given in appendix A4.6.

Table 5.2 *Predicted primary care consultation rates and rate ratios by exposure for univariable and multivariable models.*

BMI category	Unadjusted model		Adjusted model [1]	
	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)
Underweight	1,761	1.38 (1.20-1.59)**	2,127	1.25 (1.07-1.46)**
Normal Weight (Reference)	2,029	1.00	1,694	1.00
Overweight	1,962	1.02 (0.96-1.09)	1,795	1.06 (0.99-1.14)
Obese	2,234	1.19 (1.11-1.27)**	2,012	1.19 (1.10-1.28)**

1. adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

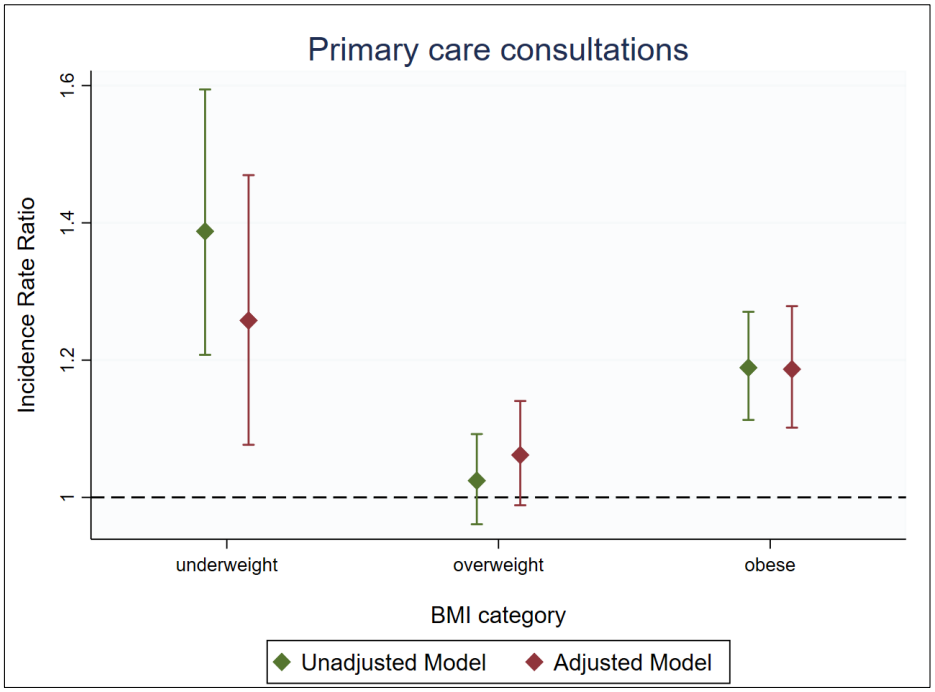

Figure 5.2 *. Incidence rate ratios (reference: normal weight) by BMI status for primary care consultations*

The predicted effect sizes in the multiple imputation model were only slightly attenuated with no change in the statistical significance of these results (Table 5.3). Pakistani children had a significantly higher rate of consultations compared to White British children. Children living in the 20% most deprived areas also showed a higher frequency of consultations (Table 5.3).

Table 5.3 *Output of multivariable negative binomial models of association between BMI status and primary care consultations*

	Adjusted Model (n=7,343)		**Multiply imputed model (n = 9,396)**	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.25 (1.07-1.46)	<0.01	1.23 (1.07-1.41)	<0.01
Overweight	1.06 (0.99-1.14)	0.10	1.06 (0.99-1.13)	0.06
Obese	1.19 (1.10-1.28)	< 0.01	1.19 (1.11-1.27)	<0.01
Ethnicity (Ref: White British)				
Pakistani	1.52 (1.44-1.60)	<0.01	1.49 (1.42-1.57)	<0.01
Other	1.27 (1.18-1.37)	<0.01	1.25 (1.18-1.34)	<0.01
Birthweight	0.99 (0.99-1.00)	0.07	0.99 (0.99-0.99)	0.02
Gestational Age	0.98 (0.96-0.99)	0.01	0.98 (0.97-0.99)	0.02
Child Sex (Ref: Male)				
Female	0.98(0.93-1.02)	0.39	0.99 (0.95-1.03)	0.77
Maternal Age	0.99 (0.99-1.00)	0.21	0.99 (0.99-1.00)	0.28
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.20 (1.05-1.37)	<0.01	1.21 (1.07-1.36)	<0.01
2nd	1.19 (1.04-1.36)	<0.01	1.19 (1.06-1.34)	<0.01
3rd	1.21 (1.06-1.38)	<0.01	1.20 (1.06-1.35)	<0.01
4th	1.13 (0.99-1.30)	0.06	1.14 (1.00-1.29)	0.03
Mother's BMI	1.00 (0.99-1.00)	0.09	1.00 (0.99-1.00)	0.29
Means tested benefits (Ref: Not in receipt)				
In receipt	0.94 (0.89-0.98)	<0.01	0.94 (0.90-0.98)	<0.01

1. Adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate Ratio, CI= Confidence intervals

5.3.2 GP doctor consultations

The direction and strength of association between BMI status and GP doctor consultations was similar to what was predicted for primary care consultations in the previous section. Underweight and obese children had a significantly higher rate of consultations both in the unadjusted and adjusted models (Table 5.4). The strength of association did however attenuate in the multivariable model. Table 5.5 presents the complete output of adjusted model before and after multiple imputation. There was slight attenuation in the effect size for underweight children in the multiple imputed model, nonetheless, obese and underweight children still had significantly higher rates in the multipy imputed model compared to normal weight children (Table 5.5).

The rates of consultations were significantly higher in Pakistani children and children of other ethnicities compared to White British children (Table 5.5). There was no evidence of an association between deprivation and consultation frequency.

Table 5.4 *Predicted GP doctor consultation rates and rate ratios by exposure for univariable and multivariable models*

	Unadjusted model		**Adjusted model [(1)]**	
BMI category	**IR per 1000 person-years**	**IRRs (95% CI)**	**IR per 1000 person-years**	**IRRs (95% CI)**
Underweight	1,655	1.36 (1.16-1.58)**	1,592	1.31 (1.10-1.56)**
Normal Weight (Reference)	1,214	1.00	1,211	1.00
Overweight	1,244	1.02 (0.95-1.09)	1,257	1.03 (0.95 – 1.12)
Obese	1,437	1.18 (1.09-1.27)**	1,429	1.17 (1.08-1.28)**

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

Table 5.5 *Output of multivariable negative binomial models of association between BMI status and GP doctor consultations*

	Adjusted Model (n=7,343)		Multiple imputed model (n = 9,396)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.31 (1.10-1.56)	<0.01	1.24 (1.06-1.44)	<0.01
Overweight	1 (0.95 – 1.12)	0.35	1.05 (0.98-1.13)	0.15
Obese	1.18 (1.09-1.28)	< 0.01	1.18 (1.09-1.27)	<0.01
Ethnicity (Ref: White British)				
Pakistani	1.41 (1.32-1.49)	<0.01	1.38 (1.31-1.46)	<0.01
Other	1.20 (1.11-1.31)	<0.01	1.20 (1.12-1.29)	<0.01
Birthweight	0.99 (0.99-1.00)	0.35	0.99 (0.99-1.00)	0.057
Gestational Age	0.97 (0.95-0.99)	<0.01	0.98 (0.96-0.99)	0.01
Child Sex (Ref: Male)				
Female	0.98 (0.93-1.03)	0.62	1.99 (0.95-1.03)	0.78
Maternal Age	0.99 (0.99-1.00)	0.50	0.99 (0.99-1.00)	0.57
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.11 (0.95-1.28)	0.16	1.12 (0.98-1.27)	0.08
2nd	1.08 (0.93-1.26)	0.26	1.08 (0.94-1.23)	0.24
3rd	1.14 (0.98-1.32)	0.07	1.13 (0.99-1.29)	0.05
4th	1.03 (0.88-1.20)	0.68	1.03 (0.89-1.18)	0.65
Mother's BMI	1.00 (0.99-1.00)	0.15	1.00 (0.99-1.00)	0.13
Means tested benefits (Ref: Not in receipt)				
In receipt	0.92 (0.87-0.97)	<0.01	0.93 (0.88-0.97)	<0.01

1. Adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate Ratio, CI= Confidence intervals

5.3.3 Primary care prescriptions

Table 5.6 presents the predicted rates per 1000 person-years of primary care prescriptions in BMI categories for unadjusted and adjusted models. There was significant evidence in both models that obese children had a higher rate of prescriptions. The predicted rate for obese children was 20% higher compared to normal weight children in the multivariable model (Table 5.6). Significant evidence of a higher rate in underweight children compared to normal weight children was predicted in the unadjusted model. However, after adjusting for covariates this higher rate was not statistically significant (Table 5.6, Figure 5.3).

Table 5.6 *Predicted prescription rates and rate ratios by exposure for univariable and multivariable models.*

BMI category	Univariable model		Multivariable model [(1)]	
	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)
Underweight	3,658	1.30 (1.09-1.55)**	3,261	1.15 (0.95-1.41)
Normal Weight (Reference)	2,798	1.00	2,814	1.00
Overweight	2,883	1.03 (0.95-1.11)	3,069	1.09 (0.99-1.19)
Obese	3,426	1.22 (1.12-1.33)**	3,384	1.20 (1.09-1.31)**

1. Adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

Table 5.7 presents the outputs of complete case and multiple imputed models for primary care prescriptions. There was no significant difference in the effect sizes by exposure categories between the two models.

There was little to no difference in the effect sizes of covariates between the two models. Pakistani children had a significantly higher rate of prescriptions (IRR 1.87, 95% CI: 1.75-2.00) compared to White British children. Children in the other ethnicity group also had a significantly higher prescription rate (Table 5.7).

There was no evidence of a statistically significant association between deprivation and rate of prescriptions in the complete case model. However, in the multiple imputed model, children living in the 20% most deprived areas were predicted to have a significantly higher prescription rate than the children living in the 20% least deprived areas (IRR 1.17, 95% CI: 1.00-1.36). Children whose parents were in receipt of means tested benefits had a lower prescription rate (IRR: 0.94, 95% CI: 0.89-0.99).

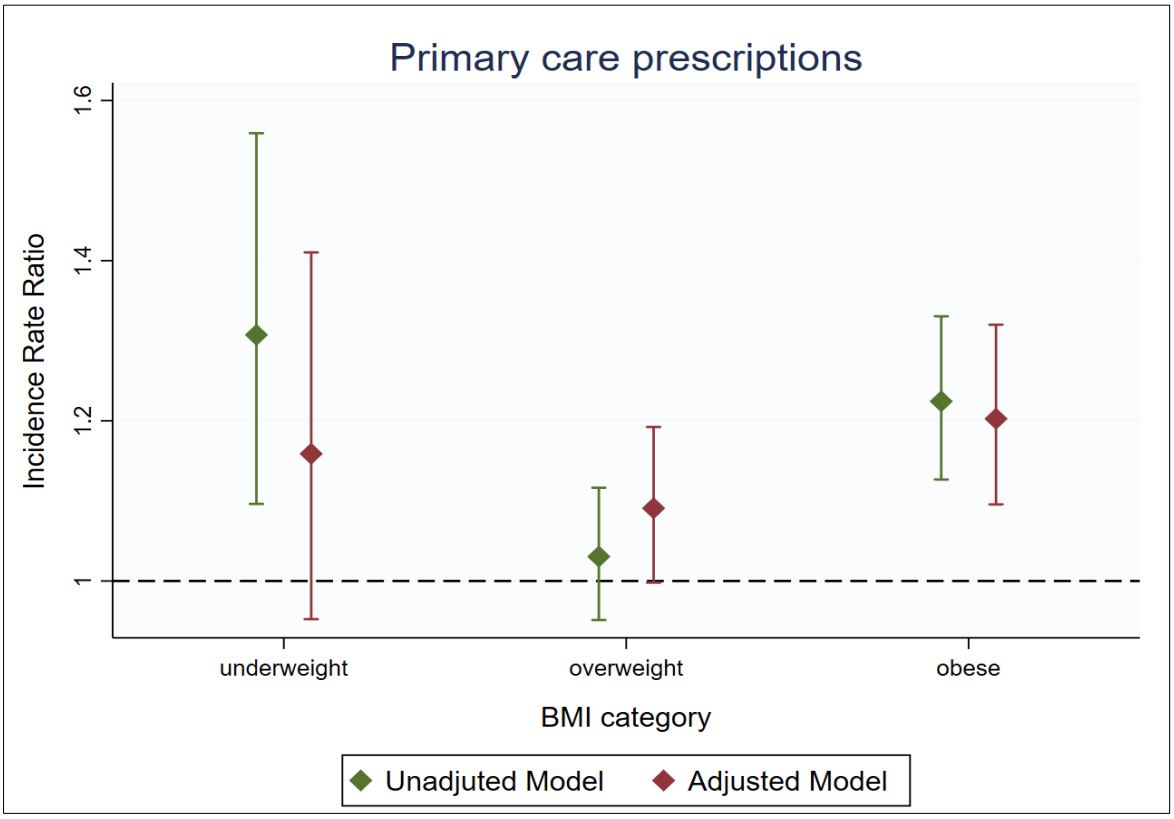

Figure 5.3 *Incidence rate ratios (reference: normal weight) by BMI status for primary care prescriptions*

Table 5.7 *Output of multivariable negative binomial models of association between BMI status and primary care prescriptions*

	Adjusted Model (n=7,344)		Multiple imputed model (n = 9,397)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.15 (0.95-1.41)	0.14	1.09 (0.91-1.29)	0.32
Overweight	1.09 (0.99-1.19)	0.05	1.09 (1.01-1.18)	0.02
Obese	1.20 (1.09-1.31)	<0.01	1.20 (1.10-1.30)	<0.01
Ethnicity (Ref: White British)				
Pakistani	1.87 (1.75-2.00)	<0.01	1.82 (1.72-1.94)	<0.01
Other	1.64 (1.50-1.79)	<0.01	1.58 (1.46-1.71)	<0.01
Birthweight	0.99 (0.99-0.99)	0.01	0.99 (0.99-0.99)	<0.01
Gestational Age	0.97 (0.96-0.99)	0.03	0.98 (0.96-0.99)	0.02
Child Sex (Ref: Male)				
Female	0.90 (0.85-0.95)	<0.01	0.93 (0.88-0.98)	<0.01
Maternal Age	1.00 (1.00-1.01)	<0.01	1.01 (1.00-1.01)	<0.01
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.12 (0.94-1.32)	0.17	1.17 (1.00-1.36)	0.03
2nd	1.10 (0.93-1.30)	0.23	1.13 (0.97-1.32)	0.09
3rd	1.09 (0.92-1.29)	0.27	1.13 (0.97-1.31)	0.09
4th	1.03 (0.87-1.22)	0.71	1.03 (0.88-1.20)	0.67
Mother's BMI	1.00 (1.00-1.01)	<0.01	1.00 (1.00-1.01)	0.01
Means tested benefits (Ref: Not in receipt)				
In receipt	0.94 (0.89-0.99)	0.04	0.93 (0.87-0.98)	0.01

1. Adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate Ratio, CI= Confidence intervals

5.4 Primary healthcare use by ethnicity

Table 5.8 presents the incidence rates per 1000 person-years by ethnicity for each outcome measure of primary care use. These incidence rates and associated IRRs by BMI status are predicted after performing separate multivariable regression models for each ethnic group. Complete outputs of these models are reported in appendix A4.7. As reported in the previous section, the IRRs for Pakistani children and children of other ethnicities were significantly higher than White British children for all measures of primary care use. Therefore, Pakistani children had higher predicted rates of consultations and prescriptions in each BMI category than the White British children. A similar trend was observed for children in the Other ethnic group (Table 5.8). Looking at the association of BMI status with consultation frequency within each ethnic group, obese children of all ethnic groups had a significantly higher rate of primary care consultations compared to their respective normal weight counterparts (Table 5.8). Overweight Pakistani children also had a significantly higher rate compared to normal weight Pakistani children (Figure 5.4).

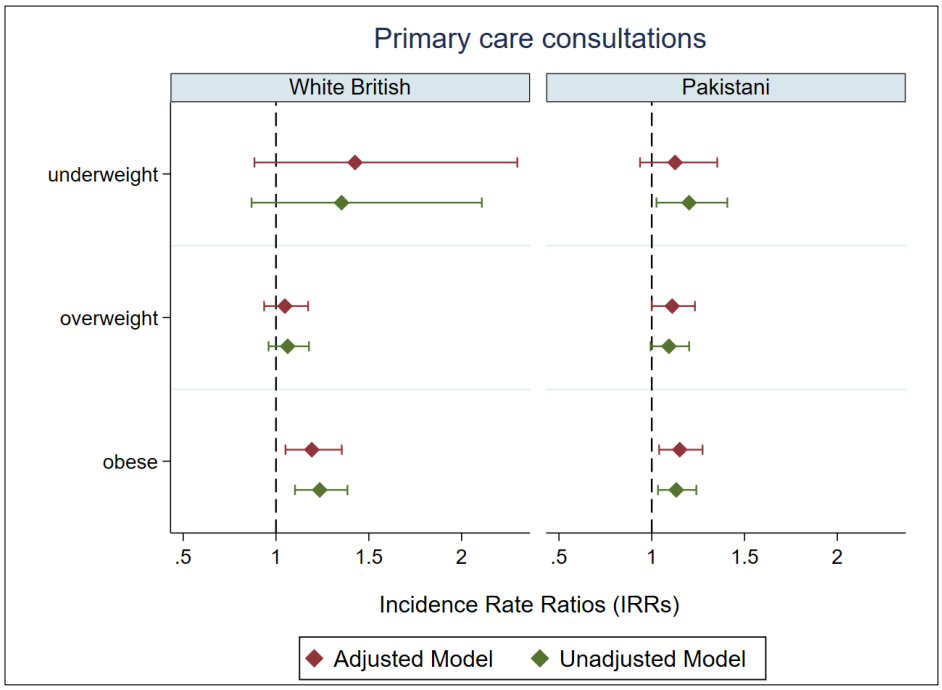

Figure 5.4 *Incidence rate ratios (reference: normal weight) for consultations by BMI status for Pakistani and White British children*

The significantly higher rate of consultations previously reported for underweight children in the analysis cohort (section 5.3.1) was only observed for children in the Other ethnic groups (Table 5.8).

Table 5.8 *Estimated incidence rates per 1000 person-years and incidence rate ratios by body mass index (BMI), stratified by ethnicity.*

BMI category	White British (3,469)		Pakistani (4,346)		Other (1,323)	
	IR per 1000 person -years	IRRs (95% CI)	IR per 1000 person -years	IRRs (95% CI)	IR per 1000 person -years	IRRs (95% CI)
Primary care consultations						
Underweight	1,876	1.43 (0.89-2.32)	2,255	1.12 (0.93-1.34)	2,577	1.53 (1.09-2.13) *
Normal Weight (Reference)	1,303	1.00	2,010	1.00	1,683	1.00
Overweight	1,371	1.05 (0.93-1.17)	2,240	1.11 (1.00-1.23) *	1,520	0.90 (0.73-1.10)
Obese	1,555	1.19 (1.05-1.35) **	2,323	1.15 (1.04-1.27) **	2,218	1.31 (1.06-1.63) *
GP doctor appointments						
Underweight	1,526	1.54 (0.93-2.55)	1,572	1.13 (0.91-1.40)	2,051	1.69 (1.16-2.46)**
Normal Weight (Reference)	989	1.00	1,386	1.00	1,211	1.00
Overweight	965	0.97 (0.86-1.10)	1,631	1.17 (1.03-1.32)*	973	0.80 (0.63-1.01)
Obese	1,154	1.16 (1.02-1.33)*	1,615	1.16 (1.03-1.30)*	1,551	1.28 (1.00-1.63)*
Primary care prescriptions						
Underweight	2,285	1.24 (0.67-2.30)	3,900	1.12 (0.89-1.40)	3,908	1.26 (0.82-1.95)
Normal Weight (Reference)	1,833	1.00	3,481	1.00	3,077	1.00
Overweight	2,021	1.10 (0.95-1.27)	3,894	1.11 (0.98-1.27)	3,182	1.03 (0.80-1.33)
Obese	2,056	1.12 (0.95-1.31)	4,421	1.27 (1.12-1.43) **	4,165	1.35 (1.02-1.78) *

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI.
2. IRR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p<0.01, *p<0.05

The rates of prescriptions in obese children, which were reported to be significantly higher in the whole cohort (section 5.3.3), were significantly higher only in the Pakistani and children of Other ethnicities compared to their respective normal weight counterparts (Table 5.8). An obese Pakistani child on average was 1.27 (95% CI: 1.12 – 1.43) times more likely to be given a prescription compared to a normal weight Pakistani child, whereas an obese White British child was 1.12 (95% CI: 0.95 – 1.31) times more likely to be given a prescription, however the association was not significant (Figure 5.5).

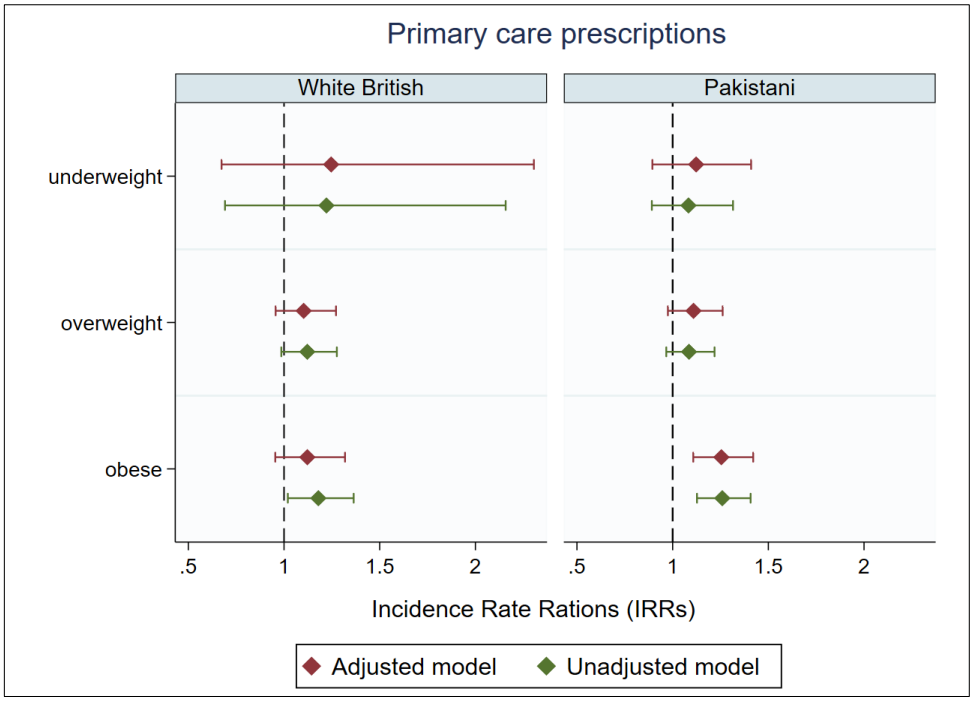

Figure 5.5 *Incidence rate ratios (reference: normal weight) of prescriptions by BMI status for Pakistani and White British children*

5.4.1 Ethnicity-specific BMI values

Table 5.9 reports the results by BMI categories (reference: normal weight) from unadjusted and adjusted analyses of primary care use in Pakistani children after application of ethnicity-specific BMI values. The association of obesity with primary care consultations was attenuated but remained significant (IRR 1.12, 95% CI: 1.04-1.22). The adjusted IRR for underweight children decreased (IRR 0.92, 95% CI: 0.50 – 1.70) but was not significant and

had a large confidence interval due to a very small number of children in the category (n = 12). Additionally, the association of obesity with prescriptions was also attenuated (IRR 1.19, 95% CI: 1.07 – 1.31). The adjusted IRR for underweight children increased but was not significant with a large confidence interval (IRR 1.35, 95% CI: 0.59-3.0) due to the small group size.

Table 5.9 *Results of negative binomial models of association between Pakistani children's BMI status and primary care use after application of ethnicity-specific BMI values**

Ethnicity-specific BMI category	Unadjusted model		Adjusted model (1)	
	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)
Primary care consultations				
Underweight	1,761	0.86 (0.49-1.51)	1,862	0.92 (0.50-1.68)
Normal Weight (Reference)	2,029	1.00	2,026	1.00
Overweight	1,962	0.96 (0.90-1.03)	1,999	0.98 (0.91-1.06)
Obese	2,234	1.10 (1.02-1.18)**	2,288	1.12 (1.04-1.22)**
GP doctor consultations				
Underweight	898	0.64 (0.32-1.24)	946	0.67 (0.32-1.39)
Normal Weight (Reference)	1,403	1.00	1,400	1.00
Overweight	1,360	0.96 (0.89-1.05)	1,387	0.99 (0.90-1.08)
Obese	1,576	1.12 (1.03-1.21)**	1,621	1.15 (1.05-1.26)**
Primary care prescriptions				
Underweight	4,020	1.15 (0.59-2.27)	4,649	1.33 (0.63-2.79)
Normal Weight (Reference)	3,472	1.00	3,493	1.00
Overweight	3,542	1.01 (0.93-1.11)	3,564	1.02 (0.92-1.12)
Obese	4,141	1.19 (1.09-1.30)**	4,155	1.19 (1.07-1.31)**

1. *Pakistani boys: +1.12 kg/m2, Pakistani girls: 1.07 kg/m2
2. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
3. IRR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
4. **p<0.01, *p<0.05

5.5 Chapter summary

This chapter has explored the relationship between BMI status and use of primary healthcare services. The findings in this chapter highlight the relationship between obesity and ill-health during childhood, assessed through analysing the primary healthcare consultation frequency and prescription rates. There is also evidence from the findings of an adverse relationship between being underweight and increased rates of healthcare use during childhood. Additionally, rates of primary healthcare use were significantly higher in Pakistani children compared to White British children, independent of their BMI status.

Chapter 6 Analyses of the relationship between BMI status and secondary healthcare use

This chapter presents the results of the analyses of secondary healthcare use in BiB children.

6.1 Introduction

In this chapter, results of the univariable (unadjusted) and multivariable (adjusted) relationship between the exposure and outcome measures of secondary healthcare use are presented. Additionally, results of the impact of ethnicity on the above-mentioned relationship between the exposure and outcomes are also presented. In addition to tabular presentations, text summaries highlight the key findings. As discussed in chapter 3 (section 3.6.1.2), two measures of secondary healthcare use were modelled separately as outcomes:

1. Hospital admission spells
2. Accidents & Emergency (A&E) visits

Figure 6.1 gives a breakdown of all secondary healthcare events by event type (hospital admission or A&E visit). Of the 9,397 children in the analysis cohort, 1,710 children had at least one admission during the study period. A comparison of these children with those without any admission on key characteristics is presented in table 6.1. As explained in detail in chapter 3 (section 3.6.2), for these children with at least one admission, I created counts of hospital Length of Stay (LoS). Results of a separate analysis with length of stay as an outcome are also presented. In total, there were 2,892 admissions spells during the study period in the analysis cohort. There were 4,635 children in the analysis cohort who had at least one A&E visit during the study period, with a total of 9,021 visits (Figure 6.1).

Table 6.1 *Comparison of key characteristic between children with at least one admission and rest of the analysis cohort*

Characteristics	At least one admission	Rest of the cohort	P-value[a]
Total	1710	7687	
Mean BMI z-score	0.16	0.20	0.22
Child sex			<0.01
Boys	982 (57.43%)	3849 (50.07%)	
Girls	728 (42.57%)	3838 (49.93%)	
BMI category			<0.01
Underweight	50 (2.92%)	139 (1.81%)	
Healthy weight	1296 (75.79%)	5948 (77.38%)	
Overweight	172 (10.06%)	856 (11.14%)	
Obese	192 (11.23%)	744 (9.68%)	
Ethnicity			<0.01
White British	571 (34.50%)	2898 (38.73%)	
Pakistani	877 (52.99%)	3469 (46.36%)	
Others	207 (12.51%)	1116 (14.91%)	
Missing	55 (3.22%)	204 (2.65%)	
Birthweight			0.12
Normal birthweight	1517 (88.71%)	6909 (89.88%)	
Low birthweight	161 (9.42%)	635 (8.26%)	
Missing	32 (1.87%)	143 (1.86%)	

*****Percentages are given by column
[A]p-value for a chi-square test
BMI: body mass index

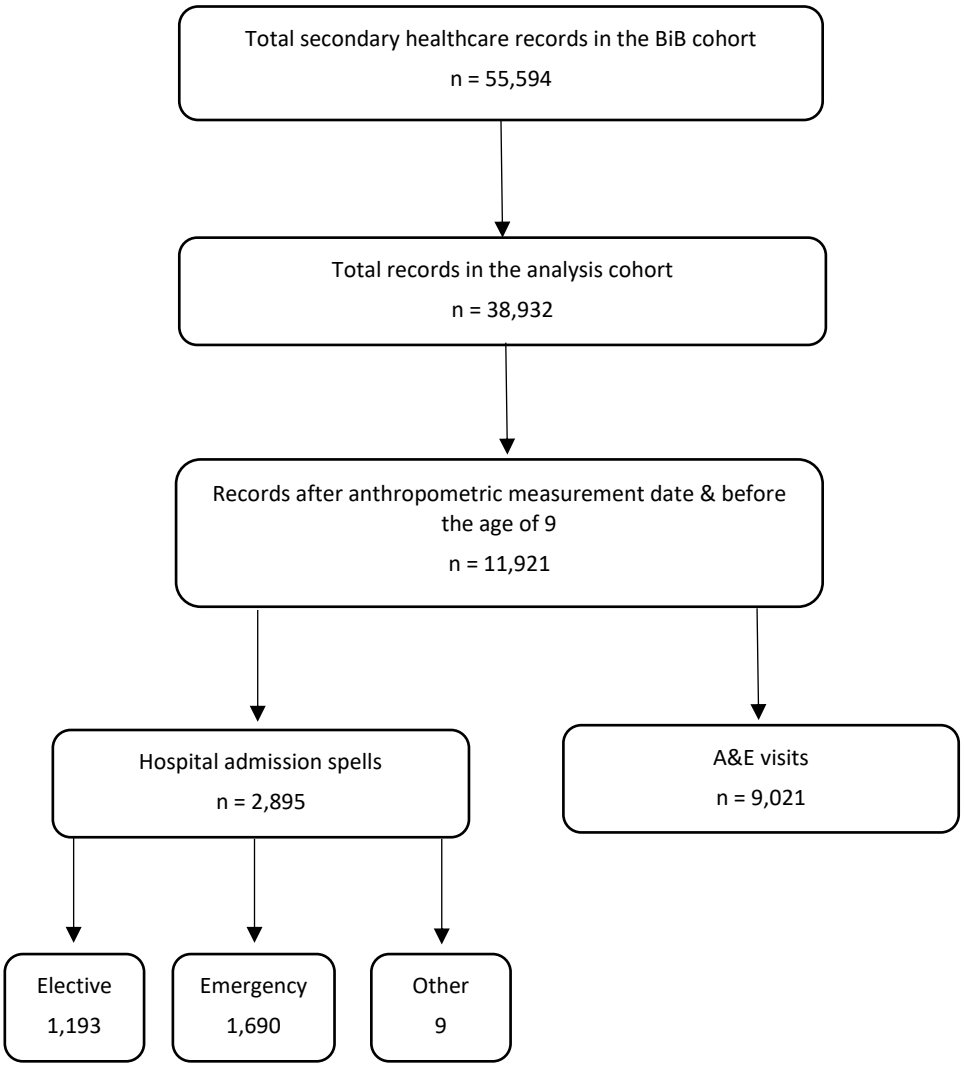

Figure 6.1 *Breakdown of secondary care events (up to July 2020) by event type*

6.2 Descriptive statistics

Distribution of hospital admissions, hospital LoS and A&E visits by BMI categories is given in table 6.1. Histograms for each outcome measure by BMI category are given in appendix A5.1**.** All outcome variables were not normally distributed (Shapiro-Wilk test: $p < 0.01$, appendix A 5.2) and had a positive (right-tailed) skew. Therefore, Mann-Whitney U tests of difference were undertaken to assess the difference in outcomes for underweight, overweight, and obese children compared to normal weight children. Table 6.2 also reports the means and variances of the outcomes. All the outcomes were over dispersed, and therefore negative binomial regression models were considered the best fit for the unadjusted and adjusted analyses.

Table 6.2 *Distribution of secondary healthcare outcomes by BMI status*

Primary healthcare outcome	Normal weight (7,244)	Underweight (189)	p-value[1]	Overweight (1,028)	p-value[1]	Obese (936)	p-value[1]
Hospital admissions							
Mean (variance)	0.30 (2.51)	0.35 (0.49)		0.31 (4.69)		0.32 (0.70)	
Median (range)	0-59	0-5	<0.01	0-61	0.31	0-10	0.04
Hospital Length of Stay							
Mean (variance)	1.56 (23.5)	1.64 (15.45)		1.48 (12.71)		1.49 (11.05)	
Median (range)	0-108	0-24	0.78	0-39	0.88	0-29	0.48
A & E visits							
Mean (variance)	0.94 (2.08)	1.08 (2.01)		0.91 (1.72)		1.10 (2.45)	
Median (range)	0-19	0-7	0.06	0-9	0.81	0-13	<0.01

[1]p-values associated with Mann-Whitney U tests of difference

6.3 Results of statistical analyses

This section presents the results of unadjusted and adjusted negative binomial regression models for hospital admissions, hospital LoS and A&E visits. Results of both complete case (n = 7,344) and multiple imputed models (n = 9,397) are presented. All multivariable models were adjusted for ethnicity, birthweight, child sex, gestational age, maternal BMI, maternal age, Index of Multiple Deprivation (IMD) and means-tested benefits. No significant interactions were observed between the predictor variables, and therefore no interaction terms were included in the adjusted analyses.

6.3.1 Zero-inflation

As discussed in chapter 3 (section 3.8.3.3), due to the presence of excess zeros, I considered the possibility of using zero-inflated negative binomial regression models to predict the variation in the outcomes of hospital admissions and A&E visits. However, none of these models performed better than the standard negative binomial models based on the AIC/BIC criteria and results of the Vuoung test. Therefore, results for each outcome in this chapter are based on modelling using the standard negative binomial regression models.

6.3.2 Analysis of hospital admissions

Table 6.3 presents the predicted rates of hospital admissions per 1000 person-years in each BMI category, along with the Incidence Rate Ratios (IRRs) using normal weight as the reference category.

Table 6.3 *Predicted hospital admission rates and rate ratios by exposure for univariable and multivariable model*

	Univariable model		Multivariable model [1]	
BMI category	**IR per 1000 person-years**	**IRRs (95% CI)**	**IR per 1000 person-years**	**IRRs (95% CI)**
Underweight	86	1.18 (0.80-1.73)	83	1.14 (0.73-1.76)
Normal Weight (Reference)	73	1.00	72	1.00
Overweight	75	1.02 (0.85-1.22)	70	0.97 (0.78-1.19)
Obese	79	1.08 (0.89-1.30)	83	1.15 (0.93-1.42)

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

The rates of hospital admissions were higher in underweight and obese children in the unadjusted and adjusted models, however the observed associations were not significant (Table 6.3). Table 6.4 presents the complete output of the multiple regression models before and after imputation of missing covariates.

Table 6.4 *Output of multivariable negative binomial models of association between BMI status and hospital admissions*

	Adjusted Model (n=7,344)		Multiple imputed model (n = 9,397)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.14 (0.73-1.76)	0.55	1.09 (0.74-1.61)	0.65
Overweight	0.97 (0.78-1.19)	0.76	1.06 (0.88-1.27)	0.49
Obese	1.15 (0.93-1.42)	0.21	1.07 (0.88-1.30)	0.46
Ethnicity (Ref: White British)				
Pakistani	1.49 (1.28-1.74)	<0.01	1.33 (1.16-1.53)	<0.01
Other	1.11 (0.90-1.36)	0.98	0.95 (0.79-1.15)	0.64
Birthweight	0.99 (0.99-0.99)	0.01	0.99 (0.99-1.00)	0.21
Gestational Age	1.01 (0.97-1.05)	0.53	0.96 (0.92-1.00)	0.05
Child Sex (Ref: Male)				
Female	0.79 (0.70-0.90)	<0.01	0.76 (0.67-0.85)	<0.01
Maternal Age	0.97 (0.96-0.99)	<0.01	0.98 (0.97-0.99)	<0.01
Mother's BMI	1.00 (0.96 –1.01)	0.38	1.00 (0.99-1.01)	0.36
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.54 (0.99-2.40)	0.05	1.72 (1.16-2.56)	<0.01
2nd	1.72 (1.10-2.68)	0.01	1.83 (1.23-2.71)	<0.01
3rd	1.85 (1.19-2.89)	< 0.01	1.91 (1.29-2.84)	<0.01
4th	1.74 (1.10-2.75)	0.01	1.70 (1.11-2.59)	0.01
Means tested benefits (Ref: Not in receipt)				
In receipt	0.98 (0.86-1.12)	0.86	0.94 (0.82-1.08)	0.41

1. adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate Ratio, CI= Confidence intervals

There was no significant impact of missing data on parameter estimates of exposure categories as shown by the output in table 6.4. Pakistani children had a significantly higher rate of admissions compared to White British children both in the complete case and multiple imputed model (Table 6.4). In comparison to children living in the 20% least

deprived areas, children in all other IMD categories had a significantly higher rate of hospital admissions.

Table 6.5 reports the odds ratios (ORs) for univariable and multivariable logistic regression models by exposure predicting the probability of at least one hospital admission. A complete output of the multivariable logistic regression model is given in appendix A5.3. Although the probability of being admitted was predicted to be higher in underweight and obese children, the associations were non-significant, with the only exception being the unadjusted odds in the underweight group (Table 6.5).

Table 6.5 *Predicted odds of being admitted to the hospital by exposure for univariable and multivariable model*

	Univariable model	**Multivariable model (1)**
BMI category	**ORs (95% CI)**	**ORs (95% CI)**
Underweight	1.65 (1.18-2.29)**	1.46 (0.99-2.15)
Normal Weight (Reference)	1.00	1.00
Overweight	0.92 (0.77-1.09)	0.95 (0.78-1.16)
Obese	1.18 (0.99-1.40)	1.07 (0.88-1.31)

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. ORs = Odds Ratios, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

Pakistani children had significantly higher odds of being admitted to the hospital compared to their White British counterparts (IRR 1.24, 95% CI 1.07-1.43, appendix A5.3). In reference to children living in the 20% least deprived areas of Bradford, children in the 1st (20% most deprived, OR 1.71, 95% CI 1.11-2.62), 2nd (OR 1.69. 95% CI 1.10-2.60) and 3rd (OR 1.76, 95% CI: 1.15-2.70) categories of IMD had significantly higher odds of being admitted to the hospital (appendix A5.3).

The predicted rates of bed days (hospital LoS) and associated IRRs (reference: normal weight) by BMI categories for unadjusted and adjusted models are given in table 6.6. There was no evidence of an association between BMI status and number of days a child was in the hospital. A complete output of the complete case and multiple imputed models for hospital LoS is given in appendix A5.4.

Table 6.6 *Predicted number of bed days per 1000 person-years and IRRS by exposure for univariable and multivariable analyses*

BMI category	Univariable model		Multivariable model [(1)]	
	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)
Underweight	394	1.04 (0.63-1.70)	390	1.04 (0.59-1.84)
Normal Weight (Reference)	377	1.00	373	1.00
Overweight	359	0.95 (0.71-1.25)	388	1.04 (0.76-1.41)
Obese	365	0.96 (0.74-1.26)	375	1.00 (0.74-1.36)

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

6.3.3 Accident and Emergency (A&E) visits

Table 6.7 reports the predicted rates per 1000 person-years and associated IRRs by BMI status for A&E visits in unadjusted and adjusted models. There was significant evidence in both models that obese children had a higher incidence rate of A&E visits compared to the normal weight children (Figure 6.2). Obese children were 1.17 (95% CI: 1.05 – 1.30) times more likely to have an A&E visit compared to normal weight children. The higher rate for underweight children was not statistically significantly in both unadjusted and adjusted models (Table 6.7, Figure 6.2).

Table 6.7 *Predicted incidence rate per 1000 person-years & IRRs for A&E visits by exposure categories*

BMI category	Univariable model		Multivariable model [1]	
	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)
Underweight	26	1.16 (0.95-1.41)	25	1.11 (0.88-1.39)
Normal Weight (Reference)	22	1.00	22	1.00
Overweight	22	0.97 (0.88-1.06)	22	1.00 (0.89-1.11)
Obese	26	1.17 (1.06-1.28)	26	1.17 (1.05-1.30)**

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
3. **p < 0.01, *p < 0.05

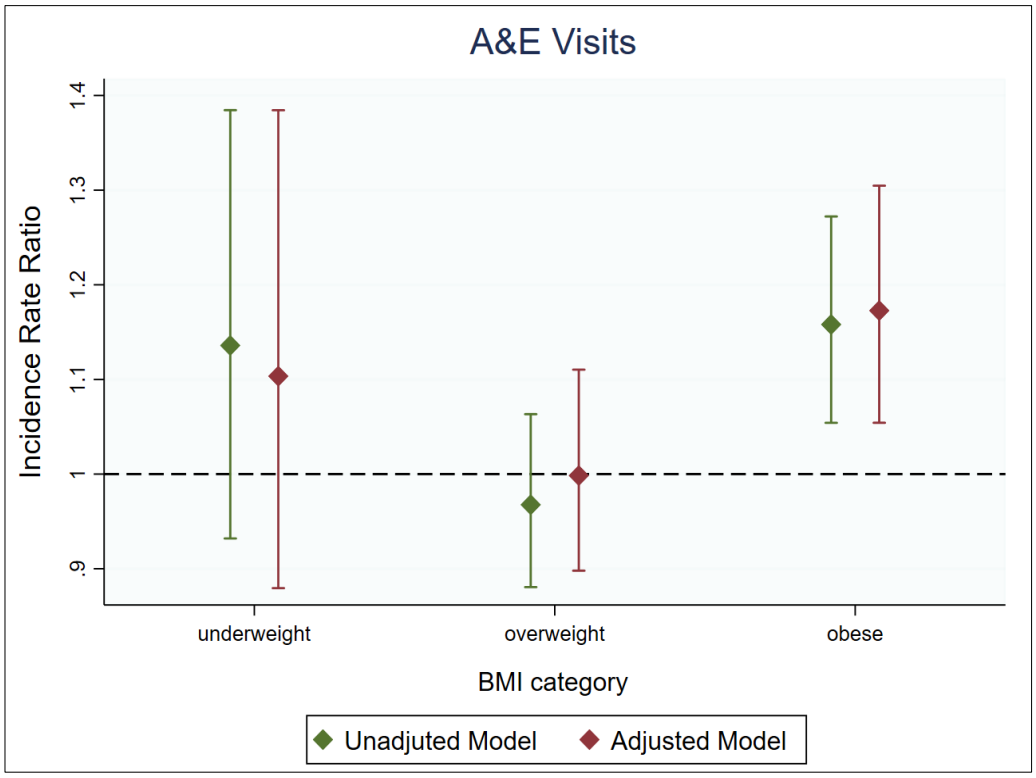

Figure 6.2 *Incidence rate ratios (reference: normal weight) by BMI status for A&E visits*

Table 6.8 presents the total output of complete case and multiple imputed model of A&E visits. There was no significant impact of missing data on the parameter estimates of exposure and covariates. Pakistani children were significantly more likely to have an A&E visit (IRR 1.38, 95% CI 1.27-1.48) compared to White British children. There was no evidence

of an association with the children in the Other ethnicity group. There was evidence of a strong association between area deprivation (IMDs) and frequency of A&E visits. In reference to the children living in the 20% least deprived areas of Bradford, children in all the other four categories of IMDs were significantly more likely to have an A&E visit (Table 6.8). A complete output of the multivariable logistic regression model for A&E visits is given in appendix A5.6.

Table 6.8 *Negative Binomial models of the association between children's BMI weight categories and outcome of A & E visits*

	Adjusted Model (n=7,344)		Multiple imputed model (n = 9,397)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.11 (0.88-1.38)	0.35	1.08 (0.87-1.34)	0.46
Overweight	1.00 (0.89-1.11)	0.99	0.97 (0.88-1.08)	0.65
Obese	1.17 (1.05-1.30)	<0.01	1.16 (1.05-1.29)	<0.01
Ethnicity (Ref: White British)				
Pakistani	1.38 (1.27-1.49)	<0.01	1.36 (1.26-1.46)	<0.01
Other	1.06 (0.95-1.19)	0.23	1.07 (0.97-1.19)	0.15
Birthweight	0.99 (0.99-1.00)	0.99	0.99 (0.99-1.00)	0.55
Gestational Age	0.98 (0.96-1.00)	0.25	0.99 (0.97-1.01)	0.34
Child Sex (Ref: Male)				
Female	0.78 (0.73-0.84)	<0.01	0.80 (0.75-0.85)	<0.01
Maternal Age	0.98 (0.97-0.99)	<0.01	0.98 (0.97-0.99)	<0.01
Mother's BMI	1.00 (1.00 –1.01)	<0.01	1.01 (1.00-1.01)	<0.01
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.68 (1.33-2.13)	<0.01	1.67 (1.33-2.09)	<0.01
2nd	1.88 (1.49-2.38)	<0.01	1.85 (1.47-2.31)	<0.01
3rd	1.82 (1.44-2.30)	<0.01	1.81 (1.45-2.27)	<0.01
4th	1.47 (1.15-1.88)	<0.01	1.44 (1.14-1.82)	<0.01
Means tested benefits (Ref: Not in receipt)				
In receipt	1.03 (0.96-1.10)	0.31	1.05 (0.98 – 1.12)	0.12

1. adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate Ratio, CI= Confidence intervals

6.4. Secondary healthcare use by ethnicity

Table 6.9 reports the incidence rates (IRs) per 1000 person-years by ethnicity for hospital admissions, hospital LoS, and A&E visits. These IRs and associated IRRs are predicted after performing separate multivariable regression models for each outcome within each ethnic group. Complete outputs of these models are given in appendix A5.5. As reported in the previous section, the rates of admissions and A&E visits for Pakistani children were significantly higher compared to White British children. Therefore, Pakistani children had higher predicted rates of hospital admissions and A&E visits within each BMI category, with the only exception being the predicted rate of hospital admissions in the underweight White British children (Table 6.9, Figure 6.3).

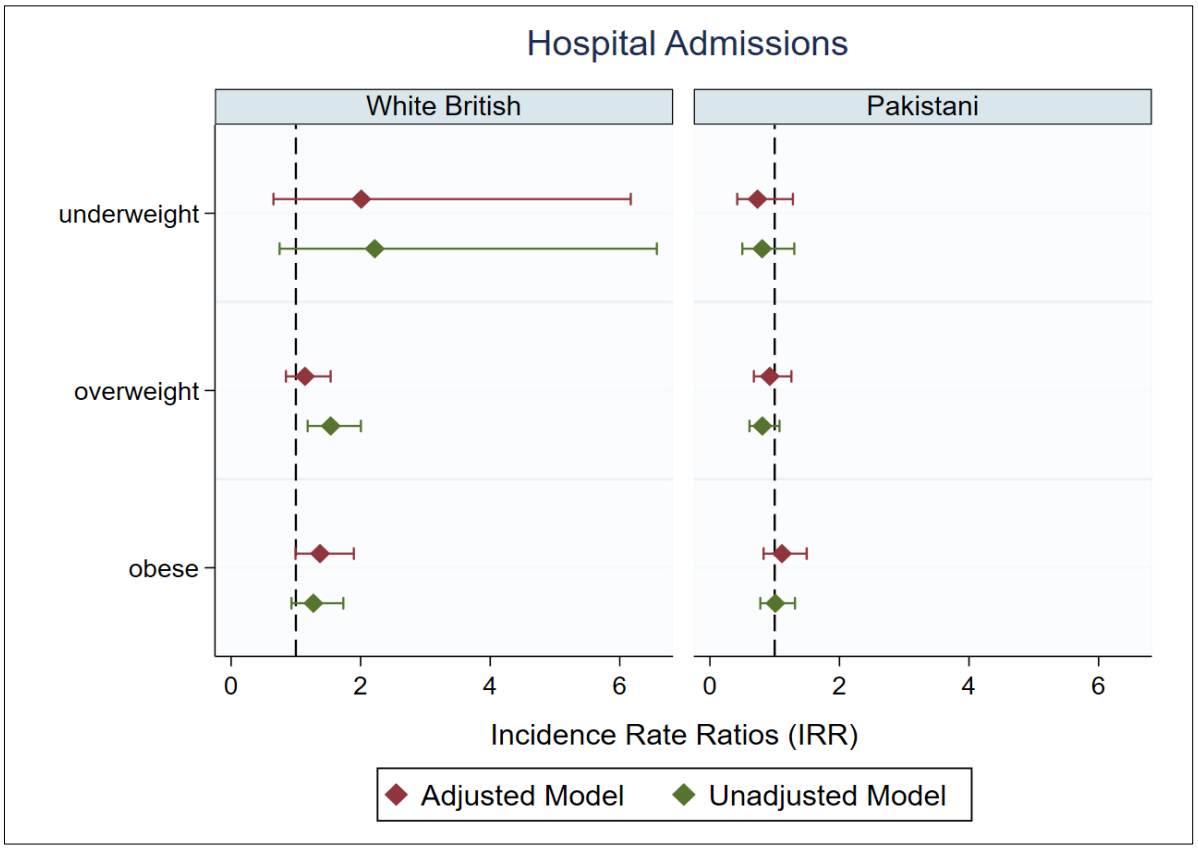

Figure 6.3 *Incidence rate ratios (reference: normal weight) for hospital admissions by BMI status for Pakistani and White British children*

Table 6.9 *Estimated incidence rates per 1000 person-years and incidence rate ratios by body mass index (BMI), stratified by ethnicity*

BMI category	White British (3,469)		Pakistani (4,346)		Other (1,323)	
	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)	IR per 1000 person-years	IRRs (95% CI)
Hospital Admissions						
Underweight	110	2.00 (0.65-6.17)	65	0.74 (0.42-1.27)	147	2.28 (0.98-5.71)
Normal Weight (Reference)	55	1.00	88	1.00	64	1.00
Overweight	63	1.14 (0.84-1.53)	82	0.93 (0.68-1.27)	35	0.54 (0.27-1.08)
Obese	76	1.37 (0.99-1.89)	99	1.12 (0.83 – 1.51)	52	0.81 (0.40-1.67)
Hospital length of stay						
Underweight	138	0.47 (0.75-2.97)	558	1.32 (0.66-2.63)	187	0.54 (0.13-2.12)
Normal Weight (Reference)	291	1.00	422	1.00	345	1.00
Overweight	398	1.36 (0.82-2.26)	385	0.91 (0.59-1.39)	471	1.36 (0.40-4.54)
Obese	295	1.01 (0.58-1.74)	423	1.00 (0.67-1.49)	575	1.66 (0.60-4.56)
Accidents & Emergency visits						
Underweight	177	0.96 (0.47-1.99)	281	1.03 (0.78-1.35)	263	1.31 (0.79-2.18)
Normal Weight (Reference)	183	1.00	272	1.00	199	1.00
Overweight	204	1.11 (0.95-1.31)	253	0.92 (0.79-1.08)	171	0.85 (0.62-1.17)
Obese	213	1.16 (0.97-1.39)	311	1.14 (0.98-1.32)	271	1.35 (0.99-1.84)

1. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals

Looking at the association of BMI status with admission rates within each ethnic group, obese children had a higher rate of admissions compared to their normal weight counterparts, however none of these associations were significant (Table 6.9).

For A&E visits, there was only weak evidence within each ethnic group that obese children had a higher episode rate when compared with normal weight children (Table 6.9, Figure 6.4). There was no evidence of significantly higher episode rate in underweight and overweight children within each ethnic group when compared with normal weight children.

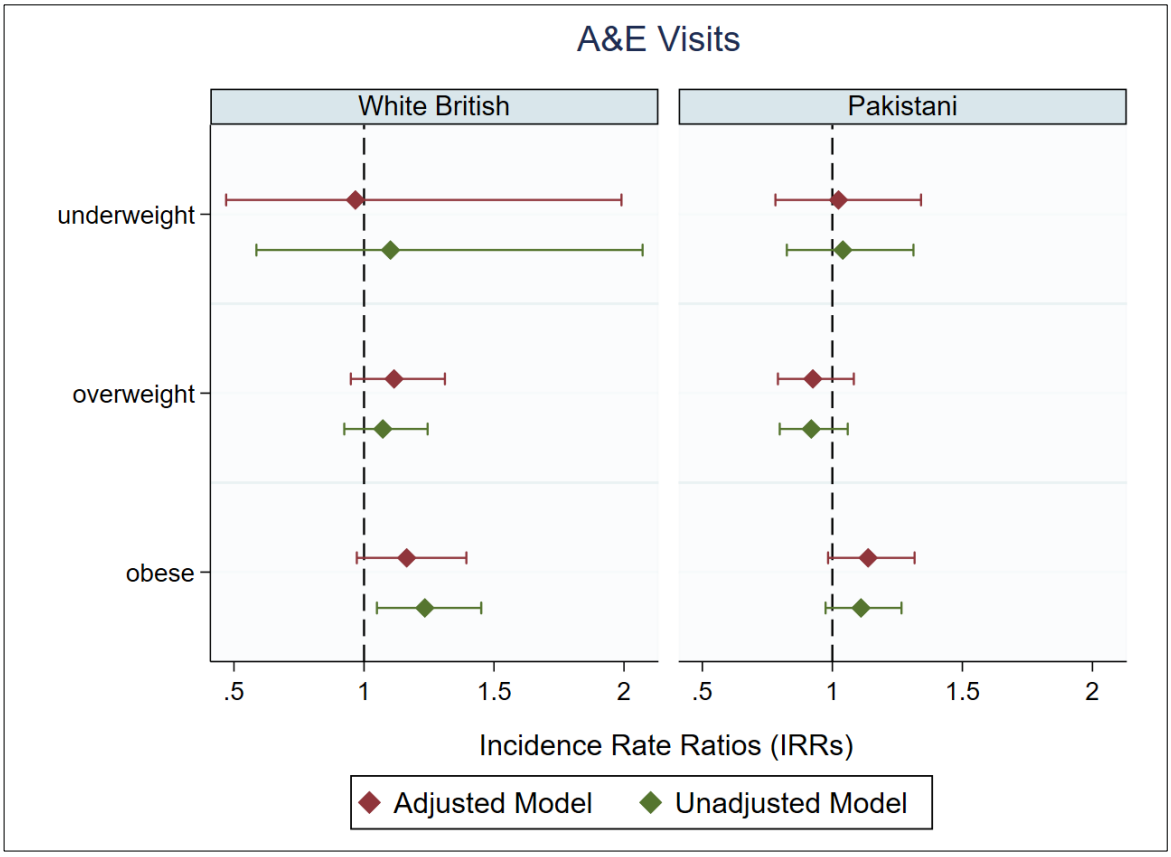

Figure 6.4 *Incidence rate ratios (reference: normal weight) for A&E visits by BMI status for Pakistani and White British children*

6.4.1 Ethnicity-specific BMI values

Table 6.10 reports the results by BMI categories (reference: normal weight) from unadjusted and adjusted analyses of secondary care use in Pakistani children after application of ethnicity-specific BMI values (section 3.3.1). There was no significant impact of these ethnicity-specific values on the association between exposure and each outcome. The adjusted IRRs for obese children attenuated for each outcome, however the associations remained non-significant.

Table 6.10 *Results of negative binomial models of association between Pakistani children's BMI status and secondary healthcare use after application of ethnicity-specific BMI values**

	Unadjusted model		Adjusted model (1)	
Ethnicity-specific BMI category	**IR per 1000 person-years**	**IRRs (95% CI)**	**IR per 1000 person-years**	**IRRs (95% CI)**
Hospital Admissions				
Underweight	51	0.55 (0.08-3.63)	29	0.30 (0.02-3.32)
Normal Weight (Reference)	91	1.00	95	1.00
Overweight	77	0.84 (0.68-1.04)	64	0.67 (0.52-0.85)
Obese	80	0.87 (0.71-1.07)	87	0.92 (0.72-1.16)
Hospital length of stay				
Underweight	334	0.64 (0.02-14.2)	869	1.67 (0.04-6.54)
Normal Weight (Reference)	514	1.00	518	1.00
Overweight	539	1.04 (0.76-1.44)	473	0.91 (0.62-1.33)
Obese	366	0.71 (0.52-0.96)*	425	0.82 (0.58-1.15)
Accidents & Emergency visits				
Underweight	253	0.93 (0.41-2.13)	311	1.15 (0.49-2.73)
Normal Weight (Reference)	270	1.00	268	1.00
Overweight	277	1.02 (0.92-1.13)	284	1.05 (0.94-1.19)
Obese	283	1.04 (0.94-1.16)	287	1.07 (0.95-1.20)

1. *Pakistani boys: +1.12 kg/m^2 , Pakistani girls: +1.07 kg/m^2
2. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
3. IRR = Incidence Rate, IRR = Incidence Rate Ratio, CIs = Confidence Intervals
4. **p<0.01, *p<0.05

6.5 Chapter summary

This chapter has focused on the relationship between BMI status and use of secondary healthcare services. These findings provide some evidence that although BMI status is possibly not associated with frequency of hospital admissions, there may still be greater risk of ill-health and being admitted to a hospital for both Pakistani and socioeconomically disadvantaged children. My findings also highlight a relationship between obesity and higher rate of A&E visits in children. Additionally, independent of their weight status, Pakistani children and children living in the deprived areas had significantly higher use of A&E services compared to White British children and children living in the 20% least deprived areas, respectively.

Chapter 7 Analysis of the relationship between BMI status and healthcare costs

In this chapter, I present the results of analyses for the outcomes of primary and secondary healthcare costs. In the first section, I describe the distribution of each measure of costs (primary care consultations, hospital admissions and A&E costs) within each BMI category. I also report the crude (observed) mean annual costs per child by BMI category in the analysis cohort, and in each ethnic group.

This is followed by presentation of results of multivariable Generalized Linear Models (GLM) with gamma distributions. Predicted mean annual costs per child are first presented for the whole cohort, followed by results in each ethnic group. As explained in detail in section 3.8.5, separate models were run for each measure of costs based on BiB children's healthcare data from the date of BMI measurements to the age of 8 years.

7.1 Descriptive statistics

7.1.1 Primary care costs

Figure 7.1 shows the positively skewed (right-tailed) distribution of primary care costs by each BMI category (Shapiro-Wilk test: $p < 0.01$). Observed mean annual costs per child are presented in table 7.1. Costs were observed to be higher in obese and underweight children compared to normal weight children in the full cohort and in each ethnic group separately. Additionally, within each BMI category, observed costs were higher in Pakistani children compared to White British children.

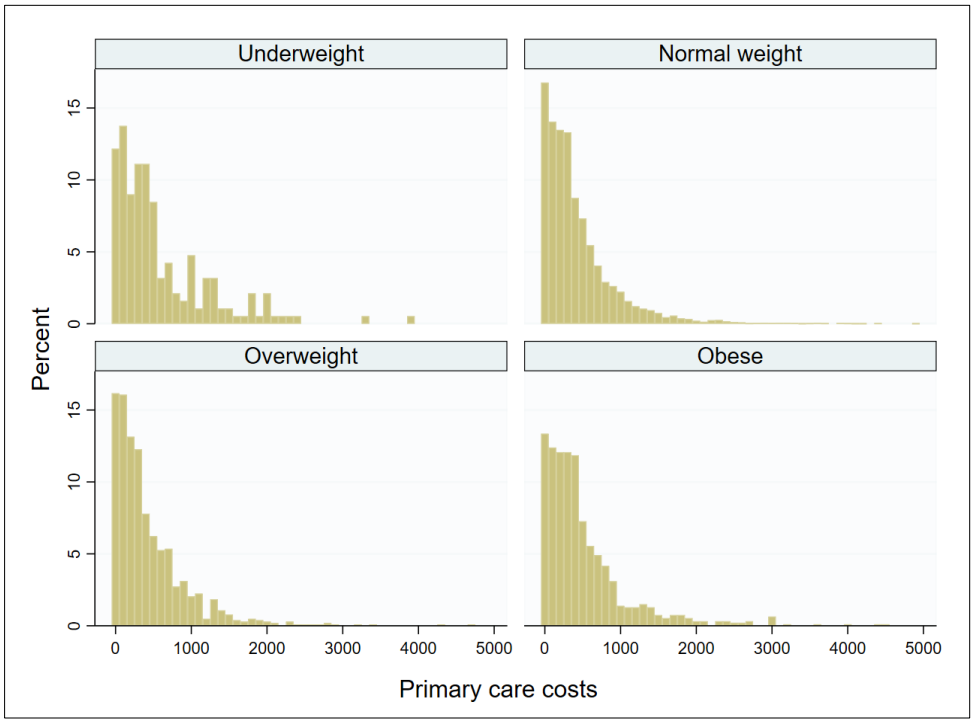

Figure 7.1 *Histograms of total primary care costs (£) for all BiB children by BMI categories*

Table 7.1 *Crude (observed) annual mean costs per child (£) by BMI and ethnicity*

BMI category	Analysis cohort (9,397)	White British (3,469)	Pakistani (4,346)	Other (1,323)
Primary care				
Underweight	£150.4	£123.4	£151.4	£165.1
Normal Weight	£109.6	£86.6	£128.1	£108.9
Overweight	£112.9	£88.8	£144.9	£99.3
Obese	£130.5	£105.3	£147.1	£127.0
Hospital Admissions				
Underweight	£132.8	£194.9	£115.3	£149.4
Normal Weight	£96.4	£81.0	£114.9	£78.7
Overweight	£93.8	£114.3	£86.8	£42.4
Obese	£107.1	£105.4	£117.4	£65.7
Emergency department visits				
Underweight	£40.0	£28.6	£43.4	£32.3
Normal Weight	£33.23	£26.9	£39.4	£29.1
Overweight	£32.31	£29.7	£35.8	£26.9
Obese	£39.25	£34.0	£43.8	£35.9

7.1.2 Secondary healthcare costs

Figure 7.2 and figure 7.3 show the positively skewed distributions of hospital admission and A&E costs within each BMI category, respectively (Shapiro-Wilk tests: $P < 0.01$).

Observed mean annual costs per child are presented in table 7.1. For hospital admissions, observed costs were higher for obese and underweight children compared to normal weight children in the whole cohort and in each ethnic group. A similar trend was also observed for A&E costs.

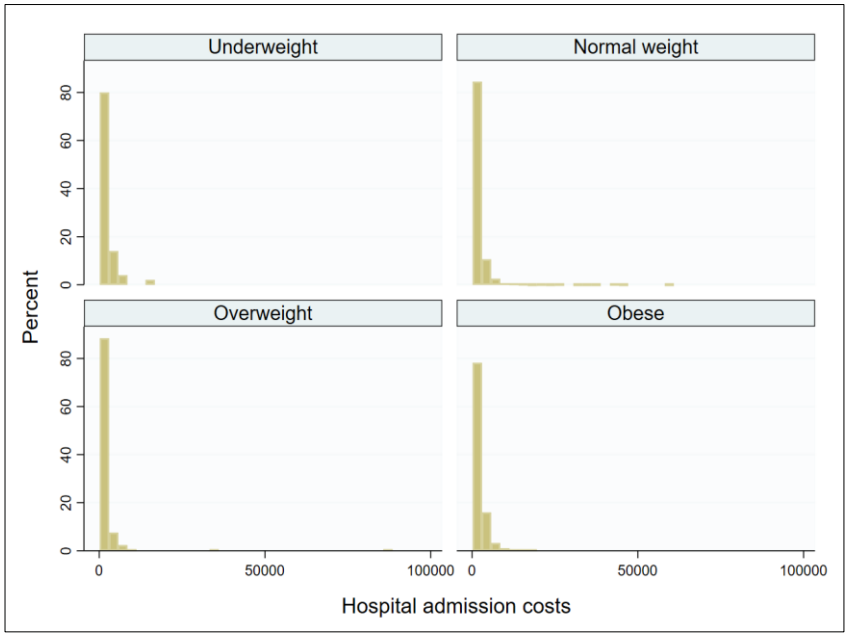

Figure 7.2 *Histograms of total hospital admission costs (£) for all BiB children by BMI categories*

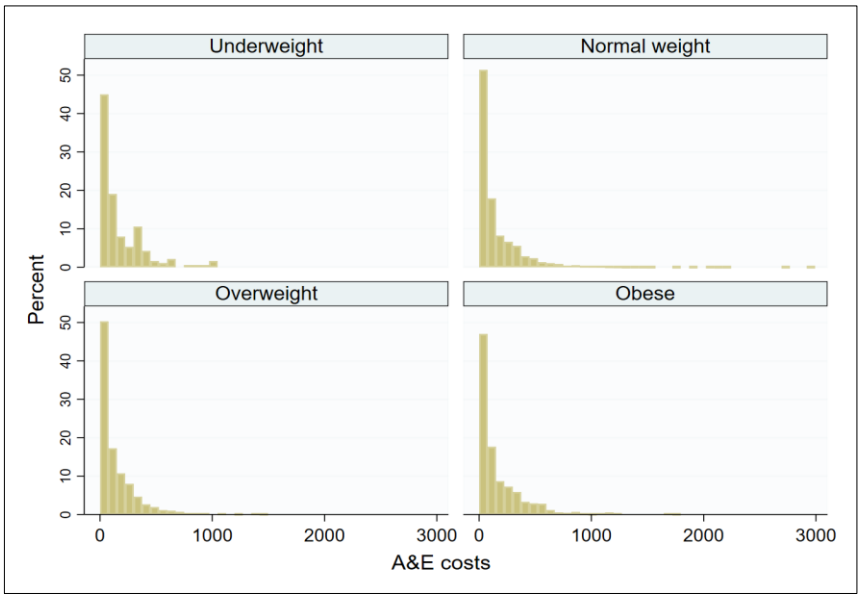

Figure 7.3 *Histograms of total A&E costs (£) for all BiB children by BMI categories*

7.2 Results of the regression models

I analysed the relationship between the exposure (BMI status), and the costs associated with primary care, hospital admissions and A&E visits in separate models, adjusting for covariates (child sex, gestational age, birthweight, ethnicity, mother's BMI, mother's age, IMDs, and means tested benefits). Results of these models are presented as annual predicted costs per child within each BMI category. Results of models stratified by ethnicity are also presented in a similar way. Additionally, estimates of absolute mean differences in these annual costs per child for each BMI category are presented using normal weight as a reference.

7.2.1 Primary healthcare costs

Table 7.2 reports the annual mean predicted costs per child by BMI categories for primary care. The left section of the table presents results for the whole cohort, while the right section presents predicted costs within each ethnic group. In the overall cohort, an obese child was predicted to cost an additional £20 per year in comparison to a normal weight child ($p < 0.01$). This annual difference was even higher for an underweight child with additional cost of £32 per child ($p < 0.01$).

Pakistani children had higher predicted costs within each BMI category than the White British children. The additional costs associated with being obese in Pakistani children was £22 per year when compared to their normal weight counterparts. Obese White British children also accrued higher predicted costs than their normal weight peers, however the difference (£15) was not significant and not as pronounced as in Pakistani children. An opposite pattern was observed for underweight children. White British children who were underweight accrued higher additional costs (£47.5) than underweight Pakistani children (£18), when compared with their respective normal weight counterparts.

Table 7.2 *Estimated mean primary and secondary care costs (£) per child per year, by body mass index (BMI) and ethnicity* [1]

	Analysis cohort (9,397)		White British (3,469)		Pakistani (4,346)		Other (1,323)	
BMI category	**Costs (£)** [2]	**Absolute Difference (95% CI)** [3]	**Costs (£)**	**Absolute Difference (95% CI)**	**Costs (£)**	**Absolute Difference (95% CI)**	**Costs (£)**	**Absolute Difference (95% CI)**
Primary care								
Underweight	142.7	32.8 (5.1-60.4)**	134.5	47.5 (-31.8-126.8)	146.7	18.2 (-15.1-51.7)	168.2	59.5 (-9.4-128.4)
Normal Weight (Reference)	109.9	0.00	87.0	0.00	128.5	0.00	108.7	0.00
Overweight	115.2	5.2 (-4.7-15.3)	86.6	-0.32 (-12.1-11.4)	150.3	21.8 (2.61-41.0)*	90.1	-18.5 (-41.2-4.11)
Obese	129.9	19.9 (8.2-31.7)**	102.2	15.2 (-0.29-30.6)	150.7	22.2 (3.6-40.9)**	131.2	22.4 (-11.5-56.4)
Hospital Admissions								
Underweight	125.7	29.2 (-62.8-121.3)	174.4	96.9 (-208.6-402.6)	97.1	-17.8 (-104.8-69.2)	171.8	86.9 (-144.8-318.7)
Normal Weight (Reference)	96.5	0.00	77.4	0.00	114.9	0.00	349.3	0.00
Overweight	82.9	-13.6 (-41.3-14.1)	72.3	-5.11 (-34.6-24.3)	101.6	-13.2 (-65.0-38.5)	162.1	-45.5 (-84.0- -6.9)*
Obese	109.7	13.2 (-24.3-50.7)	106.5	29.1 (-18.1-76.4)	127.2	12.3 (-49.4-74.0)	286.1	-15.3 (-77.3-46.6)
Accidents and Emergency								
Underweight	38.1	4.9 (-4.8-14.8)	22.9	-4.2 (-21.9-13.5)	42.9	3.8 (-8.9-16.5)	39.9	8.5 (-13.0-30.0)
Normal Weight (Reference)	33.1	0.00	27.07	0.00	39.1	0.00	28.5	0.00
Overweight	33.8	0.68 (-3.2-4.5)	30.5	3.49 (-1.8-8.8)	36.5	-2.6 (-8.8-3.5)	25.6	-2.8 (-11.3-5.7)
Obese	39.8	6.6 (1.9-11.4)**	31.4	4.3 (-1.9-10.6)	45.6	6.4 (-.86-13.7)	42.0	13.5 (-1.4-28.3)

1. Adjusted for sex, mother's BMI, IMD categories, means tested benefits, mother's age at birth and gestational age in weeks. Costs are presented as mean annual costs per child predicted through Generalised Linear Models using the BiB children's data
2. Annual mean costs per child
3. Absolute difference in mean costs (£) is derived with the normal weight as baseline
4. **p < 0.01, *p < 0.05

7.2.2 Hospital admission costs

Five percent of the admission spells were not assigned an HRG using the grouper software. However, since the results presented in table 7.2 are based on complete case analyses, the spells with missing HRGs were not part of the analysis in the first place due to missing data on other covariates.

The second part of table 7.2 presents mean predicted annual costs per child for hospital admissions. In the whole cohort, an obese child accrued £109.7 per year, £13.2 higher than a normal weight child on average. Additional costs were more pronounced for underweight children, with a difference of £29.2 per child per year. The annual cost estimate for an overweight child (£82.9) was lower than a normal weight child (£96.5).

Pakistani children accrued higher costs within each BMI category except underweight when compared with White British children. Additional costs per child associated with obesity in White British children were £29.1, while they were estimated to be £97 for underweight children. Additional costs were less pronounced in Pakistani obese children (£12.3 per year). Moreover, Pakistani underweight children had lower annual estimate of costs per child (£97.1) when compared with their normal weight counterparts (£114.9).

7.2.3 Accidents and Emergency costs

Seven percent of the A&E visits were not assigned an HRG. All visits with missing HRGs were not part of the complete case analysis due to missing data on covariates.

The third part of table 7.2 presents results of analyses for A&E costs. In the whole cohort, mean annual predicted cost per obese child (£39.8) was significantly ($p < 0.01$) higher compared to a normal weight child (£33.1). An underweight child (£38.1) also accrued higher annual costs than a normal weight child.

When stratified by ethnicity, Pakistani children accrued higher costs within each BMI category compared to White British children. Annual costs per obese child were higher than normal weight children for both Pakistani and White British children, however the mean difference was more pronounced in Pakistani children (£6.1). White British underweight children had lower annual cost per child (mean difference: £-4.2) compared to normal weight children.

7.4 Chapter Summary

This chapter has focused on the association between BMI status and healthcare costs associated with use of primary and secondary healthcare services. The predicted mean costs per child per year provide evidence of high-cost burden of obesity and underweight for all domains of healthcare. Additionally, independent of their BMI status, higher costs were predicted for healthcare use by Pakistani children compared to their White British counterparts.

Chapter 8 Discussion

This chapter begins with a summary and interpretation of the main findings of this thesis. I consider these findings in the context of relevant literature and discuss their novel aspects. This is followed by a discussion of the strengths and limitations of this thesis. The chapter ends with consideration of the implications of the findings for policy, practice, and research.

8.1 Summary and interpretation of findings

This thesis analysed the association between children's BMI status at age 4/5 years with primary and secondary healthcare use in the next four years of their lives. Under the umbrella of this overarching aim, this thesis also explored whether these associations were modified by ethnicity. Additionally, this thesis explored the direct costs associated with primary and secondary healthcare use by children's BMI status and ethnicity.

The importance of exploring these associations has been established in chapter one. In light of the rising prevalence of childhood overweight and obesity with a varying degree of rise among different ethnic groups in the UK (NHS Digital, 2020d), it is important to investigate how obesity affects the health of children during childhood in a multi-ethnic population. It has been widely established in the literature that a continuous exposure to adiposity from childhood to adulthood results in a significantly higher risk of obesity associated diseases and obesity associated mortality in adulthood (Bhaskaran et al., 2018). As explained in chapter 1, excess adipose tissue results in progressive physio-metabolic changes in an individual's body through various mechanisms (Bray et al., 2017). Long-term persistence of adiposity and associated physio-metabolic changes results in deterioration of health to a point where these manifest as associated clinical conditions (e.g., Type-2 diabetes, cardiovascular diseases) in adulthood. This is one of the reasons why most studies analysing

the burden of childhood obesity in a population do so with a long- term perspective and look at the risk of these obesity associated diseases in adulthood. Recently, studies have reported a temporal trend of increasing prevalence of obesity associated diseases such as Type-2 diabetes and metabolic syndrome during childhood (Abbasi et al., 2017, Singer and Lumeng, 2017). This increase has been attributed to the rise in prevalence of childhood obesity. However, assessing the burden of obesity during childhood through the perspective of obesity associated diseases potentially underestimates the true burden of obesity associated adverse health in a population. As these diseases require a long-term exposure to adiposity to reach a stage of clinical diagnosis, such an approach is not able to account for the adverse health that obese children would experience due to immediate cardio-metabolic changes occurring in their bodies.

A multi-ethnic population-based cohort study such as the Born in Bradford (BiB) cohort with linkage to routinely collected healthcare data presented a perfect platform to explore the adverse impact of adiposity in children through analyses of their healthcare use which is an indicator of clinical need and potential adverse health.

As presented in chapter 1, there were two primary aims of this thesis:

1. To critically review the existing literature on healthcare utilisation in overweight and obese children, and to identify gaps and avenues for further research.
2. To explore the association of overweight and obesity in White British and Pakistani children at the age of 4/5 years with the use and costs of primary and secondary healthcare services up to the age of 8 years through secondary data analyses of the BiB cohort. This aim was achieved by addressing the following two objectives:
    i. To quantify the healthcare burden of childhood obesity through analyses of the rates and costs of primary and secondary healthcare use.

ii. To explore the impact of ethnicity on the association between childhood obesity and primary and secondary healthcare use and costs.

These aims were addressed in the form of four studies, the findings of which were presented in the form of four chapters in this thesis. An overview of the key findings is given in figure 8.1.

I undertook a systematic review and meta-analysis to collate the existing evidence on the association of overweight and obesity with healthcare utilisation during childhood. Findings from the meta-analysis showed a significant increase in the use of emergency department and outpatient services for obese children, while the increase was found to be not significant in overweight children. When narratively reviewed, three of the included studies (n = 33) that analysed primary care use demonstrated a significantly higher frequency of use by obese and overweight children. This review also highlighted the limitations of the methods employed in these studies. Specifically, there were only two studies from the UK. One analysed the use of primary care services (Kelly et al., 2019) and the other analysed rate of hospital admissions (Griffiths et al., 2019). There was no analysis for Accidents and Emergency (A&E) use in the UK. Additionally, both these studies did not explore the impact of ethnicity and socio-economic status on the association. In fact, only two of the thirty-three included studies in the review analysed the impact of ethnicity, both being from the United States. Both these studies reported a lower rate of healthcare utilisation in ethnic minority obese children, compared to White obese children.

In the proceeding sections, I give a detailed summary of the findings of each study that constitute the secondary data analyses of the BiB dataset in this thesis and discuss these findings in the context of wider literature on childhood obesity. Here, I have taken an objective-centric approach, whereby findings are summarised and discussed in relation to the two objectives comprising the second aim of this thesis. Interpretation of these findings

is based on an attempt to make use of my knowledge of literature to discuss their wider relevance, their novelty and to search for explanations of why I observed what I did.

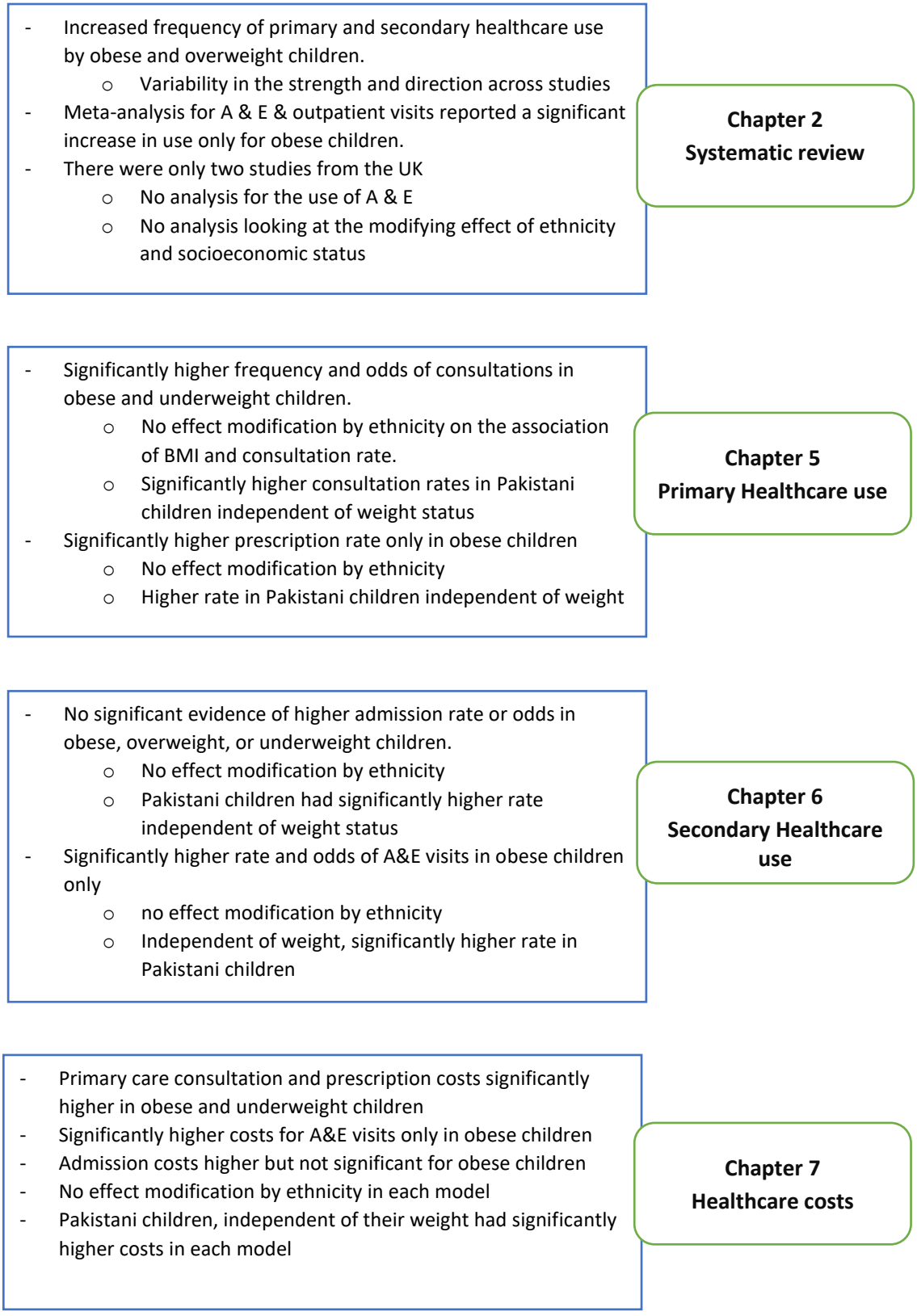

Figure 8.1 *Overview of key findings*

8.2 Weight status and healthcare utilisation and costs

In this section, results from the analyses of the association of primary and secondary healthcare use with children's BMI status at age 4/5 years are summarised in separate subsections followed by an overall interpretation of these findings. Table 8.1 shows the direction of association for relative rates of each measure of healthcare utilisation, modelled with weight status (reference: normal weight). This table also provides information on whether the observed effect was significant or not at the $p < 0.05$ level.

8.2.1 Summary of the findings

8.2.1.1 Primary healthcare use

I explored the association of children's BMI status with three outcome measures of primary healthcare use. The following measures were modelled in separate analyses:

1. Primary care consultations
2. GP doctor consultations
3. Primary care prescriptions

When the model was adjusted for all the covariates, there was significant evidence that obese children had a higher rate of primary care consultations compared to normal weight children (IRR 1.19, 95% CI: 1.10 – 1.28). Frequency of consultations was also significantly higher in underweight children (IRR 1.25, 95% CI: 1.07 – 1.46). Missing data on covariates did not have a significant impact on the strength and direction of these associations as demonstrated by results of multiple imputation analyses with 20 imputations.

Obese children also had a significantly higher rate of primary care prescriptions (IRR 1.20, 95% CI: 1.09 - 1.31) compared to normal weight children. The relative prescription rate was higher but not significant in overweight and underweight children (Table 8.1).

Table 8.1: *Strength and direction of association between children's weight status and healthcare use*

Healthcare utilisation*	BMI status (ref: normal weight) Obese (n = 189)	Overweight (n = 1,028)	Underweight (n = 936)
Primary healthcare use			
Primary care consultations	↑	↑	↑
GP Doctor consultations	↑	↔	↑
Primary care prescriptions	↑	↑	↑
Secondary healthcare use			
Hospital Admissions	↑	↔	↑
A & E visits	↑	↔	↑
Hospital Length of Stay	↔	↔	↔

Key:

↑ = significantly increased rate ($p < 0.05$) ↑ = increased rate (not significant, $p > 0.05$)

↔ = no effect or decreased rate (not significant, $p > 0.05$)

*Relative rate of healthcare use (ref: normal weight). All models adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI

8.2.1.2 Secondary healthcare use

I analysed the association of children's BMI status with outcome measures of hospital admissions and Accident & Emergency (A&E) visits. Additionally, conditional upon having a hospital admission, I also undertook an analysis of the hospital length of stay in bed days by weight status.

There was no significant difference in rates of hospital admissions between obese and normal weight children. The frequency of A&E visits was significantly higher in obese children (IRR 1.17, 95% CI, 1.05 – 1.30). There was no significant difference in the odds of being admitted to the hospital between obese and normal weight children (appendix A5.4).

The odds of visiting the A&E department were significantly higher in obese children (appendix A5.7).

8.1.1.3 Healthcare costs

Health care costs associated with primary care consultations and prescriptions were significantly higher in obese and underweight children. On average, consultations (including prescription costs) for an obese child cost £20 more than the cost for a normal weight child per year.

The costs associated with hospital admissions were higher in underweight and obese children, however these associations were not significant. For A&E use, the costs were significantly higher in obese children, with an obese child on average costing £6.60 more than a normal weight child.

8.2.2 Interpretation of findings

The findings of this thesis show that obesity in early childhood (age 4/5 years) is associated with higher use of healthcare services in the next 4-5 years of life. These findings support the hypothesis that obese children would demonstrate a higher clinical need during childhood and an indicator of this in a longitudinal cohort study like BiB is the use of primary and secondary healthcare services. This is illustrated in part by studies showing a rise in the prevalence of obesity associated health conditions during childhood (Candler et al., 2018, Dubinina et al., 2014, Barrett et al., 2020). However, these studies are isolated in terms of their context, population and the clinically diagnosed health condition being looked into and therefore do not provide a complete picture as to what extent obesity is affecting the immediate health of children and leading to a rise in immediate burden on health care services. To my knowledge, this study is the first of its kind that simultaneously quantifies in a cohort of children the impact of their weight status at age 4/5 years on their health in the next 4-5 years of life as estimated by both primary and secondary healthcare use.

A significantly higher rate of utilisation was exhibited by obese children for primary healthcare and A&E use, while there was no significant association for hospital admissions or hospital length of stay. Based on the evidence available in the literature, many potential explanations for these findings can be articulated. These findings are consistent with the conceptualisation that exposure to adiposity in childhood results in physiological and metabolic changes that lead to deterioration in a child's overall health (Weiss and Caprio, 2005, Dubinina et al., 2014, Magge et al., 2020). This deterioration of health status results in an increased clinical need exhibited here through increased rates of utilisation of primary care and A&E services. However, as previously discussed, obesity associated conditions such as Type-2 diabetes and cardiovascular disease are progressive in nature and require long term exposure to excess adipose tissue to reach a point where they are diagnosed clinically. Therefore, a possible explanation of these findings could be that these diseases associated with obesity do not normally require inpatient care unless they are progressed to an advanced stage, which is unlikely to be the case in children. Additionally, children must be quite unwell with acute illness to be admitted to a hospital. However, if we also consider the significantly higher rate of primary care prescriptions observed for obese children, a possible interpretation here could be that these changes were on average progressed to a point where therapeutic interventions were required at primary care level.

The nature of primary healthcare and A&E services is such that in addition to other determinants of healthcare behaviour, utilisation is determined by patient's or parents' perception of their or their child's clinical need. Based on the findings of higher frequency of use of primary care, and a much higher rate of drugs being prescribed to obese children once they access healthcare, it could be assumed that in the BiB cohort, the perception of parents of obese children regarding their children's clinical need was accurate to a degree, however the extent of accuracy could not be determined through the data available. This

assumption is in contrast to what is frequently reported in the literature, which largely suggests that parents of obese and overweight children significantly under-perceive their children's weight and under-assess their children's health and clinical need (Tompkins et al., 2015, Rietmeijer-Mentink et al., 2013). If this interpretation of parent's accurate assessment of their children's health status stands true in the Bradford population, it provides an optimistic picture regarding the potential effectiveness of interventions that aim to support parents in adopting healthier lifestyles for their children. This is because evidence shows that an indicator of success for weight management and obesity prevention interventions is parent's understanding of their child's excess weight and its effect on child's immediate and future health (Rhee et al., 2005, Tompkins et al., 2015).

Recent figures from Public Health England (PHE) report that almost 32% of Bradford children (under-16 years) belong to low income families (Public Health England, 2020b). Research has shown that children in Bradford experience higher rates of morbidity and mortality compared to the national average, a reason why BiB cohort study was established (Raynor, 2008, Small, 2012, Sheridan et al., 2013, West et al., 2013, City of Bradford Metropolitan District Council, 2020). To find a significant association of obesity with increased healthcare utilisation in this cohort of children living in Bradford indicates its strong association with poor health status and higher clinical need in children. It can be argued that the studies in this thesis were not designed with an aim to disentangle the impact of obesity from other indicators of health status in children (e.g., rates of infectious diseases) and adjusting for other health indicators might have shown different results. However, although it is a data limitation that I was not able to adjust for children's previous health status, interpretation of these findings with the knowledge of presence of poorer baseline health in Bradford's children could highlight how the presence of obesity interacts to further accentuate ill-health and clinical need. Further exploration of this interaction

between obesity in childhood and overall health status in children in different geographical contexts is required to identify the extent to which they independently and dependently explain variation in clinical need and healthcare utilisation.

It is widely known that the prevalence of obesity is higher in children living in deprived areas (NHS Digital, 2020d). It is also widely known that people who have obesity and people who live in deprived areas experience greater ill-health. Based on this knowledge, the finding of a non-significant interaction between deprivation and BMI status in explaining variation in healthcare utilisation for all outcome measures was unexpected. A potential explanation of this finding could lie in the larger barriers to primary healthcare that people living in deprived areas experience (Kossarova et al., 2017, Hutt and Gilmour, 2010). It has consistently been reported that GP practices in deprived areas in the UK perform poorly on all quality indicators (Fisher et al., 2020). People living in these areas experience greater barriers in accessing these services due to long waiting times, low knowledge of the healthcare systems and low understanding of their health needs (Fisher and Fraser, 2020, Hutt and Gilmour, 2010). Therefore, it could potentially be theorised that an interaction effect might have been attenuated due to these barriers to access. If we look at the effect size of deprivation categories with use of primary care services independent of a child's BMI status, the rates and odds were slightly higher in more deprived areas for primary care consultations, but not for consultations with a doctor and for primary care prescriptions. On the contrary, the rates and odds of A&E use and hospital admissions were significantly higher in children living in more deprived areas with the effect sizes much higher than what is observed for all primary care consultations (appendices A5.4 and A5.7). These findings highlight the impact of barriers of access to primary care services in the presence of deprivation and are supported by research that shows that people from deprived areas tend to visit A&E services disproportionately more due to barriers in accessing primary care

services (Cowling et al., 2014, Kossarova et al., 2017). Additionally, the Bradford Royal Infirmary is located within a very deprived and densely populated area of Bradford. Therefore, in light of the evidence of barriers of access to primary care services in deprived areas, it could be the case that children living closest to the Bradford Royal Infirmary disproportionately used the A&E services more. However, this does not explain the absence of a significant interaction between deprivation and BMI status in models for A&E visits and hospital admissions. Another potential explanation of these findings is that due to the unique deprivation profile of Bradford, whereby it is the 5th most income deprived district in England, area level deprivation factors might not be helpful in distinguishing health status of children at the level of Bradford. This explanation is discussed in further detail later in this chapter in the context of ethnicity. These findings and potential interpretations highlight that if similar research is replicated in a different context, geographical location or a different cohort, these findings could be different, and an interaction between these two predictors might be observed.

In the analysis for primary healthcare consultations, underweight status in children was found to be significantly associated with higher utilisation. The direction of associations for primary care prescriptions and secondary healthcare use in underweight children indicated a higher use across all measures; however, these associations were not significant. These analyses for underweight children were limited due to the smaller group numbers and therefore these non-significant increased rates might be due to low power. Nevertheless, these higher rates indicate a worrying trend of poor health in underweight children and warrants further exploration. An adverse impact of being underweight on health is expected due to the associated nutritional deficiencies (Mokhtar et al., 2018). A J-shaped association between BMI status and mortality and morbidity in adults is well reported, whereby underweight individuals have higher burden compared to normal weight

individuals (Bhaskaran et al., 2018). However, underweight in some cases could also be a consequence of another underlying health condition, and the inability to adjust for prior clinical health is a limitation in these analyses. Currently, there are no government strategies around underweight in children due to the priority of focus on the increasing prevalence of obesity in children. Although the proportion of underweight children in the UK is low, it is disproportionately higher in children of ethnic minority groups (NHS Digital, 2020d). This is also shown by the greater proportion of underweight in the BiB children of Pakistani origin. No matter what proportion of children are underweight in a population, they deserve a healthy start to life. Research and exploration into the determinants of underweight in children needs to be done to understand the pathways that lead to underweight. This will provide an evidence base for policy actions to implement interventions at local, regional, and healthcare level to inform parents on the health implications of being underweight and support them in developing behaviours that lead to a healthy weight in children.

Efforts to estimate the economic burden of obesity on the National Health Service (NHS) and wider community is essential for planning public health interventions and allocating resources. The most recent estimates from the UK show that obesity alone resulted in a direct-costs burden of £6.1 billion to the NHS, while the burden of overall indirect costs to society was around £27 billion (Department of Health & Social Care, 2020a). From a policy perspective, an aim of a policy - in addition to reduction of weight and improvement of population health - is to reduce the cost and resource burden on the NHS and wider community. Despite an increasing focus of policy and research on the effectiveness of childhood obesity interventions in reducing the population burden of childhood obesity, there is lack of research into evaluation of the cost utility of these interventions. This scarcity of focus on economic effectiveness is best highlighted through the lack of proposed

methods to evaluate and monitor performances of proposed interventions in the recent Childhood Obesity Plans by the UK government (HM Government, 2018). Additionally, two recent reviews collating evidence from around the world also highlight the lack of research into cost-effectiveness of childhood obesity interventions (Döring et al., 2016, Brown et al., 2019) .

Most studies that have evaluated cost-effectiveness of childhood obesity interventions have done so with a long-term perspective (Döring et al., 2016, Brown et al., 2019). These studies look at the effectiveness of a childhood obesity intervention in reducing burden of direct and indirect costs through prevention of obesity associated diseases in adulthood. This long-term perspective is based on assumptions around future sustainability of an intervention and its sustained effect and the future health and demographic profile of a population. In addition to these studies, it is important to understand the early impact of childhood obesity on the healthcare system. Such assessment of healthcare burden of obesity in childhood is important for policy makers and intervention strategists to assess real-world cost utility of a childhood obesity intervention, and to allocate resources accordingly. In the cost-analyses carried out in this thesis, I have tried to fill these gaps and shift the focus towards immediate impact of childhood obesity on increased burden of healthcare costs. The findings that obese children accrue substantially higher costs compared to normal weight children across primary and secondary healthcare highlight the impact that effective childhood obesity interventions and prevention strategies could have on reducing the immediate cost burden on the healthcare system. It is also worth mentioning that the cost estimates in this thesis are conservative, since they do not consider administrative costs of primary care consultations, and do not account for A&E visits and hospital admissions that happened outside of the Bradford Royal Infirmary. Additionally, I only analysed the costs directly attributable to clinical care, and there was

no analysis done for indirect costs associated with loss of productivity by parents and children missing school due to illness. In a recent audit by the Department of Health & Social Care (Department of Health & Social Care, 2020a), it was reported that £61.7 million was the total spent by local authorities on the obesity prevention efforts in England in 2018/2019. Because childhood obesity is a priority focus of the UK government in recent strategy documents, it could be inferred that this spending was mostly on childhood obesity interventions. However, despite this spending in recent years, there has been little to no reduction in rates of childhood obesity. Therefore, evaluation of interventions at a local authority level is required to help make them more effective. The findings of immediate costs in this thesis, or a similar analysis of direct healthcare costs could provide an objective outcome measure against which the cost utility of interventions could be evaluated to inform future policy decisions and resource allocation.

8.3 Impact of ethnicity

In this section, I summarise and interpret the findings of the analyses informed by the second objective under the second aim of this thesis: "to explore the impact of ethnicity on the association between BMI status and primary and secondary healthcare use in children". Table 8.2 shows an overview of the impact of ethnicity on the association of healthcare utilisation with BMI status in BiB children of Pakistani and White British origin.

8.3.1 Summary of findings

8.3.1.1 Primary healthcare use

The effect of BMI status on the rate of primary care consultations in children was not modified by ethnicity, demonstrated through a non-significant interaction between weight status and ethnicity. However, Pakistani children had a consultation rate 1.5 times (95% CI: 1.44 – 1.60) higher than the White British children, independent of their BMI status.

Additionally, Pakistani children had double the odds of consultations compared to the White British children, independent of their BMI status (appendix A4.6).

Table 8.2 *Direction of association of Pakistani and White British children's weight status (reference: normal weight) with primary and secondary healthcare use*

Healthcare utilisation*	Pakistani (n = 4,346)			White British (n = 3,469)		
	Obese	Overweight	Underweight	Obese	Overweight	Underweight
Primary healthcare use						
Primary care consultations	↑	↑	↑	↑	↑	↑
GP Doctor consultations	↑	↑	↑	↑	↔	↑
Primary care prescriptions	↑	↑	↑	↑	↑	↑
Secondary healthcare use						
Hospital Admissions	↑	↔	↔	↑	↑	↑
A & E visits	↑	↔	↑	↑	↑	↔
Hospital Length of Stay	↔	↔	↑	↔	↑	↔

Key:

↑ = significantly increased rate ($p < 0.05$) ↑ = increased rate (not significant, $p > 0.05$)

↔ = no effect or decreased rate (not significant, $p > 0.05$)

* Relative rate of healthcare use (ref: normal weight) within each ethnic group. All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI

There was no significant evidence of effect modification by ethnicity on the association of primary care prescriptions with weight status. However, Pakistani children independent of their BMI status had a prescription rate 1.87 times (95% CI: 1.75 – 2.00) that of White British children.

When I undertook the analyses stratified by ethnicity, the association of primary healthcare use with weight status within Pakistani and White British children showed a similar pattern for the most part. Obese children in each ethnic group had a higher rate of primary care consultations than their respective normal weight peers (Table 8.2). However, Pakistani

obese children had a significantly higher rate of prescriptions compared to normal weight Pakistani children, a finding which was not observed in the White British children.

When I ran the analysis for Pakistani children after applying the ethnicity-specific BMI values, the adjusted rates in each BMI category were attenuated. Underweight and overweight Pakistani children now had a lower rate of primary care consultations than normal weight children, but the associations were not significant. As for the obese Pakistani children, the rate of consultations was attenuated but remained significantly higher than normal weight children (Table 8.3).

8.3.1.2 Secondary healthcare use

Ethnicity did not modify the association between children's BMI status and hospital admission rate. However, Pakistani children independent of their BMI status had an hospital admission rate 1.49 times (95% CI: 1.28 – 1.74) that of White British children. In the separate analyses stratified by ethnicity, the direction and strength of associations of hospital admissions to BMI status was similar to what was observed in the whole cohort (Table 8.2).

The association of A&E visits with BMI status was also not modified by ethnicity. Pakistani children, independent of their BMI status had an A&E visits rate 1.38 times (95% CI: 1.27 – 1.49) that of the White British children. When the analyses for Pakistani children were run after application of ethnicity-specific BMI values, the effect sizes were attenuated but there was no significant change in the association by weight categories (Table 8.3).

Additionally, for both admissions and A&E visits, the odds were significantly higher in Pakistani children compared to the White British children independent of their BMI status (appendix A5.4 & appendix A5.7).

***Table 8.3**: Direction of association of Pakistani children's weight status (reference: normal weight) with primary and secondary healthcare use before and after use of ethnicity-specific BMI values*

Healthcare utilisation*	Pakistani (before ethnicity-specific BMI values)			Pakistani (after ethnicity-specific BMI values)		
	Obese	Overweight	Underweight	Obese	Overweight	Underweight
Primary healthcare use						
Primary care consultations	↑	↑	↑	↑	↔	↔
GP Doctor consultations	↑	↑	↑	↑	↔	↔
Primary care prescriptions	↑	↑	↑	↑	↑	↑
Secondary healthcare use						
Hospital Admissions	↑	↔	↔	↔	↔	↔
A & E visits	↑	↔	↑	↑	↑	↑
Hospital Length of Stay	↔	↔	↑	↔	↔	↑

Key:

↑ = significantly increased rate ($p < 0.05$) ↑ = increased rate (not significant, $p > 0.05$)

↔ = no effect or decreased rate (not significant, $p > 0.05$)

* Relative rate of healthcare use (ref: normal weight). All models adjusted for Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI

8.3.2 Interpretation

In the introductory chapter I hypothesised that the association between BMI status and utilisation of health services in children could potentially be modified by ethnicity. Due to the lack of any studies looking directly at such an association, this hypothesis was founded on a series of indirect lines of evidence. South Asian children have higher rates of obesity in the UK (NHS Digital, 2020d); they tend to carry more fat mass for a given BMI (Hudda et al., 2017, Eyre et al., 2017), a finding that has also been reported at birth in the cohort (Born in Bradford) used for the analyses in this thesis (West et al., 2013); people of South Asian origin tend to have a higher risk of cardiometabolic diseases for a given BMI (Whincup et

al., 2010); and South Asian people in the UK exhibit variation in healthcare utilisation behaviour from that of White British people (Katikireddi et al., 2018).

As summarised in the previous section, findings from the analyses in this thesis did not show any significant modification by ethnicity on the association between children's BMI and healthcare use. To my knowledge this is the first time such an association has been explored, and therefore it is not possible to explain these findings in light of what direct evidence previously exists in literature. Here I take help from the wider literature on childhood obesity and ethnicity to interpret these findings and draw a series of explanations.

It is known through evidence that ethnic minority groups in the UK face barriers to access primary healthcare services (Hull et al., 2014). A possible explanation for observed lack of effect modification by ethnicity on primary care use by BMI status could lie in it being attenuated by these barriers to access. However, this does not explain why there is no effect modification in the use of A&E services, as evidence shows that access to A&E services is disproportionately greater in the presence of barriers of access to primary care services (Cowling et al., 2013b, Hutt and Gilmour, 2010). Additionally, I found that independent of their BMI status, the rates of use of all health services and likelihoods to access these services were significantly higher in Pakistani children. This suggests poorer health and higher clinical need in Pakistani children with no evidence of any barriers to access, and therefore demonstrate that there was no effect modification by ethnicity on the association of interest in the BiB cohort. Evidence on variation in health care use behaviour between ethnic groups in the UK shows that this variation is explained to some extent by the higher proportion of ethnic minorities living in the deprived areas, which in itself presents challenges in terms of barriers of access to primary care services (Hull et al., 2014). It is well reported that the performance indicators of primary care services in

deprived areas show significantly poor performance and score low on patient satisfaction (Cecil et al., 2016), with ethnic minority groups having the highest rates of dissatisfaction from the services provided (Lyratzopoulos et al., 2012, Fisher et al., 2020). However, due to the unique deprivation profile of Bradford, a possible explanation for the observed lack of modification by ethnicity could lie in an argument that variation in healthcare utilisation behaviour and barriers to access might not be as observable between areas within Bradford as compared to what could be observed when Bradford LSOAs are ranked at a national level. This might also be a reason as to why no interaction between ethnicity and deprivation categories was observed in all models. The categories of deprivation used in the analyses in this thesis are based on relative ranking of LSOAs within Bradford. If we take a broader view, 34% of the LSOAs in Bradford actually fall in the 10% most deprived in England (City of Bradford Metropolitan District Council, 2020). Therefore, it could be argued that healthcare use variation that is observed between ethnic groups due to areas ranked by deprivation at the level of an affluent city or at national level, might not be applicable at the level of Bradford district due to little variability between different deprivation categories within Bradford. It is well reported that obesity is socio-economically patterned in the UK, whereby rates of obesity are higher in children and adults living in deprived areas. As previously discussed, it is through interaction of various factors that people living in deprived communities are at higher risk of being obese, as obesity is determined by a complex interaction of multiple factors. Among these determinants, environment plays a very important role. Low income families have few opportunities to afford healthy food options (Power et al., 2021) and the environment of deprived areas is structured to be obesogenic. There is higher density of unhealthy fast-food outlets (Public Health England, 2017), a higher population density associated with higher traffic congestion, less green spaces, and overall physically hazardous conditions

which limit the opportunities for physical activity (Noonan et al., 2016, Christian et al., 2015). Therefore, the challenges faced in preventing or controlling obesity and associated ill-health in an area like Bradford which is the 5th most income deprived local authority in the UK (City of Bradford Metropolitan District Council, 2020), are quite unique and extreme compared to the challenges in more affluent areas in the UK. This highlights how important the interaction between ethnicity and geographical context is when it comes to exploring and understanding different predictors and pathways of adverse health associated with obesity in general, and childhood obesity in particular. This also lends support to the Government's recent strategies to tackle childhood obesity where they have focused on collaboration with local authorities to look for predictors of intervention success and failures in a particular context (HM Government, 2019a). An example of this is the new "Trailblazer Programme" initiated as a trial in five different districts, one of which is Bradford (HM Government, 2019a).

When obesity is discussed in the context of ethnicity, consideration must be given to the overwhelming evidence on the presence of higher fat mass for a given BMI in people of South Asian origin compared to White British people (Hudda et al., 2017, Eyre et al., 2017). Questions have been raised in the literature on the validity of conventional BMI cut-off values for South Asian people for clinical and public health purposes (Nightingale et al., 2011, WHO Expert Consultation, 2004). Although the presence of higher fat mass for a given BMI in South Asian children is well reported in literature, research into the use of ethnicity-specific BMI values to predict cardiometabolic risk in children is limited. Additionally, the use of ethnicity-specific BMI values has resource implications, and therefore their implementation should be considered with caution. Currently in England, referral of obese children to weight management services from a healthcare setting is based on the criteria recommended by National Institute for Health and Care Excellence

(NICE) (NICE, 2019) and is built upon the categorisation of obesity in children using the conventional BMI thresholds and the presence of co-morbidities (Viner et al., 2018). This criterion currently has no recommendation for ethnic groups. Therefore, if a Pakistani child not identified as obese on conventional BMI threshold of ≥ 95th percentile but with a fat mass equivalent to an obese White British child presents to a primary care service with preclinical Type-2 Diabetes, there is a risk of him/her not being referred to an appropriate weight management service. There is a flip side however, in that the use of ethnicity-specific BMI values, as shown by the descriptive analyses in this thesis, resulted in relatively more Pakistani children being categorised as obese. Although it is known that Pakistani children in the BiB cohort and South Asian children in other birth cohorts in the UK are relatively more adipose, we don't yet know how that affects their cardiometabolic risk. Therefore, if any ethnicity-specific BMI values are not significant predictors of clinical need in a population, there is risk of unnecessary use of weight management services, straining the already burdened services (Viner et al., 2018).

In the analyses in this thesis, using the ethnicity-specific BMI values derived by Hudda et al. (2017), I did not find any evidence that their use was associated with higher clinical need and a higher rate of healthcare use in obese Pakistani children. In fact, the results showed the opposite effect, whereby effect sizes for almost all measures of healthcare use in obese Pakistani children were attenuated when compared to models with conventional BMI thresholds. A potential interpretation of this finding is that although these ethnicity-specific thresholds were developed taking data from three different cohorts, it is not known how generalisable and sensitive they are to a population structure of another cohort of children. Especially important is that these thresholds do not take into account the potential heterogeneity in adiposity between different South Asian groups. Additionally, derivation of these thresholds is sensitive to the accuracy of measures used to determine fat mass.

The use of a less accurate method, difference of fat measurement methods across cohorts, or potential of measurement errors could affect the sensitivity of these cut-offs. Therefore, based on the findings of this thesis, it could be recommended that if the aim is to identify obese and at risk of being obese South Asian children for early intervention, more research is required to develop ethnicity-specific BMI values for children of specific South Asian groups. These values, in addition to being strong predictors of fat mass, need to be strongly associated with cardiometabolic risk, perhaps through incorporating the mediating effect of cardiometabolic changes such as changes in blood pressure, insulin resistance and inflammatory biomarkers that occur due to excess adiposity (Weiss and Caprio, 2005).

8.3 Strengths and limitations

To achieve the aims and objectives of this project outlined in chapter one, I had to make various methodological and analytical decisions along the course of the project. Due to the fact that BiB is a cohort study and the data for participants is already collected and linked, these decisions were driven by the availability of the data and the nature of the data that was available to me.

In this section, I start with an overview of the strengths of the project. Following on from there, I delve into a more nuanced discussion on strengths and limitations of the methodology applied, the challenges that could arise from the limitations, and what steps were undertaken to keep these limitations to a minimum.

8.3.1 Overview of the strengths of the project

This project provides a new understanding of the association between children's BMI status and their primary and secondary healthcare use and the modifying effect of ethnicity on the association. To the best of my knowledge, this is a first of its kind study in the UK to analyse different domains of healthcare use for a cohort of children prospectively during

childhood. This is also a first of its kind study in the UK to model the direct healthcare costs associated with the use of primary and secondary healthcare by children's BMI status. Additionally, this study provides a novel insight into the use of frequently recommended ethnicity-specific BMI cut-offs to predict cardiometabolic risk and clinical need in South Asian children. I have based the analyses carried out in this thesis on the framework that healthcare use in children can be used as a marker of their clinical need and health status. I have shown how routinely collected data through primary and secondary healthcare can be used to investigate differences between health status of children categorised into different BMI categories and ethnic groups.

Due to the robust methodology of the BiB cohort, the high levels of successful data linkage and the detailed data on many covariates, I was able to investigate the extent to which each outcome was potentially explained by a wide range of factors on a large sample of children. Adjusting for a wide range of covariates selected *a priori* based on a theoretical framework, I reported a higher rate of healthcare use in obese children as theorised, though the strength of association varied across outcomes. One finding which is not covered much in literature was the higher rate of healthcare use in underweight children, albeit variation in the strength and significance of association. These findings necessitate a focus on the health status and health needs of underweight children in future research. The rate of healthcare use was much higher in Pakistani children independent of their BMI status. However, unlike what was hypothesised based on literature, I did not find any modifying effect of ethnicity and/or socioeconomic status on healthcare use by weight status.

In the proceeding sections the strengths and limitations of the study design and analytical methodology are discussed.

8.3.2 Data linkage and validity

The BiB study used an individual level linkage to link the data of children to their primary and secondary healthcare records. In individual level data linkage, an individual's information from two or more datasets are merged together using one or more unique personal identifiers. For the BiB cohort, children's information was linked to the primary and secondary healthcare datasets using their unique NHS numbers, date of birth and sex. Data linkage is widely used in the context of health-related research. Such data linkage for routinely collected healthcare data not only provides an opportunity to use data for research purpose, but there are other advantages such as reduced time and cost compared to a primary data collection. In the context of this project, linkage to prospective healthcare data for BiB children made it possible for me to analyse their healthcare use prospectively over an extended time period. This not only made it possible to analyse an association with weight status but also mitigated the risk of reverse causality, which I discuss in detail further in this section.

There are some limitations of data linkage. One of the limitations pertinent to this project and the BiB cohort is that it was not possible to verify the validity of primary and secondary healthcare data. Another limitation is that the primary healthcare data were linked only from the GP surgeries that had a data sharing agreement with the BiB, which were around 98% of the primary healthcare providers in the Bradford metropolitan area. Therefore, if a child was registered with a surgery other than these, there would be no data available. Also, the secondary healthcare data were extracted only from the health records at the Bradford Royal Infirmary (BRI). So, if children utilised secondary healthcare at a provider other than the BRI, their healthcare records would not reflect such an event. For example, seriously ill children who required care in a Paediatric Intensive Care Unit (PICU) would not be possible to be cared for at the BRI. Additionally, it was not possible to discern from the

data whether an absence of any event for a child was due to no utilisation or utilisation at a different provider. This could potentially introduce systematic bias and underestimate the healthcare rate. However, since information for 98% BiB children was matched to their BRI health records, it can be assumed that data linkage was able to capture most of the BiB cohort's secondary care uptake. Moreover, no data linkage was established for BiB children's outpatient and community healthcare services records as part of the BiB project. Therefore, lack of this data could potentially lead to an underestimation of the burden of healthcare use and costs.

8.3.3 Selection bias

Selection bias is an important consideration in cohort studies (Henderson and Page, 2007) and occurs when selection of a specific cohort population from a source population depends on both the exposure and the outcome of a study (Hernán et al., 2004, Rothman et al., 2008). Recruitment to the prospective BiB cohort study was offered to all mothers that attended the antenatal clinic at the BRI during the study recruitment period and all children born to the participating mothers were selected in the BiB cohort. Therefore, risk of potential bias due to nonparticipation in my project is low as participation of BiB children was not influenced by the exposure or the outcome. However, consideration should be given to socio-economic and demographic factors that may have influenced mothers' participation at the time of recruitment. Such factors in turn may correlate with risk factors for children's weight status and healthcare use. A comparison of the BiB cohort with all births to nonparticipant mothers at the BRI during the recruitment period reported small differences between the recruited and non-recruited cohorts (Wright et al., 2012). For example, in the recruited cohort, proportions of South Asian mothers and mothers living in deprived areas were higher compared to those who were not recruited (Wright et al., 2012). However, it was not possible to quantify the impact and direction of potential

selection bias due to these differences without any knowledge of risk of being obese and likelihood of healthcare service use in children born to non-participant mothers. Therefore, it was only possible to control for any potential bias arising through nonparticipation by adjusting the multivariable analyses for ethnicity, socio-economic status and other covariates identified through a theoretical model (section 3.7.1) that may also be associated with participation of mothers of BiB children.

The analyses in this thesis were restricted to children who had their height and weight measurements at the age of 4/5 years. In theory, in prospective cohort studies, the risk of selection bias is very low since the outcome is measured after the exposure, and therefore inclusion is not related to the outcome. However, it is important to consider the impact any correlation between unavailability of BMI measurement for BiB children and their BMI status would have on the findings of this thesis. For example, if children who were obese were more likely to be opted out of National Child Measurement Programme (NCMP) by their parents, then the inclusion is related to the exposure, and in light of the findings in this thesis and what has been reported in literature, an assumption can be made that inclusion is also related to the outcomes since obesity is significantly associated with healthcare use. However, it is not possible to formally assess the impact this bias could have on the findings of the thesis and this limitation should be considered when interpreting the findings. Loss to follow-up rate due to withdrawn consent or death was very low in the analysis cohort, and therefore it is unlikely to bias the findings. A comparison of the key characteristics between the analysis cohort and the excluded BiB children reported that the two groups did not differ significantly on all variables except their deprivation status (Table 4.1). As previously mentioned, adjusting for sociodemographic factors restricted the influence of deprivation on the relationship between the exposure and the outcome.

8.3.4 Measurement accuracy

Accurate measurement of exposure, outcomes, and covariates is essential to ensure validity of the findings of a study. A limitation of the secondary analysis of already collected cohort data was the inability to independently verify the exposure, outcomes, and covariates. Height and weight measurements of the BiB cohort were taken by trained professionals either through the NCMP or primary care at age of 4/5 years, therefore this is highly unlikely to be a source of bias. Bias could possibly be introduced due to self-reporting of key characteristics by mothers at the recruitment questionnaire. For example, ethnicity was self-reported by mothers at recruitment and there is a possibility of misclassification bias either due to misreporting or data entry errors. Similar concern could arise for other self-reported variables such as means tested benefits. Another possible source of bias, and one which I have previously touched upon, is the availability of primary and secondary healthcare data from specific primary care providers and the BRI, respectively. The impact of this, as previously discussed is most likely be an underestimation of the healthcare use frequency.

As the height and weight measurements were collected at age 4/5 years with no follow-up measurement during the time in BiB children's lives that this project covers (up to the age of 8 years), it was not possible to account for any variations in the weight status of children over the course of this project. Research has shown that a decrease in BMI during childhood is significantly associated with a rapid improvement in the cardio-metabolic biomarkers associated with access adiposity and vice versa (Savoye et al., 2007, Savoye et al., 2011). Therefore, fluctuations in the BiB children's BMI status could potentially be a source of bias, the impact of which could not be predicted without information on the direction of BMI change in each child. Additionally, a lack of repeat measurements for covariates could potentially bias the findings. For example, the socioeconomic information adjusted for in

the analyses was collected during pregnancy. Economic disadvantage and material deprivation have been reported to be correlated with the exposure and outcomes of this thesis. Therefore, the unavailability of repeated measures of covariates such as these could potentially bias the findings of the study. However, while considering this limitation, a possibility should also be considered that even if repeated measures were available, their inclusion and investigation of modifying effect might not have been possible or statistically meaningful due to small group sizes.

8.3.5 Covariates

Measured and unmeasured confounding is an important consideration in cohort studies as children in different BMI categories could differ from each other in characteristics that influence their health care use over the course of the study. As part of this thesis, I theorised a conceptual framework that identified the pathways through which different variables could act as confounders, mediators, or moderators (Figure 3.4). These potential covariates were identified from the literature *a priori,* and these were then controlled for in all the analytical models.

Not all covariates that were identified as confounders, mediators or moderators were included in the multivariable analyses. This restriction on the number of covariates was done to mitigate the issue of overfitting the models. A decision to include or exclude a covariate was predicated on the following considerations:

1. Given the scarcity of literature on childhood obesity and healthcare use, I prioritised the inclusion of covariates that are reported to have a significant association with the exposure and the outcomes.
2. Inclusion was not only driven by an established association, but also by the availability and the completeness of data for a variable.
3. Additionally, collinearity with other predictors was also a restricting factor.

As stated above, the reason to restrict the inclusion of too many covariates was to lower the risk of overfitting the data. This is better explained in the context of an excluded covariate. For example, mother's smoking status during pregnancy. The proportion of missing observations on smoking status was much higher than the included covariates, and the variable was recorded as a categorical variable with three distinct categories. Therefore, its inclusion would have further reduced the sample size of the analysis cohort in a complete case analysis and would have decreased observations per regression term in the model, leading to an increased chance of spurious associations due to overfitting the data, not to mention a reduced power (and increased type-2 error) due to smaller sample size. Additionally, smoking status was strongly correlated with ethnicity with a substantial majority of smoking women being White British**.** The introduction of this strong correlation between two categorical predictors would have further increased the chance of spurious associations due to inflated type-1 errors. Therefore, based on my knowledge of the literature, I have taken every effort to avoid spurious associations by mitigating overfitting. This ensures accuracy of the predictions and increases the precision of conclusions that are drawn about the population from the analysis sample.

A limitation of a project consisting of secondary data analysis of observational cohort data is that the collection of data is not driven by the research questions of the project. Therefore, a project like this is susceptible to residual confounding due to unmeasured covariates. As discussed in chapter 1, evidence reports variation in pattern of healthcare use and uptake among children based on how equitable a primary care service is (Cecil et al., 2016). It is frequently reported that people registered at low access practices, which are predominantly based in deprived areas, tend to have a lower primary healthcare use and a higher A&E use (Cowling et al., 2013b, Cecil et al., 2016). It would have been great to explore the variation of healthcare use in BiB children by weight status after controlling for

service level indicators in a two-level hierarchical model, however the lack of data on such variables did not allow this and this could potentially lead to residual confounding in the analyses. Additionally, there was no data on cardio-metabolic biomarkers, changes in which mediate the pathway from adiposity to healthcare use (Weiss and Caprio, 2005, Viner et al., 2012). The results of the studies carried out in this thesis support the hypothesis that adiposity causes adverse health and increased healthcare use, but due to the lack of information on these mediating factors, I could not provide insight into the differential impact of changes in different cardio-metabolic biomarkers on healthcare use in children.

8.3.6 Multiple testing

In the analyses that constitute the studies included in this thesis, the BiB data are subjected to multiple statistical tests on different outcomes with the same exposure of interest and a fixed set of covariates. Undertaking multiple comparisons in such a way could inflate the chance of type-1 errors (false positives), where the null hypothesis is mistakenly rejected (Ranganathan et al., 2016)**.** This issue of multiple comparisons has been widely debated in the statistical literature with no consensus on how to adjust for inflated type-1 errors, with some researchers questioning the need for any adjustments at all (Feise, 2002, Rothman, 1990, Althouse, 2016). Any recommendation for adjusting the inflated type-1 error involves some method to lower the threshold of significance (alpha level) in a study e.g., Bonferroni method of adjustment (Perrett et al., 2006, Streiner and Norman, 2011).

After careful consideration of the literature in the context of my thesis, I designed the methodology in each study to make every attempt to mitigate the chance of type-1 errors**.** To minimise type-1 errors, as discussed previously, selection of covariates was specified *a priori* through a theoretical framework predicated on the literature, and therefore only the variables with a known relationship with the exposure and outcomes were adjusted for in the analysis. It has been shown that selection of covariates done through univariate

exploration of associations with the outcomes in a dataset (e.g., stepwise selection) inflates the type-1 error due to the outcome in the dataset being subjected to multiple tests (Perrett et al., 2006). Therefore, due to the *a priori* selection of covariates it can be assumed with a certain degree of confidence that any significant association estimated with the outcomes in the analyses is unlikely due to chance. Additionally, in case of analyses on the whole cohort (not the subset analysis by ethnicity), all significant associations had consistently small p-values across all models, further indicating that these associations were not down to chance. Moreover, since the association of each variable in the multivariable model was estimated independent of other predictors by controlling for them, and in the absence of any significant interactions between predictors at 5% significance level (significant interactions subject an outcome to multiple tests by interacting predictors in a model), any inflation in type-1 errors was unlikely.

Inflation in type-2 errors, failure to reject a null hypothesis when it is false, was also an important consideration in this thesis. A limitation of adjusting for type-1 errors been identified in statistical literature frequently is that it inevitably leads to an increased chance of type-2 errors (Perneger, 1998, Rothman, 1990). Therefore, any upward adjustment in the significance level would have resulted in rejection of any associations significant at the 5% level. However, findings from a single study are never confirmatory, nor can they guide policy decisions unless their scientific plausibility and findings are replicated and corroborated in different populations. Therefore, an inflation in the type-2 error rate through multiple comparisons adjustment could restrict further exploration of the observed associations by identifying them as chance findings when indeed there is a 95% probability of them to be true findings. Another potential limitation of the studies in this thesis could occur when the data are subjected to multiple comparisons through subgroup analysis by ethnicity. However, since these findings are not supposed to be confirmatory

but rather a first of its kind exploration into the possible associations, with the main purpose being to inform future extensive research, restricting the significance level could result in elimination of future exploration of observed associations at a 5% significance level. Therefore, based on these considerations, I decided not to do any adjustments to lower the threshold of significance in interpretation of the findings.

8.3.7 Generalisability

The BiB cohort is unique in its ethnic and socio-demographic composition. The generalisability of the findings of my thesis might be limited due to this uniqueness. However, this limitation is unlikely to exist at the level of Bradford, since the BiB cohort is largely representative of Bradford's population, with some differences in the socio-economic deprivation (West et al., 2013). Adjustment for socioeconomic deprivation in the analyses mitigated its impact on the association of interest in each model. There might be some generalisability of findings to other deprived multi-ethnic populations in the UK cities, however any such generalisations should be treated with caution in the absence of any corroborating evidence looking at similar associations from other such cities. The generalisability of findings to children living in more affluent areas of England is limited. Adjustment for socioeconomic deprivation might not mitigate this limitation since the general health status of children living in Bradford is frequently reported to be much lower than the England average (City of Bradford Metropolitan District Council, 2020, Public Health England, 2020b). Additionally, Bradford is the 5th most income deprived district in England with 34% of its LSOAs in the 10% most deprived in England (City of Bradford Metropolitan District Council, 2020). Irrespective of how limited the generalisability of findings is to relatively affluent areas in England, it should be considered that obesity or overweight is not unique to the BiB cohort or Bradford, with over 10% of children at age 4/5 years being obese across the UK (NHS Digital, 2020d). Additionally, the adverse changes

that adiposity impart on a child's body are not solely dependent on their socio-demographic characteristics. Therefore, the mechanism through which adipose children experience ill-health and increased healthcare use is generalisable to other populations. Socio-demographic characteristics might play a role in modifying the strength of this association in a different population; however, the direction of association is expected to be what is observed in the BiB cohort.

Another limitation of this thesis which could affect the generalisability of findings is the low sample size of children in BiB from other South Asian ethnic groups. These children were grouped together with all children with ethnicities other than White British and Pakistani to preserve the study power and decrease the type-2 error rate in the estimates. Therefore, it was not possible to draw any specific assumptions about children from these ethnic groups.

8.3.8 Additional considerations

In prospective cohort studies that follow participants over time after measurement of exposure, the potential of reverse causality is low; however, it cannot be eliminated. In my thesis, a possible source of reverse causality could be if children had ill-health before the age of 4/5 years and if this led to a more obesogenic lifestyle through reduced physical activity. In such instances, residual confounding could bias the estimates since children with previous underlying conditions would have a higher health care use and a higher BMI. It would appear as an over-estimated causal link between exposure and outcome, when it is actually driven by pre-existing underlying conditions. I was unable to adjust for pre-exposure health status of children due to unavailability of data. Therefore, consideration should be given to this limitation when interpreting the findings of this thesis.

In the BiB data, there was a considerable number of missing observations for covariates that were included in the models. This issue of missingness was dealt with by undertaking

twenty imputations using multiple imputation with chained equations (MICE) under the assumption that the data was missing at random. It should be considered that imputation is a computational estimation of a true value to replace missing values randomly from a range of imputed values. Therefore, there is uncertainty around the imputed value which could lead to bias in any model estimates. However, MICE was validated as a robust method to handle missingness in this thesis based on literature, the nature of the missing data, and through checking the model assumptions.

As discussed in detail in the methods chapter (section 3.6.1 & section 3.6.2), I was not given access to information on the date and year of a primary or secondary healthcare event. This had implications for the cost-analyses done in this thesis. As it was not possible for me to ascertain from the available data when an event took place, I was unable to assign the relevant annual unit cost to the event. Therefore, I had to decide what year's unit cost figures to use. Since the primary care data was extracted up to October 2019, and the extraction of secondary healthcare was done up to July 2020, I used the latest unit cost figures (2019/20 for primary care, 2018/19 for secondary care) available at the time of analyses to assign costs to each event. The rationale behind this decision was based on the aim of the study. As the aim was to predict annual costs per child in each BMI category, using the latest cost figures would provide annual predictions that are representative of current economic climate and are up to date with the current primary and secondary care practice guidelines.

When interpreting the results of primary care costs, it should be considered that the predicted costs might be an underestimation as these were only predicted for clinical events at a primary care service and did not account for costs associated with administrative tasks. Additionally, as previously discussed, secondary healthcare data for BiB children was only extracted from the Bradford Royal Infirmary. Therefore, predicted

secondary healthcare costs might be an underestimation of the total costs for BiB children. For example, there is no PICU facility at the Bradford Royal Infirmary, therefore expensive costs associated with care of seriously unwell children in a PICU could not be accounted for since there was no way to ascertain if any such events took place for BiB children at another healthcare provider.

In this thesis, I did not analyse the diagnostic codes associated with healthcare events to explore the reasons for which children accessed primary and secondary healthcare services. Evidence using the hospital episode statistics (HES) data showed that tooth decay or dental caries was the number one reason for hospital admissions in children aged 5-9 years in the UK in 2017, followed by acute tonsillitis, viral infections, asthma, and abdominal pain (Royal College of Surgeons of England, 2018). A prospective birth cohort study carried out in 2019 in Bristol also reported tooth decay as the leading cause of hospital admissions in children aged 5-9 years (Johnson et al., 2019). As development of both obesity and tooth decay may be mediated by dietary factors such as excess sugar consumption (Te Morenga et al., 2013, Moynihan and Kelly, 2014), it is plausible that tooth decay may provide an explanation of higher rates of healthcare use in children with obesity. However, research evidence to support this plausibility is inconsistent. Several systematic reviews collating evidence from studies exploring an association between obesity in children and tooth decay have reported inconclusive findings (Li et al., 2015, Paisi et al., 2019, Manohar et al., 2020). Nevertheless, an exploration into the reasons for healthcare use in a specific population could provide a deeper understanding of the population level trends of different health conditions in children living with obesity. Such insights could potentially inform childhood obesity interventions and health service planning.

8.4 Implications for policy and practice

The findings of my thesis report higher use of primary and secondary healthcare services by obese children. This suggests a higher rate of clinical need and obesity-associated ill-health in obese children as early as the age of 4/5 years. These findings highlight the importance of implementing public health policies and interventions to prevent childhood obesity in the early years of life. Early formative years in a child's life are identified frequently in literature as an ideal time to implement healthy lifestyles and behaviour change interventions since unhealthy lifestyle and behaviours are less established and any obesity associated adverse health is less progressed (Davies et al., 2019, Theis and White, 2021). The challenge however is that obesity is multi-factorial and is determined by various individual, social, biological and environmental factors (Albuquerque et al., 2017, Ang et al., 2013). All these determinants come together to interact and produce obesogenic environments that promote obesity. Therefore, there is no single intervention or policy that can target all these determinants at once. My findings provide an evidential basis and justification to the UK government's focus on prioritising obesity interventions in children in their most recent strategies and policies, an example of which is the implementation of sugar reduction programme including the Sugar Drinks Industry Levy (SDIL) as laid out in the latest Childhood Obesity Plans for action (HM Government, 2019a, HM Government, 2016, HM Government, 2018). As mentioned in the introduction chapter, SDIL has been successful in stimulating the industry to reduce sugar content in the drinks subject to levy. This resulted in reduction of sugar consumption through soft drinks by 30 gm per household per week after one year of implementation, which equates to a 10% decrease in sugar consumption per household compared to the pre-implementation years (Pell et al., 2021). However, despite the government's policy focus on controlling childhood obesity for the most part of last decade, recent data suggests that the prevalence in children has

not seen a drop and remains high (NHS Digital, 2020d). Additionally, the socioeconomic divide in childhood obesity prevalence has been increasing with children in deprived areas and children of ethnic minority groups at a disadvantage (NHS Digital, 2020d). In this section, I do not recommend any new policy actions or interventions since evidence-based actions and interventions are already in place on paper (HM Government, 2016, HM Government, 2018, HM Government, 2019a). Instead, with help from my findings, I identify and discuss how actions and interventions that exist within the government's strategic documents could be optimally implemented at the level of local authorities to target childhood obesity, and be on track to reach the target of halving the prevalence of childhood obesity by 2030 and to reduce the socioeconomic divide (HM Government, 2019a).

Policies that are aimed at childhood obesity in the UK can be seen from two perspectives: health care and public health. The former deals with the treatment and support for already obese children through planning and implementation of multi-component weight management services. The public health perspective on the other hand is concerned with primary prevention and tackling the rise in obesity through interventions and actions that address the multiple determinants of obesity and help in giving rise to an environment that promotes healthier lifestyles and makes it easier for a population to make healthier life choices.

8.4.1 Public health perspective

Recent systematic reviews of studies that have evaluated the efficacy of public health interventions to prevent the rise in childhood obesity consistently show that multisystem community-based interventions that undertake a holistic approach and target the social, environmental, and individual determinants are most effective (Colquitt et al., 2016, Anderson and Ball, 2019, Mead et al., 2017). The UK government's initial childhood obesity

action strategies were criticised – possibly with some justification - for being too focused on individual responsibility with no clear-cut strategy for policy actions that should be taken at the environmental, local and commercial levels to build a healthier environment for families that promotes a healthy lifestyle (Jebb et al., 2013, Ulijaszek and McLennan, 2016). However, in the latter part of the last decade, the UK government has taken an evidence-based approach in acknowledging the role that local, environmental and commercial factors play in building an obesogenic environment (Theis and White, 2021, HM Government, 2019a). An example of this is the introduction of sugar tax as part of chapter one of the Childhood Obesity Plan for action (HM Government, 2016), which has resulted in successful outcomes in reduction of sugar consumption by children (HM Government, 2019a). Targeting environmental and commercial determinants of childhood obesity such as access to green spaces, affordability & advertisement of healthy food, availability of healthy food options in and around schools, and density of fast-food outlets etc. require collaboration between different stakeholders at a local authority level (Davies et al., 2019). Public Health England (PHE) has defined this networking approach as a "Whole Systems Approach" and has released a guidance resource for local authorities to bring together all the responsible stakeholders on the same page and work towards a common goal of creating an environment that promotes healthy lifestyle behaviours (Public Health England, 2018).

The approach by the government in chapter 2 of the Childhood Obesity Plan for action (HM Government, 2018) and the most recently published chapter 3 (HM Government, 2019a) has remained the same. The government reiterates its strategy to implement a whole systems approach to childhood obesity and to expand its policy actions to include other responsible actors in local authorities and commercial advertisement agencies. However, as previously discussed, despite childhood obesity being a priority strategic area for the

government in the last decade, no reduction in childhood obesity prevalence has occurred (NHS Digital, 2020d). This indicates that there is a lot more that needs to be done and asks the question about the effectiveness of these strategies and whether the government needs to reconsider its approach. To reconsider, we need to know what aspects of these policies have not worked and what aspects should be prioritised for reconsideration. Therefore, I identify here how findings of my thesis add to the debate around effectiveness of childhood obesity policy, and how these findings may be interpreted to put forward recommendations to optimise childhood obesity prevention strategies.

In this thesis, I have highlighted an ethnic and socio-economic pattern of obesity. In the BiB cohort, the proportion of obese children was higher in deprived areas and in the Pakistani ethnic group. One of the main pledges that the government put forward in chapter two of the Childhood Obesity Plan for action in 2018 was to reduce the socioeconomic divide in childhood obesity by 2030 (HM Government, 2018). However, according to the recent NCMP data, there has been no diminishing effect nationally; in fact the divide in obesity prevalence has slightly increased from where it was in 2016 (NHS Digital, 2020d). Socioeconomic deprivation in the UK has been frequently reported to be closely associated with ethnicity, with minority ethnic groups often experiencing disadvantage (Public Health England, 2019a). The findings from the BiB cohort support this, with more Pakistani children living in deprived areas compared to White British children. Despite this pledge to reduce the socio-economic divide, there is no explicit plan in recent government childhood obesity strategies to ensure equality of outcomes across all ethnic and socioeconomic groups. It can be argued that implicit within the Childhood Obesity Trailblazer Programme is the consideration of ethnic and cultural aspects. Trailblazer is a programme that the government committed to deliver in partnership with PHE in chapter 2 of the Childhood Obesity Plan for action (HM Government, 2018). This programme was put into action as

part of chapter 3 of the Childhood Obesity action plan with an aim to empower five local authorities in England to find what works for them in tackling childhood obesity in their respective populations (HM Government, 2019a). The government and PHE should make sure that this programme is undertaken in accordance with PHE's "Whole Systems Approach" evidence-based guidance for local authorities (Public Health England, 2019d). Additionally, the respective local authorities should ensure community engagement and ethnic minority representation when adapting this whole systems approach in line with the evidence published by PHE for supporting families of children from ethnic minority and other at risk of obesity groups (Ells et al., 2020). Evidence shows differential uptake (Liu et al., 2012) and differential effectiveness (White et al., 2009) of health promotion interventions in ethnic groups, with South Asian groups at a disadvantage. An important finding of this thesis is the significantly higher use of all healthcare services in Pakistani children compared to White British children across all weight groups, suggesting potentially poorer health in Pakistani children and/or marked differences in how different communities access health advice or services. This further highlights the importance of engaging with the ethnic minority community in a population to understand the barriers to and facilitators of uptake of and adherence to interventions that promote a healthier lifestyle. This engagement with ethnic minority communities should also extend to the world of digital interventions that promote healthy behaviour. An example is the upcoming new project "Our Family Health" by PHE (Department of Health & Social Care, 2019). Uptake of such digital health promotion services requires individual motivation, a common language and some digital experience, as such these services may be more sensitive to cultural and ethnicity-specific barriers. It is imperative to engage with ethnic minority communities to understand how to make these resources culturally sensitive. Otherwise, we run the risk of increasing the socioeconomic divide further.

As previously discussed, this thesis reports that the rate of use of healthcare services was significantly higher in obese children from the age of 4/5 years up to the age of 8 years, encompassing a period of 4-5 years of primary school. In England and in Bradford, the proportion of children with obesity almost doubles by the time children leave primary school compared to the proportion at reception (NHS Digital, 2020d, City of Bradford Metropolitan District Council, 2021). I did not have any repeated measures of BiB children's weight and height during the longitudinal time period that this thesis covers, however if the wider evidence from Bradford and England is considered, it could be assumed that the proportion of obese BiB children would be higher at the end of this thesis period than at the start. Therefore, an assumption could be made that there is high probability of obesity associated clinical need and higher burden of healthcare use tracking into adolescence for the BiB children. This indicates how important a role schools have in supporting children to develop healthier lifestyles. Evidence from around the world shows that schools where healthy lifestyle behaviours are promoted through their curriculum, physical education and food standards have a lower proportion of children with obesity and overweight (Gray et al., 2019, Dobbins et al., 2013). The UK government has put forward strategies and action plans for schools to tackle childhood obesity; however, they have been subjected to slow implementation, weak enforcement, misalignment in policies, and lack of evaluation (Theis and White, 2021, Chapman et al., 2020). In a recent paper, it has been reported that schools in the UK that had programmes in place to promote healthier lifestyles were unaware of the impact of the different actions due to lack of evaluation (Ofsted, 2018). Additionally, policies such as the healthy food programme are misaligned across schools with them being only mandatory for certain state schools under the jurisdiction of local authorities (Davies et al., 2019). The government should scale up their efforts to ensure participation of all schools nationwide in policy actions such as the healthy food programme and the school

rating system. Additionally, local authorities should make sure to engage with schools as part of a whole systems approach. Schools and other local stakeholders need to be on a same page to create an environment in and around schools that promotes a healthy lifestyle.

8.4.2 Healthcare perspective

Despite the UK government's efforts to prevent childhood obesity, there remain a lot of children who are already obese, 1.2 million in 2019/2020 (Davies et al., 2019). In this thesis, I have found that the annual direct costs of primary and secondary healthcare use are significantly higher in obese children from the age of 4/5 years up to the age of 8 years. As previously discussed, the proportion of obese children almost doubles by the end of primary school in England (NHS Digital, 2020d). Therefore, it could be assumed that the healthcare use and cost burden of obesity would be even higher in adolescence particularly when progressive nature of obesity associated ill-health is factored in. According to the most recent estimate, obesity annually costs the National Health Service (NHS) in England around £6.1 billion (Department of Health & Social Care, 2020a). This highlights how important effective weight management services are during childhood to not only reduce the burden of morbidity on children, but also to reduce the healthcare burden of childhood obesity. This importance of weight management services is further brought to light by the ongoing COVID-19 pandemic due to the increased rates of COVID-19 associated hospitalisations and deaths in obese individuals (Public Health England, 2020a, Razieh et al., 2020).

Evidence shows that multi-component weight management services that focus on diet, physical activity and behaviour change in children with involvement of parents are the most effective (Sutcliffe et al., 2017, Colquitt et al., 2016). In the UK, commissioning of weight management services is the responsibility of local authorities (Department of Health &

Social Care, 2012). The National Institute for Health and Care Excellence (NICE) recommends local authorities adopt an integrated approach to commissioning of these services through engagement with various local and national stakeholders (NICE, 2013). Public Health England has echoed this guideline and recommended the use of weight management services as part of the whole systems approach to tackling obesity, thereby complimenting health promotion interventions and vice versa (Public Health England, 2019d). Despite the large body of evidence through original studies and systematic reviews highlighting what sort of weight management services are most effective (Sutcliffe et al., 2017), little is known about how effective current weight management services in the UK are in reducing childhood obesity (Pallan et al., 2019). Nevertheless, one aspect of the UK's weight management services is their inadequacy to meet the demand of the obese population eligible for uptake (Davies et al., 2019). More recently, the role of the NHS in management of childhood obesity has been reported to be inadequate in the NHS Long Term Plan (NHS, 2019), in chapter 3 of the Childhood Obesity Plan for action (HM Government, 2019a), and by the UK's Chief Medical Officer in an independent report on childhood obesity (Davies et al., 2019). Primary care services are the first point of contact for most patients in the UK. My findings show that primary care services provide a perfect opportunity for General Practitioners (GPs) and other primary healthcare professionals for early identification of children at risk of obesity, and to provide early weight management support, and timely referral to external weight management services if required. However, central to the reported inadequacy of health services is the perceptions of the primary care practitioners in terms of their role in managing childhood obesity. Qualitative literature researching the barriers to provision of efficient obesity support and management at the primary care level has repeatedly shown that most GPs think that their job is to signpost to external support services available, and that it is not the requirement of their role to be

advising parents and children on weight management (Bouch, 2017, O'Donnell et al., 2017). In cases where they do consider it a part of their role, they feel that they are not being adequately trained to bring up such a sensitive issue with parents under the constraints of a short GP consultation. Therefore, based on the findings in this thesis, recommendations for the NHS are to scale up the weight management support available within primary care services, to train the primary healthcare staff to assess and identify children at risk of obesity early, and to train the staff to engage and communicate effectively with parents regarding their children's weight.

The impact of ethnicity and socioeconomic deprivation on the effectiveness of community-based and healthcare-based weight management services in the UK is unknown. But we know that people from ethnic minority groups and people living in deprived areas experience barriers in accessing primary care services, and these barriers are often not mutually exclusive (Salway et al., 2016, Hull et al., 2014). This could explain why a disproportionately higher use of A&E services is often reported in these groups (Hutt and Gilmour, 2010). In this thesis, I found that the proportion of obesity was higher in BiB children of Pakistani origin compared to White British children. Additionally, the use of healthcare services across all measures was significantly higher in Pakistani children compared to White British children, suggesting a higher clinical need and poorer health. Possible poorer health in South Asian people including people of Pakistani origin was further highlighted during the COVID-19 pandemic, with South Asian obese people having a disproportionately higher risk of COVID-19 associated severe symptoms and hospitalisations (Razieh et al., 2020, Department of Health & Social Care, 2020b). Public Health England undertook a survey of the weight management services during the first national lockdown and found that their provision was badly affected (Public Health England, 2020c). In light of the evidence of the higher risk of severe symptoms of COVID-

19 in obese individuals, the government pledged to increase the availability of weight management services for obese individuals (Department of Health & Social Care, 2020a). Interestingly, despite the evidence for a greater risk in ethnic minority groups, there was no mention of how the government would tailor these services to meet the needs of ethnic minority people. Additionally, the NHS long-term plan (NHS Digital, 2019f) and the Childhood Obesity Plan for action chapter 3 (HM Government, 2019a) put forward plans to increase the availability of weight management services in healthcare settings. However, neither of these touch upon how they are going to engage with local stakeholders to tailor these services to the specific needs of ethnic minority groups. Therefore, in accordance with the NICE guidelines (NICE, 2013) and in light of the findings of this thesis, a recommendation for local authorities is to engage with their local community to understand group specific needs. Local authorities should then collaborate with local and national stakeholders to commission tailored community-based and healthcare-based weight management services if the government's pledge to significantly reduce the socioeconomic divide is to be achieved by 2030.

8.5 Implications for future research

In this project, I started out with a systematic review to identify gaps in the literature that I could address through the BiB cohort study. As previously discussed, this is a first of its kind study that looks at the association of obesity and healthcare use from the perspective of exploring the role of ethnicity. However, I was limited in my effort to fill these gaps by the availability of data. In this section, I identify and discuss the future research approaches that could explore and provide a broader insight into the complex problem of childhood obesity and could provide further evidence to inform future policy actions.

There is a need to understand the role that context plays in childhood obesity, ill-health, and healthcare use by undertaking similar long-term cohort studies in different contexts

and at different time points during childhood and adolescence. For example, the finding that ethnicity did not modify the association between BMI status and healthcare use was unexpected based on the theoretical framework. I have discussed in detail potential explanations of this finding in section 8.3.2. The point here is that the findings from a single study could be used to put forward some policy recommendations, but policy decisions that result in the implementation of an intervention at the population level should be based on corroborated evidence from multiple studies in different contexts and/or in different populations. A similar study to mine carried out in a different cohort, or in a different context, might give different results. Therefore, more cohort studies looking at similar associations, possibly in different populations should be set-up to see if and how findings from different studies corroborate, and how the information could be used to implement effective policies and interventions. Another area of further research using data from the BiB cohort study, or other such birth cohort studies could be the analysis of the reasons for hospital admissions by children's BMI status, and an exploration of how reasons for admissions vary by context and children's characteristics such as ethnicity. As previously discussed in section 8.3.8, such analyses could provide an understanding of the population level trends of different health conditions in children living with obesity and could potentially inform childhood obesity interventions and health service planning to reduce the burden of childhood obesity on the healthcare system.

As previously discussed, despite the UK government's primary policy focus on tackling childhood obesity, the childhood obesity prevalence in England has seen no decline over the last decade and the socio-economic divide in obesity has further increased. There is limited evidence regarding the effectiveness of childhood obesity interventions and weight management services at the local authority level, particularly in a multi-ethnic and socioeconomically deprived context. Therefore, there is need for local authorities to be

partners in qualitative and quantitative research studies to understand the predictors of success of healthy lifestyle interventions and weight management services at the population level.

The establishment of a clear pathway to routine integration of the NCMP growth data with healthcare data is required. Such integration will provide a unique opportunity for more advanced and nuanced investigation into the role of adiposity in children's ill-health at different time points during childhood with a focus on the interaction between different characteristics in different contexts and on multiple outcomes. The availability of such integrated data would provide a unique opportunity to evaluate the performance of interventions and identify aspects that require modification in a timely fashion. Additionally, larger cohort studies with expanded age ranges of children would allow detailed exploration of the mediating pathways from adiposity to ill-health and higher burden of healthcare use. A suggestion to take the exploration I have done in my project further would be to understand the mediating effect of biomarkers of cardiometabolic risk (i.e., blood pressure, insulin resistance, inflammation) in explaining the effect of adiposity on variation of the burden of ill-health during childhood. This would aid healthcare professionals in timely identification of cardiometabolic changes in children who are at risk of developing serious adiposity associated conditions. Such findings could potentially be very important in the case of children of South Asian origin who have higher underlying fat mass for a given BMI on average, compared to White British children, that is not reflected in their BMI measurements. Building on this, an exploration into the mediating effect of biomarkers could also provide more nuanced development and validation of ethnicity-specific BMI values that accurately reflect the underlying fat mass and better predict the risk of poor cardiometabolic outcomes in South Asian children. Additionally, the

development of ethnicity-specific BMI values should also take into account the potential heterogeneity in fat mass between children from different South Asian groups.

As previously discussed, an important finding in this thesis was the higher burden of healthcare use in underweight children, albeit low sample numbers. There is a need for research and exploration into different determinants of underweight in children, and to understand the pathways that lead to underweight in children from different ethnic and socioeconomic backgrounds. Findings from such research studies will provide an evidence base for local authorities to engage with local, regional, and national stakeholders to develop policy actions and implement interventions that inform parents and children on the health implications of being underweight and support them in developing behaviours that lead to a healthy weight and lifestyle.

8.6 Conclusion

In this chapter, I have interpreted the findings of this thesis in the context of the relevant literature and have highlighted the contributions it makes to the current literature. Additionally, I have also discussed the recommendations of these findings for policy and their implications for future research.

In conclusion, this thesis has shown that obesity in early childhood (age 4/5 years) is associated with higher use of primary and second healthcare services during primary school years (up to the age of 8 years), indicating a higher clinical need resulting from poorer health in obese children. Additionally, this thesis reports significantly higher direct healthcare costs associated with childhood obesity. Furthermore, this thesis highlights that in a unique context like Bradford where a much larger proportion of children live in deprived neighbourhoods and experience poorer health compared to the UK average, ethnicity does not seem to modify the association of obesity with use of healthcare

services. However, a higher proportion of obesity in Pakistani children with a much higher frequency and costs of use of primary and secondary healthcare services by Pakistani children was reported independent of their weight and deprivation status, indicating a poorer health status of Pakistani children compared to White British children. These findings highlight the important role of context and population structure in research and policy decisions on childhood obesity. To tackle the rise of childhood obesity in the UK and to diminish the socioeconomic divide in childhood obesity prevalence, it is important to understand through research the needs of local populations to trigger policy actions and implement interventions that are tailored to the demands of a multi-ethnic population.

Appendices

Appendix 1 Additional information for chapter 2

A1.1 Systematic review and meta-analysis

Open access Original research

BMJ Open

Healthcare utilisation in overweight and obese children: a systematic review and meta-analysis

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ABSTRACT

Objective This systematic review and meta-analysis aims to systematically analyse the association of overweight and obesity with health service utilisation during childhood.

Data sources PubMed, MEDLINE, CINAHL, EMBASE and Web of Science.

Methods Observational studies published up to May 2020 that assessed the impact of overweight and obesity on healthcare utilisation in children and adolescents were included. Studies were eligible for inclusion if the included participants were ≤19 years of age. Findings from all included studies were summarised narratively. In addition, rate ratios (RRs) and 95% CIs were calculated in a meta-analysis on a subgroup of eligible studies.

Outcome measures Included studies reported association of weight status with healthcare utilisation measures of outpatient visits, emergency department (ED) visits, general practitioner visits, hospital admissions and hospital length of stay.

Results Thirty-three studies were included in the review. When synthesising the findings from all studies narratively, obesity and overweight were found to be positively associated with increased healthcare utilisation in children for all the outcome measures. Six studies reported sufficient data to meta-analyse association of weight with outpatient visits. Five studies were included in a separate meta-analysis for the outcome measure of ED visits. In comparison with normal-weight children, rates of ED (RR 1.34, 95% CI 1.07 to 1.68) and outpatient visits (RR 1.11, 95% CI 1.02 to 1.20) were significantly higher in obese children. The rates of ED and outpatient visits by overweight children were only slightly higher and non-significant compared with normal-weight children.

Conclusions Obesity in children is associated with increased healthcare utilisation. Future research should assess the impact of ethnicity and obesity-associated health conditions on increased healthcare utilisation in children with overweight and obesity.

PROSPERO registration number CRD42018091752

Strengths and limitations of this study

- A systematic search of the published literature in English language in major databases up to May 2020 was conducted.
- Risk of bias was assessed in the included studies and the review is reported according to Preferred Reporting Items for Systematic reviews and Meta-Analysis guidelines.
- Search of grey literature, unpublished studies and studies published in a language other than English was not conducted.
- Meta-regression analysis could not be conducted.

INTRODUCTION

In recent years, childhood obesity has emerged as one of the greatest paediatric public health concerns worldwide. According to latest report by WHO, in 2016 over 41 million children under the age of 5, and over 340 million children and adolescents aged 5–19, were overweight or obese globally.[1] The situation is of serious concern in the UK, which is reported to be the most obese country in Western Europe by the Organisation of Economic Co-operation and Development.[2] Recent reports have shown that 1 in 5 children in the reception year (age 4–5) and 1 in 3 children in year 6 (age 12–13) are obese or overweight in the UK.[3]

The burden of obesity-related morbidity is well documented. Extensive research has shown that individuals who are obese or overweight in their childhood are more likely to stay overweight or obese in adult life,[4] leading to an increased risk of developing cardiometabolic conditions such as type 2 diabetes, ischaemic heart disease and stroke.[4–6] In addition, the increasing prevalence of overweight and obesity in childhood has led to an increase in the incidence of previously unusual metabolic imbalances at this age, and a rise in associated diseases such as type 2 diabetes and metabolic syndrome.[7–11]

Given the aforementioned associations, it could be inferred that individuals with overweight and obesity would experience greater morbidity compared with individuals of normal weight, leading to increased healthcare utilisation. Several studies have reported a strong association between overweight

or obesity and increased healthcare use.[12–14] However, majority of these have quantified this association by assuming that individuals with obesity will start accruing the obesity-associated increased healthcare use at or after a certain age, with most ignoring the healthcare use during childhood.[12 15]

In order to address this issue, we conducted a systematic review and meta-analysis with the objective of evaluating the association of overweight or obesity with healthcare utilisation in children, pooling the available evidence from eligible studies. In this review, we also aim to identify the obesity-associated conditions that may explain the association of overweight or obesity with increased healthcare utilisation.

METHODS

This review is reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) recommendations.[16] The protocol for this review is registered with PROSPERO—International Prospective Register of Systematic Reviews. The PRISMA checklist is provided as online supplemental file 1.

Literature search

A systematic literature search was performed in five electronic databases (PubMed, Medline, EMBASE, Web of Science and CINAHL) from inception to July 2018. An update of database searches was conducted in May 2020. This search update covered the full data range from inception to May 2020, and records found in the previous search were removed based on the methods described by Bramer and Bain.[17] The search focused on studies reporting association between weight status and healthcare utilisation in children. Only studies published in English language were considered for inclusion. The searches were conducted by assembling terms that could relate to the three main components of the review: 'children or adolescents', 'obesity or overweight' and 'healthcare utilisation'. These terms comprised keywords, text terms or medical subject headings appropriate for each literature database. A copy of the searches conducted to identify studies is given in online supplemental file 2. We also searched the reference lists of screened publications to look for additional articles. A forward and backward reference search for all the studies meeting the inclusion criteria was carried out to identify any other relevant studies. Research reported in grey literature was not searched. Conference abstracts and review articles were not eligible for inclusion. However, reference lists of screened review articles were checked for potentially relevant studies.

Study eligibility

Observational studies assessing the impact of overweight or obesity on healthcare utilisation in children were included in the review. Studies were excluded based on the following criteria: studied the association for underweight children only; included participants over 19 years of age; included participants both less than and greater than 19 years of age but did not stratify the results by age groups; review articles. The decision for the inclusion of children/adolescents up to the age of 19 years was made based on WHO's definition of a child and adolescent.[18] In addition, instead of restricting the inclusion criteria to studies using predefined standard body mass index (BMI) cut-offs for childhood overweight (sex-specific and age-specific BMI ≥85th centile and <95th centile) and obesity (sex-specific and age-specific BMI ≥95th centile),[19 20] a decision was made to include the study-specific definitions with the aim of assessing the effect of varying BMI cut-offs on the association of overweight or obesity with healthcare utilisation.

Study selection

Titles and abstracts of records retrieved through literature search up to July 2018 were screened by a single reviewer (TH) with a random sample of 10% of these studies screened by a second reviewer (TSA). Studies were then full text screened by the first reviewer (TH) to assess their eligibility for inclusion in the review. A random sample of 10% of these full-text studies was also screened by the second reviewer (TSA). The level of agreement between the two reviewers at each stage was assessed by Cohen's kappa score. The score was classified as follows:<0.20 indicated a poor agreement; 0.21–0.40 a fair agreement; 0.41–0.60 a moderate agreement; 0.61–0.80 a good agreement; 0.81–1.00 a very good agreement.[21] All disagreements were resolved through discussion between the two reviewers and by consulting a third reviewer (LKF) if required.

Additional records retrieved from the search update in May 2020 were screened for title, abstract and full text by the first reviewer (TH).

Data extraction and risk of bias assessment

A customised data extraction form was designed to extract following information from each study: first author's surname, year of publication, study design, country, sample size, age range, time frame, definition of obesity/overweight, outcome measures and effect size for healthcare use. Data for each study were extracted by the first reviewer (TH) and reviewed by the second reviewer (TSA). Any discrepancies were discussed and resolved through consensus between the reviewers.

The Quality Assessment tool for Observational Cohort and Cross-sectional studies by the National Heart and Lung Institute (NHLBI) was used to assess the quality and risk of bias of each included study.[22] This assessment tool rates study quality along 14 criteria, with three possible outcomes for each question: 'Yes', 'No' and 'Cannot determine/Not reported/Not applicable'. For a response of 'Yes', a score of one was assigned against the criteria, whereas a score of zero was assigned for any answer other than 'Yes'. Each study was then rated Good, Fair or Poor based on a score ranging from 0 to 14; where a 'good' study was considered to have the least risk of bias, 'fair' was susceptible to some bias and 'poor' indicated a high risk of bias.

Narrative synthesis

Due to the diverse nature of healthcare utilisation outcomes, measures of effect and lack of appropriate or sufficient data

in the majority of studies to statistically analyse these effect size measurements, a decision was made to summarise the findings of the included studies narratively. A narrative synthesis was developed to explain the impact of weight status on all the reported measures of health service use in different studies: emergency department visits, outpatient visits, general practitioner (GP) visits, hospital admissions and length of stay (LOS). In addition, potential sources of heterogeneity across studies were explored.

Statistical analysis

The 'meta' command in Stata V.16.1 [23] was used to generate meta-analysis for rate ratios (RRs) of healthcare utilisation in obese and overweight children, using normal-weight children as a reference. Studies that reported RRs with corresponding measures of precision (95% CIs or SEs) were included in the meta-analysis. In addition, studies with appropriate raw data to compute crude RRs were eligible for inclusion in the meta-analysis. Meta-analysis uses effect sizes in a metric that makes them closest to normally distributed; therefore, before undertaking the analysis in Stata, RRs were log transformed and corresponding SEs were computed from effect sizes and 95% CIs using the Comprehensive Meta-Analysis software V.3.[24] Afterwards, a random-effects meta-analysis with Hartung-Knapp-Sidik-Jonkman method was carried out.[25 26] The error rates for this method have consistently been shown to be more robust than the more commonly used DerSimonian and Laird method, particularly when there are small number of studies in the meta-analysis.[27]

Publication bias was assessed using funnel plots; however, due to the number of studies included in the analysis being less than 10, statistical tests for funnel plot asymmetry were not performed.[28] Heterogeneity among studies was assessed using the I^2 statistic. Based on the interpretation provided in the Cochrane Handbook for Systematic Reviews, heterogeneity in this review is considered substantial if I^2 >50%.[29]

Patient and public involvement

No patients or members of public were involved in the conduct and reporting of this review.

RESULTS

Study selection

A PRISMA flow diagram for study selection is shown in figure 1. The search of electronic databases up to July 2018 identified 36 077 records. After removal of duplicates, 18 966 studies were screened by titles and abstracts. A random sample of 1900 studies (10%) was also reviewed by the second reviewer. The level of agreement between reviewers at this stage was reflected by a Cohen's kappa

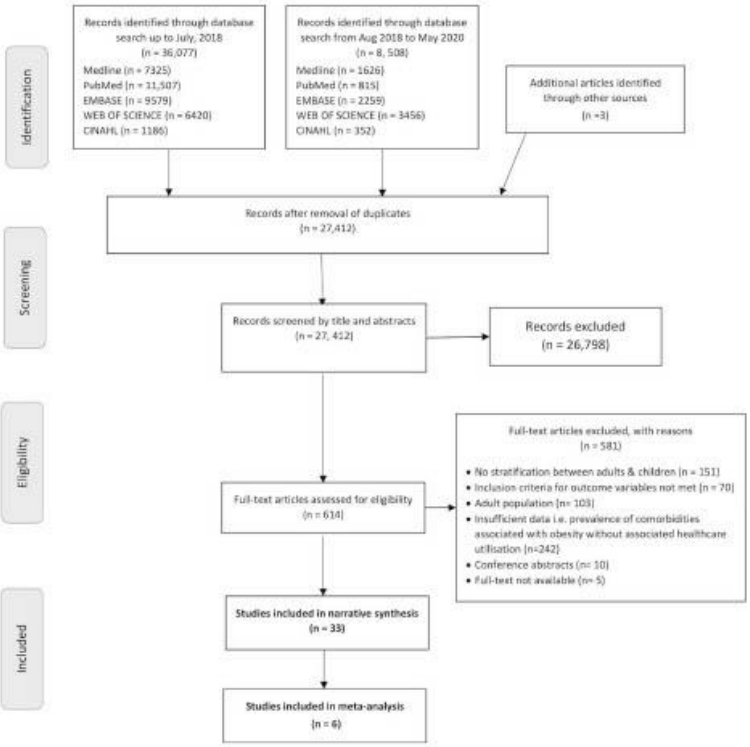

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) study selection diagram.

score of 0.86. Full texts of 578 studies were screened by the first reviewer with a random sample of 60 studies (10%) also reviewed by the second reviewer. Cohen's kappa score for level of agreement at this stage was 0.67, which indicated a good agreement. Twenty-six articles were eligible for inclusion at this stage.

The search update in May 2020 identified 8504 additional articles, of which 4 were eligible for inclusion. Three additional articles were identified through searching the reference lists of screened systematic reviews. Overall, 33 studies were eligible for inclusion. All these studies were included in the narrative synthesis, but only six were included in the meta-analysis.

Study characteristics

The basic characteristics of included studies are summarised in table 1. The majority of these studies (n=20) were conducted in the USA. Twenty-three of the included studies were cohort studies. Nine of the remaining studies used cross-sectional methods, while one study was a case–control study (table 1). Multiple studies reported data from two surveys/cohorts. The Medical Expenditure Panel Survey (MEPS) is reported in five studies[30–34] and the German Interview and Examination Survey for Children and Adolescents (KiGGS) is reported in two studies.[35 36] As studies from the same survey/cohort reported data for different years or different outcome measures, decision was made to analyse the data for each individual study.

Table 1 summarises the measures of healthcare utilisation reported across the included studies. The most commonly reported outcome measures were emergency department (ED) visits (n=10)[32–34 37–43] and outpatient (n=11) visits (including primary care and specialty visits).[32–34 36–41 43 44] Seven studies reported on healthcare use associated with respiratory diseases,[41 44–49] two reported on musculoskeletal conditions[44 50] and two on conditions concerning mental health.[37 44] The rest of the studies analysed the overall healthcare use in children with no reporting on reasons for utilisation. The studies represented children between 1 and 19 years of age. Table 1 shows that seven studies calculated BMI from anthropometric measurements (height and weight) based on self-reported or parent-reported data.[30 32–34 51 52] In all other studies, heights and weights were either measured as part of the study or recorded from the health facility records. Two studies reported data on weight only and used weight:age ratio to define obesity or overweight.[53 54] In addition, different variables were adjusted for in the multivariate analysis in respective studies. These variables are listed in table 1.

Risk of bias

The response for each study against the criteria in NHLBI's quality assessment tool to critically appraise the internal validity is shown in table 2. Fourteen studies scored a 'good' rating, sixteen had a 'fair' rating, while three had a 'poor' rating. The studies included in the meta-analysis were either of 'good' or 'fair' quality; therefore, weighting based on quality assessment was not done in the meta-analysis. However, quality assessment was used to weigh the strength of evidence during narrative synthesis.

Narrative synthesis and meta-analysis

Findings from all included studies were synthesised narratively for each outcome measure of healthcare utilisation. A subgroup synthesis was done by dividing studies based on BMI cut-offs, ethnicity and method of anthropometric measurement.

Six studies were included in the meta-analysis.[37 38 40 41 43 55] All of these studies were cohort studies (table 1). All six studies reported an association between weight status and outpatient visits and were included in the meta-analysis for outcome measure of outpatient visits. Five of these six studies also reported on association of weight status with ED visits, and were therefore included in a separate meta-analysis for outcome measure of ED visits.[37 38 40 41 43] In addition, five of these[37 38 41 43 55] used a similar definition to define obesity (age-specific and sex-specific BMI ≥95th percentile) while one study[40] defined it as age-specific and sex-specific BMI z-score ≥2, which also corresponds to BMI ≥95th percentile.[19] Moreover, five studies included in the meta-analysis for ED visits were conducted in the USA. The sixth study, which was part of analysis for outpatient visits, was conducted in Canada. For one study,[38] the appropriate effect sizes with corresponding SEs were calculated using the available raw data. One study assessed healthcare use over 1-year and 3-year periods. A decision was made to include data for 1-year period due to larger sample size as many participants were lost to follow-up by the end of the 3-year period.[37] Figures 2 and 3 show the forest plots for meta-analysis with outcome measures of ED visits and outpatients visits, respectively. Online supplemental figures 1 and 2 show forest plots for ED and outpatient visits in obese children compared with normal-weight children calculated using the pre-specified adjusted RRs reported by individual studies. Due to a small number of studies eligible for inclusion in the meta-analysis and limited to no data available on key covariates, it was not possible to perform a subgroup analysis.

ED visits

Ten studies reported ED visits as an outcome measure for healthcare utilisation.[32–34 37–41 43 53] In both obese and overweight children compared with normal-weight children, the general direction of association was an increase in visits; however, variability in the strength and direction of association was reported. For obese children compared with normal-weight children, five studies reported a significant increase in ED visits.[32 33 40 41 43] Three studies reported a non-significant increase in ED visits.[37–39] In addition, one study reported a non-significant decrease of ED visits in obese children 6–11 years old, while for obese children aged 12–17 years, a significant increase in visits was reported.[34] For overweight children, four studies reported a significant increase in ED visits compared with normal-weight children.[32 33 41 43] Two studies reported a

Table 1 Basic characteristics of included studies

First author, year	Country	Number of participants	Study design	Age in years (cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of healthcare utilisation	Covariates
Adams, 2008† [53]	USA	4263	Cross-sectional	14–19	Physical assessment measurement	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Primary care referrals Dental referrals	Not reported
Bechere Fernandes,[54] 2014	Brazil	91	Retrospective cohort	1–10	Hospital-based measurements	Weight/age ratio (W/A) for 1–3 years: excess weight W/A ≥2 z-scores, normal weight as interval from −2 to +2 z-scores. Age 3–10: excess weight BMI ≥1 z-score, normal weight BMI −2 to +1 z-score	Length of stay in the hospital	Age and sex
Bertoldi, 2010[54]	Brazil	4452	Prospective cohort	11–12	Measurement by researchers	Not given	Medicine uptake in 15 days prior to interview	Skin colour, sex, socioeconomic status, pregnancy complication, ICU admission, nutrition status, sedentary lifestyle and use of sedatives by mothers
Bettenhausen,[57] 2015†	USA	518	Cross-sectional	5–17	Hospital-based measurement	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Inpatient length of stay Readmission rates	Age, sex, race and insurance
Bianchi-Hayes,[56] 2015†	USA	17 444	Retrospective cohort study	2–18 (NHANES)	Measured by trained health technicians	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Total healthcare visits Total number of hospitalisations Mental health visits	Age, sex, ethnicity, health insurance status, household income, presence of asthma or diabetes, and the educational status of the head of household
Breitfelder,[51] 2011	Germany	3508	Cross-sectional	9–12 (GINI and LISA)	Measured or self-reported	Overweight: BMI >90th to 97th percentile. Obese >97th percentile	Expenditure associated with physician, therapist and inpatient rehabilitation visits	Sex, region, parental education and income

Continued

Table 1 Continued

First author, year	Country	Number of participants	Study design	Age in years (cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of healthcare utilisation	Covariates
Buescher,[45] 2008†	USA	30 528	Cross-sectional	12–18	Clinical measurements	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Well-child visits Respiratory-related health visits Total expenditure	Sex and ethnicity
Carroll,[47] 2006†	USA	219	Retrospective cohort	2–18	Not given	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Duration of total ICU and hospital length of stay	Age, severe persistent asthma, admission modified pulmonary index score
Dilley,[69] 2007†	USA	1216	Retrospective cohort	≥2 years	Medical record	Overweight ≥95th percentile. At risk for overweight: BMI of 85th to 94th percentile	Number of visits to private practice or public health clinics	Age, race, BMI percentile, insurance status, parental education and household tobacco use
Doherty,[68] 2017	Ireland	5924	Prospective cohort	13 (GUI)	Measurement by health professionals	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	GP visits Inpatient stay	Child characteristics: gender, birth weight, gestation age and citizenship. Mother's characteristics: age, health status, education status, marital status and depression score. Household characteristics: income, location and health insurance status
Estabrooks and Shetterly,[37] 2007*†	USA	8282	Prospective cohort	3–17	Hospital medical record	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Primary care (outpatient) visits ED visits Number of hospitalisations	Sex, age and disease status
Fleming-Dutra,[53] 2013†	USA	32 966	Retrospective cohort	2–18	Hospital medical record	Overweight >95th percentile sex-specific weight for age. Normal weight ≤95% sex-specific weight for age	Billed charges for child's visit Hospitalisation rate ED length of stay in hours	Race, age, sex, insurance, and acuity

Continued

Table 1 Continued

First author, year	Country	Number of participants	Study design	Age in years (cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of healthcare utilisation	Covariates
Griffiths,[49] 2018	UK	3269	Prospective cohort	5–14	Measured by trained interviewers	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Hospital admission	Sex, mode of delivery, preterm, long-standing illness, disability, maternal BMI
Hampl,[38] 2007*†	USA	8404	Retrospective cohort	5–18	Measured by clinical nursing staff	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Primary care visits ED visits Laboratory use	Age, sex, race and insurance status
Hering,[39] 2009	Israel	Cases: 363 Controls: 382	Retrospective case–control	4–18	Clinical measurement	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	ED visits Primary care clinic visits Hospital admissions	Control group matched for age and gender
Janicke,[40] 2010*†	USA	200	Retrospective cohort	7–15	Measured by a trained researcher	Overweight: BMI z-score ≥1 and <2. Obese: BMI z-score ≥2	ED visits Acute care claims Outpatient and medical claims	Age, sex, ethnicity, insurance status
Kelly,[48] 2019	UK	9443	Prospective cohort	4–5	Measured by trained school nurses	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	GP appointments GP prescriptions	Sex, maternal age, gestational age, means tested benefits, Index of Multiple Deprivation (2010)
Kovalerchik,[43] 2020*†	USA	30 352	Retrospective cohort	3–17	Hospital-based measurements	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Emergency department visits Outpatient visits	Age, age^2, sex, race/ethnicity, and insurance status
Kuhle,[55] 2011†	Canada	4380	Prospective cohort	10–11	Measured by research assistants	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	GP visits Specialist referrals Total healthcare costs	Sex, income, education status and geographical region
Lynch,[41] 2015*†	USA	19 528	Retrospective cohort	2–18	Hospital medical record	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Outpatient visits ED visits Number of hospitalisations	Sex, age and socioeconomic status
Monheit,[30] 2009†	USA	6738	Retrospective cohort	12–19 (MEPS)	Parent-directed and self-directed	At risk for overweight BMI ≥85th and <95th percentile. Overweight BMI ≥95th percentile	Overall health expenditure	Age, race, region, parental education attainment and parental smoking

Continued

Table 1 Continued

First author, year	Country	Number of participants	Study design	Age in years (cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of healthcare utilisation	Covariates
Ortiz Pinto,[44] 2019	Spain	1857	Prospective cohort	4–6	Measured by paediatricians	Overweight: BMI z-score ≥1 and ≤2. Obese: BMI z-score >+2	Primary care visits Drug prescriptions Hospital admissions	Sex, age in months, mother's education, breastfeeding duration, family purchasing power
Skinner,[31] 2008†	USA	Not given	Cross-sectional	6–17 (MEPS)	Physical examination in NHANES. Parent-reported in MEPS	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Healthcare expenditure	Year, sex, race, poverty and insurance status
Trasande and Chatterjee,[32] 2009*	USA	19 613	Prospective cohort	6–19 (MEPS)	Parent-reported and self-reported	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Outpatient visits ED visits Healthcare expenditure	Race, gender, insurance status and family income
Trasande,[32] 2009*	USA	Not given	Prospective cohort	2–19	Parent-reported and self-reported	Based on ICD-9 diagnostic codes	Obesity-associated hospitalisations	Age, sex, ethnicity, expected primary payer, hospital location, hospital teaching status and median household income
Turer,[33] 2013*	USA	17 224	Cross-sectional	10–17 (MEPS)	Parent-reported and self-reported	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Hospital-based outpatient, or clinic visit Specialist visits ED visits Outpatient prescriptions	Gender, age, race, insurance status, and poverty status
van Leeuwen,[50] 2018	Netherlands	617	Prospective cohort	2–18 (DOERAK)	Measured by GP or research assistant	Overweight: BMI z-score ≥1 and <2. Obese: BMI z-score ≥2	Number and type of musculoskeletal consultation Total number of consultations	Age, gender, socioeconomic status and marital status
Wake, 2010[85]	Australia	923	Prospective cohort	5–19	Measured by trained field workers	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Healthcare visits	Sex, age and Socio-Economic Indexes for Areas (SEIFA) disadvantage index

Continued

Table 1 Continued

First author, year	Country	Number of participants	Study design	Age in years (cohort/survey)	Anthropometric measurement	BMI cut-offs	Measures of healthcare utilisation	Covariates
Wenig,[35] 2011	Germany	14 592	Retrospective cohort	3–17 (KiGGS)	Measured through physical examination	Overweight: BMI >90th to 97th percentile. Obese >97th percentile	Number of pharmaceuticals taken in the last 7 days	Age, sex, socioeconomic status and migrant status
Wenig,[36] 2012	Germany	14 277	Cross-sectional	3–17 (KiGGS)	Measured through physical examination	Overweight: BMI >90th to 97th percentile. Obese >97th percentile	Physician visits	Sex, age, BMI group, socioeconomic stats, town size, and east or west Germany variable
Woolford,[46] 2007†	USA	777 274	Cross-sectional	2–18	Hospital-based measurements	Obesity was defined based on ICD-9-CM codes Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Length of stay Total charges	Sex, race, region and hospital type
Wright and Prosser,[34] 2014†	USA	23 727	Cross-sectional	6–17 (MEPS)	Parent-reported and self- reported	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	ED visits Outpatient visits Prescription of drugs	Age, BMI class, sex, ethnicity, census region, poverty status, insurance status and survey year
Wyrick,[42] 2013†	USA	1746	Prospective cohort	2–18	Hospital-based measurements	Overweight BMI ≥85th and <95th percentile. Obese BMI ≥95th percentile	Admissions from ED	Age and sex

*Studies included in the meta-analysis.
†Studies using Centers for Disease Control (CDC) criterion to define obesity and not at the level of the survey/cohort. None of the six studies included in the meta-analysis use data from the same source.
BMI, body mass index; ED, emergency department; GP, general practitioner.

Table 2 Risk of bias assessment of included studies

Study	Criteria														Rating
	Research question or objective clearly stated	Study population clearly defined	Participation rate of eligible persons at least 50%	Groups recruited from the same population with uniform eligibility criteria	Sample size justification	Exposure assessed prior to the outcome	Sufficient timeframe to see an effect	Different levels of exposure of interest (categorical/ continuous)	Exposure variables clearly defined or not were the tools used for measurement were accurate	Repeated exposure assessment	Outcome measures clearly defined and measured	Blinding of the outcome assessors	Loss to follow-up 20% or less	Statistical analysis (measurement and adjustment of confounding variables)	
Adams, 2008[43]	1	0	0	1	0	0	0	1	0	0	1	0	0	0	Poor
Bech ere Fernandes et al[54]	1	1	0	1	1	1	1	1	1	0	1	0	0	1	Good
Bertoldi, 2010[44]	1	0	0	1	0	1	1	0	1	0	0	0	0	1	Poor
Bettenhausen[9]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Fair
Bianchi-Hayes[26]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Fair
Bietekker2011	1	1	0	1	0	0	0	1	1	0	0	0	0	1	Fair
Buescher et al[45]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Fair
Carroll et al[47]	1	1	0	1	0	1	1	1	0	0	1	0	0	1	Fair
Dilley et al[50]	1	0	0	1	0	1	1	1	0	0	0	0	0	1	Poor
Doherty et al[8]	1	1	0	1	0	1	1	1	1	1	1	0	0	1	Good
Estabrooks and Shetterly[27]	1	1	0	1	0	1	1	1	1	1	1	0	0	1	Good
Fleming-Dutra et al[33]	1	1	0	0	1	1	1	1	0	0	1	0	0	1	Fair
Griffiths et al[30]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Good
Hamplet al[156]	1	1	0	1	0	1	1	1	1	0	1	0	1	1	Good
Hering et al[28]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Fair
Janicke et al[46]	1	1	0	1	0	0	0	1	1	0	1	0	0	1	Fair
Kelly et al[48]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Good
Kondarchik et al[34]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Good
Kuhle et al[55]	1	1	1	1	0	1	1	1	1	0	1	0	1	1	Good
Lynch et al[41]	1	1	0	1	0	1	1	1	1	1	1	0	1	1	Good
Monbek et al[40]	1	1	0	1	0	0	1	1	1	0	0	0	0	1	Fair
Ortiz-Pinto et al[44]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Good
Skinner et al[31]	1	1	0	1	0	1	1	1	0	0	1	0	0	1	Fair
Trasande and Chatterjee[32]	1	1	0	1	0	0	1	1	0	1	0	0	0	1	Fair
Trasande et al[52]	1	1	0	1	0	1	1	0	0	0	1	0	0	1	Fair
Turer et al[29]	1	1	0	1	0	1	1	1	0	1	0	0	0	1	Fair
van Leeuwen et al[53]	1	1	1	1	0	1	1	1	1	1	1	0	1	1	Good
Wake et al[35]	1	1	0	1	0	0	1	1	1	1	1	0	1	1	Good
Wenig et al[42]	1	1	0	1	0	1	1	1	1	0	1	0	0	1	Fair
Wenig, 2012[36]	1	1	0	1	0	1	1	1	1	0	0	0	0	1	Fair

Continued

Table 2 Continued

Study	Criteria																Rating
	Research question or objective clearly stated	Study population clearly defined	Participation rate of eligible persons at least 50%	Groups recruited from the same population with uniform eligibility criteria	Sample size justification	Exposure assessed prior to the outcome	Sufficient timeframe to see an effect	Different levels of exposure of interest (categorical/ continuous)	Exposure variables clearly defined or not were the tools used for measurement were accurate	Repeated exposure assessment	Outcome measures clearly defined and measured	Blinding of the outcome assessors	Loss to follow-up 20% or less	Statistical analysis (measurement and adjustment of confounding variables)	
Woolford et al, 2007[46]	1	1	0	1	0	0	1	1	0	0	1	0	0	1	Fair
Wright and Prosser, 2014[41]	1	1	0	1	0	1	1	1	1	1	1	0	0	1	Good
Wyrick et al, 2013[40]	1	1	0	1	0	1	1	1	1	0	1	0	1	1	Good

*1=Yes; 0=No/cannot determine/not recorded. Rating: Poor, score ≤4; Fair, score 7–4; Good, score ≥10.
†Studies included in the meta-analysis

non-significant increase[34 38] and two studies reported a non-significant decrease.[37 40]

In the five studies included in the meta-analysis for ED visits, obese children were significantly more likely to visit EDs compared with normal-weight children (figure 2A). The associated effect size (RR) was 1.34 (95% CI 1.07 to 1.68). The effect size for overweight versus healthy weight was RR 1.11 (95% CI 0.92 to 1.33) (figure 2B). The I^2 statistic showed substantial between-study heterogeneity for obese versus normal weight (I^2=94.3%, p<0.01) and overweight versus normal weight (I^2=92.5%, p<0.01).

On visual inspection of funnel plot asymmetry, there is a possibility of publication bias, with a small sized study reporting high RRs for obese children (online supplemental figure 3). A statistical test for publication bias was not performed due to small number of studies (n<10).

Outpatient visits

Eleven studies reported outpatient visits as a measure of healthcare utilisation.[32–34 36–41 43 44] In obese children compared with normal-weight children, the general direction of association was an increase in visits; however, variability in the strength of association was reported. Seven studies reported a significant increase in outpatient visits for obese children,[32 33 37 39–41 43] while four studies reported a non-significant increase.[34 36 38 44] For overweight children compared with normal-weight children, three studies reported a significant increase in outpatient visits.[37 41 43] Five studies reported a non-significant increase[32–34 36 38] while two studies reported a non-significant decrease in outpatient visits.[40 44]

Pooled unadjusted RRs for obese versus normal weight and overweight versus normal weight were 1.11 (95% CI 1.02 to 1.20) and 1.02 (95% CI 0.98 to 1.08), respectively (figure 3A,B). Significant between-study heterogeneity was observed for both obese versus normal-weight children (I^2=87.6%, p<0.01) and overweight versus normal-weight children (I^2=73%, p<0.01).

Visual inspection of funnel plot asymmetry for outpatient visits in obese children suggests publication bias (online supplemental figure 4). Statistical tests to assess publication bias were not performed due to the small number of studies (n<10).

Hospital admissions and LOS

Seven studies reported hospital admissions as a measure of healthcare use.[37 39 41 42 44 49 56] One study reported a significant increase[39] while two studies reported a non-significant increase[37 49] in hospital admissions for obese children compared with normal weight. Two studies reported a non-significant decrease in admissions.[44 56] In addition, one study reported that 14.5% of obese or overweight children were admitted, compared with 16.5% normal-weight children.[42] For overweight children, one study reported a significant decrease[56] while one reported a non-significant decrease[37] in admissions compared with normal-weight children.

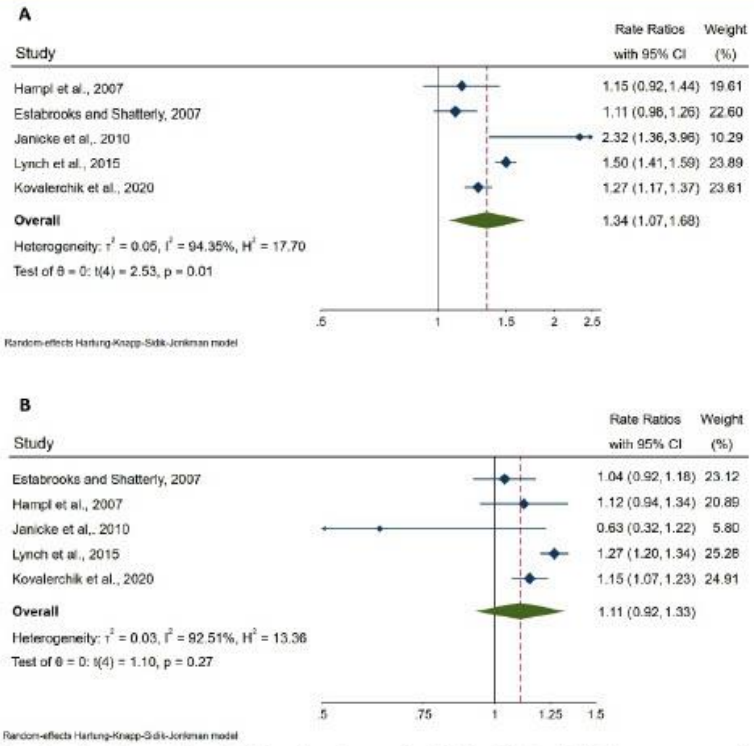

Figure 2 Forest plots showing the unadjusted effect sizes (rate ratios (RRs) with 95% CIs) for emergency department visits in (A) obese children, (B) overweight children. RRs are computed with normal-weight children as the reference category.

Hospital LOS was reported as a measure of healthcare utilisation by six studies.[46 47 52–54 57] Four studies found a significant increase in LOS for obese children compared with normal weight.[46 47 52 54] One study reported a slight significant decrease in LOS for obese children,[57] while one study reported no association between obese and normal-weight children.[58]

GP visits

Three studies reported GP visits as a measure for healthcare utilisation.[48 55 58] All three studies reported a significant increase in GP visits for overweight and obese children, compared with their normal-weight peers.

Associated medical conditions

Five studies reported on the effect of asthma or acute respiratory disorders on healthcare utilisation in obese children.[41 45–48] Of these studies, four reported that obese children significantly incurred increased healthcare use for asthma compared with normal-weight children.[45–48] In addition, two studies found that other acute respiratory conditions are also significantly associated with increased healthcare use in obese children.[41 45] Furthermore, two studies reported a non-significant increase for respiratory conditions in obese children.[44 46]

Two studies reported that obese children are at a significantly greater risk of seeking healthcare for mental health problems compared with normal-weight children.[37 44] The risk for overweight children was also reported to be higher but non-significant. Two studies reported a non-significant increase in visits for musculoskeletal problems in obese children compared with normal-weight children.[44 50]

BMI cut-offs

Table 1 shows that 20 of the included studies used the Centers for Disease Control or the International Obesity task force cut-off points to classify children into weight categories. However, some studies used the term 'overweight' in place of obese for ≥95% percentile, while using the term 'at-risk of overweight (AROW)' in place of overweight for children with BMI percentiles ≥85% and ≤95%. During the analysis, we adjusted for this difference in terminologies.

Two studies used the weight for age BMI z-score classification.[40 54] The effect size reported by these two studies for obese children was significant and much stronger than the studies not using this criterion. Three studies using data from German survey KiGGs and GINI and

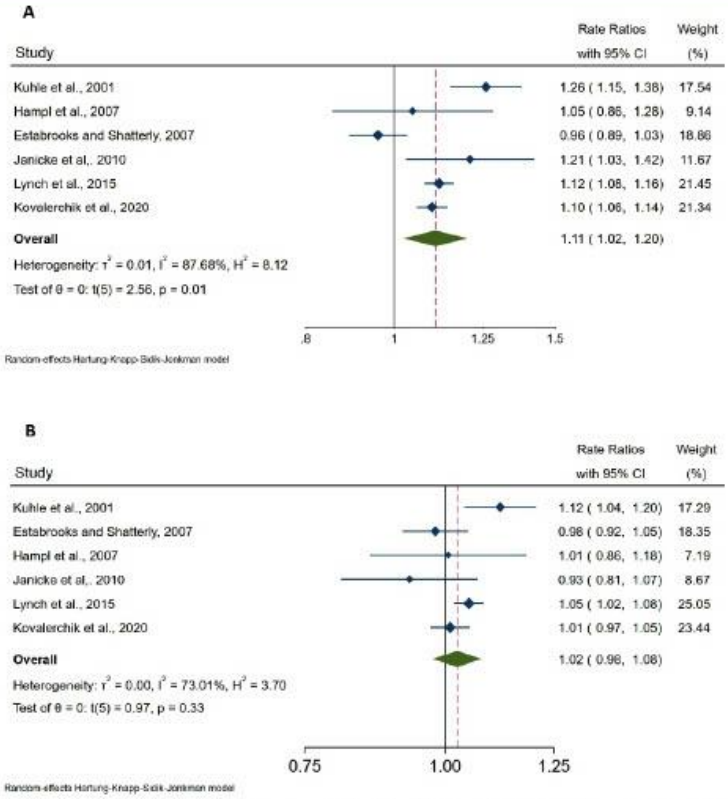

Figure 3 Forest plots showing the unadjusted effect sizes (rate ratios (RRs) with 95% CIs) for outpatient visits in (A) obese children, (B) overweight children. RRs are computed with normal-weight children as a reference category.

LISA cohorts used the country-specific BMI cut-off values with obesity defined as >97th percentile.[35 36 51] It was not possible to formally establish a comparison based on BMI cut-off criteria due to the small number of studies using respective BMI cut-offs and the use of different outcome measures across these studies.

Ethnicity

Two studies reported the effect of ethnicity on the association of weight status with healthcare utilisation.[30 59] Both these studies were from the USA. They reported a decrease in healthcare utilisation in black overweight or obese children compared with white overweight or obese children. In addition, one study also reported decreased healthcare use in obese Asian or Hispanic children compared with white obese children.[30]

Anthropometric measurements

Seven studies recorded the height and weight by self-reporting or parental reporting without validation.[30–34 51 52] Five of these studies used data from MEPS survey in the USA. Variability in the direction and strength of association between weight status and healthcare use was observed across these studies. This heterogeneity could be subject to reporting bias due to self-reporting or parent-reporting; however, not enough data were available to formally assess this.

DISCUSSION

This systematic review and meta-analysis has demonstrated an association between excess weight and increased healthcare use in children. Thirty-three studies were included in the review, of which six had appropriate data to be included in the meta-analysis. Attesting to the diverse nature of health services and the variability in their provision in different countries, the studies used multiple outcome measures to define healthcare utilisation. Commonly examined outcome measures were outpatient visit, ED visit, hospital admission and hospital LOS. Studies included in the meta-analysis reported an increased risk of healthcare utilisation in obese children compared with normal-weight children. A significant

unadjusted positive association of obesity with increased outpatient and ED visits was observed in the meta-analysis. The results of the narrative synthesis supported these findings and indicated that obese children are much more likely to have higher healthcare utilisation for all the reported outcome measures. However, variability in the direction and strength of association was observed across studies, with a few studies reporting a negative or no association.

A vast body of research and associated systematic reviews exist which have analysed the burden of adult obesity on healthcare systems and also the incremental health burden of child obesity during adulthood.[60–62] Such studies have indicated repeatedly that obesity is significantly related to a greater risk of morbidity in adult life and associated increase in healthcare utilisation. Our review builds on this knowledge and suggests that much like adult life, obesity during childhood results in an increased burden of morbidity on healthcare services. These findings can be explained in the light of recent clinical research reporting an increasing prevalence of obesity-related conditions in childhood that were more commonly associated with adulthood in the past.[7 63]

This leads our discussion into one of the secondary objectives of the review: to analyse the most common obesity-associated health conditions that are contributing to an increased healthcare use in children with obesity. Most of the included studies did not attempt to ascertain the reason for increased healthcare utilisation. Two studies included in the review analysed the rate of mental health related visits in obese children, with both reporting an increased risk. These findings support the previous evidence that has shown obesity to be a strong risk factor for stigmatisation and development of low self-esteem and other mental health issues in children.[64 65] The role of obesity in increasing the risk of asthma in children is well founded.[66] Five studies in the review supported the previous evidence and reported that obesity leads to increased health service utilisation in asthmatic children and also in children with other respiratory diseases.

Regional variation in rates of healthcare utilisation is well reported in literature.[67–69] When studies conducted in different regions or countries with different population characteristics and healthcare systems are systematically reviewed and analysed together, regional variation in healthcare utilisation may result in between-study heterogeneity. Evidence suggests that this regional variation is in part driven by population-specific factors such as ethnicity, socioeconomic status, health status, cultural beliefs and preferences.[68] The prevalence of childhood obesity varies between different regions and countries. It is also well reported that within a population, the prevalence of obesity varies between children of different ethnic origins.[3 70 71] In addition, evidence shows an inverse relationship between the prevalence of obesity and low socioeconomic status.[3 72] The extent to which this variability in prevalence translates into variability in associated morbidity and healthcare use is not known. There is evidence that healthcare seeking behaviour and healthcare uptake varies across ethnic groups and socioeconomic classes.[73–76] Most of this evidence suggest that people belonging to black and other minority ethnic groups are at a disadvantage in accessing health services.[77 78] In addition, cultural beliefs and perceptions towards health status in general and weight status in particular may contribute to ethnic disparities in healthcare utilisation.[79 80] None of the studies included in the review analysed the impact of socioeconomic status while only two studies analysed the impact of ethnicity. They reported a significantly lower use of health services in obese children of black, Asian and other ethnic minority groups compared with white children. To what extent this lower use is a result of disadvantage in access to healthcare and what results from differences in prevalence and in levels of morbidity remains unclear. In addition, both of these studies were from the USA, which has specific health insurance programmes for children.[81 82] Therefore, care should be taken in generalising these findings to other countries with different healthcare systems. In the light of these two studies and previous research evidence, we can infer that ethnicity and socioeconomic status could be sources of between-study heterogeneity reported in this review; however, as the studies did not report the ethnic and socioeconomic characteristics of the populations studied, it was not possible to explore this further. Evidence also suggests that in addition to population-specific factors, regional variation in healthcare is in part due to differences in region-specific factors such as access to health services, healthcare resources, health policies and physician beliefs.[68 69] For example, some percentage of the between-study heterogeneity reported in our review may be attributable to regional variations in physician beliefs towards excess weight or barriers and facilitators to healthcare access. However, exploring the extent of heterogeneity due to region-specific variables was beyond the scope of this review.

Strengths and limitations

This review has a number of strengths. First, to our knowledge this is the first systematic review and meta-analysis of the utilisation of healthcare services in obese and overweight children. Second, we have used a comprehensive search strategy, with publications not restricted by region or year of publication which resulted in the inclusion of 33 studies reporting outcome measures from primary and secondary healthcare. In addition, a protocol was developed and registered a priori and methodological guidelines were followed on conducting and reporting a review.

A limitation of this review was the restriction of studies to English-language reports only. A limitation of the meta-analysis was the inclusion of only six studies which meant we were unable to include all the outcomes described in the review. In addition, there was uncertainty over the weighted effect sizes due to between-study heterogeneity in methods and outcomes.

There were some further limitations in terms of the characteristics of the included studies. First, the majority of the studies were from the USA, with the remainder being from eight first-world countries, therefore limiting the extent to which the findings may be generalised beyond certain national contexts due to differences in healthcare services and systems. Second, there was poor reporting of data for key study characteristics. For example, none of the studies included in the meta-analysis reported the use of healthcare services stratified by sex. Therefore, it was not possible to run a subset analysis and adjust for covariates in a meta-regression to formally analyse sources of between-study heterogeneity.

CONCLUSIONS

In summary, this systematic review has shown that overweight and obesity in children is positively associated with increased utilisation of ED and outpatient healthcare services during childhood. This finding remained in the meta-analysis although with potential heterogeneity between studies. The reported evidence for inpatient health service use is mixed. The studies included in the review are limited to only a few developed countries; therefore, it is difficult to generalise these findings to other countries due to differences in healthcare systems and delivery of health services. The substantial between-study heterogeneity reported in the review might be due to these differences across countries; however, it was not possible to formally analyse this due to insufficient data. The review has identified areas of research where gaps exist. In particular, further research is required in understanding the dynamics of obesity-associated health conditions that may drive increased healthcare utilisation in children. In addition, the driving factors behind the varying effect of ethnicities and socioeconomic status on association of obesity with healthcare utilisation are yet to be explored. Such evidence is necessary for the development of policies for clinical practice and research, and for their implementation in a way that, while being cost-effective, can successfully target the therapeutic needs of obese and overweight children from different ethnic and socioeconomic backgrounds.

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Contributors TH conceptualised and designed the protocol, conducted the literature search and screening, assessed risk of bias, extracted data, conducted the narrative synthesis and meta-analysis, drafted the initial manuscript and revised the manuscript. TSA screened the studies, reviewed the extraction of data and quality assessment, and revised the initial and subsequent drafts. JW and LKF designed the protocol, revised the initial and subsequent manuscript drafts and approved the final version for publication. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of work.

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A1.2 Search strategy

1. MEDLINE (Ovid)

1. child*.mp. or Child/
2. Adolescent/ or adolescent*.mp.
3. pediatric*.mp.
4. teen*.mp.
5. infant*.mp. or exp INFANT/
6. 1 or 2 or 3 or 4 or 5
7. Body Weight/ or body weight*.mp.
8. Obesity/
9. Body Mass Index/
10. obese.mp. or Overweight/
11. 7 or 8 or 9 or 10
12. tertiary care.mp. or exp Tertiary Healthcare/
13. primary care.mp. or exp Primary Health Care/
14. secondary care.mp. or exp Secondary Care/
15. prescription*.mp. or exp PRESCRIPTION DRUGS/.
16. health visit*.mp
17. health resource*.mp. or exp Health Resources/
18. outpatient*.mp. or OUTPATIENT CLINICS, HOSPITAL/
19. hospital*.mp.
20. exp Health Services/ or health servic*.mp.
21. emergency care.mp. or exp Emergency Medical Services/
22. exp HEALTH EXPENDITURES/ or expenditure*.mp.
23. exp Health Care Costs/ or health care cost*.mp.
24. General Practice/ or general practi*.mp.
25. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24
26. 6 and 11 and 25
27. limit 26 to (english language and humans)

2. PubMed

((((((("Child"[Mesh]) OR "Adolescent"[Mesh]) OR "Infant"[Mesh]) OR teen[Text Word] OR child [Text Word] OR adolescent[Text Word] AND ((((("Pediatric Obesity"[Mesh]) OR "Body Mass Index"[Mesh]) OR obesity[Text Word] OR adiposity[Text Word] AND (((((((("Emergency Medical Services"[Mesh]) OR "Primary Health Care"[Mesh]) OR "Child Health Services"[Mesh]) OR "Adolescent Health Services"[Mesh]) OR "Health Services"[Mesh]) OR "Outpatient Clinics, Hospital"[Mesh]) OR "General Practice"[Mesh]) OR "Emergency Service, Hospital"[Mesh]) OR health visit[Text Word] AND "Humans"[Mesh] AND (english[Filter])

3. Web of Science

1. TOPIC: (child*) OR TOPIC: (pediatric*) OR TOPIC: (adolescen*) OR TOPIC: (infant*)
2. TOPIC: (primary care) OR TOPIC: (medical care) OR TOPIC: (healthcare) OR TOPIC: (tertiary care) OR TOPIC: (emergency care) OR TOPIC: (outpatient*) OR TOPIC: (prescription*) OR TOPIC: (health service*) OR TOPIC: (healthcare utilisation) OR TOPIC: (healthcare cost) OR TOPIC: (general practi*) OR TOPIC: (health visit*)
3. TS=(obes*) OR TS=(adipos*) OR TS=(body mass index*) OR TS=(overweight*)
4. #3 AND #2 AND #1
5. #3 AND #2 AND #1
6. Refined by: LANGUAGES: (ENGLISH)

4. EMBASE

1. child*.mp. or exp CHILD/
2. pediatric*.mp.
3. exp Adolescent/ or adolescen*.mp.
4. exp INFANT/ or infant*.mp
5. 1 or 2 or 3 or 4
6. exp Obesity/ or obes*.mp.
7. exp Body Mass Index/
8. adipos*.mp. or exp Adiposity/
9. exp OVERWEIGHT/ or overweight*.mp.
10. 6 or 7 or 8 or 9

11. primary care.mp. or exp Primary Health Care/
12. tertiary care.mp. or exp Tertiary Healthcare/
13. prescription*.mp. or exp PRESCRIPTION DRUGS/
14. health visit*.mp.
15. outpatient*.mp. or exp OUTPATIENT CLINICS, HOSPITAL/
16. exp Emergency Medical Services/ or emergency care*.mp.
17. exp HEALTH EXPENDITURES/ or expenditure*.mp
18. exp General Practice/ or general practi*.mp.
19. exp Health Care Costs/ or health care cost*.mp.
20. health resource*.mp. or exp Health Resources/
21. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
22. 5 and 10 and 21
23. limit 22 to (human and english language)

A1.3 Data extraction form

Study	**(Lynch et al., 2015)**
Study design	Retrospective cohort study
Year of publication	2015
Location	Olmstead County
Country	USA
Journal	Academic paediatrics
Setting	Emergency department, outpatient clinics,
Sampling frame	Children, aged 2-18 years, residing in Olmstead County in 2015
Age-range	2-18 years
Sample size	19,528
Time Frame	January 2005 - December 2013
Definition of Obesity/BMI levels	Under/healthy weight <85 percentile. overweight ≥85 -<95 percentile. Obese ≥ 95th percentile

AIMS/objectives	outpatient clinic visits, ED visits, and hospitalisations from the first BMI measurement after January 1, 2005, through last follow-up or December 31, 2013 for each child.
Stratification/adjustments/Covariates	Adjusted for sex, age, and socioeconomic status.
Methods	Rates of utilisation were compared across BMI levels using Poisson and negative binomial models to model utilisation counts, with the natural log of the person-years of follow-up used as an offset. Multivariable negative binomial models were used toadjust for age, race, sex, SES, and chronic medical conditions.
Outcome Measures	Outpatient clinic visits. Emergency department visits. No. of hospitalisations.
Key findings	ED visits increased from 0.28 per person year in children who were healthy weight or underweight to 0.42 per person year in children with obesity ($p<0.05$).
Description of results/findings	Compared to children with BMI < 85th percentile, children who were overweight and obese had increased ED visits [adjusted incident rate ratio (IRR):1.16, 95% confidence interval (CI):1.10, 1.23 and IRR: 1.27, 95% CI: 1.19, 1.35, respectively (p for trend <0.0001)]. No increased risk of hospitalisations by baseline BMI category and a minimally increased risk of outpatient clinic visits for both children who were overweight (IRR: 1.05, 95% CI: 1.02-1.08) or obese (IRR: 1.07, 95% CI: 1.04-1.11) in the adjusted model
associated health conditions	Children who were overweight or obese were more likely to have an ED visit for an accident/injury or acute respiratory disease than children who were under/healthy weight (no significance given)
Cost estimates	Not Analysed

A1.4. ED visits in obese children compared to normal weight (adjusted)

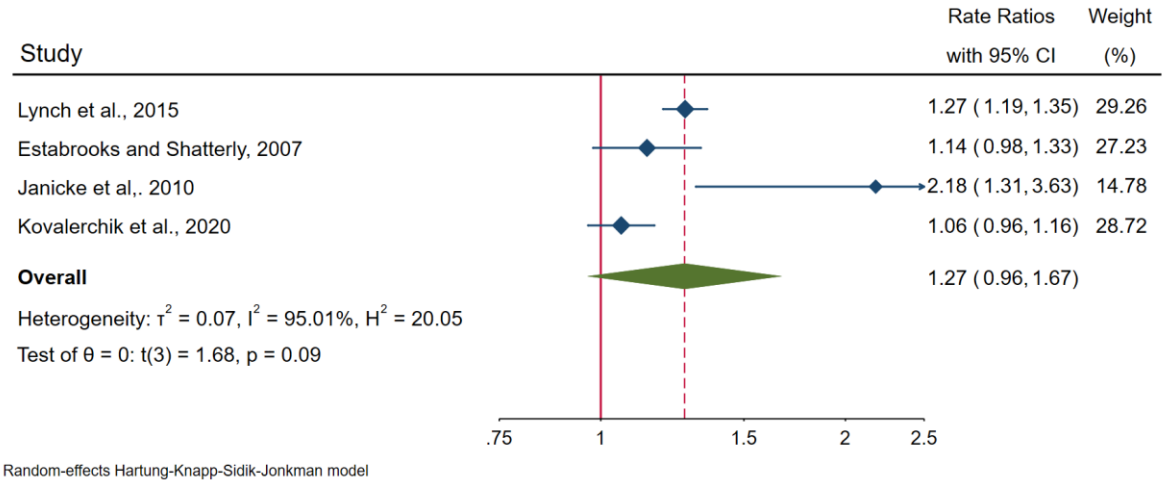

Figure A1.4. Forest plots showing the adjusted* effect sizes (with 95% CIs) for ED visits

A1.5. Outpatient visits in obese children compared to normal weight (adjusted)

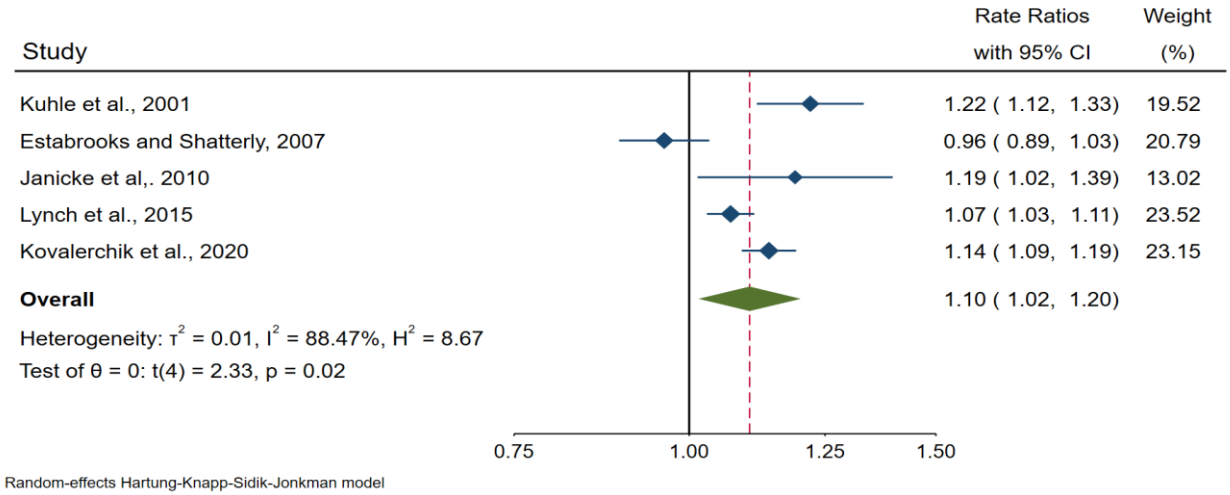

Figure 1.5. Forest plots showing the adjusted* effect sizes (with 95% CIs) for outpatient visits.

A1.6: Summary of cost-analysis by each study

First author, Year	Country	No. of participants	Study Design	Cost-analysis
Adams, 2008[a]	USA	4,263	Cross-sectional	No analysis of costs
Bechere Fernandes et al, 2014	Brazil	91	Retrospective cohort	No analysis of associated costs
Bertoldi, 2010	Brazil	4,452	Prospective cohort	No analysis of costs
Bettenhausen, 2015[a]	USA	518	Cross-sectional	No analysis of associated costs
Bianchi-Hayes, 2015[a]	USA	17,444	Retrospective cohort study	No analysis of costs
Breitfelder et al., 2011	Germany	3,508	Cross-sectional	Based on reporting by parents of the visits to physicians, number of hospital days. Price per physician contact for each medical specialty. Although non-significant, obese children had the highest mean annual direct medical costs: 680 euros. Underweight: 468 euros Normal weight: 402 euros Overweight: 468 euros
Buescher et al., 2008[a]	USA	30,528	Cross-sectional	Based on Medicaid's paid claims and enrollment records. Hospital costs, physician costs and prescription drug costs. Simple differences of mean tests to check differences in costs. Total avg medical expenditure during 2004: Underweight: $6598 Normal weight: $3604 Overweight: $4791 Obese: $4491
Carroll et al., 2006[a]	USA	219	Retrospective cohort	No analysis of costs
Dilley et al., 2007[a]	USA	1,216	Retrospective cohort	No analysis of costs

First author, Year	Country	No. of participants	Study Design	Cost-analysis
Doherty et al., 2017	Ireland	5,924	Prospective cohort	No analysis of costs
Estabrooks and Shetterly, 2007[*a]	USA	8,282	Prospective cohort	No analysis of costs
Fleming-Dutra et al., 2013[a]	USA	32,966	Retrospective cohort	Costs of acute care/visits to the ED. Only use normal and overweight categories. No difference in costs between normal weight and overweight for all ED visits. Normal weight: $6302 Overweight: $6067
Griffiths et al., 2018	United Kingdom	3,269	Prospective cohort	No analysis of costs
Hampl et al., 2007[*a]	USA	8,404	Retrospective cohort	Mean difference of costs of primary, ED and outpatient, inpatient combined per year. Medicaid paid claims. Obese: 617 (533 sd) Normal: 445 (450) Overweight: 473 (461)
Hering et al., 2009	Israel	Cases: 363 Controls: 382	Retrospective case control	No analysis of costs done
Janicke et al., 2010[*a]	USA	2,00	Retrospective cohort	Medicaid claims paid to the providers. gamma regression Outpatient/Physician expenditures: Obese: $1813 Normal: $1176 Overweight: $1070 ED expenditure: Normal: $132 Overweight: $122 Obese $212

First author, Year	Country	No. of participants	Study Design	Cost-analysis
Kelly et al., 2019	United Kingdom	9,443	Prospective cohort	Crude analysis (unadjusted). Obese children had estimated $28 (18 – 37) additional costs. Underweight children had estimated $49 (12-87) additional costs
Kovalerchik et al., 2020[*a]	USA	30,352	Retrospective cohort	No analysis of costs
Kuhle et al., 2011[*]	Canada	4,380	Prospective cohort	Aggregate costs of physician visits and hospitalisations. For obese children, the difference of costs (ES 1.21 (1.02-1.43) from normal weight was statistically significant. Specific cost estimates were not given. Cost estimates are not given
Lynch et al., 2015[*a]	USA	19,528	Retrospective cohort	No analysis of costs
Monheit et al., 2009[a]	USA	6,738	Retrospective cohort	Medicaid claims paid to the providers. Estimates are only given for females Overweight (obese) females: $2101 ($p < 0.01$) Normal weight: $1311 Overweight: $1778 ($p = 0.10$) Underweight: $1565
Ortiz Pinto et al., 2019	Spain	1,857	Prospective cohort	No analysis of costs
Skinner et al., 2008[a]	USA	Not given	Cross-sectional	No analysis of costs

First author, Year	Country	No. of participants	Study Design	Cost-analysis
Trasande and Chatterjee, 2009[a]	USA	19,613	Prospective cohort	Medicare and Medicaid claims. No estimates by exposure given. Obese children: $194 additional costs for outpatient, $114 additional costs for prescriptions. $12 additional Ed costs Overweight: $79 additional costs for outpatient, $64 additional costs for prescriptions. $25 additional Ed costs
Trasande et al., 2009[a]	USA	Not given	Prospective cohort	Total costs for hospitalisations with any diagnosis of obesity increased from $125.9 million in 2001 to $237.6 million in 2005 (2005 dollars)
Turer et al., 2013[a]	USA	17,224	Cross-sectional	No analysis of costs
van Leeuwen et al., 2018	Netherlands	617	Prospective cohort	No analysis of costs
Wake et al., 2010	Australia	923	Prospective cohort	No analysis of costs
Wenig et al., 2011	Germany	14,592	Retrospective cohort	Analysis of costs of drugs. Adjusted two-part regression analysis Obese: 211 euros/year (167-195) Overweight: 172 (143-205) Normal weight: 170 (158-184) Underweight: (236 (181-303)

First author, Year	Country	No. of participants	Study Design	Cost-analysis
Wenig, 2012	Germany	14,277	Cross-sectional	Self-reported use of healthcare services. Physician costs: Obese: 136 euros (123-150) Overweight: 122 (112-134) Normal weight: 111 (109-114) Underweight: 103 (94-112)
Woolford et al., 2007[a]	USA	7,77,274	Cross-sectional	Charges for hospitalisations. adjusted mean hospital charges were significantly higher for dis-charges with obesity as a secondary diagnosis vs. those without: appendicitis ($14,134 vs. $11,049; p ↕ 0.01),asthma ($7766 vs. $6043; p ↕ 0.05), pneumonia ($12,228vs. $9688; p ↕ 0.05), and affective disorders ($8292 vs.$7769; p ↕ 0.01)
Wright and Prosser, 2014[a]	USA	23,727	Cross-sectional	Medicaid claims paid to the providers. overweight and obese youth have higher, but not significantly higher medical expenditures than normal weight youth. reported results from multiple statistical models (used multiple models to model costs)
Wyrick et al., 2013[a]	USA	1,746	Prospective cohort	No analysis of costs

Appendix 2 Additional information for chapter 3

A2.1 Letter from the University of York's Health Sciences Research Governance Committee

DEPARTMENT OF HEALTH SCIENCES

c/o Department of Philosophy
Heslington
York YO10 5DD

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Dr Stephen Holland
Chair, Health Sciences Research Governance Committee

www.york.ac.uk/healthsciences

5 October 2018

Mr T Hasan
University of York
Department of Health Sciences
York
YO10 5DD

Dear Taimoor

Healthcare utilisation by obese & overweight children in the Born in Bradford cohort

Thank you for submitting the above project to the Health Sciences Research Governance Committee for approval. Your application was considered by the committee at its meeting on 1 October 2018.

I am pleased to report that the committee approved the project.

If you have any queries regarding the decision or make any substantial amendments to the study, please contact me. Finally, if you intend to submit this letter or any other correspondence from the HSRGC as part of your assessed work (e.g., to demonstrate that your study has ethical approval) please make sure you edit the letter so as to maintain anonymity.

Yours sincerely

S. Holland

Stephen Holland
Chair: HSRGC

cc: Dr Lorna Fraser

A2.2 Variables requested from BiB children's secondary healthcare records

Admitted Patient Care	
Information	**HES variable code**
Child ID	
Admission ID	
Age on admission if months	
Age on admission in years	
Patient Classification	CLASSPAT
Source of Admission	ADMISORC
Admission Method	ADMIMETH
Discharge Destination	DISDEST
Discharge Method	DISMETH
Episode Duration	EPIDUR
Duration of Spell	SPELDUR
Main Specialty	MAINSPEF
Treatment Specialty	TRETSPEF
Primary diagnosis	DIAG_01
Secondary Diagnosis	DIAG_02 – DIAG_20
Primary procedure	OPER_01
Secondary procedure	OPER_01 – OPER_24
Episode Order	EPIORDER
Accidents and Emergency	
Child ID	
Age in months	
Age in years	
Patient group	AEPATGROUP
Treatment Code	TREAT_N
Investigation code	INVEST_N

A2.3 Methodology to assign costs to primary care events

Staff roles	Consultation type (avg. length)	Cost	Description
General Practitioner	GP surgery (9.22 minutes)	£56.1	(£255/60) * 9.22
	Clinic (17.2 minutes)	£73.1	(£255/60) * 17.2
	Home visit (23.4 minutes)	£99.4	(£255/60) * 23.4
	Telephone (7.1 minutes)	£30.1	(£255/60) * 7.1
Practice Nurse	(15.5 minutes)	£10.9	(£42/60) * 15.5

Appendix 3 Additional information for chapter 4

A3.1: Tests of normality for continuous variables included as covariates in the analyses

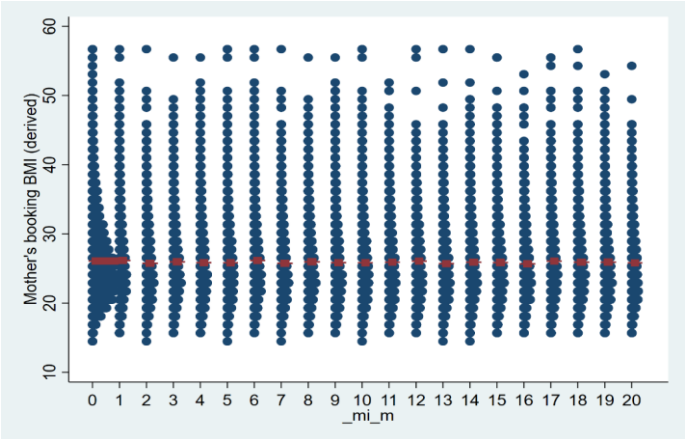
Variable	Skewness, p[1]	Kurtosis, p[1]	Shapiro-Wilk test, z (p[1])
Birthweight	P < 0.01	P < 0.01	11.36 (p < 0.01)
Gestational age	P < 0.01	P < 0.01	17.09 (p < 0.01)
Maternal BMI	P < 0.01	P < 0.01	14.4 (p < 0.01)
Maternal age	P < 0.01	P < 0.01	10.86 (p < 0.01)
[1]p ≤ 0.05 indicates that the data are not normally distributed			

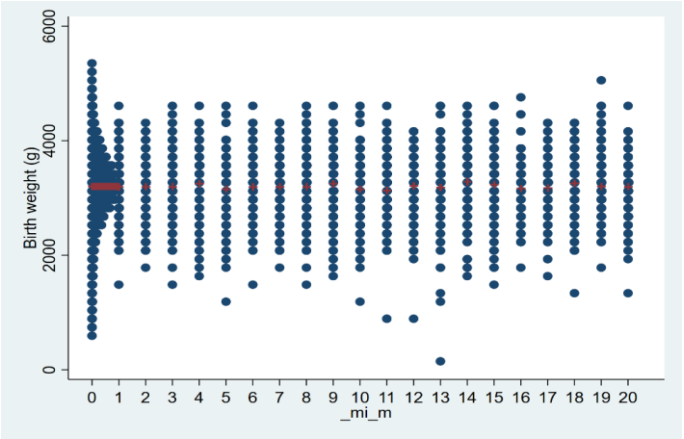
A3.2 Non-monotone pattern of missing data

1. IMDs (91)
2. Gestational age (175) <-> Birthweight (175)
3. Ethnicity (259) -> Maternal BMI (1966)
4. Ethnicity (259) -> Means Tested Benefits (1451)

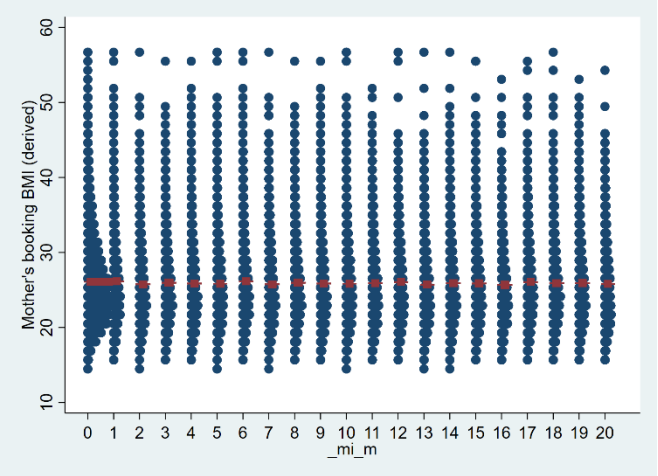
A3.3 Comparison of observed and imputed datasets on key variables

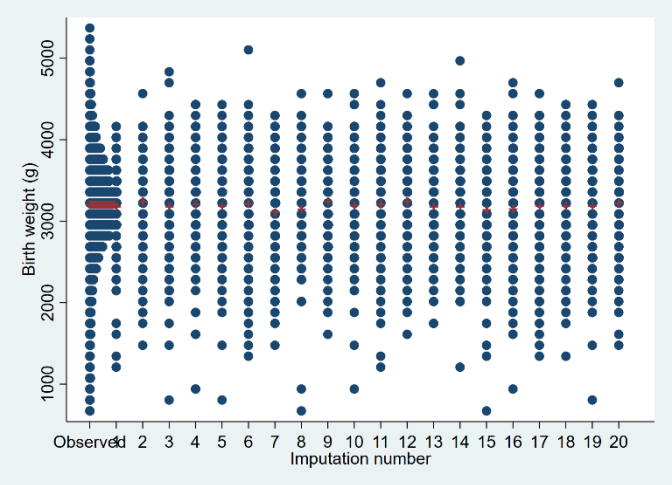
Primary care consultations:



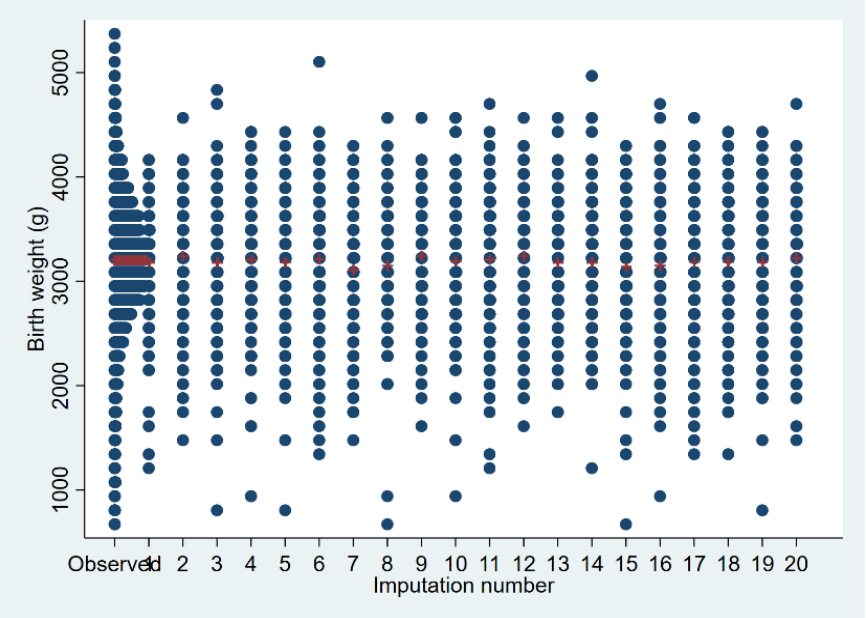


Primary care prescriptions:





Hospital Admissions:



A3.4 Pre-pregnancy diabetes as an auxiliary variable

Characteristics	n	Means tested benefits			Mother's BMI		
		Missing (%)	Not missing (%)	p-value	Missing (%)	Not missing (%)	p-value
Ethnicity				<0.01			<0.01
White British	3,477	363 (10.4%)	3,114 (89.6%)		586 (16.85%)	2,891 (83.15%)	
Pakistani	4,377	573 (13.09%)	3,804 86.91%)		808 (18.46%)	3,569 (81.54%)	
Others	1,326	257 (19.38%)	1,069 (80.62%)		319 (24.06%)	1,007 (75.94%)	
Missing	260	260 (100%)	0		260 (100%)	0	
Pre-pregnancy diabetes*				<0.01			<0.01
No	8,870	1,337 (15.07%)	7,533 (84.93%)		1,620 (18.26%)	7250 (81.74%)	
Yes	51	28 (54.9%)	23 (45.1%)		34 (66.6%)	17 (33.4%)	
Missing	519	88 (16.96%)	431 (83.04%)		319 (61.46%)	200 (38.54%)	

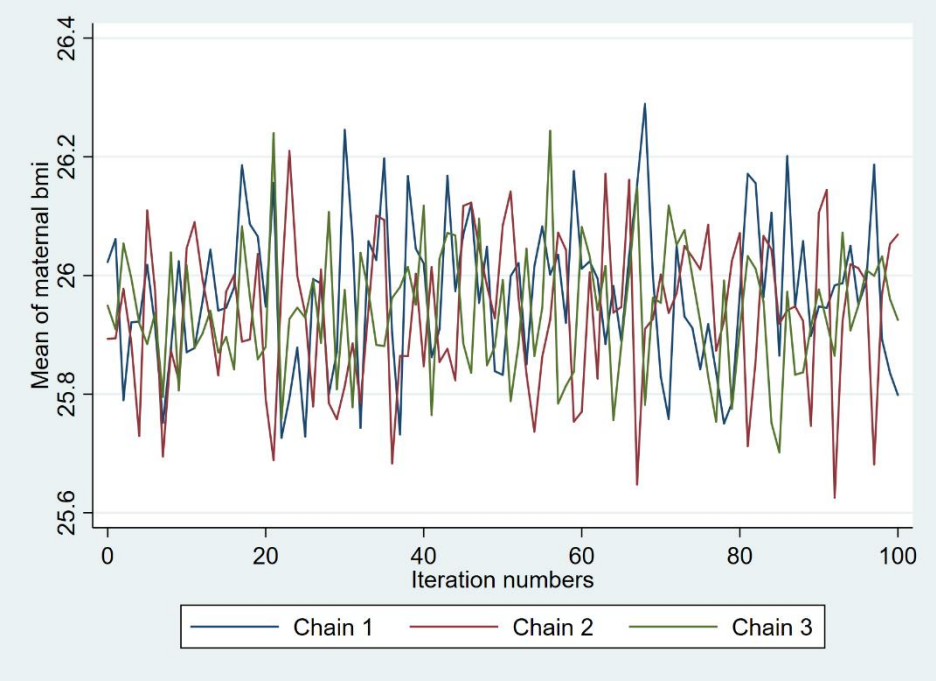
Percentages are given by rows.
[1]p-values are given for Chi-square tests
BMI: Body Mass Index
***Auxiliary variable**

```
. logit mben0mentst i.bkfdiabete, or

Iteration 0:   log likelihood = -3817.2466
Iteration 1:   log likelihood = -3803.4231
Iteration 2:   log likelihood = -3796.5303
Iteration 3:   log likelihood = -3795.7909
Iteration 4:   log likelihood = -3795.7909

Logistic regression                             Number of obs     =      8,921
                                                LR chi2(1)        =      42.91
                                                Prob > chi2       =     0.0000
Log likelihood = -3795.7909                     Pseudo R2         =     0.0056

------------------------------------------------------------------------------
  mben0mentst | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
--------------+---------------------------------------------------------------
  bkfdiabete |
         Yes |   6.859094   1.940933     6.80   0.000     3.939131    11.94354
       _cons |   .1774857   .0052671   -58.26   0.000     .1674568    .1881153
------------------------------------------------------------------------------
Note: _cons estimates baseline odds.
```

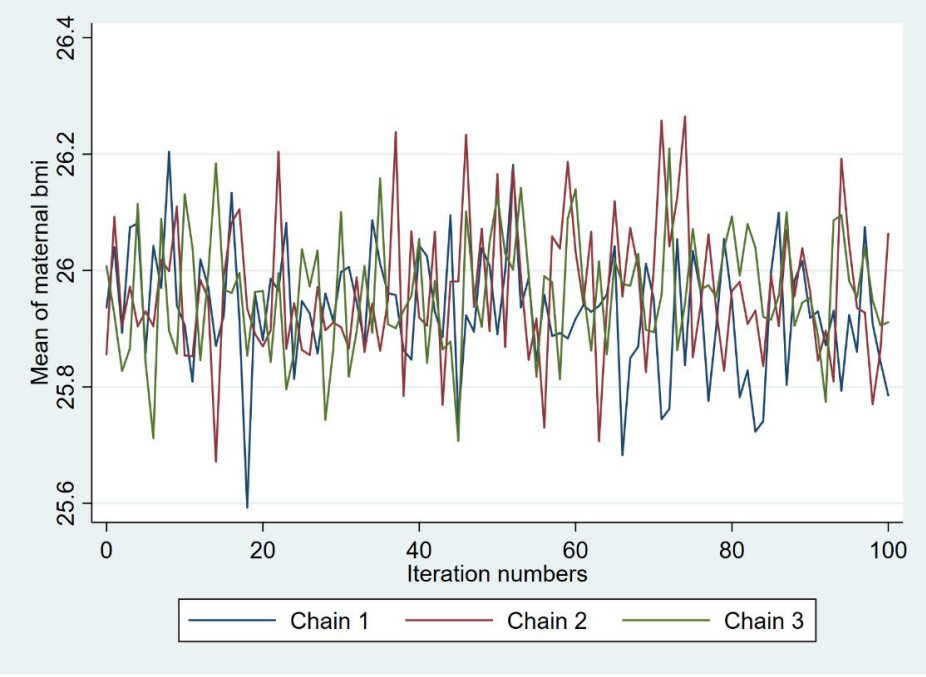
mmms0mbkbmi: Missingness in mother's BMI

A3.5 Trace plots

Primary care consultations:



A&E visits:

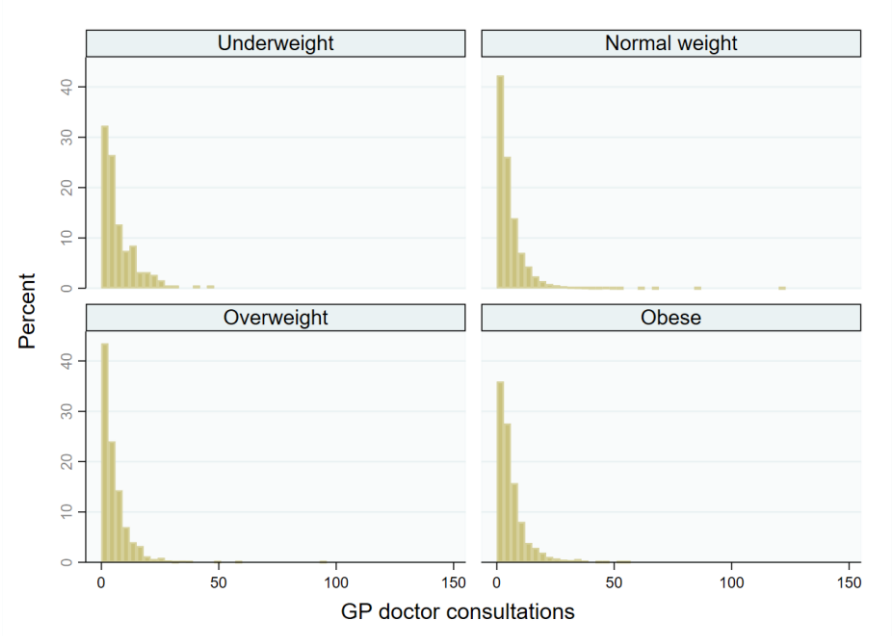


Appendix 4 Additional information for chapter 5

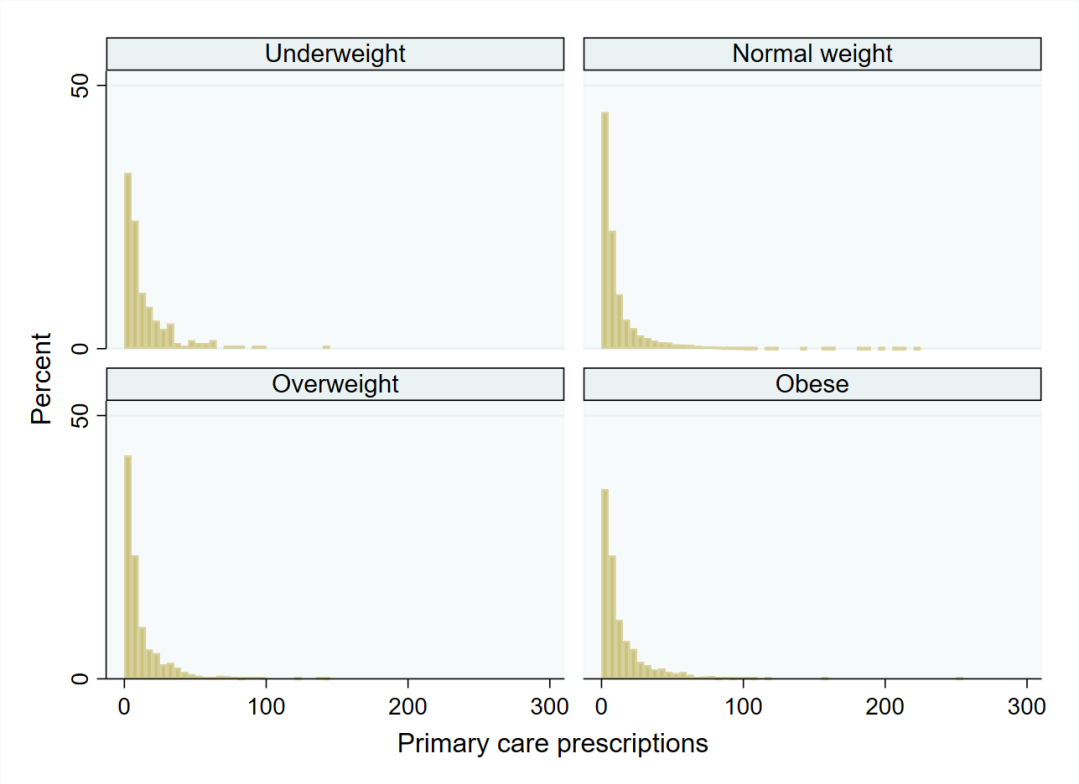
A4.1 Distribution of outcome variables

Primary care consultations:

GP doctor consultations:



Primary care prescriptions:



A4.2 Variance inflation factors

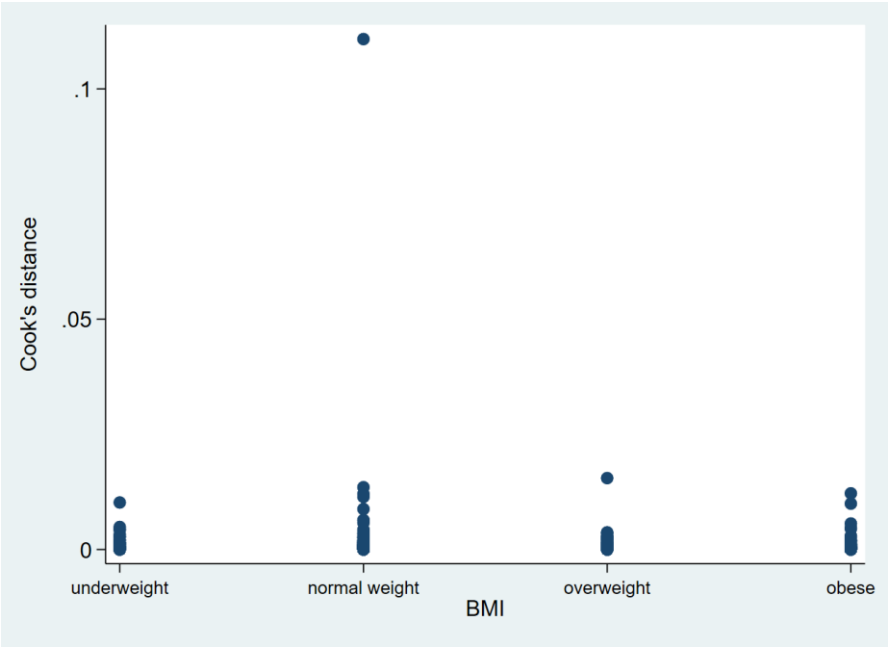
Collinearity Diagnostics

Variable	VIF	SQRT VIF	Tolerance	R-Squared
eclgestwks	1.61	1.27	0.6227	0.3773
eclbirthwt	1.66	1.29	0.6028	0.3972
mms0mbkbmi	1.10	1.05	0.9115	0.0885
adminpagerecmy	1.05	1.03	0.9483	0.0517
Mean VIF	1.35			

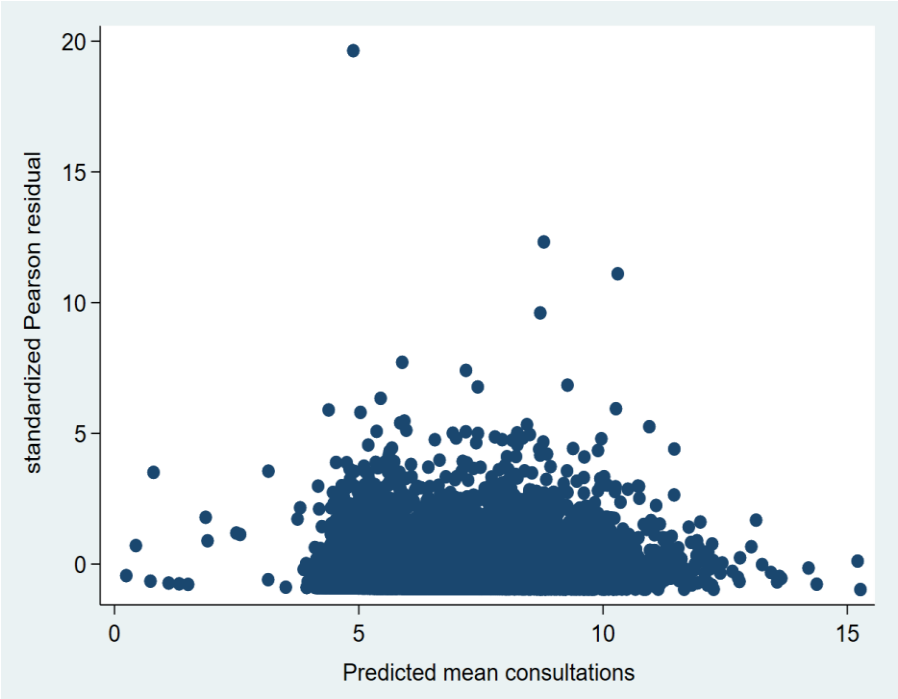
Eclgestwks: Gestational age in weeks
eclbirthwtL Birthweight in grams
adminpagerecmy: Maternal age
mms0mbkbmi: Maternal BMI

A4.3 Influential observation

Cook's distance

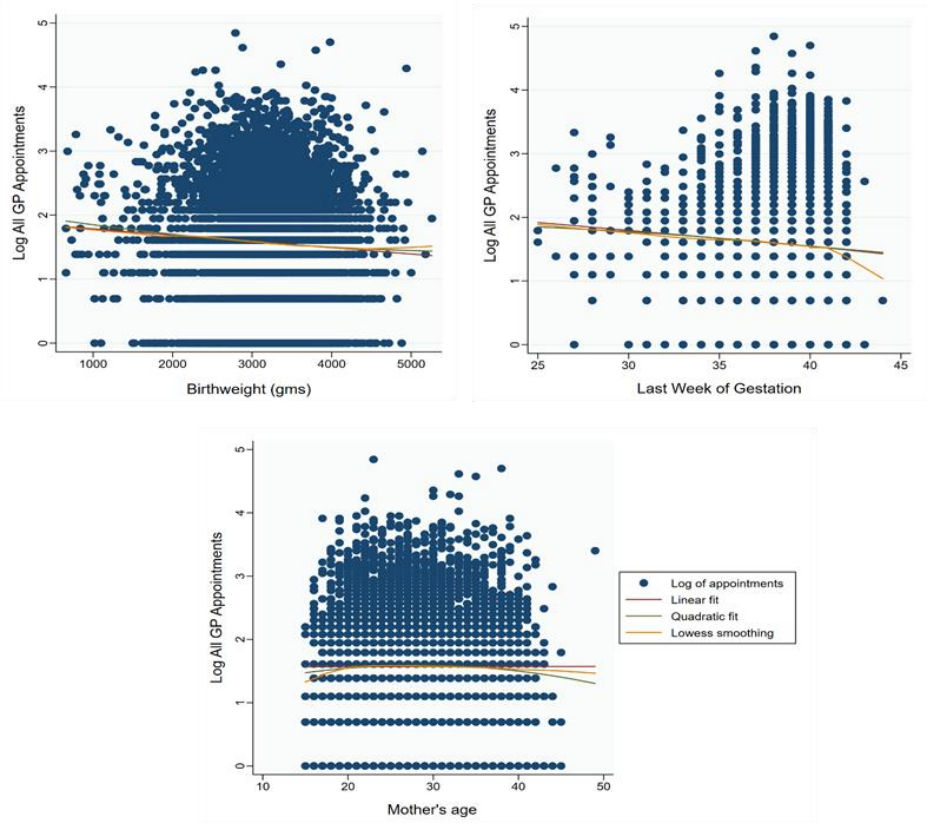


Pearson residual:

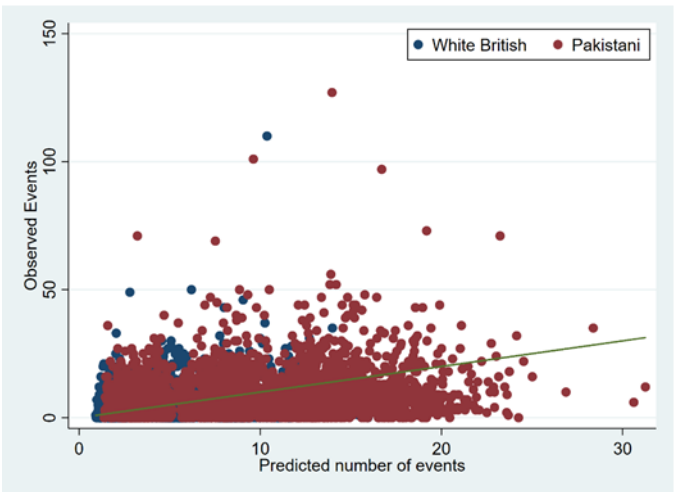


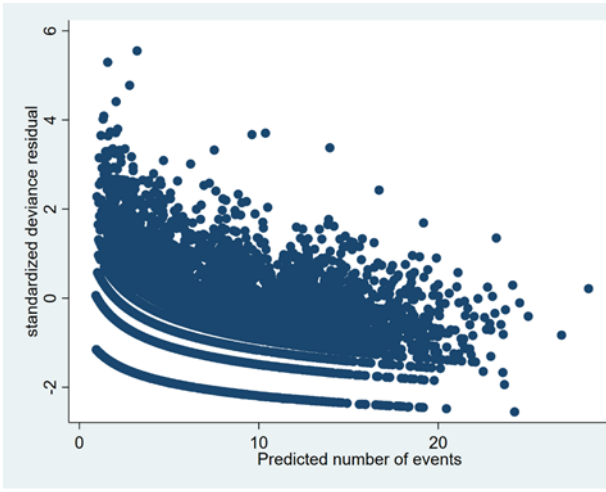
A4.4 Model diagnostics for primary care consultations

Assessment of linearity – primary care consultations

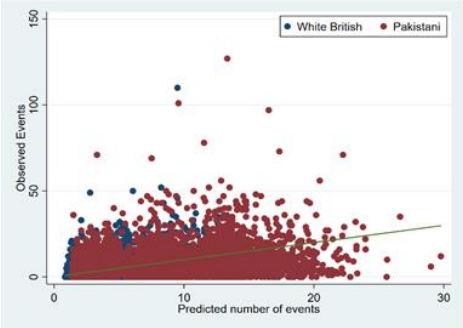


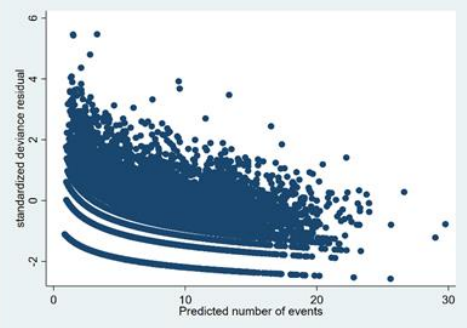
Assessments of model fit - Primary care consultations

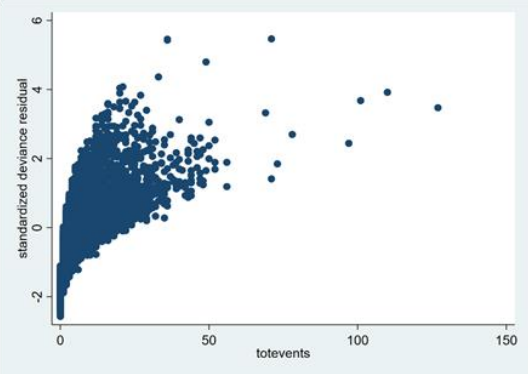




A4.5 Assessment of fit of multiple imputed model for primary care consultations







Appendix 4.6 Results of logistic regression model for primary care consultations

Characteristics	Adjusted Model (n=7,344)	
	OR (95% CI)	P-value
Child BMI (Ref: Normal Weight)		
Underweight	1.39 (0.67 – 2.88)	0.36
Overweight	1.06 (0.82 – 1.37)	0.64
Obese	1.34 (0.99 – 1.82)	0.05
Ethnicity (Ref: White British)		
Pakistani	2.01 (1.65 – 2.45)	<0.01
Other	1.43 (1.10 – 1.85)	<0.01
Birthweight	0.99 (0.99 – 1.00)	0.69
Gestational Age	0.99 (0.94 – 1.05)	0.90
Child Sex (Ref: Male)		
Female	1.02 (0.87 – 1.21)	0.72
Maternal Age	0.99 (0.97 – 1.00)	0.37
Mother's BMI	0.99 (0.98 – 1.01)	0.76
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)		
1st	1.84 (1.26 – 2.68)	<0.01
2nd	1.71 (1.17 – 2.49)	<0.01
3rd	1.72 (1.18 – 2.50)	<0.01
4th	1.47 (1.01 – 2.15)	<0.05
Means tested benefits. (Ref: Not in receipt)		
In receipt	0.98 (0.82 – 1.16)	0.82

1. adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI
2. IRR = Incidence Rate Ratio, CI= Confidence intervals

A4.7x. Negative Binomial regression models for Pakistani and White British children

Table A4.8 Primary care consultations

	White British (n=2,829)		Pakistani (n = 3,524)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.43 (0.89-2.32)	0.13	1.12 (0.93-1.34)	0.22
Overweight	1.05 (0.93-1.17)	0.37	1.11 (1.00-1.23)	0.04
Obese	1.19 (1.05-1.35)	<0.01	1.15 (1.04-1.27)	<0.01
Birthweight	0.99 (0.99-1.00)	0.71	0.99 (0.99-1.00)	0.36
Gestational Age	0.95 (0.93-0.98)	<0.01	0.99 (0.97-1.01)	0.51
Child Sex (Ref: Male)				
Female	1.02 (0.94-1.10)	0.55	0.94 (0.88-1.00)	0.06
Maternal Age	0.98 (0.98-0.99)	<0.01	1.01 (1.00-1.01)	<0.01
Mother's BMI	1.01 (1.00-1.01)	<0.01	0.99 (0.99-1.00)	0.30
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.12 (0.95-1.31)	0.17	1.08 (0.68-1.73)	0.72
2nd	1.21 (1.03-1.43)	0.01	1.08 (0.68-1.73)	0.73
3rd	1.12 (0.96-1.32)	0.13	1.12 (0.70-1.79)	0.63
4th	1.09 (0.93-1.28)	0.26	1.04 (0.63-1.72)	0.85
Means tested benefits (Ref: Not in receipt)				
In receipt	0.99 (0.91-1.08)	0.95	0.87 (0.81-0.92)	<0.01

1. **Adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI**
2. **IRR = Incidence Rate Ratio, CI= Confidence intervals**

Table A4.8: Primary care prescriptions

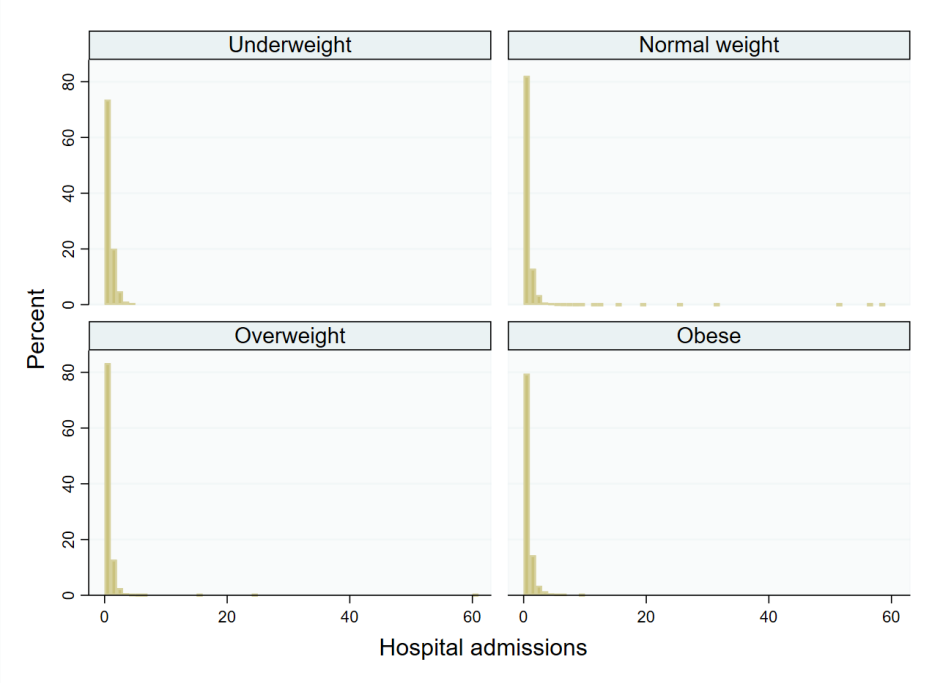
	White British (n=2,829)		Pakistani (n = 3,524)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.24 (0.67-2.30)	0.48	1.12 (0.89-1.40)	0.32
Overweight	1.10 (0.95-1.27)	0.17	1.11 (0.98-1.27)	0.08
Obese	1.12 (0.95-1.31)	0.16	1.27 (1.12-1.43)	<0.01
Birthweight	0.99 (0.99-0.99)	0.03	0.99 (0.99-1.00)	0.18
Gestational Age	0.95 (0.92-0.98)	<0.01	0.99 (0.97-1.02)	0.79
Child Sex (Ref: Male)				
Female	0.87 (0.79-0.96)	<0.01	0.92 (0.85-0.99)	0.03
Maternal Age	1.00 (0.99-1.01)	0.21	1.01 (1.00-1.01)	<0.01
Mother's BMI	1.01 (1.00-1.02)	<0.01	0.99 (0.83-0.97)	0.01
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	0.92 (0.75-1.13)	0.46	1.39 (0.78-2.47)	0.26
2nd	1.03 (0.84-1.27)	0.75	1.33 (0.75-2.37)	0.32
3rd	0.98 (0.80-1.20)	0.90	1.34 (0.75-2.39)	0.32
4th	0.91 (0.75-1.11)	0.39	1.42 (0.77-2.62)	0.26
Means tested benefits (Ref: Not in receipt)				
In receipt	1.04 (0.94-1.15)	0.39	0.90 (0.83-0.97)	0.01

1. **Adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI**
2. **IRR = Incidence Rate Ratio, CI= Confidence intervals**

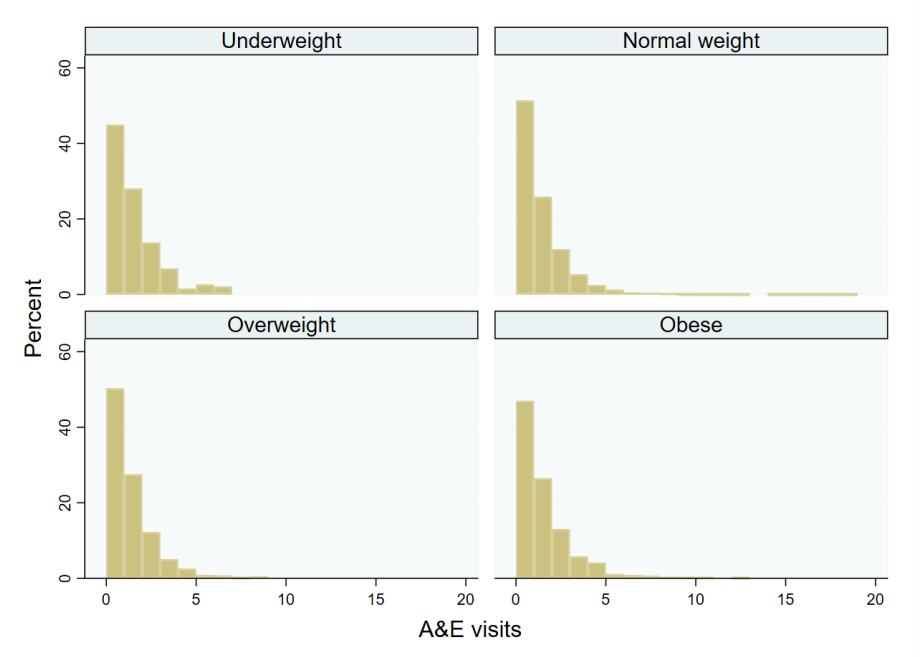
Appendix 5 Additional information for chapter 6

A5.1 Histograms

Hospital admissions



A&E visits



A5.2 Tests for normality

Variable	Skewness, p^1	Kurtosis, p^1	Shapiro-Wilk test, z (p^1)
Hospital Admissions	P < 0.01	P < 0.01	21.69 (p < 0.01)
Hospital Length of stay	P < 0.01	P < 0.01	16.33 (p < 0.01)
A & E visits	P < 0.01	P < 0.01	17.31 (p < 0.01)
[1]p ≤ 0.05 indicates that the data are not normally distributed			

A5.3. Output of multivariable logistic model for Hospital Admissions

Characteristics	Adjusted Model (n=7,344) OR (95% CI)	P-value
Child BMI (Ref: Normal Weight)		
Underweight	1.46 (0.99-2.15)	0.05
Overweight	0.95 (0.78-1.16)	0.64
Obese	1.07 (0.88-1.31)	0.45
Ethnicity (Ref: White British)		
Pakistani	1.24 (1.07-1.43)	<0.01
Other	0.90 (0.73-1.11)	0.34
Birthweight	0.99 (0.99-1.00)	0.90
Gestational Age	0.95 (0.91-0.99)	0.04
Child Sex (Ref: Male)		
Female	0.73 (0.65-0.83)	<0.01
Maternal Age	0.99 (0.98-1.00)	0.13
Mother's BMI	1.01 (0.85-2.08)	0.20
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)		
1st	1.71 (1.11-2.62)	0.01
2nd	1.69 (1.10-2.60)	0.01
3rd	1.76 (1.15-2.70)	<0.01
4th	1.33 (0.85-2.08)	0.20
Means tested benefits. (Ref: Not in receipt)		
In receipt	0.98 (0.87-1.11)	0.84

1. **adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI**
2. **IRR = Incidence Rate Ratio, CI= Confidence intervals**

A5.4. Multivariable negative binomial model for hospital LoS

	Adjusted Model (n=1,326)		Multiple imputed model (n = 1,433)	
Characteristics	**IRR (95% CI)**	**P-value**	**IRR (95% CI)**	**P-value**
Child BMI (Ref: Normal Weight)				
Underweight	1.04 (0.59-1.84)	0.87	0.94 (0.53-1.65)	0.83
Overweight	1.04 (0.76-1.41)	0.79	0.95 (0.70-1.29)	0.77
Obese	1.00 (0.74-1.36)	0.96	0.97 (0.72-1.32)	0 87
Ethnicity (Ref: White British)				
Pakistani	1.34 (1.06-1.69)	0.01	1.24 (0.99-1.57)	0.05
Other	1.10 (0.79-1.54)	0.55	1.04 (0.74-1.45)	0.80
Birthweight	0.99 (0.99-0.99)	<0.01	0.99 (0.99-0.99)	<0.01
Gestational Age	1.05 (0.99-1.13)	0.08	1.06 (0.99-1.13)	0.09
Child Sex (Ref: Male)				
Female	0.89 (0.74-1.08)	0.27	0.94 (0.78-1.14)	0.56
Maternal Age	1.00 (0.98-1.02)	0.45	1.01 (0.99-1.03)	0.21
Mother's BMI	1.01 (0.99-1.02)	0.22	1.01 (0.98-1.03)	0.42
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.79 (0.81-3.95)	0.14	1.89 (0.89-4.00)	0.09
2nd	1.85 (0.84-4.05)	0.12	1.91 (0.91-4.03)	0.08
3rd	2.89 (1.31-6.37)	<0.01	3.00 (1.41-6.37)	<0.01
4th	2.53 (1.12-5.74)	0.02	2.29 (1.05-4.99)	0.03
Means tested benefits (Ref: Not in receipt)				
In receipt	1.04 (0.86-1.26)	0.66	1.04 (0.86-1.26)	0.61

1. **adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI**
2. **IRR = Incidence Rate Ratio, CI= Confidence intervals**

A5.5 Negative Binomial Model output for A & E visits

Characteristics	White British (n=2,829)		Pakistani (n = 3,524)	
	IRR (95% CI)	P-value	IRR (95% CI)	P-value
Child BMI (Ref: Normal Weight)				
Underweight	0.96 (0.47-1.99)	0.93	1.03 (0.78-1.35)	0.81
Overweight	1.11 (0.95-1.31)	0.18	0.92 (0.79-1.08)	0.34
Obese	1.16 (0.97-1.39)	0.09	1.14 (0.98-1.32)	0.07
Birthweight	1.00 (0.99-1.00)	0.38	0.99 (0.99-1.00)	0.21
Gestational Age	0.97 (0.93-1.00)	0.12	0.99 (0.96-1.02)	0.84
Child Sex (Ref: Male)				
Female	0.90 (0.80-1.00)	0.07	0.70 (0.64-0.77)	<0.01
Maternal Age	0.97 (0.96-0.98)	<0.01	0.99 (0.98-1.00)	0.30
Mother's BMI	1.01 (1.00-1.02)	0.01	1.00 (0.99-1.01)	0.07
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)				
1st	1.44 (1.10-1.87)	<0.01	4.33 (1.44-12.96)	<0.01
2nd	1.60 (1.23-2.09)	<0.01	4.90 (1.64-14.68)	<0.01
3rd	1.43 (1.10-1.86)	<0.01	4.81 (1.60-14.44)	<0.01
4th	1.28 (0.98-1.66)	0.06	3.81 (1.23-11.78)	0.02
Means tested benefits (Ref: Not in receipt)				
In receipt	1.13 (1.00-1.27)	0.04	0.97 (0.988-1.06)	0.51

1. **Adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI**
2. **IRR = Incidence Rate Ratio, CI= Confidence intervals**

A5.6 Output of multivariable logistic model for A&E visits

Characteristics	Adjusted Model (n=7,344) OR (95% CI)	P-value
Child BMI (Ref: Normal Weight)		
Underweight	1.25 (0.89 – 1.75)	0.18
Overweight	1.09 (0.91 – 1.26)	0.26
Obese	1.20 (1.02 – 1.40)	<0.05
Ethnicity (Ref: White British)		
Pakistani	1.45 (1.29 – 1.62)	<0.01
Other	1.10 (0.95 – 1.29)	0.18
Birthweight	1.00 (0.99 – 1.00)	0.90
Gestational Age	0.99 (0.96 – 1.02)	0.65
Child Sex (Ref: Male)		
Female	0.72 (0.66 – 0.80)	<0.01
Maternal Age	0.98 (0.97 – 0.99)	<0.01
Mother's BMI	1.00 (0.99 – 1.01)	0.18
Index of Multiple Deprivation (Ref: 5th = 20% least deprived)		
1st	1.75 (1.31 – 2.35)	<0.01
2nd	1.84 (1.37 – 2.47)	<0.01
3rd	1.89 (1.41 – 2.53)	<0.01
4th	1.51 (1.11 – 2.05)	<0.01
Means tested benefits. (Ref: Not in receipt)		
In receipt	1.14 (1.04 – 1.26)	<0.01

1. **adjusted for Ethnicity, Birthweight, Gestational Age, Sex, Maternal Age, IMD, means tested benefits and maternal BMI**
2. **IRR = Incidence Rate Ratio, CI= Confidence intervals**

Abbreviations

APC	Admitted Patient Care
AIC	Akaike Information Criterion
BiB	Born in Bradford
BIC	Bayesian Information Criterion
BMI	Body Mass Index
BNF	British National Formulatory
BRI	Bradford Royal Infirmary
DAG	Directed Acyclic Graph
GLM	Generalised Linear Models
HES	Hospital Episode Statistics
HRGs	Healthcare Resource Groupers
IMD	Index of Multiple Deprivation
IOTF	International Obesity Task Force
IRRs	Incidence Rate Ratios
KIGGS	German Interview and Examination Survey for Children and Adolescents
LOS	Length of Stay
LSOA	Lower Super Output Area
MAR	Missing at Random
MCAR	Missing Completely at Random
MEPS	Medical Expenditure Panel Survey
MICE	Multiple Imputation with Chained Equations
MNAR	Missing Not at Random
NCMP	National Child Measurement Programme
NHS	National Health Service
NICE	National Institute for Health and Care Excellence

OECD	Organisation for Economic Co-operation and Development
OGTT	Oral Glucose Tolerance Test
OLS	Ordinary Least Squares
ONS	Office of National Statistics
ORs	Odds Ratios
PHE	Public Health England
PICU	Paediatric Intensive Care Unit
PMM	Predictive Mean Matching
PSSRU	Personal Social Service Research Unit
SDIL	Soft Drinks Industry Levy
SES	Socio-Economic Status
VIF	Variance Inflation Factor
WHO	World Health Organisation

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