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Early adiposity rebound, birthweight, and ethnicity: evidence from the millennium cohort study

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Centre for Longitudinal Studies
Working paper 2016/4

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This working paper was first published in October 2016
by the Centre for Longitudinal Studies,
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www.cls.ioe.ac.uk

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Acknowledgements

Thanks go to my supervisors, Dr Arjan Gjonca and Professor Michael Murphy, for their advice and guidance. I am indebted to the UK Data Archive and The Centre for Longitudinal Studies, Institute of Education, for access to, and use of, the Millennium Cohort Survey data (who assume no accountability for the current interpretation and analysis). Finally, I would like to thank my family and friends for their help, patience, and support through the dissertation process.

Abbreviations

AR	Adiposity Rebound
BMI	Body Mass Index
CHD	Coronary Heart Disease
CI	Confidence Interval
CVD	Cardio-vascular Disease
EAR	Early Adiposity Rebound
GDM	Gestational Diabetes Mellitus
IHD	Ischemic Heart Disease
ILGF-1	Insulin-like growth-factor-1
IOTF	International Obesity Task Force
LBW	Lower Birthweight
MCS	Millennium Cohort Study
T2D	Type 2 Diabetes

Tables, figures, and appendices

1. Introduction

Childhood obesity is a leading problem of industrialised nations, with 42 million children under 5 overweight globally in 2013 according to the WHO (WHO 2013). In the UK the National Child Measurement Programme (NCMP) estimated that 9.5% of children age 4-5 were obese, and 13.1% were overweight in 2013/14 (England 2014). Health Survey for England results showed that '28% of children aged 2 to 15' were overweight or obese in 2012 (England 2014) and this was higher for Afro-Caribbean or South Asian children (Boonpleng *et al*. 2012; Saxena *et al*. 2004). Obesity in childhood has multiple detrimental physical and psychological consequences, especially increased risk of 'obesity-related conditions' such as type 2 diabetes developing in childhood (England 2014).

Not only does childhood obesity have its own detrimental health effects, it also holds implications for later-life health as 'childhood obesity has been shown to confer long-term effects on mortality and morbidity' (Scerri and Savona-Ventura 2010: 177). This is particularly true of early childhood obesity known as 'Early Adiposity Rebound (EAR)' (Tabacchi *et al.* 2007: 596) when rapid weight gain occurs before age 5, instead of the usual 5-7 years. This is seen as a risk indicator for obesity, diabetes, and CVD (M. F. Rolland-Cachera *et al*. 2006) and is considered a marker for metabolic diseases in later life, EAR being associated with increased fat mass, not lean mass (M. F. Rolland-Cachera *et al*. 2006) and with rapid weight velocity, as opposed to slow height velocity (S. M. Williams 2005).

Multiple studies have investigated the possible causes of EAR in order to prevent its occurrence, in turn to reduce the level of childhood obesity and its negative impacts, as prevention is much easier than cure. A systematic review by Ong and Loos, 2006, found in all 21 studies examined a 'significant positive association between rapid infant weight gain and increased subsequent risk of obesity' (K. K. Ong and Loos 2006: 906). Risk factors range from biological (birthweight, parental weight, ethnicity) and environmental (smoking) to socio-economical (income, education) and behavioral (protein intake, exercise levels). An in-depth study of all of these factors is beyond the scope of this study, which will focus primarily on the role of lower birthweight (LBW) and ethnicity.

Studies have observed that some of the greatest gains in truncal fat in childhood occur through EAR following low BMI pre-rebound, suggesting nutritional and energy deficit during the fetal or/and early postnatal life (M. F. Rolland-Cachera *et al.* 2006). LBW is itself linked to greater risk of adult obesity (Argente *et al.* 2010) and metabolic syndrome, with birthweight being 'inversely associated with the development of type-2 diabetes' (Norris *et al*. 2012: 72). Yet it is the combination of LBW and increased weight gain velocity that poses the highest risk (Eriksson *et al*. 1999; Nobili *et al.* 2008; Norris *et al. 2012)* and this is more common in South Asian and Black ethnicities (Boonpleng *et al*. 2012), groups with higher obesity related death rates (Katzmarzyk *et al*. 2012), yet the presence of combined LBW and EAR has largely not been considered together, particularly in ethnic groups. Hence this period should

be seen as critical for the development of childhood and later life obesity risk (Prentice 2011) worthy of further investigation.

It is this proposed link between birthweight and EAR that this study aims to explore. The confirmation of an association between LBW and greater risk of childhood obesity and adult metabolic syndrome, via EAR, would be of great use in intervention and prevention strategies, as to where and whom to target, and who may be of greatest risk. The objective is to analyse data from the Millennium Cohort Study to look for the presence of EAR. This will be followed by an ANCOVA analysis between those displaying EAR and birthweight. Finally, the association of ethnicity with EAR will be investigated.

This study is separated into the following chapters: Chapter 2 reviews the current literature on AR, sets out a conceptual framework for the causes and consequences of AR and LBW, and this study's research aims and questions. The data sample and methods are set out in Chapter 3, and the results of the data analysis follow in Chapter 4. Chapter 5 is a discussion of these findings along with their limitations, and avenues for future study. Finally, Chapter 6 concludes with the inferences of these findings.

2. Literature review

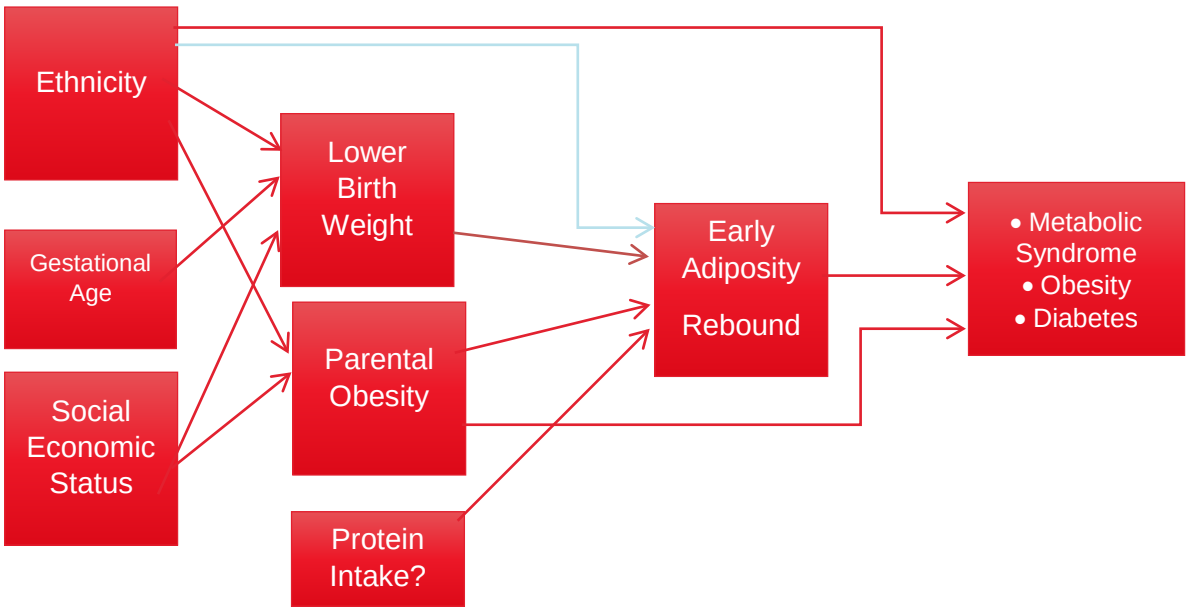
The lifecourse approach to disease, first established by Kermack in 1934, has posited that certain critical periods of childhood growth and exposure hold great significance for later-life health (Smith and Kuh 2001). The 'period of adiposity rebound' and its timing has been proposed as a key phase influential in the development of obesity and its co-morbidities, both in childhood and adult life (W. H. Dietz 1994: 955) corroborated by evidence that those who develop metabolic syndrome 'show different patterns of weight gain from their peers' (McCarthy *et al.* 2007: 907). However, obesity is a highly complex multi-factorial condition, making inferences on causation and possible prevention and treatment problematic (Parsons *et al*. 1999; Tabacchi *et al.* 2007). The identification of critical periods for weight gain and increased risk of obesity, as well as relationships with distal factors, is essential to expand the knowledge basis on which to develop solutions.

2.1. Early adiposity rebound

The adiposity rebound is the period when the velocity of weight gain rises due to an increase in the number and size of adipocytes, causing 'rapid growth in body fat' (M.-F. Rolland-Cachera *et al.* 1984: 129). This rapid growth is defined by the IOTF as a difference in z-scores between two ages 'greater than 0.67' (Monteiro and Victora 2005: 143). The normal age of adiposity rebound is 5-7 years (M. F. Rolland-Cachera *et al.* 2006) and multiple empirical studies have established that children experiencing EAR, defined as below age 5, have a greater risk of obesity, and related conditions such as T2D, than those with Normal or Late rebound (Chivers *et al.* 2010; Monteiro and Victora 2005; M.-F. Rolland-Cachera *et al.* 1984) with the odds ratio for obesity in adulthood calculated as 6.0 for Early vs. Late AR (Whitaker *et al.* 1998).

The physiological changes occurring during EAR have been established by Taylor et al to be an increase in the 'deposition of weight' as opposed to a decrease in 'rate of height gain' (Taylor *et al*. 2005: 607; S. M. Williams 2005). Moreover, this additional weight represents an increase in fat mass as opposed to lean mass, with 'early rebounders' showing rates of gain in fat mass more than double those of 'late rebounders' (Taylor *et al.* 2004: 1228) but no difference in skeletal development or lean mass (Cameron *et al.* 2003). This results in children who experience EAR developing different body compositions, with increased (predominantly central) adiposity (Boonpleng *et al.* 2012). Figure 1 shows some of the associations cited in the literature, the red lines indicating associations under consideration in this study.

Figure 1: Conceptual framework for analysis



2.1.1. Consequences of EAR

The most significant impact of EAR is increased level of obesity both in childhood and adulthood. Multiple studies have established the relationship between EAR and obesity (He and Karlberg 2002) with reports from France and the US showing greater increases in BMI with 'each year decrease in age at AR' (M. F. Rolland-Cachera *et al*. 2006: S12). This is suggested to be due to EAR allowing greater time for 'adipose tissue accumulation', and implying a difference in underlying metabolic functions leading to 'growth acceleration' (Freedman *et al.* 2001: 543) and changes in body fat composition *(Taylor et al.* 2004). Moreover, this accelerated growth then continues into adulthood, evident in changes in z-scores analysed in several longitudinal studies (S. M. Williams and Goulding 2009) and it has been proposed that EAR could account for the 30% of 'adult obesity that begins in childhood' (William H. Dietz 2000: 2027) particularly as the increases in BMI between ages 3 and 5 show a stronger positive association with adult truncal fat mass and waist and hip circumference than lean mass (Corvalán *et al*. 2007; González *et al.* 2010).

Positive associations are also shown between EAR and the development of 'impaired glucose tolerance' and T2D in both children and adults, especially those with a sustained exponential rise in BMI following EAR (Bhargava *et al.* 2004: 1). This is demonstrated in Norris *et al's* multi-country study, where rapid weight gain in early childhood was shown to be a risk factor for T2D, especially in combination with LBW (Norris *et al*. 2012). This risk has its origins in the proportional increase in body fat that typifies EAR, particularly truncal fat, which has been linked to lower levels of the protein adiponectin, considered a proximate determinate of insulin resistance (Cnop *et al.* 2003). Ratification can also be found in studies by Eriksson *et al,* which demonstrate that children who experience EAR are at greater risk of T2D; 8.6% of EAR children developed T2D compared to only 1.8% of late rebound children (after

age 7) (Eriksson *et al*. 2003). Studies have also shown a greater risk of high blood pressure and other metabolic syndrome morbidities, such as CVD, with EAR (Horta *et al.* 2003).

However, the practicality and conceptual utility of EAR is not free from criticism. Several authors consider the identification of EAR redundant as a predictor of adult obesity, as BMI age 7 or 8 shows a correlation with adult obesity of equal magnitude (Freedman *et al.* 2001; S. Williams *et al*. 1999). Moreover, Dietz has questioned EAR's utility as it can only be identified 'retrospectively', and goes further to suggest that the link between EAR and adult obesity is an 'epiphenomenon' with the real cause being the higher BMI at age of rebound, as opposed to the rebound itself (William H. Dietz 2000: 2028). This is expanded by Cole, stating a more 'direct indicator' would be the rate of BMI centile crossing in general, of which EAR is just one measure (Cole 2004: 1). Yet the significance of EAR as an indication of changes in body composition provides justification for its use, especially in relation to increased risk of T2D diabetes and metabolic syndrome, thereby rationalising further investigation.

2.1.2. Causes of EAR

There remains considerable debate over the causes of EAR, particularly the role of protein intake, several authors (Chivers *et al.* 2010; M. F. Rolland-Cachera *et al.* 1995) have suggested that a high protein diet can induce EAR through the suppression of growth hormone and stimulation of ILGF-1, resulting in greater adipose deposition (Günther *et al.* 2006). This is corroborated by the protective effects of breastfeeding, with its high-fat low-protein content encouraging slow growth, the Raine Study finding that those breastfed for less than 4 months were at greater risk of EAR (Chivers *et al.* 2010). However, this position has been dismissed by Dorosty *et al,* who found no dietary influences on AR timing (Dorosty *et al.* 2000).

Parental overweight is another cited association, with multiple studies showing a correlation between parental obesity (particularly maternal) and EAR. This implies a possible combination of genetic and behavioural factors, such as feeding and exercise habits (Sherburne Hawkins and Law 2006), and provides a basis for the higher levels of EAR seen in low socioeconomic status families due to the 'social patterning of risk factors' (Layte *et al.* 2014; Sherburne Hawkins and Law 2006: 20). A study on the MCS by Griffiths ratifies this view, finding that parental overweight is a risk factor for rapid weight gain between ages 3 and 5 (Griffiths *et al.* 2010). This forms part of the approach of this paper, as maternal BMI is a covariate of the ANCOVA when assessing the relationship between EAR and LBW.

2.2. Lower birthweight

LBW is a proxy for fetal undernutrition and has been suggested as another determinant of EAR via the induction of a thrifty phenotype which in turn encourages rapid accumulation of centrally stored fat (Barker *et al.* 1997). LBW is caused by maternal and fetal restriction of nutrition through exposure to toxins or maternal undernutrition, as seen in the Dutch Hunger Famine 1944, where maternal exposure to undernutrition in the 1st/2nd trimester lead to LBW offspring who went on to have higher rates of adult CVD mortality (Harding 2001).

This is corroborated by Barker's hypothesis of fetal programming, which states that undernutrition in utero establishes a 'thrifty metabolism and mechanisms of adaptive thermogenesis' (M. F. Rolland-Cachera *et al.* 2006: S16) known as the predictive adaptive response (Tabacchi *et al.* 2007). While in early humans this would have been advantageous and ensured survival in harsh environments, in modern industrialised society where there is abundant high-energy food it creates an imbalance between the expected and realised 'postnatal environment', leading to a high risk of overshooting the healthy BMI trajectory during rapid catch-up growth (Tabacchi *et al*. 2007: 591).

Hence, many children born LBW are found to be 'heavier, taller, and fatter' by age 5 (K. Ong *et al*. 2000: 967). Moreover, they also have higher levels of centrally distributed fat, also linked to metabolic risk in later life (Barker *et al.* 1997; K. Ong *et al.* 2000) and rapid weight gain after 12 months, which is primarily linked with greater adiposity, not larger overall size (Wells *et al*. 2012). This is due to 'suppressed thermogenesis' redistributing glucose from 'skeletal muscle to adipose tissue' (Argente *et al.* 2010: 681) resulting in a lack of muscle 'cell replication after birth' causing weight gained to be adipose based (Eriksson *et al.* 2003: 193); these 'alterations in body composition' persist into later life (Eriksson *et al*. 2003: 193) and also induce 'hyperinsulinemia and insulin resistance' (Crescenzo *et al.* 2003: 1090). Moreover, it is individuals that rapidly gain weight after having been small in infancy, that are at highest risk (González *et al*. 2010).

Many studies have supported the link between LBW and the risk of metabolic syndrome (Nobili *et al*. 2008; Prentice 2011), particularly T2D, with Whincup *et al's* 2008 systematic review identifying 23 populations where an inverse association was found between birthweight and T2D, 9 of which were statistically significant (Whincup *et al.* 2008). Other studies such as those in New Delhi (Bhargava *et al.* 2004) have also found this association between LBW and diabetes, as well as insulin resistance (Bavdekar *et al.* 1999), and an association between the rate of catch-up growth in LBW children and CHD deaths (Eriksson *et al.* 1999). While the relationship between birthweight and T2D initially appears to be J-shaped, this becomes inverse correlation when controlling for maternal diabetes and BMI (Rich-Edwards *et al.* 1999). Rich-Edwards *et al* suggest that this may be because LBW indicates deficient 'pancreatic endocrine function' which in turn affects insulin resistance (Rich-Edwards *et al.* 1999: 283) and a possible underdevelopment of the kidneys; another predisposing factor to metabolic syndrome (Argente *et al.* 2010).

EAR has been proposed in several empirical studies to be the possible missing link between LBW, T2D, and adult obesity, as summarised in the SACN 2011 report, with LBW stated as associated with the high fat mass pattern seen in EAR (Prentice 2011) giving further justification to this paper. Eriksson *et al's* Helsinki study provided significant evidence that EAR was 'preceded by low ponderal index at birth' (Prentice 2011: 79) and the subsequent changes in body composition considerably increased the risk of T2D (Eriksson *et al*. 2003). This is further supported by Norris *et al's* study which showed that the highest risk of T2D comes from LBW followed by rapid weight gain in early childhood (Norris *et al.* 2012) and the evidence from the Pelotas study that places those LBW followed by rapid weight gain at highest risk of metabolic syndrome due to the greater 'increase of visceral adipose tissue' (González *et al.* 2010: 201). This provides the context for this paper, as the identification of an association between EAR and LBW in a nationally representative sample, as opposed to previously small, local samples studied, would add further to the body of knowledge being used to elucidate this pattern of growth.

2.3. Other factors

There are several other factors that need to be taken into consideration, and form the covariates of this study, along with maternal BMI prior to birth. Gestational age plays a key role in birthweight, as those born prematurely are likely to be LBW and so gestation needs to be controlled for in analysis, as seen in the majority of studies on AR timing (Ekelund *et al*. 2006; Layte et al. 2014; McCarthy *et al*. 2007). Smoking has been linked to both LBW and rapid childhood weight gain (Sullivan *et al*. 2010; Tabacchi *et al.* 2007) and was found to have a direct and 'dose-response relationship' with childhood overweight risk (Sherburne Hawkins and Law 2006: 18). This is proposed to be due to nicotine interfering with the 'catecholaminergic neurotransmitter system' resulting in reduced 'appetite and impulse control' in the child (Layte *et al*. 2014: 89), with a 14-study meta-analysis showing a 50% increase in child obesity odds for smoking during pregnancy (Dixon *et al.* 2012).

Finally, maternal diabetes is also a significant factor in birthweight, child weight gain, body composition, and insulin resistance. Higher glucose transferal across the placenta leads to 'increased fetal insulin release' resulting in 'greater adipogenesis' (Gluckman and Hanson 2008: S67). This has the effect of increasing birthweight but also increasing the rate of child weight gain, particularly fat mass, and so a higher chance of childhood obesity and T2D (Gluckman and Hanson 2008). This can be seen in Whincup *et al's* systematic review, which found the presence of maternal diabetes reversed the birthweight-T2D association, making high birthweight more predictive of T2D (Whincup *et al.* 2008).

2.4. Ethnicity

Ethnicity's role in determining EAR is another area of debate. Studies have shown that body composition varies between ethnic groups, with higher proportionate body fat mass in South Asians compared to Whites, even at identical BMI and age (Sachdev *et al.* 2005) resulting in greater health risks at lower BMI, as reported by Public Health England (Gatineau and Mathrani 2011). This premise is supported by the call for 'revised BMI thresholds' to be used for those of South Asian origin to account for this higher risk by Public Health England (Gatineau and Mathrani 2011: 3).

Moreover, studies in America account obesity-related conditions for 51-64% of the difference in life expectancy between White and African-American groups (Katzmarzyk *et al.* 2012). This suggests that the pattern of weight gain may differ between ethnic groups and there could be greater propensity for EAR in some ethnic groups, particularly Black and South Asian, especially as these children show higher obesity levels age 4-5 compared to White-British according to the NCMP 2009/10 (Gatineau and Mathrani 2011). Furthermore, the Bongalusa Heart Study found that Black obese children were more prone to adult obesity than White obese children, 83% vs. 68% respectively (Caprio *et al.* 2008) and that 5 times as many African-American children are diagnosed with T2D vs. White (Caprio *et al.* 2008).

Studies in India support this showing Indians to have the lowest mean birthweight in the world at 2.6-7kg, but a high tendency for central obesity and metabolic syndrome (Bavdekar *et al.* 1999). However, the nutritional profile of mothers in India must be considered, as there are higher levels of maternal undernutrition resulting in LBW and thrifty phenotypes (Bavdekar *et al.* 1999). Nevertheless, the role of ethnicity is still shown to be important through studies in developed countries, such as that of the MCS, showing a higher level of rapid weight gain in children of Bangladeshi or Black ethnicity (Griffiths *et al.* 2010) and that there is a significant difference between both the risk of LBW and average BW of UK ethnic groups, with South Asian and Black ethnicity having lower birthweights than White-European according to the Office for National Statistics (Prentice 2011).

However, it must not be ignored that ethnicity is a 'multi-dimensional concept' involving differences in health behaviour, SES, and attitudes to obesity, and is also highly likely to be self-reported in sample data, and so subject to individual perception (Gatineau and Mathrani 2011: 4). Yet the significance of understanding ethnic differences in weight gain must not be underestimated due to their increasing representation, with ethnic groups comprising 73% of UK population growth and set to account for 20% of the UK population by 2051 (Gatineau and Mathrani 2011). Hence, there is demand for greater study of differences underpinning ethnic disparities in 'obesity and associated health risks' (Gatineau and Mathrani 2011: 22).

2.5. Study aims and research questions

This study aims to further the evidence base for EAR, addressing issues of LBW and ethnicity. While a previous study using the MCS of rapid weight gain considered the second and third MCS sweeps (Griffiths *et al.* 2010), this current study has the benefit of access to the fourth MCS sweep. This means that it will be possible to analyse the pattern between ages 5 and 7, as well as 3 and 5. Moreover, Griffith's study examined increase in weight whereas this current study will consider BMI to take into account height changes. This study aims to answer the questions:

- Is there EAR in the Millennium Cohort Study? And is exponential weight gain sustained after the initial rebound?

- Is there any association with LBW?

- How does AR timing compare between ethnic groups?

3. Methodology

3.1. Data source

The datasets under analysis in this paper are from MCS sweeps 1-4, downloaded with permission from UK Data Service. This is a longitudinal study following individuals born in the UK between September 2000 and August 2001, commissioned by the Economic and Social Research Council to chart the impact of early life on subsequent 'outcomes and achievements' (Hansen 2012: 7). Initial data on family background, pregnancy, birth, and infancy were collected in MCS1 in 2001/2 via surveys, interviews, and anthropomorphic measures. MCS2 followed up on the children aged 3 in 2004/5, MCS3 aged 5 in 2006, and MCS4 aged 7 in 2008. The initial sample of 18,819 children from 18,553 families was found using Child Benefit Records and used a clustered, stratified design to over-represent ethnic minorities, 'areas of high child poverty' and families from Wales, Scotland, and Northern Ireland (Hansen 2012: 10).

Only children who were present in all four sweeps were included in this current analysis, data for birthweight, gestational age, maternal BMI, and ethnicity were taken from the MCS1 Derived Variables dataset. Maternal smoking, and diabetes data was from the MCS1 Parent Interview dataset. Subsequent cohort member BMI measures were taken from MCS2, 3, and 4 Derived Variables datasets, and the relevant data was merged into one dataset. Cases were excluded if they lacked data for BMI, birthweight or gender. This resulted in 10,654 cases being included in the final analysis.

3.2. Methods

The timing of AR was calculated from BMI scores recorded in MCS sweeps 2-4. From this a new categorical variable was created. ANCOVA analysis was used to examine the association between AR timing and the continuous birthweight variable, while controlling for covariates. Ethnicity was then introduced as a second factor in the ANCOVA, to investigate the relationship between AR timing, birthweight, and ethnicity. Any association between ethnicity and AR timing was then further assessed using a Chi-square analysis.

3.2.1. Constructing AR timing variable

At MCS2-4 the children's height to the nearest 0.1cm and weight to the nearest 0.1kg were recorded by interviewers. These measurements were used to calculate the BMI of each child at the time of measurement. The present study converted these BMIs into sex-specific z-scores to create new variables with means of 0 and standard deviations of 1. The change in BMI z-scores between MCS2 and 3 (age 3 and 5) and

MCS3 and 4 (age 5 and 7) were then calculated and formed new variables. These change in BMI z-score variables were then used to create categorical variables using visual binning with a cut point of 0.67, as 0.67 'represents the distance between each displayed percentile line on standard growth charts' (Ekelund *et al.* 2006: 325) and so a change in BMI z-scores higher than 0.67 can be taken as upward centile crossing. These categorical variables were combined to create the final categorical variable for AR timing, which is comprised of 4 groups:

1. Late AR = change in zBMI<0.67 between sweeps 2, 3, and 4
2. Normal AR = change in zBMI<0.67 between sweeps 2 and 3, but >0.67 between sweeps 3 and 4
3. Early AR = change in zBMI>0.67 between sweeps 2 and 3, but >0.67 between sweeps 3 and 4
4. Early-sustained AR = changes in zBMI>0.67 between sweeps 2, 3, and 4.

The syntax for this can be found in Appendix 1. The frequency distribution of AR timing is displayed in Table 1 and Figure 2 below:

Table 1: AR Timing Frequency Distribution

S1 HHQ Cohort Member Sex C1		Frequency	Percent	Cumulative Percent
Male	Late AR	5923	80.4	80.4
	Normal AR	603	8.2	88.6
	Early AR	652	8.8	97.4
	Early-sustained AR	191	2.6	100.0
	Total	7369	100.0	
Female	Late AR	5788	77.9	77.9
	Normal AR	684	9.2	87.1
	Early AR	804	10.8	97.9
	Early-sustained AR	153	2.1	100.0
	Total	7429	100.0	

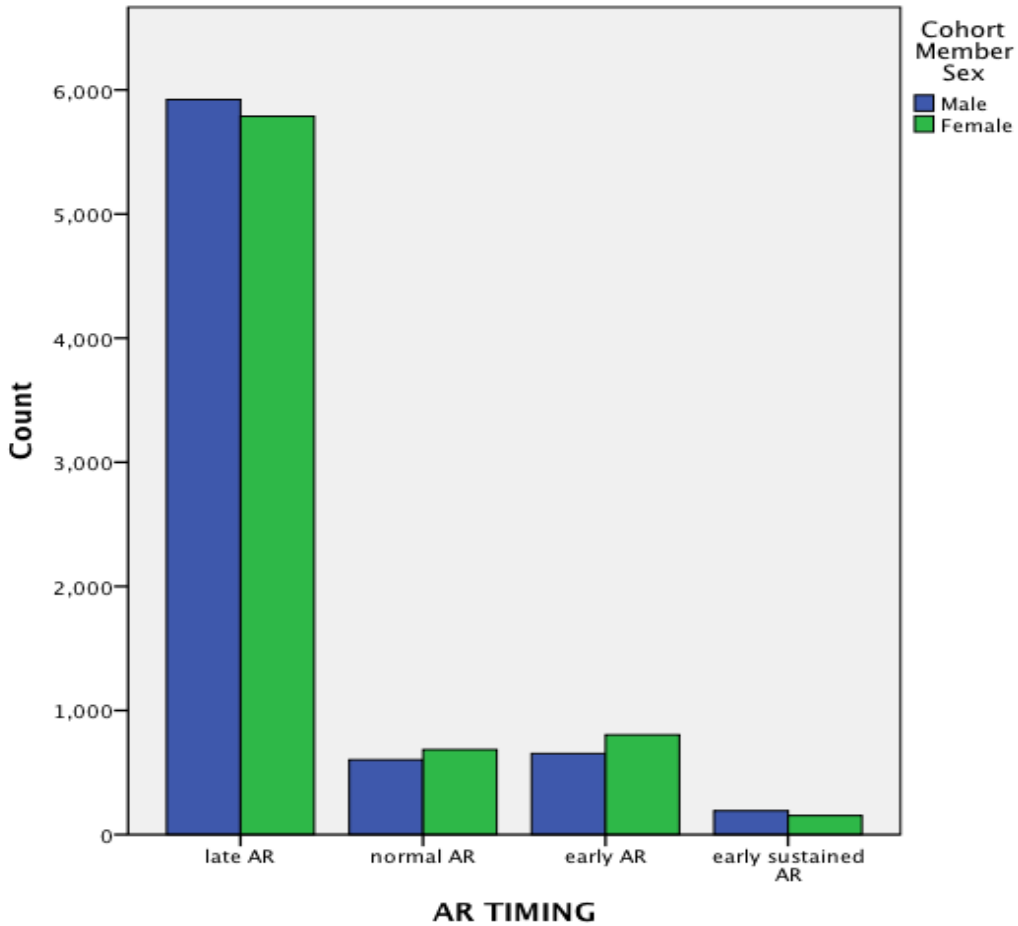


Figure 2: Distribution of AR timing

This variable shows that 11.4% of males and 12.9% of females show an Early or Early-sustained AR, and that the majority of both sexes show a Late AR (after the age of 7). This variable formed the main factor used in this study, and so would be considered the independent variable.

3.2.2. Birthweight variable

As this study is only looking to find the indication of an association and not a directional relationship, the labeling of variables as dependent and independent is misleading. However for the purpose of clarity, birthweight would be considered the dependent variable if such labels were being applied, and was coded as a continuous variable.

3.2.3. Ethnicity variable

The second factor, or independent variable, used in the subsequent analysis of this study is ethnicity. Due to the oversampling of ethnic minorities in the sample design

they are sufficiently represented to enable separate analysis (Plewis 2007). Main respondents were asked which ethnic identity they considered their baby belonged to in MCS1 using the '2001 Census ethnicity categories' (Plewis 2007: 8) and these were aggregated into the following 8 categories:

- White
- Mixed
- Indian
- Pakistani
- Bangladeshi
- Black Caribbean
- Black African
- Other Ethnic Group

10,633 out of the 10,654 cases used in this study provided valid ethnicity data. The frequency distributions can be found in Appendix 2.

3.2.4. Covariates

Based on current literature, 4 covariates were chosen based on their association with both birthweight and/or AR timing as discussed in Chapter 2. These were gestational time, maternal BMI prior to the birth, maternal smoking status, and maternal diabetes status. The response coding for these is detailed in Appendix 3 and the frequency distributions in Appendix 2.

3.3 Statistical methods

Statistical analysis was performed using SPSS Version 21. The first analyses performed was an ANOVA between birthweight and AR timing, this was followed by a General Linear Model (GLM) ANCOVA, which combines ANOVA and regression, to enable the examination of the association between birthweight and AR timing while controlling for covariates. This was necessary as this study used a secondary data source and so couldn't control for covariates in the study design (Field 2013).

Assumption of normality in the birthweight variable was confirmed using a histogram. Scatterplots of each covariate with birthweight were created to ensure linearity. Homogeneity of regression slope was tested to confirm that there was no significant interaction between the covariates and the independent. Homogeneity of variance was confirmed for both the ANOVA and ANCOVA by Levene's F-test with $\alpha=0.01$. Details of this can be found in Appendix 4. Statistically significant results were further investigated using planned contrasts and post-hoc tests. In the ANOVA Games-Howell pairwise test procedure was chosen as the sample sizes and variances varied between the AR groups, and this test provided the greatest power and control for Type 1 errors (Field 2013). In the ANCOVA Bonferroni adjustment was used in post-hoc pairwise comparisons to give the best control for Type 1 errors (Field 2013).

The relationship with ethnicity was first examined via its inclusion as another factor in the ANCOVA. This was followed by Chi-square analysis between AR timing and ethnicity, as both are nominal variables, the large sample size justifying the use of this method over Fisher's exact test. For all tests statistical significance was set as $\alpha=0.01$ for the 99% confidence interval and $\alpha=0.05$ for the 95% confidence interval.

4. Results

This Chapter details the findings of the statistical analysis performed on the sample taken from the MCS. Firstly the presence of EAR is confirmed, followed by the ANOVA and ANCOVA investigations into the association with birthweight. This is followed by the introduction of ethnicity as a factor in the ANCOVA, and the results of the Chi-square analysis of ethnicity and AR timing.

4.1. Presence of EAR

The sample frequency distributions for AR are given in Table 1 in Chapter 3 and confirm the presence of EAR in the MCS. This was sub-divided into Early AR and Early-sustained AR to account for those cases in which the increasing velocity of weight gain continued after age 5. 652 males and 804 females show Early AR representing 8.8% and 10.8% respectively. Early-sustained AR is scarcer with only 191 males (2.6%) and 153 females (2.1%). Normal AR is seen in only 603 males (8.2%) and 684 females (9.2%) whereas the majority of both sexes show Late AR; 5923 males (80.4%) and 5788 females (77.9%).

4.2. Association with birthweight

4.2.1 ANOVA

The results of the ANOVA between birthweight and AR timing can be seen in Table 2, and are displayed graphically in Appendix 5. Homogeneity of variance was met with $p>0.01$ for both sexes as can be seen in Appendix 4. For both sexes it is clear that there is a significant difference between the mean birthweights of the different AR timing groups; male $F(3,7346)=4.11$ $p=0.006$, female $F(3,7415)=4.90$ $p=0.002$.

Table 2: ANOVA results

Cohort Member birthweight in kilos

Cohort Member Sex		Sum of Squares	df	Mean Square	F	Sig.
Male	Between Groups	4.336	3	1.445	4.110	.006
	Within Groups	2583.136	7346	.352		
	Total	2587.472	7349			
Female	Between Groups	4.894	3	1.631	4.898	.002
	Within Groups	2469.659	7415	.333		
	Total	2474.554	7418			

Post-hoc analysis with Games-Howell tests, the output of which can be seen in Appendix 5, and the calculation of Cohen's *d* revealed that for males there are significant differences between the Early AR and both the Late AR, p=0.018, d=0.119, and the Normal AR, p=0.011, d=0.175, groups. For females there are significant differences between Early-sustained AR and all other groups; Late AR, p=0.001, d=-0.311, Normal AR, p=0.003, d=-0.312, Early AR, p=0.01, d=-0.281. There are no significant differences between any of the other pairwise comparisons at the 95% confidence interval, α=0.05.

4.2.2 ANCOVA

The results of the ANCOVA between birthweight and AR timing can be seen in Table 3 and can be seen graphically in Appendix 6. Homogeneity of variance was met with p>0.01 for both sexes as can be seen in Appendix 4. There is a significant difference in birthweight between the AR timing groups for both sexes, after controlling for the effects of maternal diabetes, maternal smoking, maternal BMI, and gestation time; male $F(3,4454)=3.332$, p=0.19, partial η^2=0.002, and female $F(3,4656)=8.671$, p=0.000, partial η^2=0.006. However, the partial Eta Squared values are very small, so only 0.2% of male variance in birthweight, and 0.6% of female variance in birthweight are associated solely with AR timing.

Table 3: ANCOVA Tests of Between-Subjects Effects

Dependent Variable: Cohort Member birthweight in kilos

Cohort Member Sex	Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Male	Corrected Model	544.218[a]	7	77.745	353.670	.000	.357
	Intercept	76.832	1	76.832	349.514	.000	.073
	Maternal diabetes	8.066	1	8.066	36.693	.000	.008
	Ever smoked	8.794	1	8.794	40.003	.000	.009
	Maternal BMI	22.961	1	22.961	104.451	.000	.023
	Gestation time	498.325	1	498.325	2266.917	.000	.337
	AR TIMING	2.197	3	.732	3.332	.019	.002
	Error	979.100	4454	.220			
	Total	52738.101	4462				
	Corrected Total	1523.318	4461				
Female	Corrected Model	547.458[b]	7	78.208	374.396	.000	.360
	Intercept	82.263	1	82.263	393.808	.000	.078
	Maternal diabetes	.691	1	.691	3.308	.069	.001
	Ever smoked	2.704	1	2.704	12.943	.000	.003
	Maternal BMI	33.468	1	33.468	160.216	.000	.033
	Gestation time	488.321	1	488.321	2337.674	.000	.334
	AR TIMING	5.434	3	1.811	8.671	.000	.006
	Error	972.601	4656	.209			
	Total	51415.422	4664				
	Corrected Total	1520.058	4663				

a. R Squared = .357 (Adjusted R Squared = .356)

b. R Squared = .360 (Adjusted R Squared = .359)

All of the covariates included in the analysis are significantly associated with birthweight, except for maternal diabetes in females; $F(1,4656)=3.308$, $p=0.069$.

The planned contrast, the output for which can be found in Appendix 6, between Early-sustained AR and the other AR timing groups in males reveals that birthweight

in Early-sustained AR is significantly different to birthweight in Early AR p=0.02, 95% CI [0.019, 0.224], but not to birthweight in Late AR, p=0.162, 95% CI [-0.027, 0.159], or Normal AR, p=0.668, 95% CI [-0.081, 0.127]. This is consistent with the findings from the ANOVA that birthweight in Early AR differs from the other groups.

The planned contrast for females reveals birthweight in Early-sustained AR is significantly different to all other AR timing groups; Late AR p=0.00, 95% CI [0.139, 0.334], Normal AR p=0.00, 95% CI [0.140, 0.353], and Early AR p=0.00, 95% CI [0.165, 0.374]. This is consistent with the findings from the ANOVA that birthweight in Early-sustained AR differed from the other groups.

This is confirmed by the estimated marginal means, see Appendix 6, which show that Early AR has a slightly higher mean birthweight (3.443kg, 95% CI [3.396, 3.491]) in males and Early-sustained AR has a considerably lower mean birthweight (3.034kg, 95% CI [2.938, 3.131]) in females. Ratification can also be found in the parameter estimates, which show a significant difference between Early-sustained AR and the Early AR group for males t(4454)=2.324, p=0.02, 95% CI [0.019, 0.224], and a significant difference between Early-sustained AR and all other AR timing groups for females, Late AR t(4656)=4.744 p=0.00 95% CI [0.139, 0.334], Normal AR t(4656)=4.541, p=0.00, 95% CI [0.140, 0.353], Early AR t(4656)=5.067, p=0.00, 95% CI [0.165, 0.374].

Pairwise comparisons, using the Bonferrroni procedure to control for Type 1 errors, (the output for which can be found in Appendix 6) between all groups are consistent with the previously observed differences between the AR timing groups. The significant differences in male birthweight between Early AR and Normal AR are evident, mean difference=0.099, p=0.034, 95% CI [0.005, 0.193], but the significant difference between Early AR and Late AR seen in the ANOVA is no longer present, as the mean difference=0.056, p=0.18, 95% CI [-0.012, 0.123].

In females the significant differences in birthweight between Early-sustained AR and all other AR groups is also evident, with Late AR mean difference=-0.236, p=0.00, 95% CI [-0.368, -0.105], Normal AR mean difference=-0.247, p=0.00, 95% CI [-0.390, -0.103], Early AR mean difference=-0.269, p=0.00, 95% CI [-0.410, -0.129].

4.3. Role of Ethnicity

4.3.1. Ethnicity as another factor of ANCOVA

Table 4 shows the output for the factorial ANCOVA with ethnicity added as another factor alongside AR timing. There is a significant main effect of ethnicity on birthweight between the different ethnic groups after controlling for covariates; male F(7,4429)=24.093, p=0.00, partial η^2=0.037, and female F(7,4629)=19.704, p=0.000, partial η^2=0.029. After the inclusion of ethnicity, AR timing no longer has a significant

association with birthweight for males, $F(3,4429)= 2.570$, $p=0.053$, partial $\eta^2=0.002$, but remains significant for females, $F(3,4629)= 4.492$, $p=0.004$, partial $\eta^2=0.003$. The interaction effect between AR timing and ethnicity is also significant at male $F(18,4429)=2.668$, $p=0.00$, partial $\eta^2=0.011$, and female $F(20,4629)=3.859$, $p=0.000$, partial $\eta^2=0.016$. These results are displayed graphically in Appendix 7, and indicate that the association between AR timing and birthweight differs between ethnic groups, particularly for Normal AR and Early-sustained AR in males, and Early AR and Early-sustained AR in females.

Ethnicity had a slightly lower partial η^2 than gestation (0.037 vs. 0.351) and (0.029 vs. 0.344) for male and female respectively. But a higher partial η^2 than both AR timing and the interaction effect between AR timing and ethnicity. So ethnicity had a greater association with birthweight than AR timing does.

Estimated marginal means, see Appendix 7, show that male mean birthweight is lowest in Indian (3.130kg, 95% CI [3.048, 3.211]) and Other Ethnic group (3.127kg, 95% CI [3.048, 3.206]) and highest in Black Caribbean (3.517kg, 95% CI [3.365, 3.699]) and White (3.498kg, 95% CI [3.457, 3.539]). Female mean birthweight is lowest in Bangladeshi (2.945kg, 95% CI [2.830, 3.061]) and Black African (3.052kg, 95% CI [2.972, 3.133]) and highest in White (3.394kg, 95% CI [3.349, 3.438]). Confidence intervals are based on 1000 bootstrap samples to reduce bias.

Table 4: Tests of Between-Subjects Effects

Dependent Variable: Cohort Member birth weight in kilos

S1 HHQ Cohort Member Sex C1	Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Male	Corrected Model	658.536[a]	32	20.579	105.397	.000	.432
	Intercept	72.905	1	72.905	373.383	.000	.078
	Maternal diabetes	10.696	1	10.696	54.782	.000	.012
	Ever smoked	.356	1	.356	1.823	.177	.000
	Maternal BMI	13.561	1	13.561	69.452	.000	.015
	Gestation time	467.146	1	467.146	2392.496	.000	.351
	AR TIMING	1.505	3	.502	2.570	.053	.002
	Ethnicity	32.930	7	4.704	24.093	.000	.037
	AR TIMING * Ethnicity	9.375	18	.521	2.668	.000	.011
	Error	864.782	4429	.195			
	Total	52738.101	4462				
	Corrected Total	1523.318	4461				
Female	Corrected Model	648.769[b]	34	19.081	101.376	.000	.427
	Intercept	80.326	1	80.326	426.756	.000	.084
	Maternal diabetes	1.139	1	1.139	6.051	.014	.001
	Ever smoked	.482	1	.482	2.559	.110	.001
	Maternal BMI	23.621	1	23.621	125.494	.000	.026
	Gestation time	457.286	1	457.286	2429.478	.000	.344
	AR TIMING	2.537	3	.846	4.492	.004	.003
	Ethnicity	25.962	7	3.709	19.704	.000	.029
	AR TIMING * Ethnicity	14.528	20	.726	3.859	.000	.016
	Error	871.289	4629	.188			
	Total	51415.422	4664				
	Corrected Total	1520.058	4663				

a. R Squared = .432 (Adjusted R Squared = .428)

b. R Squared = .427 (Adjusted R Squared = .423)

Pairwise comparison, the output for which can be found in Appendix 7, using Bonferroni post-hoc tests, with bias-corrected and accelerated confidence intervals based on 1000 bootstrap samples, show significant differences between the White ethnic group and different ethnic groups in both sexes. This reveals that birthweight in White males was significantly higher than birthweight in Indian (mean

difference=0.368, p=0.000, 95% CI [0.288, 0.452]), Pakistani (mean difference=0.165, p=0.001, 95% CI [0.066, 0.273]), Bangladeshi (mean difference=0.550, p=0.000, 95% CI [0.425, 0.684]), and Other Ethnic group males (mean difference=0.371, p=0.000, 95% CI [0.301, 0.441]), but not significantly different to birthweight in Mixed (mean difference=0.166, p=1.000, 95% CI [-0.001, 0.322]), Black Caribbean (mean difference=-0.019, p=1.000, 95% CI [-0.091, 0.057]), or Black African males (mean difference=0.081, p=1.000, 95% CI [0.005, 0.163]). Black Caribbean males being the only group to have a higher mean birthweight than White.

White female birthweight was significantly higher than birthweight in Indian (mean difference=0.319, p=0.000, 95% CI [0.259, 0.381]), Pakistani (mean difference=0.333, p=0.000, 95% CI [0.260, 0.416]), Bangladeshi (mean difference=0.448, p=0.000, 95% CI [0.375, 0.522]), Black African (mean difference=0.341, p=0.000, 95% CI [0.234, 0.461]), and Other ethnic groups females (mean difference=0.190, p=0.001, 95% CI [0.101, 0.278]). But not significantly higher than Mixed (mean difference=0.032, p=1.000, 95% CI [-0.037, 0.225]), or Black Caribbean females (mean difference=0.026, p=1.000, 95% CI [-0.086, 0.150]).

4.3.2. Chi-Square comparing AR timing between ethnic groups

A Chi-square was used to compare AR timing between ethnic groups; the large sample size justified the use of Chi-square over Fisher's exact test. Assumptions for Chi-square was met as each case contributes to only one cell of the contingency table, and all expected frequencies were greater than 5.

Table 5 shows the results of the Chi-Square test. There is a significant association between ethnicity and AR timing for both male, $\chi^2(21)=221.916$, p=0.000, and female, $\chi^2(21)=206.692$, p=0.000. Consequently, we can reject the null hypothesis that AR timing and ethnicity are independent. Cramer's V was also calculated, using 1000 bootstrap samples to increase the robustness of the confidence intervals, males ϕ=0.100, 95% CI [0.090, 0.122], females ϕ=0.096, 95% CI [0.086, 0.119]. This implies that the association is weak, and so ethnicity would be of little benefit in predicting AR timing.

Table 5: Chi-Square Tests

Cohort Member Sex		Value	df	Asymp. Sig. (2-sided)
Male	Pearson Chi-Square	221.916[a]	21	.000
	Likelihood Ratio	202.541	21	.000
	Linear-by-Linear Association	40.773	1	.000
	N of Valid Cases	7369		
Female	Pearson Chi-Square	206.692[b]	21	.000
	Likelihood Ratio	181.080	21	.000
	Linear-by-Linear Association	62.279	1	.000
	N of Valid Cases	7429		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.01.
b. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.05.

Crosstabulation, (which can be found in Appendix 7) with the calculation of adjusted residuals (where z>+/-1.96 indicates significance at the α=0.05 level, z>+/-2.58 indicates significance at the α=0.01 level, and z>+/-3.29 indicates significance at the α=0.001 level) revealed that for males significantly more White (z=7.6) and significantly less Indian (z=-3.1), Bangladeshi (z=-5.8), Black Caribbean (z=-2.8), Black African (z=-3.9), and Other Ethnic Group (z=-2.8), cases experienced Late AR than expected were there no association between AR timing and ethnicity present.

Significantly less White males (z=-6.0) and significantly more Indian (z=3.8), Black African (z=4.1), and Other Ethnic Group (z=3.4) males experienced Normal AR than expected. For Early AR there were significantly less White (z=-2.4), Mixed (z=-3.0), Indian (z=-2.2), and Pakistani (z=-2.0) male cases, and significantly more Bangladeshi (z=5.5), Black Caribbean (z=3.6), Black African (z=2.5), and Other Ethnic Group (z=2.6) male cases than expected. For Early-sustained AR there were significantly less White (z=-4.2) and Other Ethnic Group (z=-3.5) males and significantly more Indian (z=5.2), and Bangladeshi (z=5.9) males than expected.

In the female cases there were significantly more White (z=9.3) and significantly less Mixed (z=-2.7), Indian (z=-2.2), Pakistani (z=-3.2), Bangladeshi (z=-2.3), Black Caribbean (z=-4.1), and Black African (z=-6.3), cases that experienced Late AR than expected were no association between AR timing and ethnicity present.

Significantly less White females (z=-6.2) and significantly more Mixed (z=3.4), Indian (z=4.7), and Black African (z=2.4) females experienced Normal AR than expected. For Early AR there were significantly less White (z=-4.8) female cases, and significantly more Pakistani (z=2.6), Bangladeshi (z=3.8), and Black African (z=3.9) female cases than expected. For Early-sustained AR there were significantly less White (z=-4.1) and Other Ethnic Group (z=-3.0) females and significantly more Black Caribbean (z=6.8), and Black African (z=4.9) females than expected.

These results are displayed graphically in Figures 3 and 4.

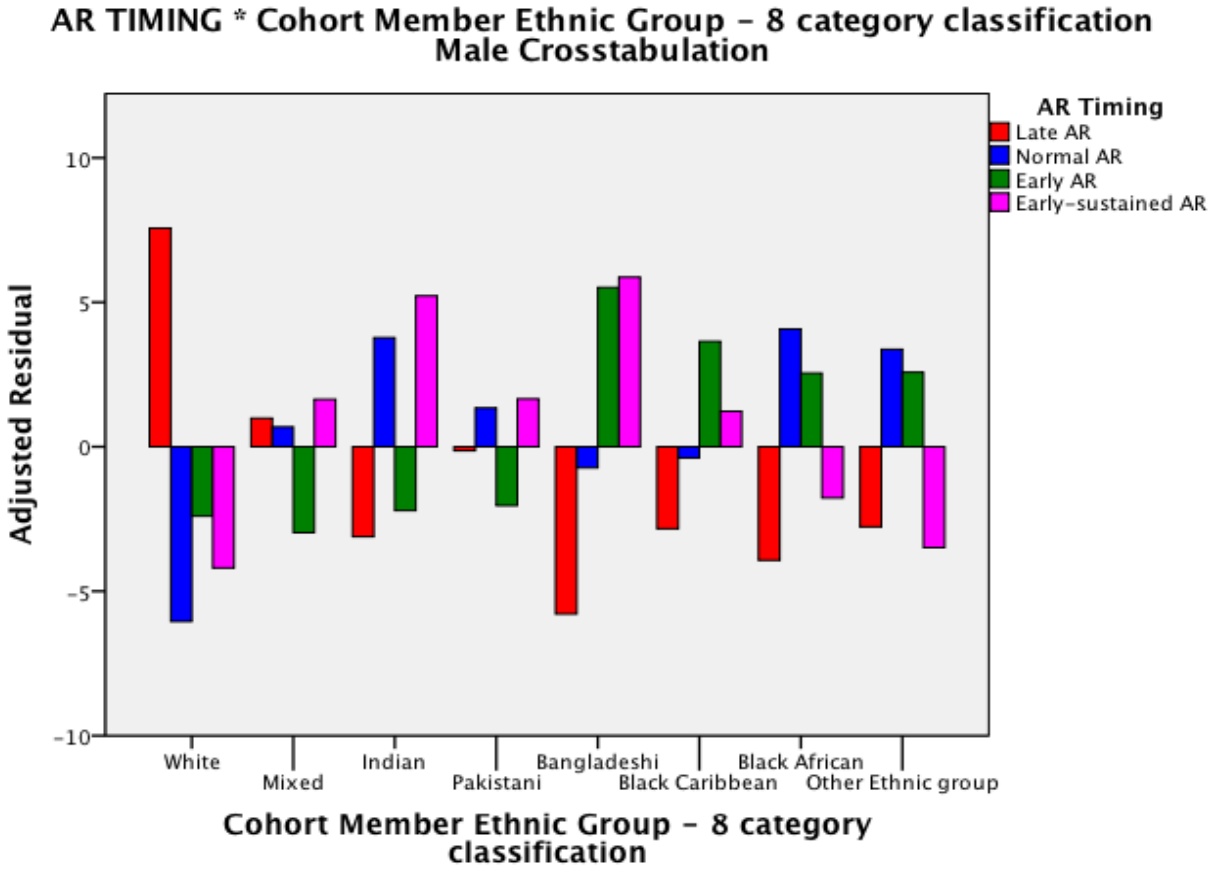


Figure 3: Plot of male AR timing, ethnicity crosstabulation

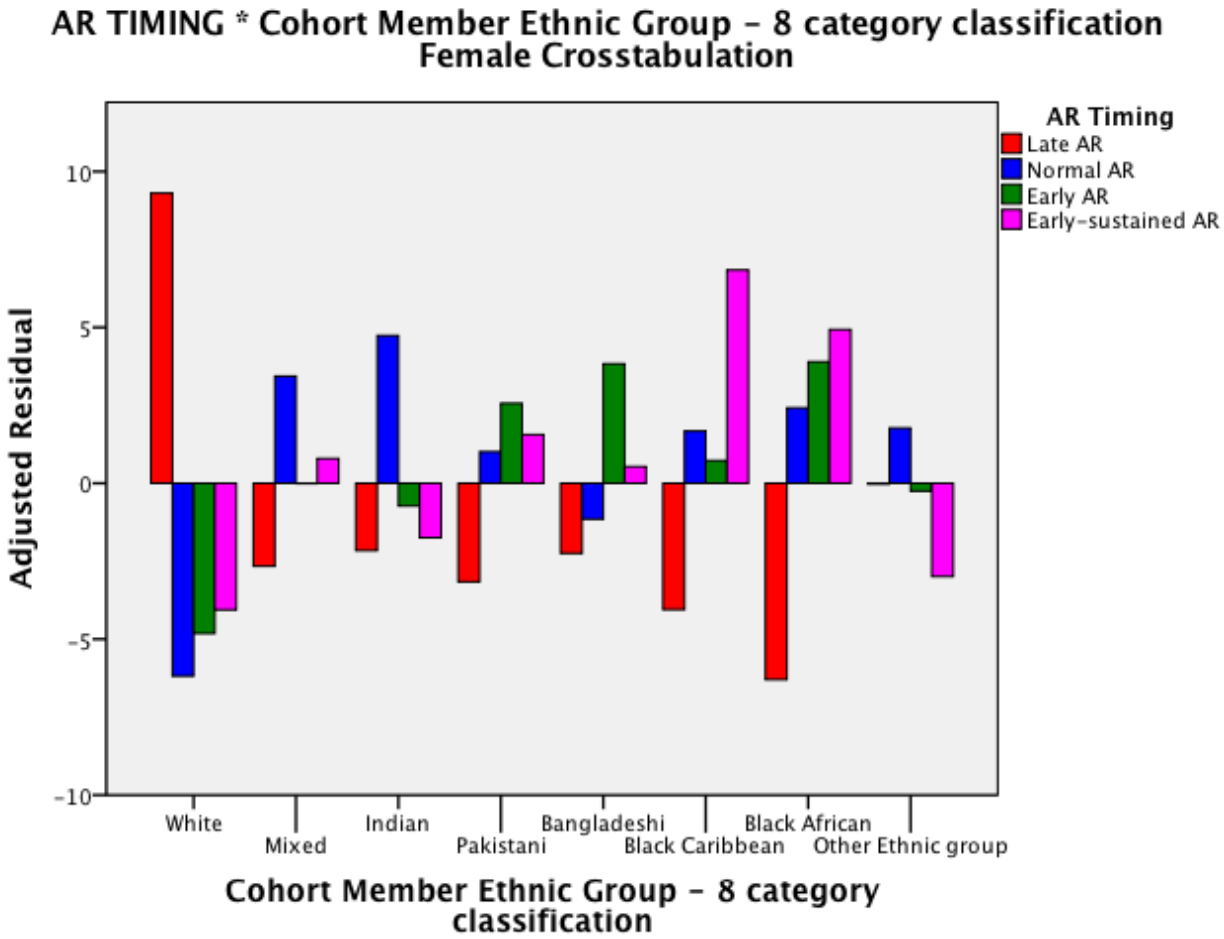


Figure 4: Plot of female AR timing, ethnicity crosstabulation

5. Discussion

This study investigated the timing of adiposity rebounds in the MCS. Having identified the presence of Early AR cases, the association with LBW was assessed. The role of ethnicity was then considered both in relation to birthweight and AR timing.

Early AR and Early-sustained AR were both found to be present in the MCS. 652 males (8.8%) and 804 females (10.8%) showed an Early AR and 191 males (2.6%) and 153 females (2.1%) showed an Early-sustained AR. The majority of cases in both males and females were Late AR, with 80.4% and 77.9% respectively, compared with only 8.2% of males and 9.2% of females experiencing what has been classified as a Normal AR, i.e. between the age of 5 and 7 years. This differs from previous studies in which the majority of children experience Normal AR, for example in Whitaker *et al's* study the mean age of AR was 5.5 years (Whitaker *et al.* 1998). To my knowledge this is the first study to distinguish between those that experience Early AR and then return to a slower rate of BMI increase, and those in whom the rate is sustained.

Early AR has been considered an indicator of greater risk of obesity and diabetes in later life, with Rolland-Cachera stating that as much as 30% of obesity that starts in childhood could be due to Early AR (William H. Dietz 2000). Multiple studies ratify this association (Cole 2004; González *et al.* 2010; Whitaker *et al.* 1998) with children who experience Early AR gaining adipose tissue twice as fast as those experiencing Late AR (Boonpleng *et al.* 2012; Taylor *et al.* 2005), having greater adult fat mass (Corvalán *et al.* 2007), and with their age at rebound negatively correlated to 'subsequent BMI' (S. M. Williams 2005). Consequently, it is of potential value that this risk could be highlighted via the identification of those children with Early AR/Early-sustained AR.

5.1. Birthweight

Univariate analysis using a GLM (ANCOVA) showed that there was a significant difference in birthweights between the AR timing groups for both sexes after controlling for covariates of maternal diabetes, BMI, and smoking, and gestational time. Male cases with Early AR had significantly higher mean birthweight (3.443kg, 95% CI [3.396, 3.491]) which supports views from previous literature that there is no association between LBW and Early AR (Griffiths *et al.* 2010; McCarthy *et al*. 2007; K. K. Ong and Loos 2006; S. M. Williams and Goulding 2009) and suggests that in males, Early AR is not linked to catch-up growth resulting from restricted fetal nutrition, as had been proposed by Rolland-Cachera *et al.* On the contrary this study implies that it is those males born high birthweight that are at greater risk of Early AR, as males in the Normal and Late AR timing groups all had lower mean birthweights; (3.345kg, 95% CI [3.293, 3.396]) and (3.388kg, 95% CI [3.373, 3.403]) respectively. This finding adds to the observation by Yu *et al.* that those of higher birthweight are at 'increased risk of obesity' (Yu *et al.* 2011), and further research into the role of AR

in high birthweight children who subsequently develop obesity would be of value in establishing causal pathways.

A slight anomaly in the male results was that the Early-sustained AR group had the lowest mean birthweight (3.322kg, 95% CI [3.231, 3.413]) yet this was not significantly different to the mean birthweight for either Normal or Late AR at the α=0.05 level, as shown in the planned contrast results in Appendix 6.

Female cases showed a considerably different pattern, Early-sustained AR cases had significantly lower mean birthweight (3.034kg, 95% CI [2.938, 3.131]) than all the other AR timing groups. This suggests that females of LBW are at greater risk of Early-sustained AR. As LBW is a proxy for fetal undernutrition, this finding implies that Early-sustained AR could be the result of the stimulation of a thrifty phenotype and the predictive adaptive response which induces the rapid accumulation of centrally stored fat (Barker *et al.* 1997) due to the expectation of a 'nutritionally poor postnatal environment' (Tabacchi *et al.* 2007: 591). This pattern has been found in previous studies where fetal undernutrition results in supressed thermogenesis (M. F. Rolland-Cachera *et al.* 2006) with glucose redirected to truncal adipose tissue instead of 'skeletal muscle' (Argente *et al.* 2010: 681). Consequently, body composition is altered, resulting in a greater proportion of body fat mass which affects 'metabolic competence' (Prentice 2011: 15) and insulin resistance, and increases the risk of obesity, T2D (Eriksson *et al.* 2003), high blood pressure (Horta *et al*. 2003), and other features of metabolic syndrome.

The work of Barker *et al.* has confirmed that there is a correlation between children of LBW and greater levels of truncal fat storage (Argente *et al.* 2010; Barker *et al.* 1997). Rat studies have identified suppressed thermogenesis as key in the induction of insulin resistance and metabolic syndrome during catch-up growth (Cettour-Rose *et al.* 2005) and this has also been seen in children born small for gestational age (Argente *et al.* 2010). The findings from this study suggest that the timing of adiposity rebound could be key in the pathway from LBW to high adiposity and further research into this pathway would be of value.

5.2. Ethnicity

The introduction of ethnicity as a factor into the GLM ANCOVA revealed significant differences in mean birthweight between ethnic groups, having controlled for covariates of maternal diabetes, BMI, smoking, and cohort member gestation time. Male mean birthweight was highest in Black Caribbean (3.517kg, 95% CI [3.365, 3.699]) and White (3.498kg, 95% CI [3.457, 3.539]) cases. Female mean birthweight was also highest in White cases (3.394kg, 95% CI [3.349, 3.438]). The lowest mean birthweights were in Indian (3.130kg, 95% CI [3.048, 3.211]) and Other Ethnic group (3.127kg, 95% CI [3.048, 3.206]) for males and in Bangladeshi (2.945kg, 95% CI [2.830, 3.061]) and Black African (3.052kg, 95% CI [2.972, 3.133]) females. While there is evidence from studies in the Indian subcontinent of high rates of poor fetal growth and LBW (Bavdekar *et al.* 1999), it is of interest to see that the same pattern

is observed in a UK sample. This suggests that genetic factors may be significant in the lower birthweight of South Asian children, however birthweight is a complex and multifactorial entity, and so cultural and environmental factors must also be taken into consideration, which is beyond the scope of this study.

Examination of the literature shows great differentials in metabolic syndrome risk between ethnic groups. The Bongalusa Heart Study found higher levels of childhood obesity persisting into adulthood among Black children than White in America (Caprio *et al.* 2008). This result was corroborated by the NCMP 2009/10 revealing greater childhood obesity in both sexes in Black, Mixed, and South-Asian ethnic groups than White British (Gatineau and Mathrani 2011) together with higher prevalence of T2D. The SEARCH study revealed that T2D onset between age 10-19 was fivefold higher for African-American children than their White counterparts (33% vs. 6% respectively) (Caprio *et al.* 2008).

In studies of South-Asian populations the risk of T2D and metabolic syndrome was elevated compared to White populations of similar BMI (Gatineau and Mathrani 2011). This is suggested to be due to 'different physiological responses to fat storage' (Gatineau and Mathrani 2011: 5) and greater levels of fat vs. lean body-mass plus higher truncal adiposity (Bavdekar *et al*. 1999).

The implication is that there may be biological underpinnings to this variation, such as 'thrifty genotypes', however so far no specific genes have been identified, and caution is necessary as many cultural and socioeconomic factors may also be influential (Caprio *et al.* 2008: 2213). Nevertheless, studies demonstrate that there are 'fundamental metabolic differences' such as adiponectin levels, and insulin resistance, as well as differences in body composition and fat distribution between ethnic groups (Caprio *et al*. 2008: 2213). There is the possibility that this variation could be influenced by differences in AR timing between ethnic groups as revealed by the current study.

The interaction effect between AR timing and birthweight was statistically significant for both sexes; male $F(18,4429)=2.668$, $p=0.00$, partial $\eta^2=0.011$, and female $F(20,4629)=3.859$, $p=0.000$, partial $\eta^2=0.016$, implying a difference in the association between birthweight and AR timing for different ethnic groups. This finding may imply that the relationship between birthweight and subsequent risk of obesity and diabetes varies between ethnic groups, and that AR timing is instrumental in this variation.

Chi-square examination of AR timing and ethnicity revealed a significant association for both sexes; male $\chi^2(21)=221.916$, $p=0.000$, and female $\chi^2(21)=206.692$, $p=0.000$.

Analysis of adjusted residuals in males showed Late AR timing was experienced by significantly more White, and significantly less Indian, Bangladeshi, Black Caribbean, Black African, and Other Ethnic Group cases. Normal AR timing was significantly

higher in Indian, Black African, and Other Ethnic Group. Early AR was also significantly higher in Bangladeshi, Black Caribbean, Black African, and Other Ethnic Group cases. Early-sustained AR was significantly higher in Indian and Bangladeshi males, which could also potentially correspond to the greater levels of LBW in South Asian males, although this is only speculation. These findings corroborate previous studies showing variation in the rate of childhood weight gain between ethnic groups, with Bangladeshi and Black children showing the highest rate of weight gain between 3 and 5 years (Griffiths *et al.* 2010). However, the discovery that it was only those of South-Asian ethnicity that sustained this rate of BMI increase to age 7 implies that there could be additional variation between ethnic groups which would benefit from further investigation.

The analysis of adjusted residuals in females showed a similar pattern for Late AR timing with significantly more White females and significantly less Mixed, Indian, Pakistani, Bangladeshi, Black Caribbean, and Black African experiencing Late AR timing. Normal AR timing was also significantly higher in Indian and Black African, but also Mixed ethnicity females. Early AR was significantly more common in Pakistani, Bangladeshi, and Black African cases. In contrast to the males results, Early-sustained AR was significantly higher in Black Caribbean and Black African females and was actually lower than expected in Indian females, which again could be seen to correspond to greater levels of LBW in Black African females. This sharp contrast between genders for Early-sustained AR suggests other factors need to be considered such as differences in fat storage and distribution. This is verified by evidence from literature of gender differences in obesity prevalence between ethnic groups with significantly higher levels seen in Black African, and Black Caribbean women than men (Gatineau and Mathrani 2011). Consequently, AR timing may be influential in the variation of fat storage and so the difference in risk of obesity, T2D, and metabolic syndrome between ethnicities, and genders, and partially account for the greater rates of obesity-related mortality in individuals of Black and South Asian ethnicity (Katzmarzyk *et al*. 2012).

5.3. Strengths of the study

This study has contributed to the literature on AR and provided insight into the variations of AR timing in relation to birthweight and ethnicity. A primary strength was the use of the MCS, which, due to its large study size and wide sampling, can be considered representative of the UK population (Ketende 2010). The high percentage of productive responses at each sweep (over 70%) also helps to increase the statistical power and reduce response bias (Ketende 2010). Moreover, the ‘two-stage stratified and cluster sampling design’ of the MCS meant that in England ethnic minorities were oversampled, and enabled these minority groups to be analysed separately (Dex *et al.* 2008: 6).

Another strength of the study was access to multiple sweeps of the MCS, this longitudinal data enabled comparison of cohort members at four different ages; birth, age 3, 5, and 7 years. Consequently, a life-course perspective could be formed with

regards to the variables considered, and the classification of Early-sustained AR could be created. This takes the current study further than previous examinations of the MCS with regards to AR timing and childhood weight gain, such as that by Griffiths *et al.*

5.4. Limitations

One of this study's main limitations was that only data from the MCS up to sweep 4 (age 7) could be utilised and so it is not clear what the long-term consequences of different AR timings, birthweight, and ethnicity are in terms of obesity, diabetes, and metabolic syndrome.

The data itself has several limitations in that there is some reliance on self-reporting, such as for smoking status, and so there is the risk of recall bias or deliberate concealment. Refusal to answer survey questions was low, and these were set as missing data and so eliminated from the current study, yet this does risk introducing bias, especially as the final complete case data set was not weighted to account for non-respondents, however studies into non-response in the MCS have implied that the impact of non-response are 'small' compared to the bias built into the sample design (Plewis 2007: 325).

Birthweight as a variable is limited in its use as a proxy for fetal growth as it fails to account for metabolic and compositional differences between newborns, gives no indication of 'growth trajectory', and is open to influence by multiple environmental and genetic factors (Prentice 2011: 41), therefore only providing a weak representation of nutritional state and other 'prenatal risk factors' significant in the development of metabolic syndrome (Rich-Edwards *et al*. 1999: 283). A better measure would have been ponderal index, however this data was not available.

The choice of BMI, as opposed to weight, to calculate AR timing has been discussed in Chapter 2, and while this variable has its strengths in taking height changes into account, there are also several limitations that have been raised in the literature. Similar to birthweight, BMI does not account for variations in body composition and provides no information on fat vs. lean mass ratio (Prentice 2011). Data on levels of truncal adiposity would have been of great value, as this is one of the main observed outcomes of suppressed thermogenesis (Cettour-Rose *et al*. 2005), and is seen to differ between ethnicities (Sachdev *et al.* 2005), and be higher in those of LBW (Barker *et al*. 1997). Moreover, with regards to ethnicity, BMI thresholds were initially established for use in European populations and it has been observed that the risk thresholds for chronic diseases for those of South Asian background need to be altered, as advised by the South Asian Health Foundation (Gatineau and Mathrani 2011). While this does not pose such a problem to the current study, it will need to be taken into consideration in future studies of the MCS.

The multifactorial nature of rate of weight gain also creates limitations to the study, as there are numerous potential cofounders that could have an impact. While this study has taken what are considered in the literature to be the main cofounders: gestational time, maternal smoking, BMI, and diabetes, into account, there are many others that data was unavailable for, or were beyond the scope of this study to consider. These include the social economic status of the cohort member and their family, duration and intensity of breast-feeding, introduction of solid foods, diet, level of physical activity, TV watching, and sleep duration (Askie *et al.* 2010; Dixon *et al*. 2012; Layte *et al.* 2014).

A final limitation of the results themselves is that due to the 2-year gap between sweeps of the MCS, the current study is unable to give precise age of AR, which could have been useful to give greater precision as to the associations with birthweight and ethnicity.

5.5.Further research

This study has revealed variation in children experiencing adiposity rebound earlier than expected, in that this can be classified as either Early AR or Early-sustained AR. Variation can also be seen between AR timing groups with gender, birthweight, and ethnicity, which all warrant further investigation, particularly with regards to causal pathways, and taking into account the other potential cofounders indicated in the limitations. Studies with greater data and investigation of body fat distribution would also be of value with regards to identifying the key factors in rising childhood-onset obesity and metabolic syndrome. Moreover, it will be of interest to see what future studies of the MCS reveal regarding long-term impacts of AR timing on adolescent and adult health and risk of metabolic syndrome.

6. Conclusion

The aim of this study has been to investigate AR timing, LBW, and ethnicity, and their associations, in the MCS, through the examination of the change in rate of BMI increase between sweeps 2, 3, and 4. Early AR was found to be present in approximately 10% of both sexes in the MCS, approximately 2% of cases showed sustained upward BMI centile crossing between all sweeps considered and consequently were classified as Early-sustained AR.

The association with birthweight was analysed using a GLM ANCOVA and revealed differences between the AR timing groups, with the male Early AR group having a significantly higher mean birthweight than the other AR timing groups. While females in the Early-sustained AR group had a significantly lower mean birthweight. This implies that both birthweight and gender influence the timing of AR and warrant further investigation.

The consideration of ethnicity revealed a difference in the association between birthweight and AR timing between ethnic groups due to the significant interaction effect seen in the ANCOVA, the exact details of which could form the basis of a PHD investigation. AR timing was found to vary between ethnic groups using a Chi-square analysis, which indicated that Early AR was significantly higher in Bangladeshi, Black Caribbean, Black African, and Other Ethnic group males, and in Pakistani, Bangladeshi, and Black African females. Early-sustained AR was found to be significantly higher in Indian and Bangladeshi males, and Black Caribbean and Black African females. These findings contribute to the current gap in knowledge about the differences underpinning variation in obesity and metabolic syndrome between ethnic groups, and future sweeps of the MCS will prove a valuable resource to provide further insight into the obesity pathway.

Finally, it is crucial to highlight that birthweight, AR timing, obesity, and metabolic syndrome are multifactorial variables and so public policy and interventions will need to be equally multi-faceted in their approach, taking into consideration both the cofounding factors highlighted in this study and others mentioned in Chapter 5. While AR timing itself can only be ascertained retrospectively, this study highlights those groups that are at highest risk of experiencing an Early or Early-sustained AR, and so at greater risk of subsequently developing obesity and metabolic syndrome. Childhood and adult obesity and associated morbidities continue to rise in the UK, as do ethnic groups as a proportion of the population. Hence, the identification of those at greater risk will become of increasing significance in the future in order to take pre-emptive action and slow the advancement of what has the potential to be one of the 21st century's biggest health threats.

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Appendix 1: Creating the AR timing variable

Categorical variables were created from the changes in zBMI using visual binning with a cut point of 0.67 this created two new variables:
"ARtiming" for the change in zBMI between sweeps 2 and 3 (ages 3 and 5) with <0.67 = 1 and >0.67 = 2
"ARtiming2" for the change in zBMI between sweeps 3 and 4 (age 5 and 7) with <0.67 = 1 and >0.67 = 2
these were combined to make a new variable using the following syntax:

COMPUTE ARTIMING = (ARtiming -1)*2 + (ARtiming2-1) + 1

This created a categorical variable with 4 groups:
1 = No AR between ages 3 & 5 or 5 & 7 = late AR
2 = No AR between ages 3 & 5, but AR between ages 5 & 7 = Normal AR
3 = AR between ages 3 & 5 with rate not maintained between ages 5 & 7 = Early AR
4 = AR between ages 3 & 5 with rate maintained between ages 5 & 7 = Early-sustained AR

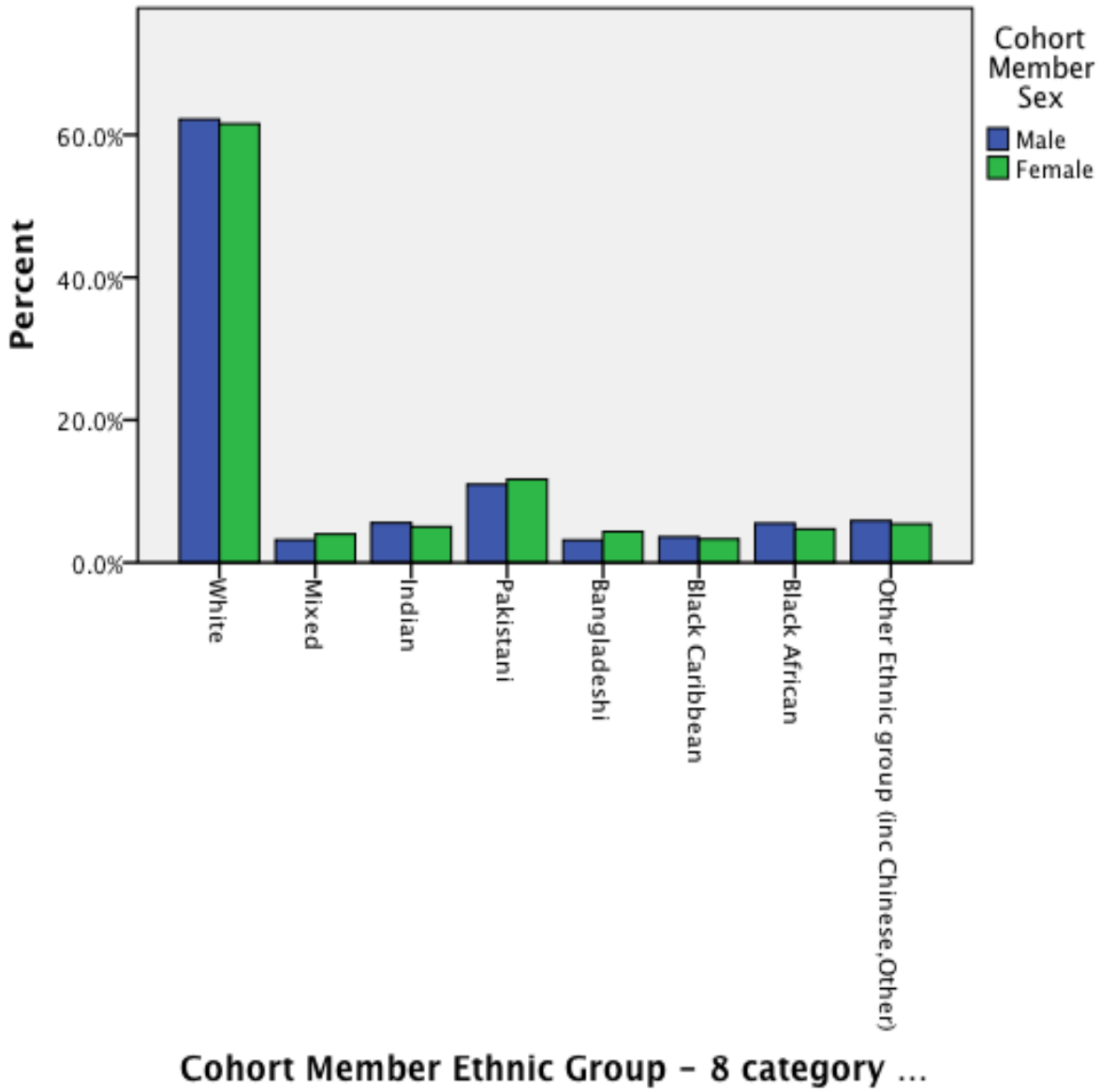
Appendix 2: Variable frequency distributions

Ethnicity:

Cohort Member Ethnic Group - 8 category classification

Cohort Member Sex			Frequency	Percent	Valid Percent	Cumulative Percent
Male	Valid	White	4582	62.2	62.2	62.2
		Mixed	234	3.2	3.2	65.4
		Indian	411	5.6	5.6	70.9
		Pakistani	808	11.0	11.0	81.9
		Bangladeshi	232	3.1	3.1	85.0
		Black Caribbean	265	3.6	3.6	88.6
		Black African	405	5.5	5.5	94.1
		Other Ethnic group (inc Chinese,Other)	432	5.9	5.9	100.0
		Total	7369	100.0	100.0	
Female	Valid	White	4572	61.5	61.5	61.5
		Mixed	296	4.0	4.0	65.5
		Indian	372	5.0	5.0	70.5
		Pakistani	868	11.7	11.7	82.2
		Bangladeshi	324	4.4	4.4	86.6
		Black Caribbean	245	3.3	3.3	89.9
		Black African	350	4.7	4.7	94.6
		Other Ethnic group (inc Chinese,Other)	402	5.4	5.4	100.0
		Total	7429	100.0	100.0	

Ethnicity percentage frequency distribution:



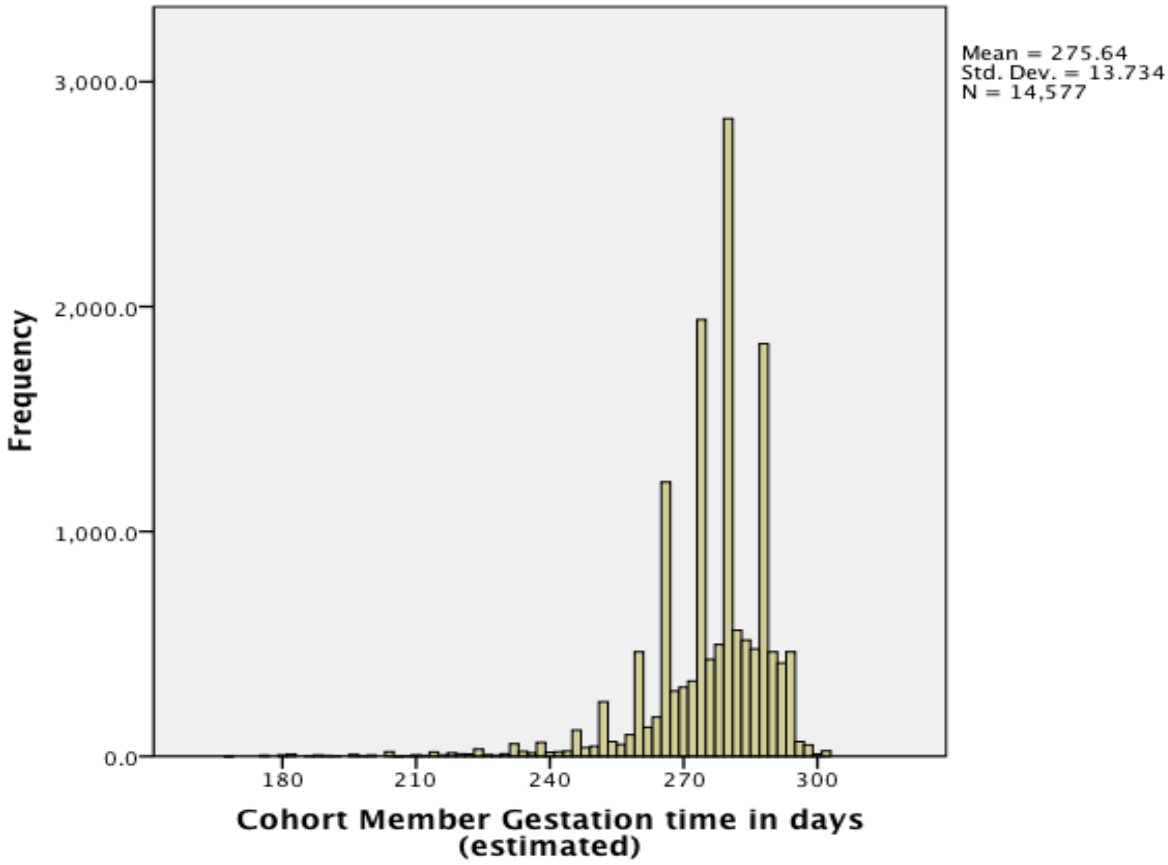
Gestation time:

Statistics

Cohort Member Gestation time in days (estimated)

Male	N	Valid	7239
		Missing	130
	Mean		275.42
	Median		280.00
	Std. Deviation		13.601
	Range		126
	Minimum		175
	Maximum		301
Female	N	Valid	7338
		Missing	91
	Mean		275.85
	Median		280.00
	Std. Deviation		13.862
	Range		133
	Minimum		168
	Maximum		301

Gestation time frequency distribution:



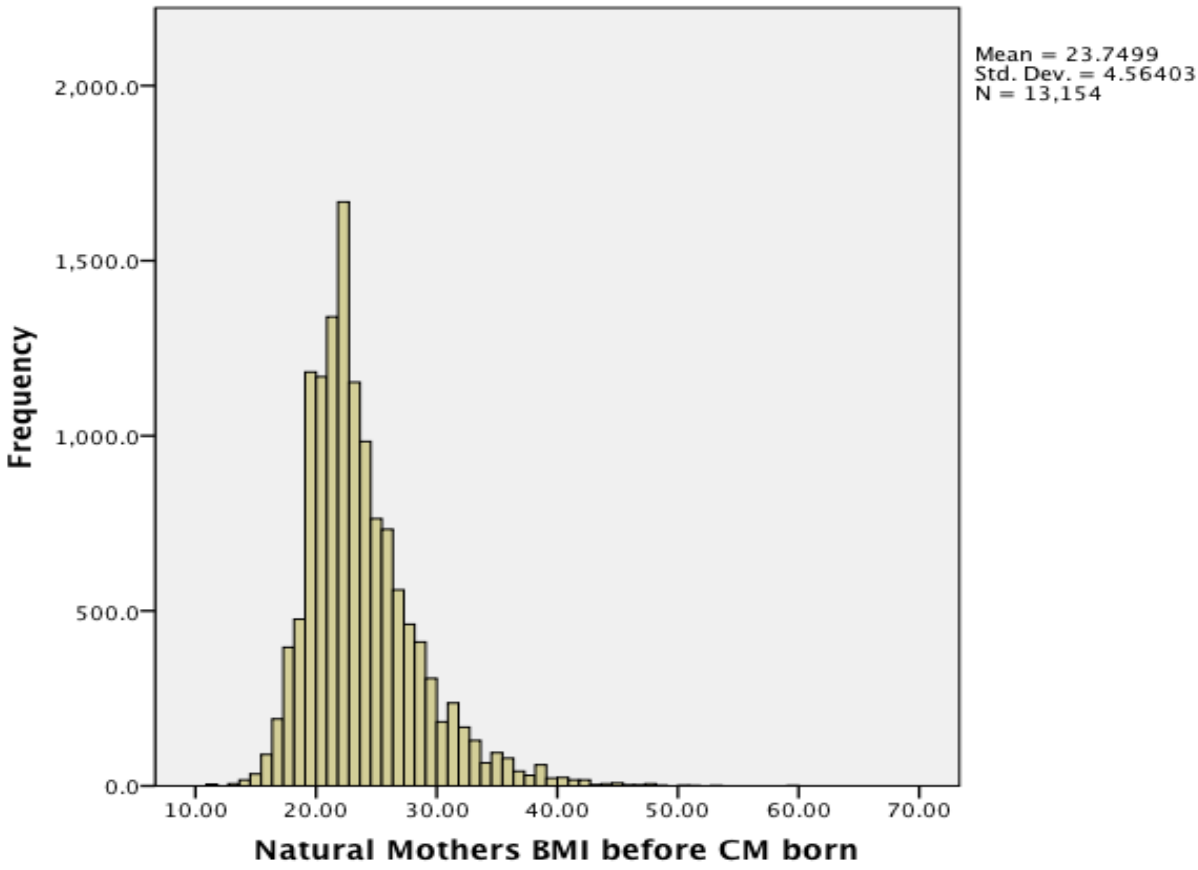
Maternal BMI prior to birth:

Statistics

Natural Mothers BMI before CM born

Male	N	Valid	6513
		Missing	856
	Mean		23.7537
	Median		22.8100
	Std. Deviation		4.47924
	Range		39.72
	Minimum		13.15
	Maximum		52.87
Female	N	Valid	6641
		Missing	788
	Mean		23.7461
	Median		22.7100
	Std. Deviation		4.64601
	Range		47.53
	Minimum		11.65
	Maximum		59.18

Maternal BMI frequency distribution:

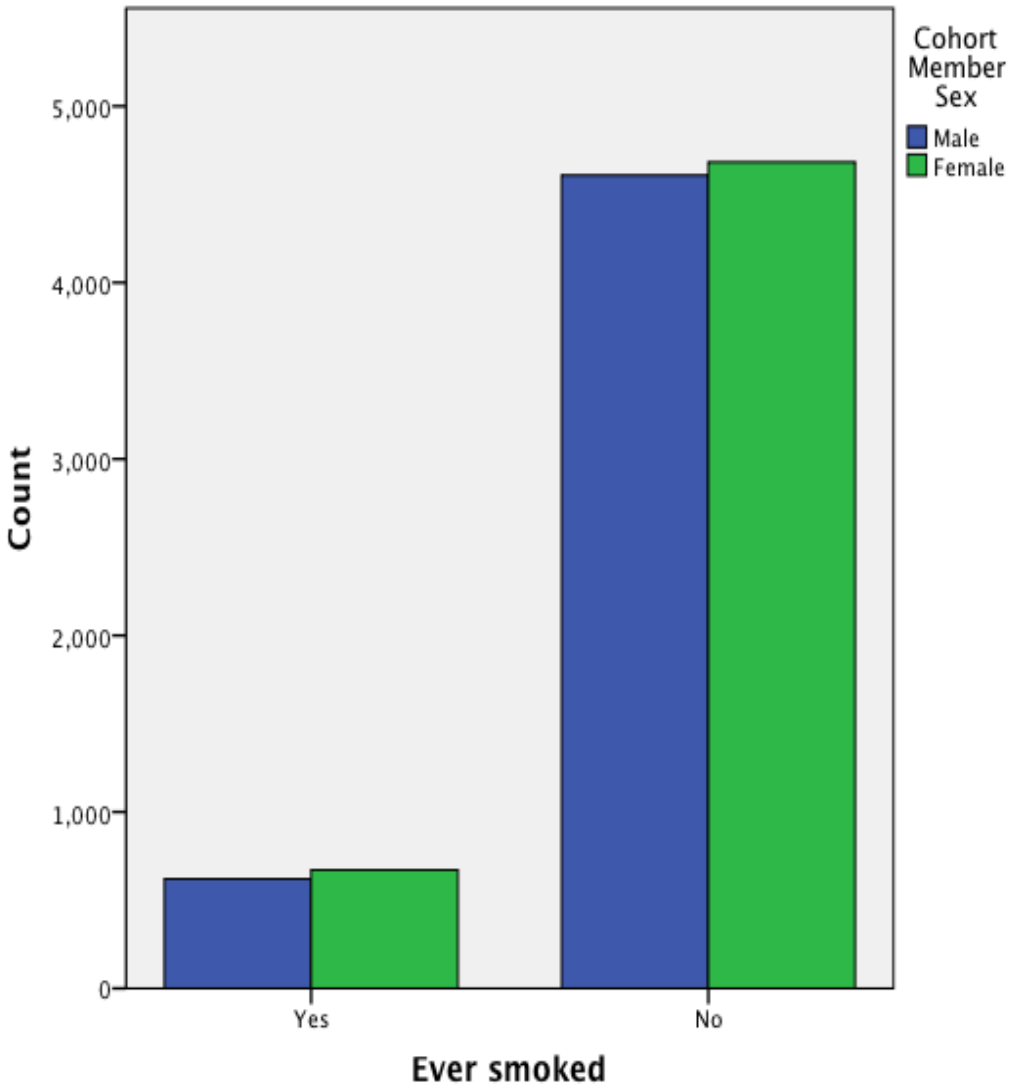


Maternal smoking status:

Ever smoked

Cohort Member Sex			Frequency	Percent	Valid Percent	Cumulative Percent
Male	Valid	Yes	620	8.4	11.9	11.9
		No	4609	62.5	88.1	100.0
		Total	5229	71.0	100.0	
	Missing	Not applicable	2140	29.0		
	Total		7369	100.0		
Female	Valid	Yes	672	9.0	12.5	12.5
		No	4683	63.0	87.5	100.0
		Total	5355	72.1	100.0	
	Missing	Not applicable	2074	27.9		
	Total		7429	100.0		

Maternal smoking frequency distribution:

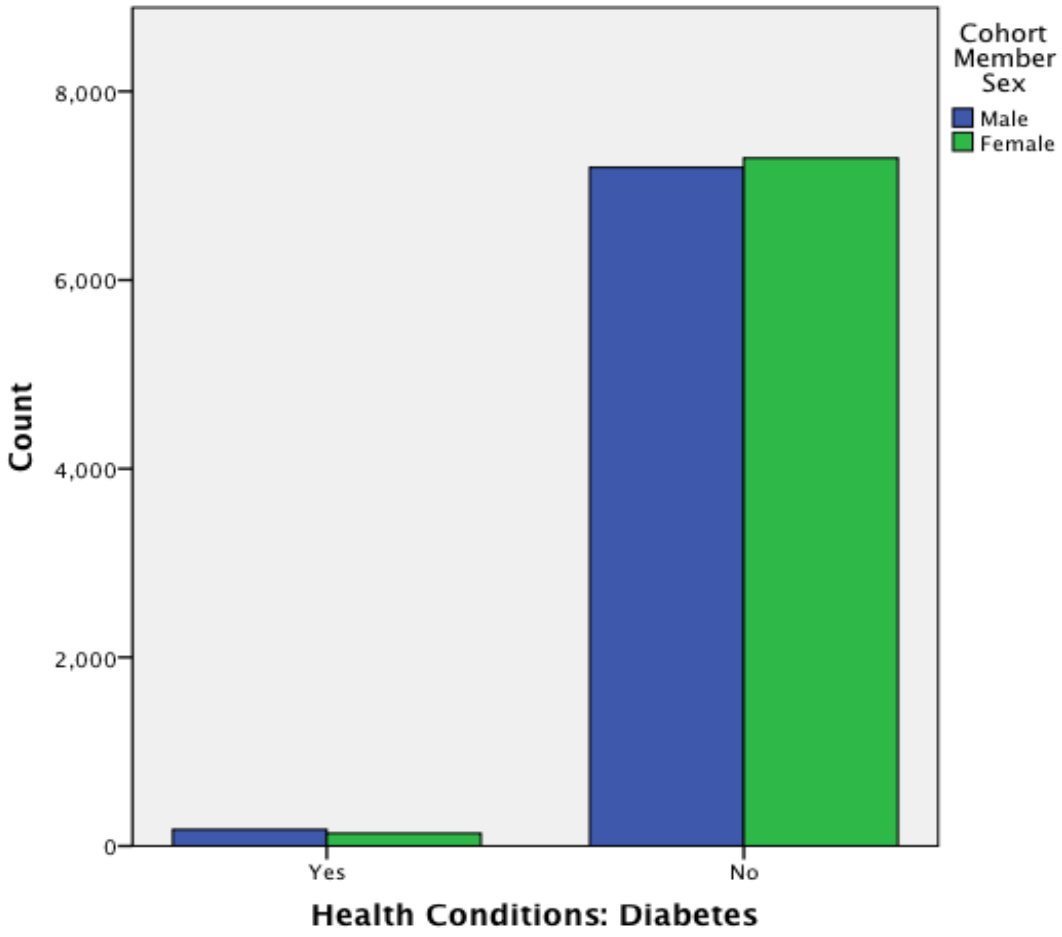


Maternal diabetes status:

Health Conditions: Diabetes

Cohort Member Sex			Frequency	Percent	Valid Percent	Cumulative Percent
Male	Valid	Yes	174	2.4	2.4	2.4
		No	7193	97.6	97.6	100.0
		Total	7367	100.0	100.0	
	Missing	Don't Know	1	.0		
		Not applicable	1	.0		
		Total	2	.0		
	Total		7369	100.0		
Female	Valid	Yes	135	1.8	1.8	1.8
		No	7293	98.2	98.2	100.0
		Total	7428	100.0	100.0	
	Missing	Don't Know	1	.0		
	Total		7429	100.0		

Maternal diabetes frequency distribution:



Appendix 3: Coding of responses

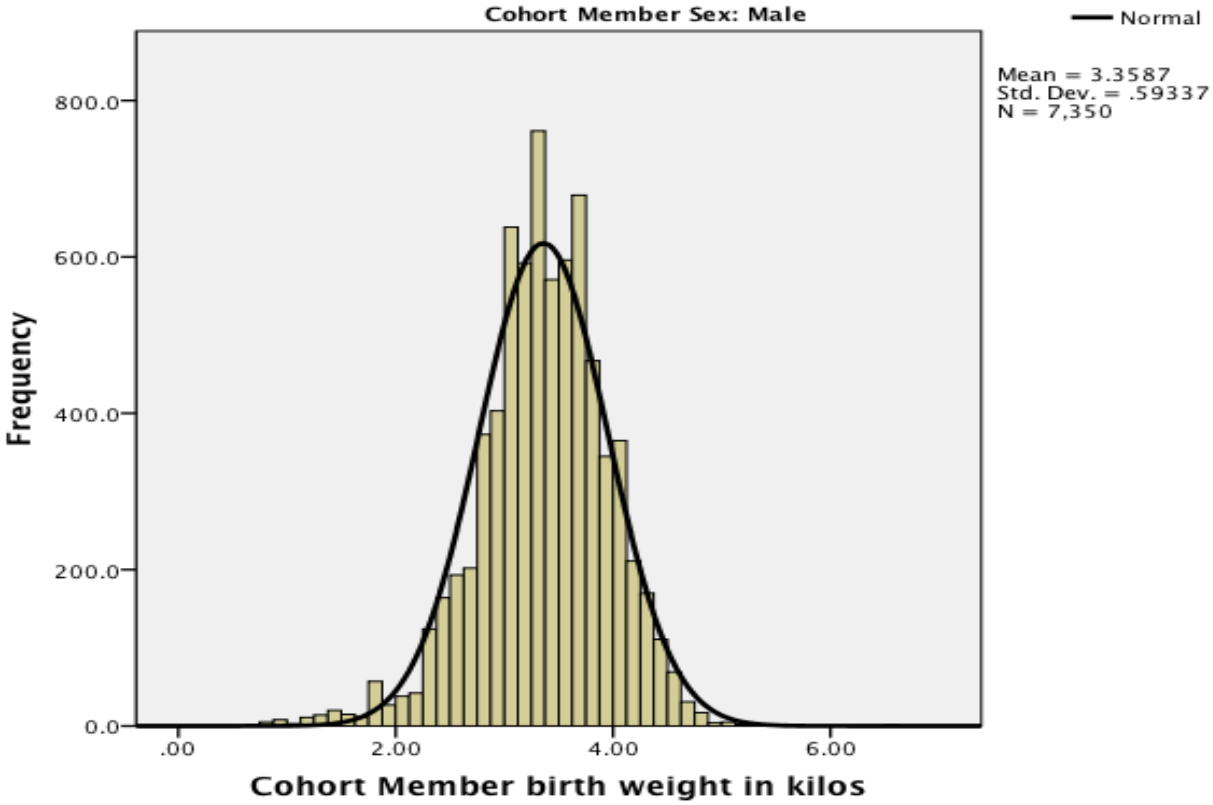
Variable interview questions, sweep, and dataset:

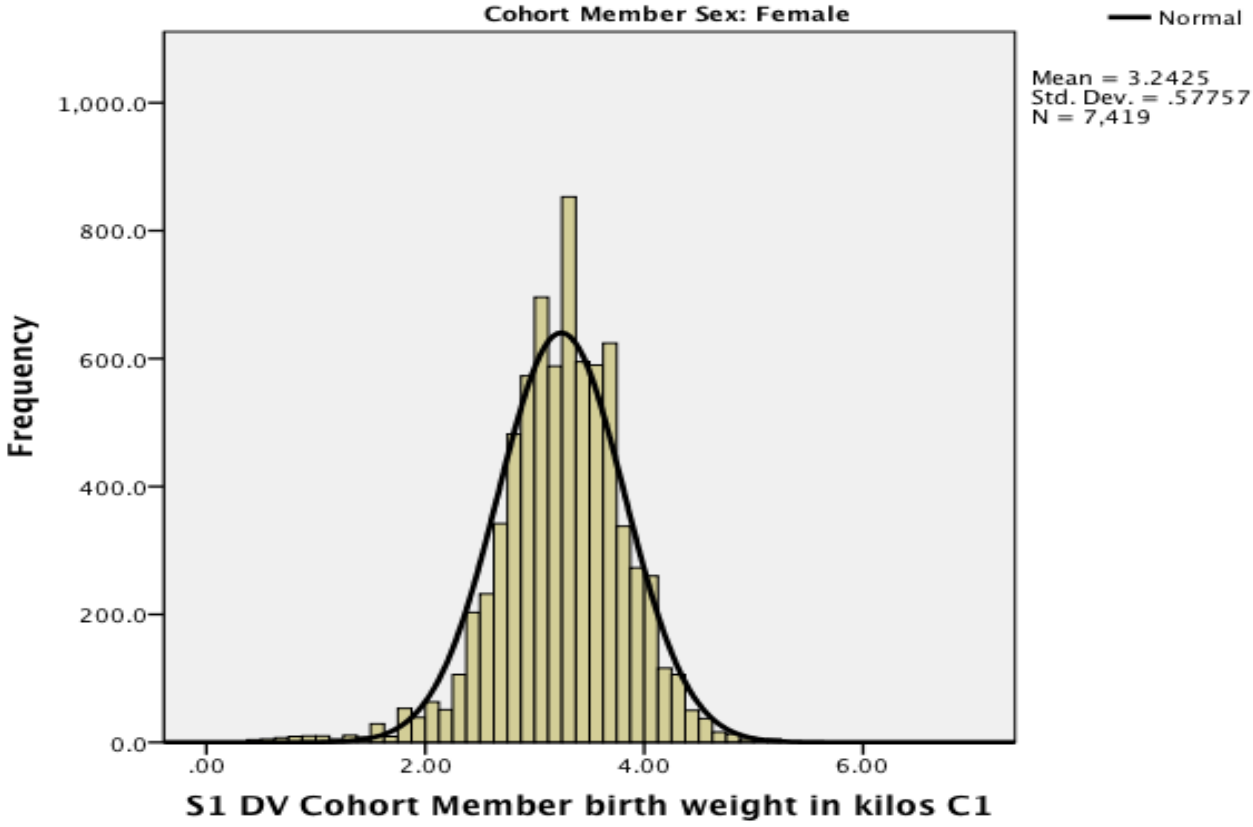
Variables	Sweep and Dataset	Question (if applicable)	Responses/Label (if applicable)
Cohort Member birthweight in kilos	MCS1 Parent Interview; Derived Variables	"How much did ^*Jack* weight when ^*he* was born?"	Response converted into kilos to the closest 0.1kg -8 = "Don't Know" -1 = "Not applicable"
S2 DV Cohort Member BMI according to present weight	MCS2 Child Measurement; Derived Variables		-1 = "insufficient data to calculate"
Body Mass Index calculated from height and weight data (where both exist)	MSC3 Child Measurement and Assessment; Height and Weight		-1 = "insufficient data to calculate"
S4 CM Body Mass Index calculated (CLS)	MSC4 Child Measurement and Assessment; Measurement		-1 = "insufficient data to calculate"
Cohort Member Sex	MCS1 Parent Interview; Main Interview		1 = "Male" 2 = "Female" -1 = "Not applicable"
Cohort Member Ethnic Group	MCS1 Parent Interview; Derived Variables	"Which of these groups do you regard ^*Jack* as belonging to?"	Responses aggregated into 8 categories: 1= "White" 2 = "Mixed" 3 = "Indian" 4 = "Pakistani" 5 = "Bangladeshi" 6 = "Black Caribbean" 7 = "Black African" 8 = "Other Ethnic Group (inc Chinese,Other)" -9 = "Refusal" -8 = "Don't Know" -1 = "Not applicable"
Cohort member gestation time in day (estimated)	MCS1 Parent Interview; Derived Variables		Response recorded in days -9 = "Refusal" -8 = "Don't Know" -1 = "Not applicable"

Natural mother's BMI before CM born	MCS1 Parent Interview; Derived Variables		-9 = "Refusal" -8 = "Don't Know" -1 = "Not applicable"
Ever smoked	MCS1 Parent Interview; Main Interview	"Have you ever regularly smoked tobacco products. By regularly, I mean 1 or more a day for 12 months or more?"	1 = "Yes 2 = "No" -9 = "Refusal" -8 = "Don't Know" -1 = "Not applicable"
S1 MAIN Health Conditions: Diabetes	MCS1 Parent Interview; Main Interview	"Have you ever been told by a doctor or nurse that you had diabetes?"	1 = "Yes" 2 = "No" -9 = "Refusal" -8 = "Don't Know" -1 = "Not applicable"

Sources: (CLS 2007; Studies, 2003)

Appendix 4: ANCOVA assumption tests
Birthweight histograms:





Case Summaries

Cohort Member birth weight in kilos

Cohort Member Sex	AR TIMING	N	Mean	Std. Deviation
Male	Late AR	5905	3.3568	.59116
	Normal AR	603	3.3223	.61315
	Early AR	652	3.4256	.56425
	Early-sustained AR	190	3.3025	.67577
	Total	7350	3.3587	.59337
Female	Late AR	5779	3.2473	.56511
	Normal AR	684	3.2534	.60130
	Early AR	803	3.2320	.63808
	Early-sustained AR	153	3.0692	.57906
	Total	7419	3.2425	.57757

Levene's test for ANOVA:

Test of Homogeneity of Variances

Cohort Member birth weight in kilos

Cohort Member Sex	Levene Statistic	df1	df2	Sig.
Male	3.064	3	7346	.027
Female	2.220	3	7415	.084

Levene's test for ANCOVA:

Levene's Test of Equality of Error Variances[a]

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	F	df1	df2	Sig.
Male	1.248	3	4458	.291
Female	3.053	3	4660	.027

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.

a. Design: Intercept + AR TIMING + Maternal diabetes + Gestation time + Maternal BMI + Ever smoked + AR TIMING * Maternal diabetes * Gestation time * Maternal BMI * Ever smoked

Test of Homogeneity of Variances

Cohort Member birth weight in kilos

Cohort Member Sex	Levene Statistic	df1	df2	Sig.
Male	3.064	3	7346	.027
Female	2.220	3	7415	.084

Levene's test shows that homogeneity of variance has been met as for both genders $p > \alpha$ if $\alpha = 0.01$ and when the largest variance is divided by the smallest variance the

result is less than 2 for both sexes so homogeneity of variance can be assumed, male = 1.953, female = 1.432.

Tests of Between-Subjects Effects

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Male	Corrected Model	545.195[a]	11	49.563	225.489	.000	.358
	Intercept	5.252	1	5.252	23.895	.000	.005
	AR TIMING	1.276	3	.425	1.935	.122	.001
	Maternal Diabetes	2.608	1	2.608	11.863	.001	.003
	Gestation time	201.555	1	201.555	916.980	.000	.171
	Maternal BMI	.448	1	.448	2.037	.154	.000
	Ever Smoked	1.172	1	1.172	5.331	.021	.001
	AR TIMING * Maternal diabetes * Gestation time * Maternal BMI * Ever Smoked	.977	4	.244	1.111	.349	.001
	Error	978.123	4450	.220			
	Total	52738.101	4462				
	Corrected Total	1523.318	4461				
Female	Corrected Model	550.640[b]	11	50.058	240.217	.000	.362
	Intercept	2.600	1	2.600	12.475	.000	.003
	AR TIMING	.366	3	.122	.586	.624	.000
	Maternal diabetes	3.051	1	3.051	14.641	.000	.003
	Gestation time	183.865	1	183.865	882.323	.000	.159
	Maternal BMI	.034	1	.034	.162	.688	.000
	Ever smoked	3.443	1	3.443	16.521	.000	.004
	AR TIMING * Maternal diabetes * Gestation time * Maternal BMI * Ever Smoked	3.183	4	.796	3.818	.034	.003
	Error	969.418	4652	.208			
	Total	51415.422	4664				
	Corrected Total	1520.058	4663				

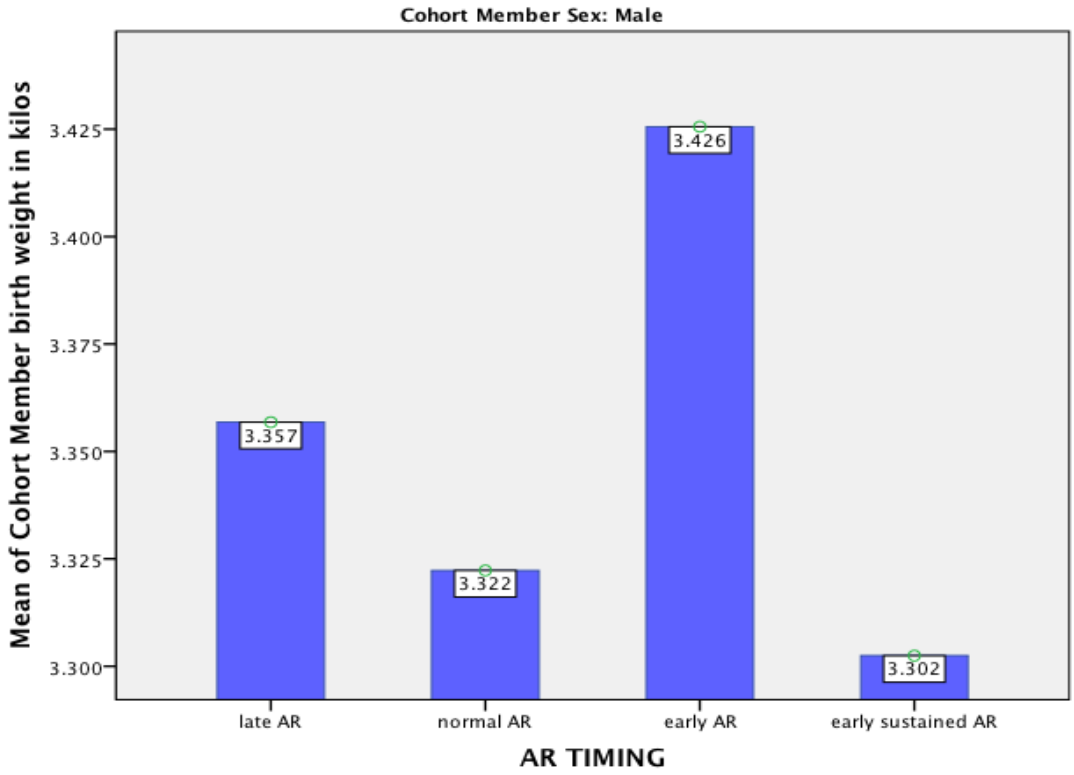
a. R Squared = .358 (Adjusted R Squared = .356)

b. R Squared = .362 (Adjusted R Squared = .361)

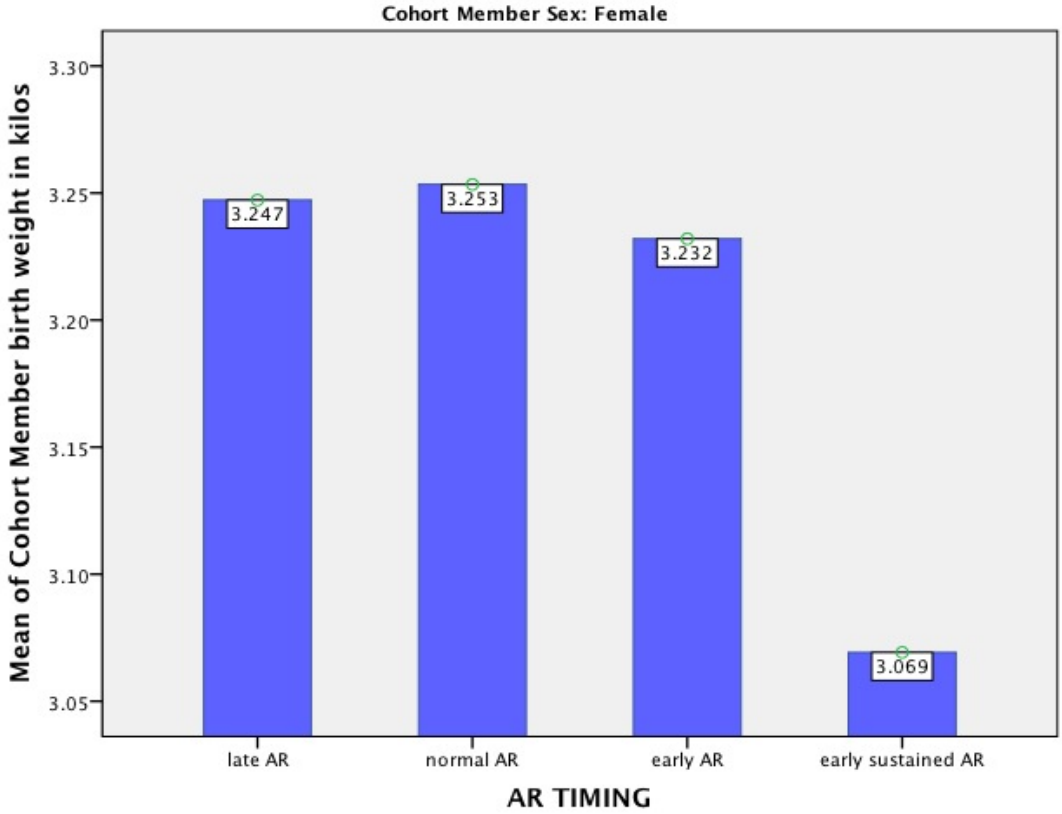
As p= 0.349 for male, and p= 0.034 for female and α = 0.01 p> α so there is no significant interaction and we can proceed with the ANCOVA.

Appendix 5: ANOVA mean birthweight plots and post-hoc test outputs

ANOVA mean birthweight plots:
Male:



Female:



ANOVA post-hoc tests output:

Multiple Comparisons

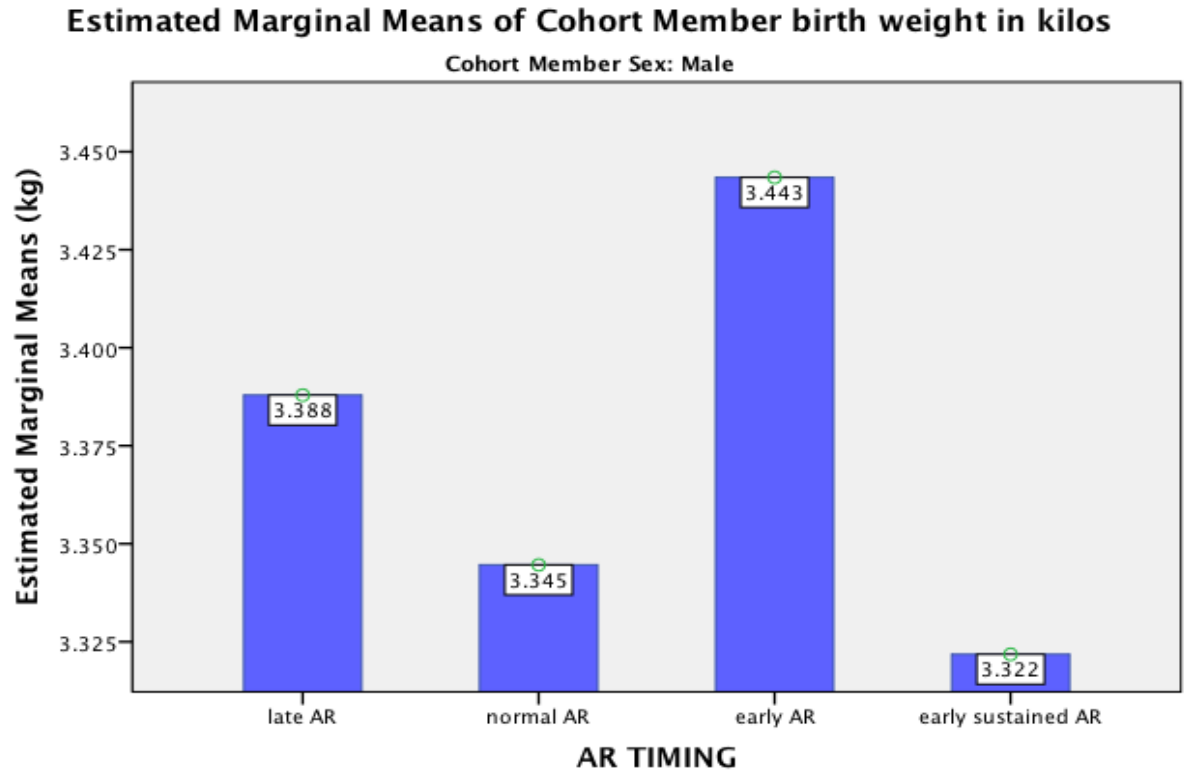
Dependent Variable: Cohort Member birth weight in kilos

Games-Howell

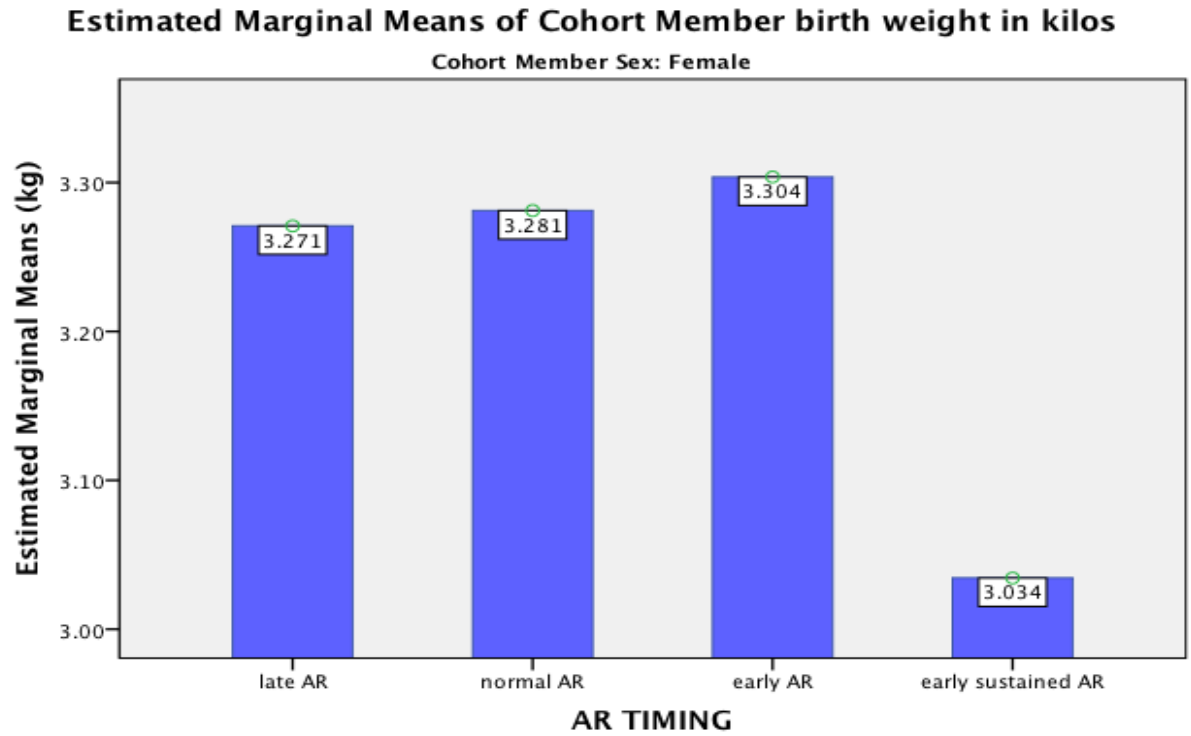
Cohort Member Sex	(I) AR TIMING	(J) AR TIMING	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Male	Late AR	Normal AR	.03451	.02613	.550	-.0328	.1018
		Early AR	-.06875*	.02340	.018	-.1290	-.0085
		Early-sustained AR	.05434	.04963	.693	-.0742	.1829
	Normal AR	Late AR	-.03451	.02613	.550	-.1018	.0328
		Early AR	-.10326*	.03334	.011	-.1890	-.0175
		Early-sustained AR	.01983	.05502	.984	-.1223	.1620
	Early AR	Late AR	.06875*	.02340	.018	.0085	.1290
		Normal AR	.10326*	.03334	.011	.0175	.1890
		Early-sustained AR	.12309	.05378	.103	-.0159	.2621
	Early-sustained AR	Late AR	-.05434	.04963	.693	-.1829	.0742
		Normal AR	-.01983	.05502	.984	-.1620	.1223
		Early AR	-.12309	.05378	.103	-.2621	.0159
Female	Late AR	Normal AR	-.00616	.02416	.994	-.0684	.0560
		Early AR	.01523	.02371	.918	-.0458	.0763
		Early-sustained AR	.17803*	.04740	.001	.0550	.3011
	Normal AR	Late AR	.00616	.02416	.994	-.0560	.0684
		Early AR	.02139	.03218	.910	-.0614	.1042
		Early-sustained AR	.18419*	.05216	.003	.0492	.3192
	Early AR	late AR	-.01523	.02371	.918	-.0763	.0458
		normal AR	-.02139	.03218	.910	-.1042	.0614
		early sustained AR	.16280*	.05195	.010	.0284	.2972
	Early-sustained AR	Late AR	-.17803*	.04740	.001	-.3011	-.0550
		Normal AR	-.18419*	.05216	.003	-.3192	-.0492
		Early AR	-.16280*	.05195	.010	-.2972	-.0284

*. The mean difference is significant at the 0.05 level.

Appendix 6: ANCOVA mean birthweight plots and outputs



Covariates appearing in the model are evaluated at the following values: Health Conditions: Diabetes = 1.97, Natural Mothers BMI before CM born = 23.8602, Cohort Member Gestation time in days (estimated) = 275.57, Ever smoked = 1.87



Covariates appearing in the model are evaluated at the following values: Health Conditions: Diabetes = 1.98, Natural Mothers BMI before CM born = 23.8720, Cohort Member Gestation time in days (estimated) = 276.02, Ever smoked = 1.86

Planned contrast between Early-sustained AR and other AR groups:

Cohort Member Sex =Male

AR TIMING Simple Contrast[a]			Dependent Variable: Cohort Member birth weight in kilos
Late AR vs. Early-sustained AR	Contrast Estimate		.066
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.066
	Std. Error		.047
	Sig.		.162
	95% Confidence Interval for Difference	Lower Bound	-.027
		Upper Bound	.159
Normal AR vs. Early-sustained AR	Contrast Estimate		.023
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.023
	Std. Error		.053
	Sig.		.668
	95% Confidence Interval for Difference	Lower Bound	-.081
		Upper Bound	.127
Early AR vs. Early-sustained AR	Contrast Estimate		.122
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.122
	Std. Error		.052
	Sig.		.020
	95% Confidence Interval for Difference	Lower Bound	.019
		Upper Bound	.224

a. Reference category = Early-sustained AR

Cohort Member Sex =Female

AR TIMING Simple Contrast[a]			Dependent Variable: Cohort Member birth weight in kilos
Late AR vs. Early-sustained AR	Contrast Estimate		.236
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.236
	Std. Error		.050
	Sig.		.000
	95% Confidence Interval for Difference	Lower Bound	.139
		Upper Bound	.334
Normal AR vs. Early-sustained AR	Contrast Estimate		.247
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.247
	Std. Error		.054
	Sig.		.000
	95% Confidence Interval for Difference	Lower Bound	.140
		Upper Bound	.353
Early AR vs. Early-sustained AR	Contrast Estimate		.269
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.269
	Std. Error		.053
	Sig.		.000
	95% Confidence Interval for Difference	Lower Bound	.165
		Upper Bound	.374

a. Reference category = Early-sustained AR

ANCOVA Estimated Marginal Means:

Estimates

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	AR TIMING	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Male	Late AR	3.388[a]	.008	3.373	3.403
	Normal AR	3.345[a]	.026	3.293	3.396
	Early AR	3.443[a]	.024	3.396	3.491
	Early-sustained AR	3.322[a]	.047	3.231	3.413
Female	Late AR	3.271[b]	.008	3.256	3.286
	Normal AR	3.281[b]	.023	3.235	3.327
	Early AR	3.304[b]	.021	3.263	3.344
	Early-sustained AR	3.034[b]	.049	2.938	3.131

a. Covariates appearing in the model are evaluated at the following values: Health Conditions: Diabetes = 1.97, Mothers BMI before CM born = 23.8602, Cohort Member Gestation time in days (estimated) = 275.57, Ever smoked = 1.87.

b. Covariates appearing in the model are evaluated at the following values: Health Conditions: Diabetes = 1.98, Mothers BMI before CM born = 23.8720, Cohort Member Gestation time in days (estimated) = 276.02, Ever smoked = 1.86.

ANCOVA parameter estimates:

Parameter Estimates

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	Parameter	B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared
						Lower Bound	Upper Bound	
Male	Intercept	-3.336	.180	-18.485	.000	-3.690	-2.982	.071
	Maternal diabetes	-.267	.044	-6.057	.000	-.353	-.181	.008
	Maternal BMI	.017	.002	10.220	.000	.014	.020	.023
	Gestation time	.026	.001	47.612	.000	.024	.027	.337
	Ever smoked	-.131	.021	-6.325	.000	-.172	-.091	.009
	[AR TIMING=1]	.066	.047	1.399	.162	-.027	.159	.000
	[AR TIMING=2]	.023	.053	.429	.668	-.081	.127	.000
	[AR TIMING=3]	.122	.052	2.324	.020	.019	.224	.001
	[AR TIMING=4]	0[a]	.	.	.	.	.	.
Female	Intercept	-3.767	.187	-20.186	.000	-4.133	-3.401	.080
	Maternal diabetes	-.096	.053	-1.819	.069	-.200	.007	.001
	Maternal BMI	.019	.001	12.658	.000	.016	.021	.033
	Gestation time	.024	.001	48.350	.000	.023	.025	.334
	Ever smoked	-.071	.020	-3.598	.000	-.109	-.032	.003
	[AR TIMING=1]	.236	.050	4.744	.000	.139	.334	.005
	[AR TIMING=2]	.247	.054	4.541	.000	.140	.353	.004
	[AR TIMING=3]	.269	.053	5.067	.000	.165	.374	.005
	[AR TIMING=4]	0[a]	.	.	.	.	.	.

a. This parameter is set to zero because it is redundant.

AR TIMING=1 = Late AR

AR TIMING =2 = Normal AR

AR TIMING = 3 = Early AR

AR TIMING = 4 = Early-sustained AR

ANCOVA pairwise comparison:

Pairwise Comparisons

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	(I) AR TIMING	(J) AR TIMING	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
Male	Late AR	Normal AR	.043	.028	.694	-.029	.116
		Early AR	-.056	.026	.180	-.123	.012
		Early-sustained AR	.066	.047	.971	-.059	.191
	Normal AR	Late AR	-.043	.028	.694	-.116	.029
		Early AR	-.099*	.036	.034	-.193	-.005
		Early-sustained AR	.023	.053	1.000	-.117	.163
	Early AR	Late AR	.056	.026	.180	-.012	.123
		Normal AR	.099*	.036	.034	.005	.193
		Early-sustained AR	.122	.052	.121	-.017	.260
	Early-sustained AR	Late AR	-.066	.047	.971	-.191	.059
		Normal AR	-.023	.053	1.000	-.163	.117
		Early AR	-.122	.052	.121	-.260	.017
Female	Late AR	Normal AR	-.010	.025	1.000	-.075	.055
		Early AR	-.033	.022	.808	-.091	.025
		Early-sustained AR	.236*	.050	.000	.105	.368
	Normal AR	Late AR	.010	.025	1.000	-.055	.075
		Early AR	-.023	.031	1.000	-.105	.059
		Early-sustained AR	.247*	.054	.000	.103	.390
	Early AR	Late AR	.033	.022	.808	-.025	.091
		Normal AR	.023	.031	1.000	-.059	.105
		Early-sustained AR	.269*	.053	.000	.129	.410
	Early-sustained AR	Late AR	-.236*	.050	.000	-.368	-.105
		Normal AR	-.247*	.054	.000	-.390	-.103
		Early AR	-.269*	.053	.000	-.410	-.129

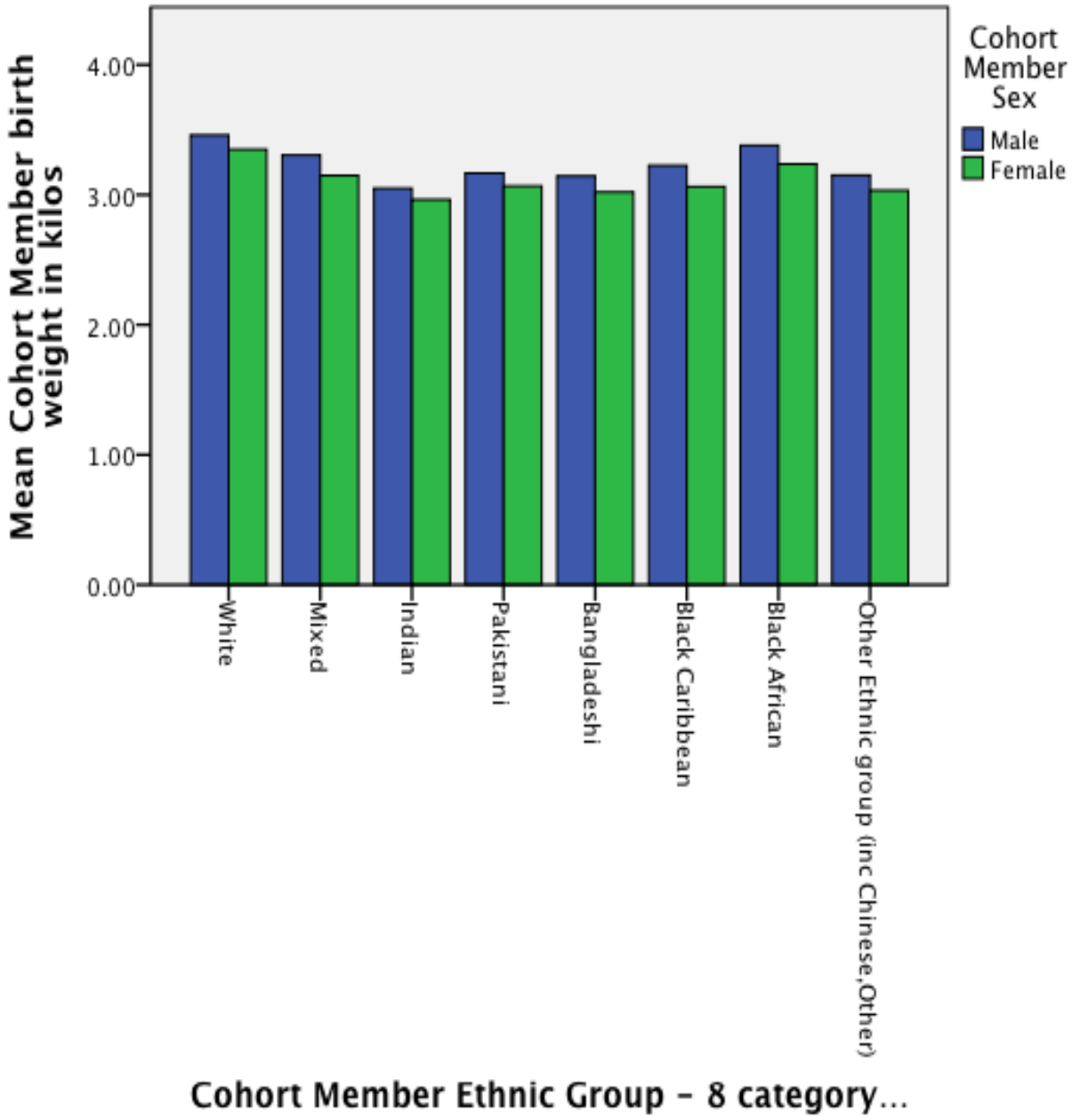
Based on estimated marginal means

*. The mean difference is significant at the

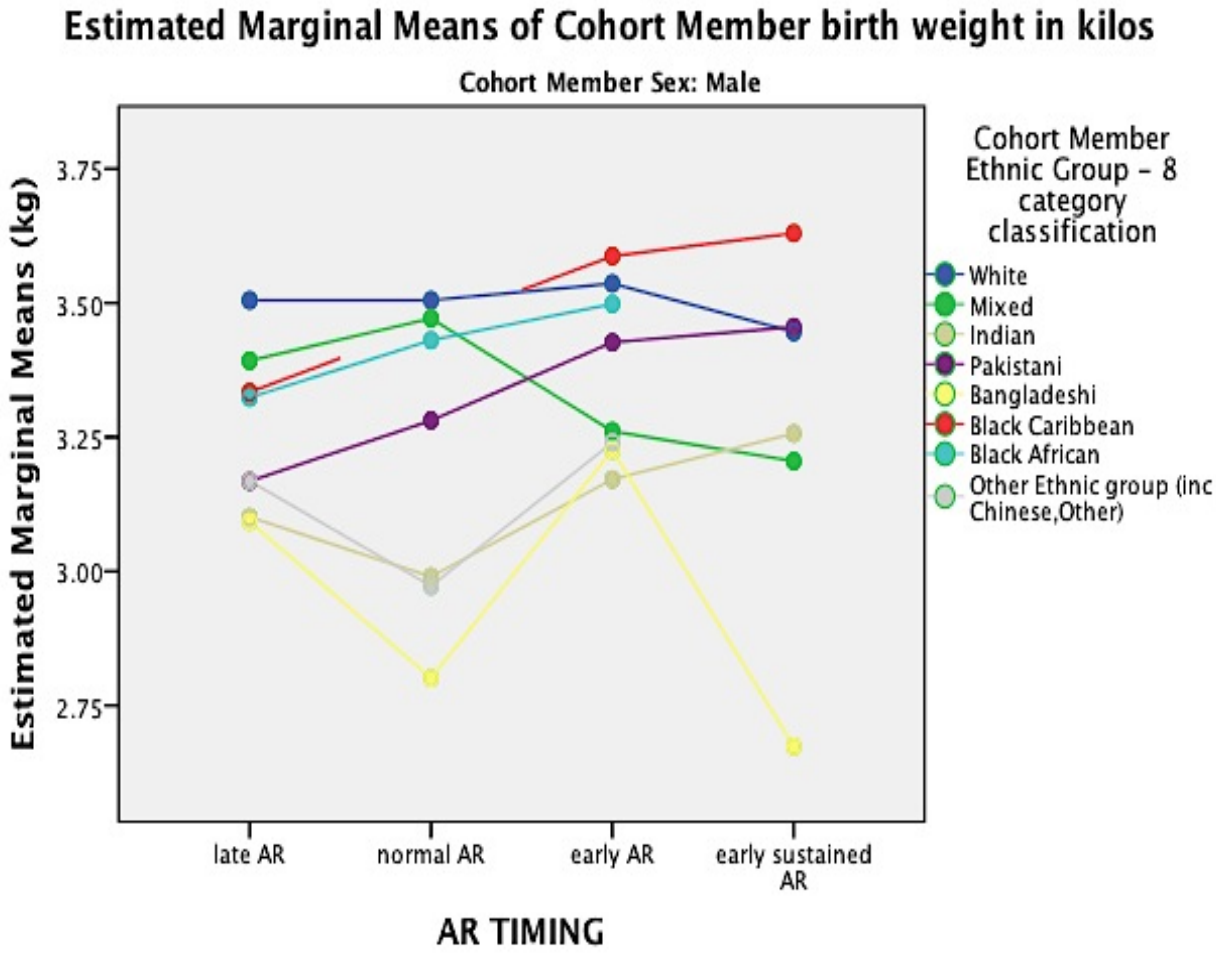
b. Adjustment for multiple comparisons: Bonferroni.

Appendix 7 Ethnicity plots, ANCOVA outputs, and Chi-square crosstabulation

Plot of mean birthweights for ethnic groups:

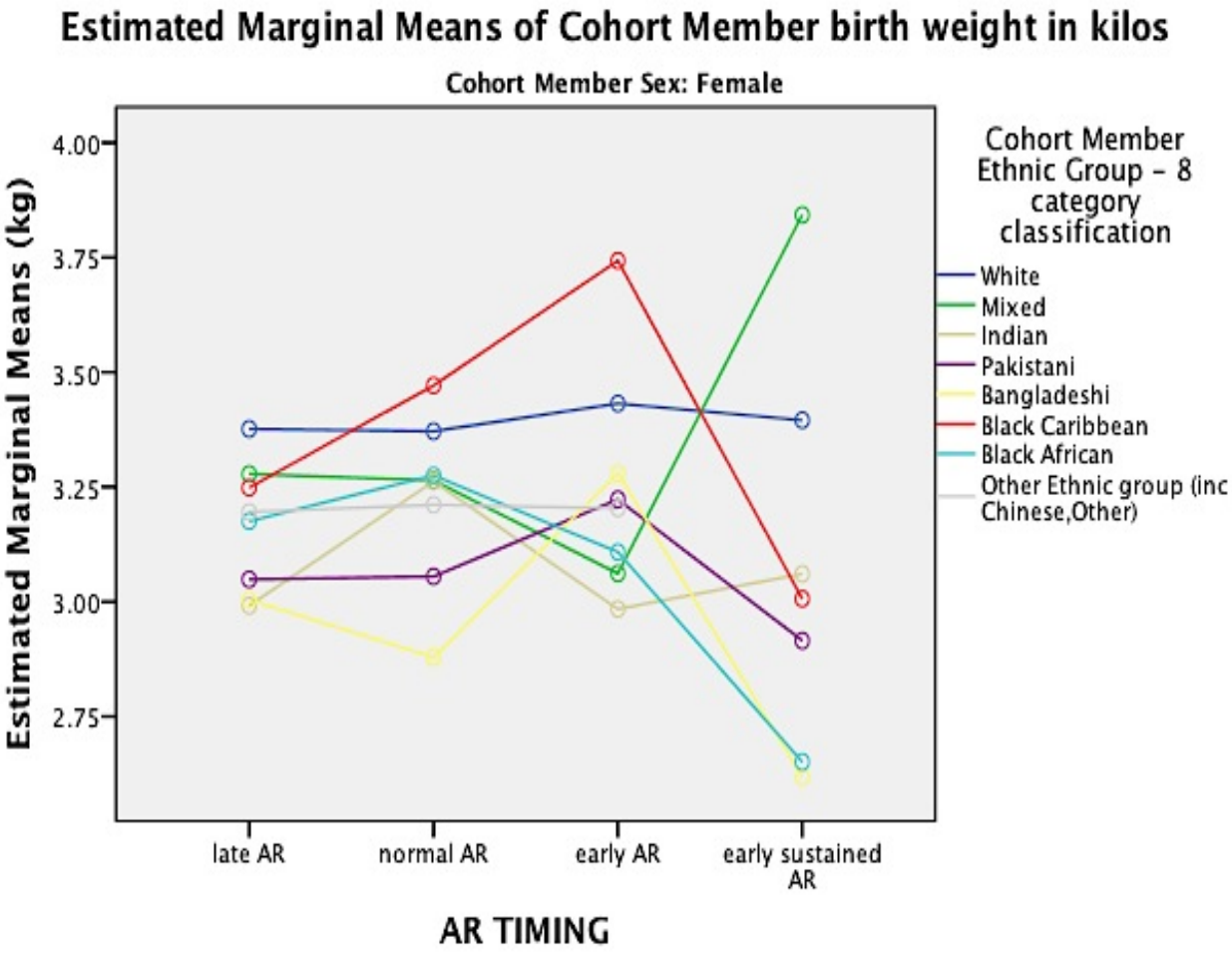


Plots of interaction effect AR timing*Ethnicity:



Covariates appearing in the model are evaluated at the following values: Cohort Member Gestation time in days (estimated) = 275.57, Natural Mothers BMI before CM born = 23.8602, Ever smoked = 1.87, Health Conditions: Diabetes = 1.97

Non-estimable means are not plotted



Covariates appearing in the model are evaluated at the following values: Cohort Member Gestation time in days (estimated) = 276.02, Natural Mothers BMI before CM born = 23.8720, Ever smoked = 1.86, Health Conditions: Diabetes = 1.98

Non-estimable means are not plotted

ANCOVA estimated marginal means:

Estimates

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	Cohort Member Ethnic Group - 8 category classification	Mean	Std. Error	95% Confidence Interval		Bootstrap for Mean[byb]			
				Lower Bound	Upper Bound	Bias	Std. Error	95% Confidence Interval	
								Lower	Upper
Male	White	3.498[a]	.021	3.457	3.539	.001	.023	3.453	3.543
	Mixed	3.332[a]	.107	3.123	3.542	.001	.078	3.185	3.494
	Indian	3.130[a]	.042	3.048	3.211	.000	.036	3.057	3.204
	Pakistani	3.333[a]	.034	3.267	3.399	6.748E-005	.048	3.236	3.424
	Bangladeshi	2.948[a]	.055	2.840	3.057	.000	.064	2.819	3.068
	Black Caribbean	3.517[a,b]	.078	3.365	3.669	-.001	.031	3.455	3.574
	Black African	3.417[a,b]	.036	3.347	3.488	-.002	.033	3.351	3.479
	Other Ethnic group (inc Chinese, Other)	3.127[a,b]	.040	3.048	3.206	.002	.027	3.075	3.181
Female	White	3.394[c]	.023	3.349	3.438	.001	.023	3.348	3.439
	Mixed	3.362[c]	.086	3.194	3.529	-.020	.063	3.174	3.421
	Indian	3.074[c]	.068	2.942	3.207	.000	.023	3.031	3.119
	Pakistani	3.060[c]	.031	2.999	3.122	-.001	.033	2.997	3.126
	Bangladeshi	2.945[c]	.059	2.830	3.061	.000	.028	2.886	3.001
	Black Caribbean	3.367[c]	.052	3.265	3.470	-.001	.057	3.260	3.476
	Black African	3.052[c]	.041	2.972	3.133	.001	.054	2.947	3.157
	Other Ethnic group (inc Chinese, Other)	3.203[b,c]	.039	3.128	3.279	.001	.039	3.130	3.280

a. Covariates appearing in the model are evaluated at the following values: Health Conditions: Diabetes = 1.97, Mothers BMI before CM born = 23.8602, Cohort Member Gestation time in days (estimated) = 275.57, Ever smoked = 1.87.

b. Based on modified population marginal mean.

c. Covariates appearing in the model are evaluated at the following values: Health Conditions: Diabetes = 1.98, Mothers BMI before CM born = 23.8720, Cohort Member Gestation time in days (estimated) = 276.02, Ever smoked = 1.86.

byb. Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

Bootstrapped pairwise comparison:

Dependent Variable: Cohort Member birth weight in kilos

Cohort Member Sex	(I) Cohort Member Ethnic Group - 8 category classification	(J) Cohort Member Ethnic Group - 8 category classification	Mean Difference (I-J)	Bootstrap[a]				
				Bias	Std. Error	Sig. (2-tailed)	95% Confidence Interval	
							Lower	Upper
Male	White	Mixed	.166	.000	.080	.034	-.001	.322
		Indian	.368	.001	.042	.001	.288	.452
		Pakistani	.165	.001	.052	.001	.066	.273
		Bangladeshi	.550	.001	.067	.001	.425	.684
		Black Caribbean	-.019	.002	.038	.600	-.091	.057
		Black African	.081	.003	.041	.050	.005	.163
		Other Ethnic group (inc Chinese, Other)	.371	-.001	.036	.001	.301	.441
	Mixed	White	-.166	.000	.080	.034	-.322	.001
		Indian	.203	.002	.087	.017	.032	.383
		Pakistani	.000	.001	.093	.997	-.182	.191
		Bangladeshi	.384	.002	.100	.001	.202	.593
		Black Caribbean	-.185	.002	.084	.024	-.350	-.018
		Black African	-.085	.003	.084	.273	-.248	.096
		Other Ethnic group (inc Chinese, Other)	.206	-.001	.081	.014	.047	.382
	Indian	White	-.368	-.001	.042	.001	-.452	-.288
		Mixed	-.203	-.002	.087	.017	-.383	-.032
		Pakistani	-.203	.000	.059	.002	-.320	-.075
		Bangladeshi	.182	3.604E-005	.073	.012	.033	.327
		Black Caribbean	-.387	.001	.047	.001	-.478	-.290
		Black African	-.288	.001	.049	.001	-.383	-.193
		Other Ethnic group (inc Chinese, Other)	.003	-.002	.045	.944	-.085	.091
	Pakistani	White	-.165	-.001	.052	.001	-.273	-.066
		Mixed	.000	-.001	.093	.997	-.191	.182
		Indian	.203	.000	.059	.002	.075	.320
		Bangladeshi	.384	.000	.082	.001	.233	.550
		Black Caribbean	-.184	.001	.057	.003	-.295	-.076
		Black African	-.085	.002	.057	.138	-.196	.023
		Other Ethnic group (inc Chinese, Other)	.206	-.002	.057	.001	.090	.308

Bootstrap pairwise comparison cont.

		White	-.550	-.001	.067	.001	-.684	-.425
		Mixed	-.384	-.002	.100	.001	-.593	-.202
		Indian	-.182	-3.604E-005	.073	.012	-.327	-.033
	Bangladeshi	Pakistani	-.384	.000	.082	.001	-.550	-.233
		Black Caribbean	-.569	.001	.070	.001	-.709	-.433
		Black African	-.469	.001	.073	.001	-.622	-.336
		Other Ethnic group (inc Chinese, Other)	-.179	-.002	.069	.008	-.319	-.044
		White	.019	-.002	.038	.600	-.057	.091
		Mixed	.185	-.002	.084	.024	.018	.350
		Indian	.387	-.001	.047	.001	.290	.478
	Black Caribbean	Pakistani	.184	-.001	.057	.003	.076	.295
		Bangladeshi	.569	-.001	.070	.001	.433	.709
		Black African	.100	.000	.045	.035	.006	.183
		Other Ethnic group (inc Chinese, Other)	.390	-.003	.041	.001	.306	.463
		White	-.081	-.003	.041	.050	-.163	-.005
		Mixed	.085	-.003	.084	.273	-.096	.248
		Indian	.288	-.001	.049	.001	.193	.383
	Black African	Pakistani	.085	-.002	.057	.138	-.023	.196
		Bangladeshi	.469	-.001	.073	.001	.336	.622
		Black Caribbean	-.100	.000	.045	.035	-.183	-.006
		Other Ethnic group (inc Chinese, Other)	.291	-.003	.042	.001	.206	.372
		White	-.371	.001	.036	.001	-.441	-.301
		Mixed	-.206	.001	.081	.014	-.382	-.047
	Other Ethnic group (inc Chinese, Other)	Indian	-.003	.002	.045	.944	-.091	.085
		Pakistani	-.206	.002	.057	.001	-.308	-.090
		Bangladeshi	.179	.002	.069	.008	.044	.319
		Black Caribbean	-.390	.003	.041	.001	-.463	-.306
		Black African	-.291	.003	.042	.001	-.372	-.206

Bootstrap pairwise comparison cont.

Female	White	Mixed	.032	.021	.066	.484	-.037	.225
		Indian	.319	.002	.032	.001	.259	.381
		Pakistani	.333	.002	.040	.001	.260	.416
		Bangladeshi	.448	.002	.037	.001	.375	.522
		Black Caribbean	.026	.002	.060	.674	-.086	.150
		Black African	.341	-3.877E-005	.058	.001	.234	.461
		Other Ethnic group (inc Chinese,Other)	.190	.000	.045	.001	.101	.278
	Mixed	White	-.032	-.021	.066	.484	-.225	.037
		Indian	.287	-.019	.065	.013	.099	.359
		Pakistani	.301	-.019	.070	.033	.097	.387
		Bangladeshi	.416	-.019	.069	.003	.217	.499
		Black Caribbean	-.006	-.019	.081	.944	-.215	.112
		Black African	.309	-.021	.083	.032	.092	.434
		Other Ethnic group (inc Chinese,Other)	.158	-.021	.074	.109	-.051	.254
	Indian	White	-.319	-.002	.032	.001	-.381	-.259
		Mixed	-.287	.019	.065	.013	-.359	-.099
		Pakistani	.014	9.679E-005	.040	.714	-.066	.090
		Bangladeshi	.129	.000	.036	.004	.059	.198
		Black Caribbean	-.293	.000	.061	.001	-.410	-.181
		Black African	.022	-.002	.059	.684	-.087	.141
		Other Ethnic group (inc Chinese,Other)	-.129	-.002	.045	.013	-.215	-.043
	Pakistani	White	-.333	-.002	.040	.001	-.416	-.260
		Mixed	-.301	.019	.070	.033	-.387	-.097
		Indian	-.014	-9.679E-005	.040	.714	-.090	.066
		Bangladeshi	.115	.000	.043	.006	.030	.201
		Black Caribbean	-.307	.000	.065	.001	-.426	-.180
		Black African	.008	-.002	.063	.900	-.117	.129
		Other Ethnic group (inc Chinese,Other)	-.143	-.002	.050	.005	-.248	-.046

Bootstrap pairwise comparison cont.

Bangladeshi	White	-.448	-.002	.037	.001	-.522	-.375
	Mixed	-.416	.019	.069	.003	-.499	-.217
	Indian	-.129	.000	.036	.004	-.198	-.059
	Pakistani	-.115	.000	.043	.006	-.201	-.030
	Black Caribbean	-.422	.001	.064	.001	-.541	-.300
	Black African	-.107	-.002	.061	.069	-.230	.015
	Other Ethnic group (inc Chinese, Other)	-.258	-.002	.048	.001	-.356	-.166
Black Caribbean	White	-.026	-.002	.060	.674	-.150	.086
	Mixed	.006	.019	.081	.944	-.112	.215
	Indian	.293	.000	.061	.001	.181	.410
	Pakistani	.307	.000	.065	.001	.180	.426
	Bangladeshi	.422	-.001	.064	.001	.300	.541
	Black African	.315	-.002	.078	.001	.152	.460
	Other Ethnic group (inc Chinese, Other)	.164	-.002	.069	.013	.024	.297
Black African	White	-.341	3.877E-005	.058	.001	-.461	-.234
	Mixed	-.309	.021	.083	.032	-.434	-.092
	Indian	-.022	.002	.059	.684	-.141	.087
	Pakistani	-.008	.002	.063	.900	-.129	.117
	Bangladeshi	.107	.002	.061	.069	-.015	.230
	Black Caribbean	-.315	.002	.078	.001	-.460	-.152
	Other Ethnic group (inc Chinese, Other)	-.151	.000	.068	.022	-.286	-.027
Other Ethnic group (inc Chinese, Other)	White	-.190	.000	.045	.001	-.278	-.101
	Mixed	-.158	.021	.074	.109	-.254	.051
	Indian	.129	.002	.045	.013	.043	.215
	Pakistani	.143	.002	.050	.005	.046	.248
	Bangladeshi	.258	.002	.048	.001	.166	.356
	Black Caribbean	-.164	.002	.069	.013	-.297	-.024
	Black African	.151	.000	.068	.022	.027	.286

a. Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples

AR Timing vs. Ethnicity crosstabulation:

AR Timing		Cohort Member Ethnic Group - 8 category classification								Total
		White	Mixed	Indian	Pakistani	Bangladeshi	Black Caribbean	Black African	Other Ethnicity	
MALE Late AR	Count	3808	194	306	648	152	195	295	325	5923
	Expected Count	3682.9	188.1	330.4	649.4	186.5	213.0	325.5	347.2	5923.0
	% within CM Ethnic Group	83.1%	82.9%	74.5%	80.2%	65.5%	73.6%	72.8%	75.2%	80.4%
	% of Total	51.7%	2.6%	4.2%	8.8%	2.1%	2.6%	4.0%	4.4%	80.4%
	Adj. Residual	7.6	1.0	-3.1	-.1	-5.8	-2.8	-3.9	-2.8	
MALE Normal AR	Count	306	22	54	76	16	20	55	54	603
	Expected Count	374.9	19.1	33.6	66.1	19.0	21.7	33.1	35.4	603.0
	% within CM Ethnic Group	6.7%	9.4%	13.1%	9.4%	6.9%	7.5%	13.6%	12.5%	8.2%
	% of Total	4.2%	0.3%	0.7%	1.0%	0.2%	0.3%	0.7%	0.7%	8.2%
	Adj. Residual	-6.0	.7	3.8	1.3	-.7	-.4	4.1	3.4	
MALE Early AR	Count	377	8	24	56	44	40	50	53	652
	Expected Count	405.4	20.7	36.4	71.5	20.5	23.4	35.8	38.2	652.0
	% within CM Ethnic Group	8.2%	3.4%	5.8%	6.9%	19.0%	15.1%	12.3%	12.3%	8.8%
	% of Total	5.1%	0.1%	0.3%	0.8%	0.6%	0.5%	0.7%	0.7%	8.8%
	Adj. Residual	-2.4	-3.0	-2.2	-2.0	5.5	3.6	2.5	2.6	
MALE Early-sustained AR	Count	91	10	27	28	20	10	5	0	191
	Expected Count	118.8	6.1	10.7	20.9	6.0	6.9	10.5	11.2	191.0
	% within CM Ethnic Group	2.0%	4.3%	6.6%	3.5%	8.6%	3.8%	1.2%	0.0%	2.6%
	% of Total	1.2%	0.1%	0.4%	0.4%	0.3%	0.1%	0.1%	0.0%	2.6%
	Adj. Residual	-4.2	1.6	5.2	1.7	5.9	1.2	-1.8	-3.5	
MALE Total	Count	4582	234	411	808	232	265	405	432	7369
	Expected Count	4582.0	234.0	411.0	808.0	232.0	265.0	405.0	432.0	7369.0
	% within CM Ethnic Group	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	% of Total	62.2%	3.2%	5.6%	11.0%	3.1%	3.6%	5.5%	5.9%	100.0%

AR Timing vs. Ethnicity crosstabulation cont.:

FEMALE Late AR	Count	3724	212	273	640	236	165	225	313	5788
	Expected Count	3562.1	230.6	289.8	676.3	252.4	190.9	272.7	313.2	5788.0
	% within CM Ethnic Group	81.5%	71.6%	73.4%	73.7%	72.8%	67.3%	64.3%	77.9%	77.9%
	% of Total	50.1%	2.9%	3.7%	8.6%	3.2%	2.2%	3.0%	4.2%	77.9%
	Adj. Residual	9.3	-2.7	-2.2	-3.2	-2.3	-4.1	-6.3	.0	
FEMALE Normal AR	Count	346	44	60	88	24	30	45	47	684
	Expected Count	421.0	27.3	34.3	79.9	29.8	22.6	32.2	37.0	684.0
	% within CM Ethnic Group	7.6%	14.9%	16.1%	10.1%	7.4%	12.2%	12.9%	11.7%	9.2%
	% of Total	4.7%	0.6%	0.8%	1.2%	0.3%	0.4%	0.6%	0.6%	9.2%
	Adj. Residual	-6.2	3.4	4.7	1.0	-1.1	1.7	2.4	1.8	
FEMALE Early AR	Count	432	32	36	116	56	30	60	42	804
	Expected Count	494.8	32.0	40.3	93.9	35.1	26.5	37.9	43.5	804.0
	% within CM Ethnic Group	9.4%	10.8%	9.7%	13.4%	17.3%	12.2%	17.1%	10.4%	10.8%
	% of Total	5.8%	0.4%	0.5%	1.6%	0.8%	0.4%	0.8%	0.6%	10.8%
	Adj. Residual	-4.8	.0	-.7	2.6	3.8	.7	3.9	-.2	
FEMALE Early-sustained AR	Count	70	8	3	24	8	20	20	0	153
	Expected Count	94.2	6.1	7.7	17.9	6.7	5.0	7.2	8.3	153.0
	% within CM Ethnic Group	1.5%	2.7%	0.8%	2.8%	2.5%	8.2%	5.7%	0.0%	2.1%
	% of Total	0.9%	0.1%	0.0%	0.3%	0.1%	0.3%	0.3%	0.0%	2.1%
	Adj. Residual	-4.1	.8	-1.7	1.6	.5	6.8	4.9	-3.0	
FEMALE Total	Count	4572	296	372	868	324	245	350	402	7429
	Expected Count	4572.0	296.0	372.0	868.0	324.0	245.0	350.0	402.0	7429.0
	% within CM Ethnic Group	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	% of Total	61.5%	4.0%	5.0%	11.7%	4.4%	3.3%	4.7%	5.4%	100.0%