The biological and social determinants of childhood obesity: comparison of two cohorts 50 years apart

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Abstract

Objective

To determine whether the same relationships between early life risk factors and socioeconomic status with childhood BMI are observed in a modern cohort (2000) compared to a historic cohort (1947).

Study design

The relationships between early life factors and SES with childhood BMI were examined in two prospective birth cohorts from the same region, born 50 years apart: 711 children in the 1947 Newcastle Thousand Families Study (NTFS) and 475 from the 2000 Gateshead Millennium Study (GMS). The associations between birthweight, breastfeeding, rapid infancy growth (0-12 months), early life adversity (0-12 months) and parental SES (birth and childhood) with childhood BMI z-scores, and whether overweight/obese (BMI >91st centile using UK 1990) aged 9 were examined using linear regression, path analyses and logistic regression.

Results

In the NTFS, the most advantaged children were taller than the least (+0.91 height z-score, p=0.001), while in GMS they had lower odds of overweight/obese than the least (0.35 (0.14, 0.86)). Rapid infancy growth was associated with increased BMIz in both cohorts, and with increased likelihood of overweight/obese in GMS.

Conclusions

This suggests that children exposed to socioeconomic disadvantage or who have rapid infancy growth in modern environments are now at lower risk of growth restriction, but greater risk of overweight.

Keywords: BMI, socioeconomic status, childhood obesity, DOHAD, rapid weight gain, path analysis

Introduction

Worldwide, there has been an estimated 10-fold increase in the prevalence of childhood obesity over the last forty years [1, 2], which has been partly attributed to the changes in the environment and shifts in socioeconomic inequalities [3, 4]. There is a well-recognised association between socioeconomic status (SES) and obesity [5, 6], evident in children as young as 5 years; for example, in England, 13% of the most deprived children are obese, compared to only 6% in the least deprived areas [5]. It has been suggested that there have been recent changes in social patterning of childhood overweight due to widening social inequalities [4, 7], hence it is not clear if these associations are an enduring feature of childhood obesity, or a characteristic of the emerging obesity epidemic. Increases in obesity in young children and increasing evidence for the developmental origins of health and disease (DOHaD) in the context of obesity, suggests that factors very early in life may play an important role [8]. Potential early life risk factors for childhood overweight/obesity (OWOB) that have been repeatedly identified in multiple, modern cohorts include: birthweight, rapid weight gain (RWG) in infancy, adverse childhood experiences, and a small protective effect of breastfeeding [9-13]. All these factors have the

capacity to be influenced by SES, which highlights the need to understand how they fit together in potential pathways to obesity.

This study therefore compares data from two birth cohorts from the same geographical area, but at different time points, that were not subject to the same confounding influences: a post-World War II cohort with low prevalence of obesity compared to a modern cohort with a higher prevalence of obesity. Our aim was to investigate if the relationships between early life risk factors, socioeconomic status and childhood overweight/obesity have changed over time. Specifically, we hypothesised that the environment and socioeconomic determinants in early life will impact on childhood BMI in both cohorts, but that the relative importance of early life factors and SES as predictors of childhood BMI and pathways and interactions between them will vary.

Research design and methods

Cohorts

The two birth cohorts, were both form North-East England, the region with the highest prevalence of childhood obesity in England [5].

The Newcastle thousand families study (NTFS) is an ongoing birth cohort based in Newcastle upon Tyne, who were recruited shortly after birth in May-June 1947 [14, 15]. The cohort included nearly all eligible births (99.5%, *n*=1142). The cohort were followed throughout childhood utilising data collected by health visitors and schools until 15 years of age. Exhaustive information was recorded, including infant feeding, various social conditions, and height and weight throughout childhood. Further details on key findings and data collected can be found in the cohort profile [14, 15].

The Gateshead millennium study (GMS) birth cohort, is an ongoing study which recruited participants shortly after birth in Gateshead, on the southern bank of the River Tyne opposite the city of Newcastle upon Tyne. The cohort included 83% of eligible infants (n=1029) born in recruiting weeks between June 1999 and May 2000 [16]. The cohort has been followed up throughout infancy and childhood with detailed questionnaires on growth, feeding, behaviour, illness and social factors, as well as having

anthropometric measures taken by trained researchers. Further details on key findings and data collected can be found in the cohort profile [16].

Measurement of early life factors and other predictor variables

The early life factors (SES, growth, feeding and adversity) and covariates (gestational and maternal age) that were directly comparable across the two cohorts and measured at similar ages (compared in Table 1; online). In NTFS, maternal age and birthweight were recorded at the time of delivery and taken from hospital records. All other factors were recorded by health visitors. In GMS, birthweight, gestational age, maternal age and postcode (to determine Townsend deprivation score [17]) were recorded at recruitment (shortly after birth). Child weight was measured in a clinic at the 13-month health check. Other variables were collected via questionnaires, including adversity (at 4 months), SES (at age 8-10), and breastfeeding (from recurrent questionnaires between birth – 12 months).

Recoding of the variables was the same for both cohorts, except for SES and adversity (Table 1; online). Whilst SES indicators at birth were not identical, the aim was to examine social gradients in BMI, and therefore data were compared using 5 ordinal groups. In NTFS, this corresponded to father's occupation at birth coded according to the Registrar-General's Social Classes: a longstanding method for individual-level socioeconomic classification [18]. For GMS, the socioeconomic indicator was Townsend deprivation index from 1991 census, which uses enumeration districts as the unit of analysis with the northern region of England as the population for comparison for the calculation of the quintiles (with 1 being the most advantaged and 5 the least). Although an area-level measure, Townsend score is a measure of material deprivation and was the most comparable classification for SES at birth in GMS. Comparative parental occupational data were available in childhood for both cohorts, although collected at slightly different time points (age 9-10 in NTFS and age 7-8 in GMS). To increase group sizes, childhood parental occupation data were re-categorised into most advantaged (I to II), middle (class III) and least advantaged (IV to V) [18]. Adversity encompassed 8 months prenatal to 4 months postnatal in GMS and birth to 1 year in NTFS (Table 1; online) and included

parental separation, police involvement, abuse, debt, death or illness in the family. Breastfeeding categories were harmonised for both cohorts to: 'never' , '<4 weeks', '4 weeks-6 months' and '6 months+'.

Rapid infancy weight gain is a known risk factor for childhood OWOB. As there were large differences in birthweight between the cohorts, weight gain conditional on birthweight (i.e. rapid thrive) was examined. Conditional weight gain, or thrive index (TI), accounts for normal catch-up growth from low birthweight as a linear measure of weight gain adjusted for regression to the mean [19]. Birthweight and weight-for-age (12 months) z-scores were calculated using the British 1990 growth reference [20], and were used to determine rapid weight gain (RWG) and rapid thrive (RT). RWG was determined as $z\text{-score}_{12m} - z\text{-score}_{birth}$). Rapid thrive was determined as RT = ($z\text{-score}_{12m} - r \times z\text{-score}_{birth}$)[19], where r is the cohort regression coefficient (NTFS, r=0.23; GMS, r=0.37) of birthweight-z on weight-z (12 months). Both RWG and RT were analysed as dichotomised variables, a >0.67 standard deviation change in weight-for-age z-score (first year), equivalent to crossing a growth centile band on a standard child growth chart [9].

Outcome data: body mass index

Height and weight measures were available at age 9 for both cohorts (1954 in NTFS, 2009 in GMS) and were used to calculate BMI (kg/m^2). Height and BMI were transformed in standard deviation (SD) z-scores using the British 1990 growth reference (adjusted for age and sex)[21] using the Zanthro program in STATA [22]. Weight categories of 'healthy weight' (2^{nd} <BMIz<91^{st} centiles) and 'overweight/obese' (>91^{st} centile) were based on UK90 clinical cut-offs [20, 23]. The UK 91st centile is close to the IOTF overweight threshold [24], while the 2nd is equivalent to -2 SD WHO threshold for moderate malnutrition.

Analytical design

The analysis had 4 stages:

1. We first examined differences between cohorts in exposures at baseline.

2. Next, we examined socioeconomic gradients in anthropometric measures (BMIz, height-z, OWOB at age 9) across cohorts.
3. We then evaluated associations between early life exposures and BMI outcomes and whether there were any interactions between cohort and early life exposures, and between early SES and early life exposures.
4. We then further examined changes in childhood BMIz (across childhood and adolescence) stratified by early life rapid growth.

Due to the differences in health risks for underweight (UW) and obesity, UW were excluded from all regression analyses.

Statistical analysis

The representativeness of the study participants (age 9) compared to the original cohort within cohorts, as well as baseline differences between the two cohorts, were examined using t-tests, chi-squared or Wilcoxon rank-sum tests as appropriate. To examine socioeconomic gradients in outcomes, variation in OWOB, BMIz, and height-z by SES (birth and childhood) was assessed using Chi-square tests, or one-way analysis of variance (ANOVA) with Bonferroni correction.

Multivariable linear regression was used to estimate associations between BMIz and exposures stratified by cohort. To examine the effects of SES on exposure-BMIz associations, bivariate models were sequentially adjusted for SES at birth and childhood SES. Odds ratios (OR) with corresponding 95% CI for OWOB and explanatory variables were estimated using logistic regression. Combining data from both cohorts, SES-exposure (stratified by cohort) and cohort-exposure interactions (pooled data) were tested within models using likelihood ratio tests. Final models were adjusted for covariates (maternal age and gestational age) with the best model informed by goodness of fit statistics (R-squared and Bayesian information criterion). Although BMI assesses weight independent of height, it remains correlated with height in children [25]. In GMS, there was a stronger correlation ($r=0.4$, $p<0.0001$) between height and BMIz (age 9), which was not evident in NTFS ($r=0.003$, $p=0.3$). Using

measures that remain correlated may introduce greater bias when comparing groups that differ markedly in height (GMS children were taller) [26]. Therefore models were adjusted for height to evaluate the associations that reflect adiposity independent of height [27, 28].

As study members measured at age 9 were different for some characteristics, compared to the remaining study members in both cohorts (Table 2; online), models were refitted using sampling weights (inverse probability weighting), weighting on the variables that differed between cohorts ($p<0.05$) as a sensitivity analysis. However, weighting minimally altered results, therefore unweighted results are presented. Additional sensitivity analyses examined rapid growth as it is frequently defined [9] (which includes catch up growth from low birthweight), by substituting RWG (instead of RT) in regression models.

To assess the relative importance of the early life predictors of BMIz, the final multivariable regression models were reconstructed as path models. Path analysis is an extension of linear regression which models relationships between dependent variables and two or more independent variables. Additional paths were added to the baseline (i.e. adjusted multivariable) model informed by *a priori* hypothesises and modification indices. Good model fit was a χ^2 value >0.05, root mean square error of approximation (RMSEA)<0.05 and p of close fit (PCLOSE)>0.05, and a comparative fit index (CFI) and goodness-of-fit index (GFI) >0.95. All direct paths with $p<0.05$ were modelled and standardised β coefficients are presented to demonstrate the relative effects across the cohorts. Confidence intervals (CI) were estimated using bootstrapping (50,000 replications).

RT emerged as an important factor, and therefore utilising the longitudinal data available, BMIz trajectories were plotted based on early life growth (RT). BMI z-scores were derived as formerly described using data available at various points in childhood for GMS (ages 0, 1, 3, 6-8, 8-10, 14-16) and NTFS (ages 0, 1, 9, 13).

Statistical analyses were conducted in STATA 14 (StataCorp, College Station, TX) and path diagrams using SPSS Amos 24.0 (SPSS Inc, Chicago, IL).

Results

At age 9, anthropometric measures and socioeconomic measures were available for 676-711 members of NTFS and 302-475 of GMS (Table 3), while there were 313 NTFS and 269 GMS with full data for the multivariable models. NTFS children on average had a lower BMIz than GMS children and were shorter (Table 3). There were only 7% OWOB in NTFS, compared to 33% in GMS. UW were excluded from all regression analyses (NTFS, *n*=17 (2.3%); GMS, *n*=6 (1.2%)).

Table 3 Relationship between socioeconomic differences and anthropometric variables (age 9) in the two cohorts

	NTFS					GMS				
	n	Healthy (%)	OWOB (%)	Mean BMIz (SD)	Mean height-z (SD)	N	Healthy (%)	OWOB (%)	Mean BMIz (SD)	Mean height-z (SD)
All	734	93.1	6.9	0.08 (-0.88)	-0.93 (1.17)	481	76.5	23.5	0.60 (1.06)	0.16 (1.02)
SES (birth)										
Least advantaged	123	91.9	8.1	0.07 (0.90)	-1.25 (1.08)	84	76.2	23.8	0.63 (1.04)	0.12 (0.97)
2nd to least	113	98.2	1.8	-0.01 (0.82)	-1.07 (1.18)	108	78.7	21.3	0.58 (1.07)	0.31 (0.95)
Mid	414	92	8	0.11 (0.89)	-0.81 (1.16)	104	76	24	0.61 (1.1)	0.17 (1.08)
2nd to most	47	91.5	8.5	0.18 (0.98)	-0.92 (1.29)	88	70.5	29.5	0.72 (1.05)	0.00 (1.00)
Most advantaged	14	92.9	7.1	-0.03 (0.87)	-0.34 (1.15)	91	80.2	19.8	0.5 (1.02)	0.17 (1.09)
Total	711					475				
P value		0.22 [a]		0.66 [b]	**0.001** [b]		0.59 [a]		0.74 [b]	0.33 [b]
SES (age 9)										
Least advantaged	250	94	6	0.04 (0.92)	-0.94 (1.11)	87	67.8	32.2	0.63 (1.13)	-0.01 (0.94)
Mid	379	92.9	7.1	0.08 (0.85)	-0.85 (1.13)	110	80.9	19.1	0.53 (1.01)	0.16 (1.05)
Most advantaged	47	91.5	8.5	0.17 (0.85)	-0.77 (1.16)	105	79	21	0.70 (0.99)	0.33 (0.99)
Total	676					302				
P value		0.77 [a]		0.63 [b]	0.53 [b]		**0.07** [a]		0.49 [b]	**0.06** [b]

Category totals (N); corresponding row percentages (row %); Standard deviation (SD); Socioeconomic status at birth (SES) was fathers occupational social class in NTFS or Townsend quintile in GMS.
a Chi-square test p value presented for differences between socioeconomic group and weight categories.
b ANOVA p value for differences between socioeconomic groups and BMIz/height-z.

Cohort differences in early life exposures

There were differences in early life exposures and SES between the time periods (Table 4). In NTFS, mothers were slightly older, gestational length was slightly shorter with fewer extreme gestation age groups, rapid growth (RWG and RT) was more common, and adversity was less common. On average, birthweights were smaller (Table 4), however there were no differences in birthweight categories (SGA, LGA). In NTFS, breastfeeding initiation was more likely and duration was longer: 85.5% were breastfed and 39% for over 4 months. Less than 7% of the NTFS cohort were in the highest occupational group (at either time point), compared to 34.9% in GMS in childhood ($p<0.001$).

Table 4 *Descriptive characteristics of the cohorts*

	Cohort						
	NTFS			GMS			
Continuous variables	n	Mean (SD)	Range	n	Mean (SD)	Range	P value
Maternal age (years)	995	28.48 (5.80)	16 - 45	993	27.94 (5.97)	15 - 46	**0.035**
Gestational age (weeks)	990	39.82 (1.28)	26 - 44	993	39.48 (1.70)	27 - 43	**<0.001**
Birthweight (z-score)	1,002	-0.15 (1.06)	-3.28 - 4.69	993	-0.02 (1.02)	-2.74 - 4.52	**0.009**
BMI (z-score)	734	0.08 (0.88)	-1.95 - 3.80	481	0.60 (1.06)	-1.91 - 3.43	**<0.001**
Height (z-score)	734	-0.93 (1.17)	-4.92 - 3.78	481	0.16 (1.02)	-2.70 - 3.35	**<0.001**
Categorical variables	n	Col %		n	Col %		P value
Sex	1,114			994			
Male	570	51.2		506	50.9		0.905
Female	544	48.8		488	49.1		
Gestation categories	990			993			
Pre-term	34	3.4		107	10.78		
Normal	914	92.3		823	82.88		**<0.001**
Post-term	42	4.2		63	6.34		
Categories of birthweight	990			993			
SGA	115	11.6		89	9		0.1
Normal	796	80.4		810	81.6		
LGA	79	8		94	9.5		
RWG	360			813			
No	218	60.6		567	69.6		**0.002**
Yes	142	39.4		246	30.4		
RT	360			813			
No	227	63.1		577	71		**0.007**
Yes	133	36.9		236	29		
Breastfeeding categories	469			993			
Never	68	14.5		468	49.1		**<0.001**
<6 weeks	75	16		237	24.9		
>6 weeks	143	30.5		89	9.3		
>4 months	183	39		159	16.7		
Adversity	352			934			
No	303	86.1		719	77		**<0.001**
Yes	49	13.9		215	23		
SES at birth	1,036			987			
Least advantaged	158	15.3		188	19.1		**<0.001**
2nd to least advantaged	165	15.9		201	20.4		
Mid	589	56.9		221	22.4		
2nd to most advantaged	92	8.9		223	22.6		
Most advantaged	32	3.1		154	15.6		
SES at age 9	718			373			
Least advantaged	265	36.9		110	29.5		**<0.001**
Mid	404	56.3		133	35.7		
Most advantaged	49	6.8		130	34.9		

Number of study members in each category (n) and corresponding column percentage (Col %) or mean and standard deviation (SD). P values shown for Chi-square test for differences between NTFS and GMS for categorical variables, and t-tests for continuous variables. SGA, Small for gestational age; LGA, Large-for-gestational age; RWG, rapid weight gain; RT, rapid thrive; SES, socioeconomic status.

Relationship between socioeconomic status and anthropometry

There were no overall trends in BMIz by SES in either cohort (Table 3). There were more OWOB in the least advantaged group in childhood in the GMS, but no socioeconomic differences in BMI categories in NTFS. However, there were early life socioeconomic differences in height in NTFS: the most advantaged were taller than the least (+0.91 height z-score, p=0.001) (Table 3). The socioeconomic differences in height were smaller in GMS and did not attain statistical significance (+0.34 height-z, p=0.06).

Inter-relationships between early life risk factors, SES and childhood BMI

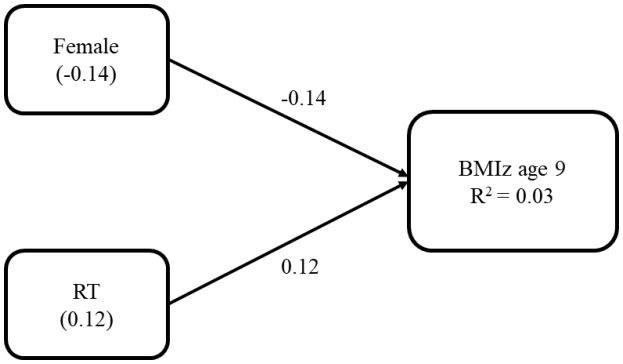
Cohort-exposure interactions were examined using pooled data with NTFS as the reference group. There were interactions between cohort and birthweight (0.15 difference in BMIz, 95% CI 0.02,0.28), RT (0.50 difference in BMIz, 95% CI 0.18, 0.82), and height (0.36 difference in BMIz, 95% CI 0.23, 0.48) (Table 5; online). No other statistically significant interactions were observed. There was an interaction for adversity (0.51 increase in BMIz in GMS, 95% CI 0.11,0.91); however, this did not remain after adjustment for childhood SES (Table 5; online).

Path analysis

The relationships between exposures and the indirect pathways to BMI are presented in the path model (Figure 1). Similar direct associations were also observed in the stratified regression models (Table 6; online), and in both cohorts RT had the largest effect on BMIz (and OWOB in GMS). The early life factors explained more variation in BMIz in GMS than NTFS (GMS R^2=21%, TFS R^2=3%, Figure 1). In GMS, adversity, RT and birthweight all had similar positive, direct effects on BMIz (Figure 1). RT and birthweight were also positively associated with height.

In NTFS, sex and RT were the only factors that predicted BMIz in adjusted regression analyses (Figure 2 and Table 6; online). SES was not directly associated with BMIz in either cohort (Table 7; online), and there were no consistent SES-exposure interactions ($p>0.05$). However, SES had indirect effects in the GMS cohort: SES (at birth) was associated with birthweight and height (Figure 1), and attenuated the effects of adversity on BMIz (Table 7; online).

a. NTFS



b. GMS

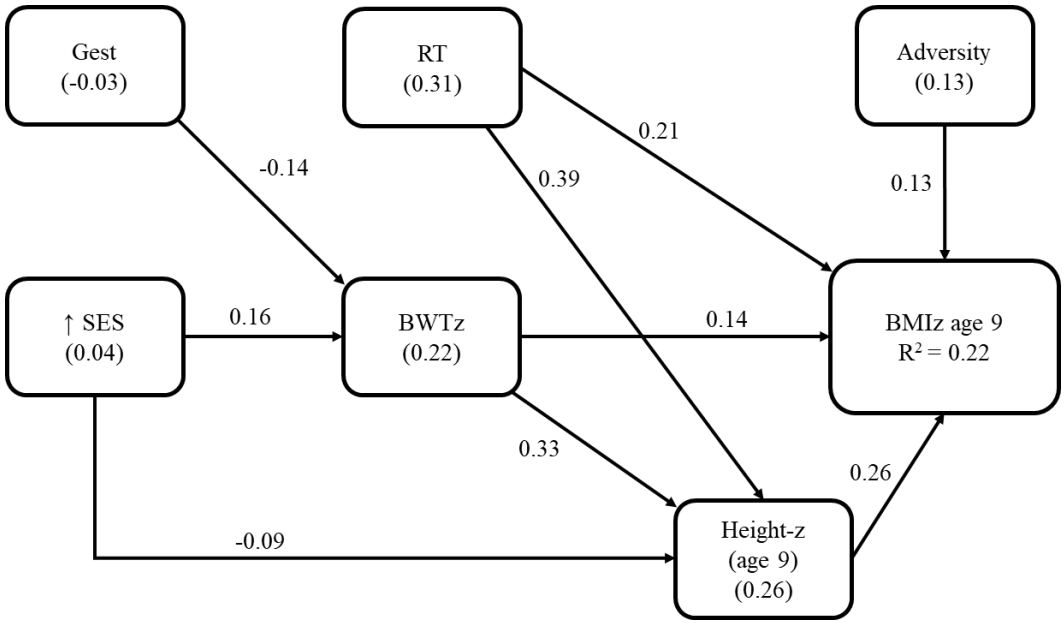


Figure 1 Path diagrams showing the direct and indirect predictors of BMIz in NTFS (a) and GMS (b).
The path model shows the relationships between early life variables with BMIz at age 9.
Arrows show the direction of the direct effects between variables. The direct effects are the straightforward relationships not going through any other variable (coefficients above lines), the indirect effect is the product of each component path (to BMIz), and the total effects (brackets) are the sum of direct and indirect paths. All exposures had significant total (the sum of direct and indirect effects) and indirect effects on BMIz. Standardised beta coefficients are presented, which represent partial regression coefficients between connected variables, controlling for all prior variables [29]. All direct effects (with $p<0.05$) were modelled and are represented by solid lines. Total effects (if significant $p<0.05$) are presented in brackets. SES, socioeconomic status; BWTz, birthweight z-score; RT, rapid thrive; gest, gestational age.

Although group sizes were too small to estimate a multivariable model for NTFS, RT was associated with increased odds of OWOB in the bivariate model (OR 2.24, 95% CI 1.01,4.96) (Table 8; online). In the multivariable model for GMS, RT was associated with increased odds of OWOB at age 9 (OR 2.34, 95% CI 1.14-4.83) (Table 6; online). Socioeconomic advantage (childhood) was associated with decreased odds of OWOB in GMS, however there were no significant SES-exposure interactions for either cohort. After adjusting for height, the model explained more variation in OWOB and birthweight was no longer a significant predictor.

In the sensitivity analysis, RWG was also associated with BMIz and the coefficients for both cohorts were similar (Table 9; online). In the GMS OWOB sensitivity model (Table 9; online), adjusting for height removed the significant positive associations for RWG.

Investigating early life rapid growth and BMIz throughout childhood

RT was the factor associated with higher BMIz in both cohorts and increased odds of OWOB, and no other tested variables predicted RT (Figure 1). The impact of RT on BMI z-scores over time was examined further (Figure 2). By definition, those with RT show a sizeable increase in z-score from birth to 12 months. Within cohorts, those who had RT had higher BMI z-scores throughout childhood compared to those who did not. However, in NTFS at age 13 (the last available time point before adulthood), it was not significantly different. In GMS, those who had RT also had a large initial increase in z-score (0-12 months) (albeit to a lower z-score), but BMIz remained elevated and on average these children were 1SD above average BMIz throughout childhood.

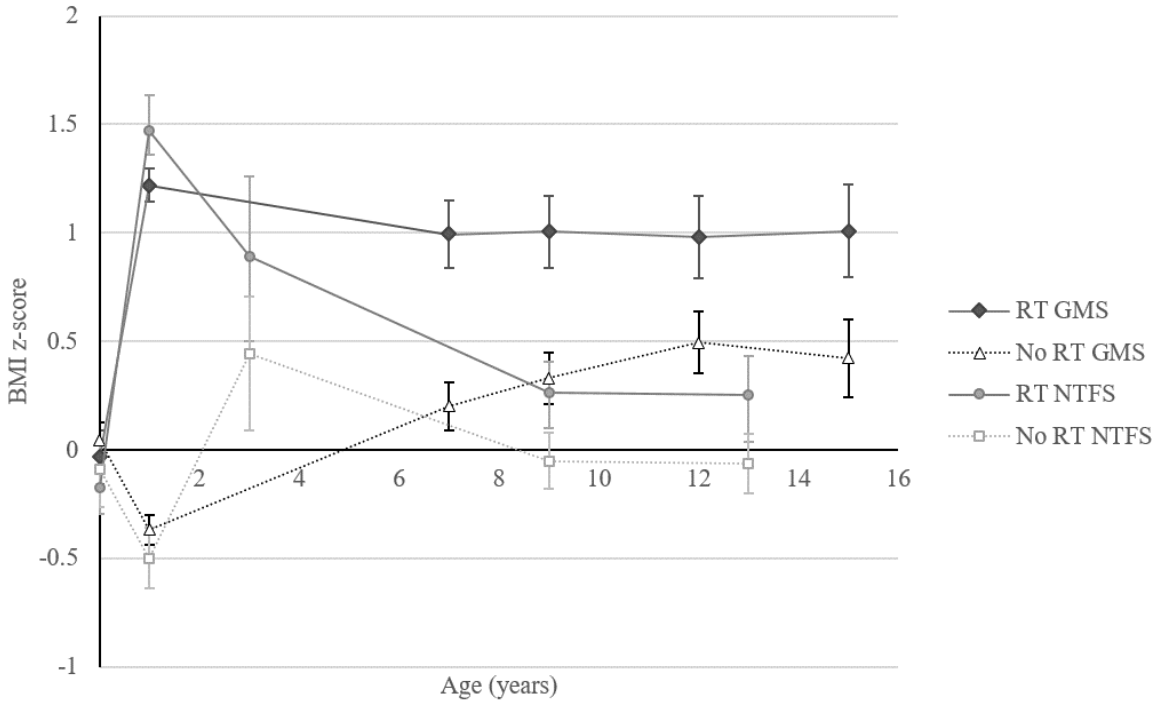


Figure 2 Changes in mean z-score over time by cohort and RT
Error bars represent 95% confidence intervals. Average values were used for the interval ages for GMS.

Discussion

Summary of results

These data provided an opportunity to consider whether risk factors for raised childhood BMI were the same in two different cohorts in the same geographical area: one recorded before and the other during the obesity epidemic. Between the two periods, height and prevalence of OWOB had greatly increased. The social class differences in height that were evident in the historic cohort have diminished over time, and instead socioeconomic differences in OWOB have emerged in the modern cohort. There have been increases in birthweight, and decreases in the duration of breastfeeding and of rapid infancy growth. Those who had rapid growth had higher BMI throughout childhood in both cohorts, but there was increased likelihood of subsequent OWOB only in the modern cohort. Early life exposures that were unrelated to BMI (birthweight, adversity) in the historic cohort explained substantially more variation in childhood BMI in the modern cohort, which may be related to the environmental changes that have occurred between the two time points.

Consistency with previous findings

This study is one of many to demonstrate that early rapid growth is associated with a higher child BMI and increased likelihood of childhood obesity [9, 10]. Genetic variants for adult BMI are also associated with infancy growth, suggesting that early infancy weight gain is on the pathway to adult obesity risk [29]. Therefore, rapid growth in infancy may be a precursor to childhood obesity, or could reflect the individual's predestined growth trajectory. Height mediated the effects of birthweight and RT on BMIz, which may suggest that some of these associations were related to lean rather than fat mass [30]. Other studies have suggested that the relationship between RWG and subsequent adiposity is a marker of fast growth and later height [31]. This may be a product of modern environments, as the effects of rapid growth were previously unrelated to height (NTFS), but are now somewhat mediated through height (GMS).

Early life risk factors that may have changed over time included birthweight and adversity, which were only associated with BMIz in the modern cohort. GMS children had higher birthweights, which is in line with previous findings that birthweight has increased over a generation [32]. Early life postnatal factors were the focus of these analyses; however, there are many maternal factors that can influence birthweight and offspring BMI (e.g. maternal smoking, BMI and diabetes) [30, 33, 34].

This study does not support associations between breastfeeding with early childhood growth and BMI [35, 36], although previous findings are not consistent and may be due to confounding by SES [37-39]. Previous analyses in the GMS cohort have found a positive association between SES and breastfeeding duration [40]. Wright et al,. also noted more rapid growth in the GMS cohort (0-13 months) in those who stopped breastfeeding earliest, although this is likely a result of reverse causation; that babies genetically destined to be larger make greater demands on their mother for breastmilk, and this greater demand increases likelihood of earlier cessation [41].

We hypothesised that early life risk factors may interact with early SES but did not find strong evidence of this, however we did identify socioeconomic differences in anthropometric outcome measures. Early life SES may reflect developmental programming effects, whilst childhood SES may more likely be a marker of detrimental environmental factors (although depending on the degree of social mobility there is likely to be overlap between the measures). Whilst we did not identify strong direct effects of early life SES, a single marker may not capture the downstream effects of inequality on numerous social, economic, academic and behavioural factors, which can influence development of obesity over the life course. Adversity included prenatal exposure in the modern cohort and had direct effects on BMI, therefore there is the possibility the cohort differences observed could be due to the earlier timing of the exposure (vs postnatal adversity in NTFS) and perhaps some *in utero* programming effects [42].

The socioeconomic gradients in height were less prominent in the modern cohort. A previous study comparing NTFS children (at age 9 in 1954) and a later born Newcastle cohort (1987) found that both had similar socioeconomic gradients in height [43], which when taken with our results suggests that socioeconomic height differences have narrowed since 1954, and possibly post-1987. Similar to our findings, Wright and Parker did not find socioeconomic differences in childhood BMI between 1947 and 1987 in Newcastle [48]. However we observed socioeconomic differences in OWOB in the GMS cohort (2000), suggesting socioeconomic inequalities on childhood OWOB have broadened over time [4, 5], perhaps due to greater exposure to an increasingly obesity-promoting environment [6, 44, 45]. We did not identify socioeconomic differences in OWOB in NTFS, which could be due to the low prevalence of OWOB and the time period (age 9 in 1956). Post-war rationing (until 1954) permitted fairer distribution and consistency of resources, which somewhat reduced class differences in nutrient intake and improved public health [48], perhaps explaining the similarities in birthweights and infant weights across deprivation indices in NTFS [43]. These historical factors likely produced a more uniform pregnancy and early life experience (in contrast to modern environments), and may explain why there were few early life exposures influenced by SES or associated with BMI in NTFS. In this case, from a

developmental origins perspective, the postnatal environment aligns with the prenatal anticipated environment, in theory meaning appropriate adaptation and decreased risk of metabolic disease (i.e. the predictive adaptive response) [49]. This is in contrast to findings in the modern cohort, which may be a consequence of evolutionary and developmental mismatches and extensive environmental changes [50]. Examples include nutritional transition and changes to the food environment amongst the other lifestyle changes between 1947 and 2000, such as: increases in the female labour force, technological advances, differing work practices and increased sedentary time and screen time [46-48]. Furthermore, findings in GMS may also reflect the cycle of higher birthweights and increased obesity across generations [1, 50, 51]

An important distinguishing feature of the historical cohort was the relatively low levels of OWOB, although this meant it was not possible to estimate a multivariable OWOB model. As the majority of NTFS children had a healthy BMI, increases in BMI in this cohort may not necessarily have negative health effects. However, the higher prevalence of rapid infancy growth but lower levels of OWOB in NTFS is yet more suggestive of the implications of environmental changes. Similarly, whilst it was not possible to adjust for all potential unmeasured confounders such as maternal BMI, rapid infant growth remained a significant predictor in NTFS when there was lower prevalence of maternal obesity [52].

The strengths of these cohorts is that they provide good coverage of the regional area and had rich prospective data collection. Study recruitment provided a representative sample of both locations at the given time. As with most longitudinal studies there is attrition, however as there were fewer advantaged families initially represented in the original GMS cohort, this bias resulted in a sample that is then more representative of North East England over time [53]. Although neighbouring areas, Newcastle and Gateshead have some differences in social compositions and there will have been many other socioeconomic and environmental changes over 50 years, apart from the onset of the obesity epidemic, so we cannot assume that the differences observed solely reflect this. Aside from

birthweight in GMS, the early life factors appeared independent of SES, although this could be related to the socioeconomic measure(s) used. Although the method used to classify deprivation between the studies was different, Registrar General's occupational social class was the only socioeconomic classification widely used at the time of the NTFS, and Townsend deprivation index was the only feasible means of comparing household deprivation in GMS. Although the two might not be directly comparable, when both have been used in other studies, associations have been consistent across both measures and produced similar socioeconomic gradients in height [43, 54].

Although anthropometric measures were utilised at age 9 to minimise the bias from puberty, earlier onset of puberty can occur and some children may have been more developed [55]. However, earlier onset may be more likely in children with a higher BMI [56, 57], and so it may not be appropriate to adjust for pubertal status if BMI is causally related to early puberty [58]. Path analysis was utilised to model the relationships to examine the relative influence of each early life factors, mediators and the indirect pathways to BMI, however causal inference methods would be required to examine causality. Whilst early life rapid growth was an important factor, there remained variation in childhood BMIz in those who had rapid growth in GMS. As many children with rapid infancy weight gain do not go on to have increased adiposity in childhood [31] further research is required to detect those most at-risk.

Conclusion

In conclusion, analysis of two North East England birth cohorts born over 50 years apart demonstrated that children exposed to both socioeconomic disadvantage and the modern environments now have little evidence of growth restriction, but a greater risk of OWOB. Rapid growth in infancy has remained a consistent antecedent of raised BMI, but the association was stronger in the modern cohort, which may indicate the effects are exacerbated by environmental changes.

Online Supplementary tables

Table 1 Description of exposures and cohort differences.

Time point	Variable	Description	Type of variable	Cohort differences
Birth	Maternal age	Years	Continuous*	No
	Gestational age	Weeks (continuous) and categorised as; pre-term, <38 weeks; post-term >41 weeks.	Continuous and categorical*	No
	Birthweight	Birthweight z-score, standardised using the British 1990 growth reference (adjusted for sex and gestational age). Categorised as small for gestational age (SGA, <10th percentile), normal (10th-90th) and large for gestational age (LGA, >90th percentile).	Continuous and categorical	No
	Socioeconomic status (SES)	In NTFS social class based on occupation, where in GMS Townsend score based on postcode was used (quintiles). Both measures used five ranked categories from the most to the least advantaged.	Categorical	Yes
First year	Rapid weight gain (RWG)	If experienced a 0.67 SD change in weight for age z-score (z-score12m − z-scorebirth) [9]	Dichotomous	No
	Rapid thrive (RT)	If experienced a 0.67 SD change in conditional weight gain (z-score12m − r × z-scorebirth) [20]	Dichotomous	No
	Breastfeeding	Duration of breastfeeding (non-exclusive). GMS had predefined categories of never, <4 weeks, 4 weeks-6 months and 6 months+. For NTFS, weeks were transformed into the same categories to match GMS.	Categorical	No
	Adversity	Experiencing any of the following; parental separation, police involvement, abuse, debt, death or illness in the family: - In the first year in NTFS (0-12 months) - From the GMS 4 month postnatal questionnaire and spanned 8 months prenatal to 4 months postnatal	Dichotomous	Yes

*Continuous measures were used as covariates in multivariable models.

Table 2 Sample representativeness for early life factors for those with BMI measures at age 9 for each cohort

	NTFS					GMS				
Continuous	**Not measured**		**Measured**			**Not measured**		**Measured**		
	n	Mean (SD)	n	Mean (SD)	p	n	Mean (SD)	n	Mean (SD)	p
Birthweight (z-score)	251	-0.23 (1.11)	734	-0.11 (1.04)	0.14	506	-0.02 (-1.00)	481	0.01 (-1.03)	0.94
Maternal age (years)	244	26.99 (5.42)	734	28.97 (5.84)	**<0.001**	506	27.1 (-6.08)	481	28.82 (-5.72)	**<0.001**
Gestation (weeks)	246	39.67 (1.77)	727	39.87 (1.07)	**0.032**	506	39.42 (1.82)	481	39.55 (-1.55)	0.22

	NTFS				GMS			
Categorical	**Total**	**Not measured**	**Measured**	**p**	**Total**	**Not measured**	**Measured**	**p**
	n	Col %	Col %		n	Col %	Col %	
Sex	1,097	363	734		988	507	481	
Male	561	54.5	49.5	0.11	501	51.7	49.7	0.53
Female	536	45.5	50.5		487	48.3	50.3	
Birthweight	973	246	727		987	506	481	
SGA	111	15	10.2		87	8.7	8.9	
Normal	784	78	81.4	0.1	806	82.4	80.9	0.77
LGA	78	6.9	8.4		94	8.9	10.2	
Gestation categories	983	250	733		987	506	481	
Pre-term	34	7.2	2.2		105	11.9	9.4	
Normal	907	87.2	94	**<0.001**	819	81.2	84.8	0.32
Post-term	42	5.6	3.8		63	6.9	5.8	
RWG	354	17	337		808	354	454	
No	213	58.8	60.2	0.91	562	70.9	68.5	0.46
Yes	141	41.2	39.8		246	29.1	31.5	
RT	354	17	337		808	354	454	
No	219	58.8	62	0.79	572	72.9	69.2	0.25
Yes	135	41.2	38		236	27.1	30.8	
Breastfeeding categories	460	114	346		948	483	465	
None	65	8.8	15.9		465	56.1	41.7	
<6 weeks	73	21.1	14.2	**0.004**	237	25.1	24.9	**<0.001**
>6wk	143	21.9	34.1		89	6.8	12	
>4m	179	48.2	35.8		157	12	21.3	
Adversity	346	97	249		928	475	453	
No	298	89.7	84.7	0.23	715	80.8	73.1	**0.005**
Yes	48	10.3	15.3		213	19.2	26.9	
SES at birth	1021	310	711		981	506	475	
Least advantaged	158	11.3	17.3		186	20.2	17.7	
2nd to least	162	15.8	15.9		200	18.2	22.7	
Mid advantaged	577	52.6	58.2	**<0.001**	221	23.1	21.9	**0.001**
2nd to most	92	14.5	6.6		222	26.5	18.5	
Most advantaged	32	5.8	2		152	12.1	19.2	

Number of study members in each category (n) and corresponding column percentage (Col %) or mean and standard deviation (SD). P values shown for Chi-square test for significant differences between those with data (BMI measured) and those without for categorical variables, and t-tests for continuous variables. SGA, Small for gestational age; LGA, Large-for-gestational age; RWG, rapid weight gain; RT, rapid thrive; SES, socioeconomic status.

Table 5 The model interaction effects (p<0.05)

Cohort* exposure interactions						
	Unadjusted		**Adjusted for SES (birth)**		**Adjusted for SES (age 9)**	
	Coef	95% CI	Coef	95% CI	Coef	95% CI
Birthweight (z-score)	**0.16**	(0.05,0.26)	**0.17**	(0.07,0.28)	**0.15**	(0.02,0.28)
RT	**0.40**	(0.11,0.68)	**0.44**	(0.15,0.73)	**0.50**	(0.18,0.82)
Adversity	**0.51**	(0.11,0.91)	**0.47**	(0.05,0.89)	0.30	(-0.16,0.77)
Height (z-score)	**0.38**	(0.28,0.48)	**0.38**	(0.29,0.48)	**0.36**	(0.23,0.48)

Coef, coefficient; 95% CI, 95% confidence interval; Ref, reference category. SES, socioeconomic status; Bwtz, birthweight z-score; RT, rapid thrive. The reference group for the cohort interactions was NTFS.

Table 6 Multivariable linear (BMIz) and logistic (OWOB) regression models by cohort

	NTFS (BMIz)		GMS (BMIz)		GMS (OWOB)	
	coef	95% CI	coef	95% CI	OR	95% CI
Female	**-0.22**	(-0.41,-0.02)	-0.18	(-0.40,0.05)	0.68	(0.35,1.33)
RT	**0.22**	(0.01,0.43)	**0.51**	(0.25,0.78)	**2.34**	(1.14,4.83)
Birthweight z-score	0.02	(-0.08,0.11)	**0.17**	(0.05,0.29)	1.38	(0.97,1.97)
SES at birth						
Least advantaged	Ref		Ref		Ref	
2nd to least	0.05	(-0.31,0.41)	-0.24	(-0.62,0.14)	1.13	(0.38,3.34)
Mid advantaged	0.1	(-0.21,0.41)	-0.33	(-0.72,0.06)	0.65	(0.20,2.10)
2nd to most	0.04	(-0.45,0.53)	-0.19	(-0.58,0.20)	1.09	(0.36,3.29)
Most advantaged	-0.93	(-1.87,0.01)	-0.21	(-0.61,0.19)	0.91	(0.29,2.79)
SES (age 9)						
Mid advantaged	-0.15	(-0.39,0.08)	-0.13	(-0.44,0.17)	**0.36**	(0.15,0.88)
Most advantaged	0.21	(-0.30,0.70)	-0.04	(-0.36,0.28)	**0.35**	(0.14,0.86)
Height z-score	-0.02	(-0.12,0.07)	**0.24**	(0.11,0.37)	**1.98**	(1.34,2.93)
Adversity	-		**0.30**	(0.05,0.55)	1.65	(0.83,3.28)
Adjusted R^2	0.022		0.205		0.17	
N	313		269		269	

Models additionally adjusted for maternal age and gestational age. There were too few OWOB to estimate a multivariable model for OWOB in NTFS. Least advantaged socioeconomic group was the reference group. Coef, coefficient; 95% CI, 95% confidence interval; Ref, reference category; n, number of observations; RT, rapid thrive; SES, socioeconomic status.

Table 7 Results of linear regression analysis for all included exposures on BMIz at age 9 years in the cohorts adjusted for SES

Exposure	NTFS						GMS					
	Unadjusted		Adjusted for SES (birth)		Adjusted for SES (age 9)		Unadjusted		Adjusted for SES (birth)		Adjusted for SES (age 9)	
	Coef	95% CI	Coef	95% CI	Coef	95% CI	Coef	95% CI	Coef	95% CI	Coef	95% CI
Female	**-0.23**	(-0.36,-0.11)	**-0.24**	(-0.37,-0.11)	**-0.25**	(-0.38,-0.11)	-0.03	(-0.22,0.16)	-0.05	(-0.24,0.15)	-0.15	(-0.39,0.09)
Birthweight z-score	0.05	(-0.01,0.11)	0.05	(-0.01,0.11)	0.04	(-0.02,0.11)	**0.21**	(0.12,0.30)	**0.23**	(0.13,0.32)	**0.22**	(0.10,0.33)
Birthweight categories												
SGA	-0.14	(-0.35,0.07)	-0.15	(-0.37,0.08)	-0.18	(-0.41,0.05)	-0.2	(-0.53,0.13)	-0.19	(-0.53,0.15)	-0.15	(-0.61,0.30)
Normal	Ref		Ref		Ref		Ref		Ref		Ref	
LGA	0.09	(-0.15,0.32)	0.08	(-0.15,0.32)	0.04	(-0.21,0.29)	0.22	(-0.09,0.53)	0.25	(-0.07,0.57)	0.25	(-0.14,0.64)
Maternal age (years)	**-0.01**	(-0.02,0.00)	**-0.01**	(-0.02,0.00)	**-0.01**	(-0.03,0.00)	0	(-0.02,0.01)	0	(-0.02,0.02)	-0.02	(-0.04,0.01)
Adverse events	-0.09	(-0.39,0.21)	-0.03	(-0.35,0.30)	0.07	(-0.29,0.43)	**0.42**	(0.20,0.64)	**0.43**	(0.21,0.65)	**0.34**	(0.07,0.61)
RWG	**0.29**	(0.10,0.48)	**0.27**	(0.08,0.46)	**0.27**	(0.08,0.47)	**0.36**	(0.16,0.57)	**0.37**	(0.16,0.58)	**0.32**	(0.05,0.59)
RT	**0.29**	(0.10,0.48)	**-0.03**	(-0.35,0.30)	**0.20**	(-0.00,0.40)	**0.63**	(0.43,0.83)	**0.65**	(0.44,0.86)	**0.70**	(0.45,0.96)
Breastfeeding categories												
Never	Ref		Ref		Ref		Ref		Ref		Ref	
<6 weeks	0.19	(-0.17,0.54)	0.18	(-0.16,0.52)	0.18	(-0.16,0.52)	-0.05	(-0.30,0.19)	-0.04	(-0.29,0.21)	-0.04	(-0.29,0.21)
>6 weeks	0.12	(-0.17,0.42)	0.11	(-0.18,0.39)	0.11	(-0.18,0.39)	-0.28	(-0.59,0.04)	-0.24	(-0.57,0.10)	-0.24	(-0.57,0.10)
>4 months	0.08	(-0.22,0.38)	0.08	(-0.20,0.36)	0.08	(-0.20,0.36)	-0.16	(-0.42,0.09)	-0.17	(-0.45,0.10)	-0.17	(-0.45,0.10)
SES at birth												
Least advantaged			Ref		Ref				Ref		Ref	
2nd to least advantaged			-0.07	(-0.30,0.16)	-0.01	(-0.25,0.23)			-0.09	(-0.39,0.22)	-0.21	(-0.61,0.18)
Mid			0.04	(-0.14,0.22)	0.05	(-0.16,0.26)			-0.06	(-0.36,0.25)	-0.29	(-0.69,0.10)
2nd to most advantaged			0.11	(-0.19,0.41)	-0.02	(-0.36,0.32)			0.07	(-0.25,0.38)	-0.21	(-0.61,0.19)
Most advantaged			-0.07	(-0.58,0.44)	-0.28	(-0.90,0.34)			-0.18	(-0.50,0.14)	-0.18	(-0.59,0.23)
SES age 9												
Least advantaged					Ref						Ref	
Mid					0.02	(-0.14,0.18)					-0.09	(-0.40,0.22)
Most advantaged					0.25	(-0.11,0.61)					0.05	(-0.27,0.37)
Height z-score (age 9)	0.04	(-0.02,0.09)	0.03	(-0.03,0.09)	0.04	(-0.02,0.11)	**0.42**	(0.33,0.50)	**0.42**	(0.33,0.50)	**0.41**	(0.30,0.51)

The unadjusted model is the relationship between the exposure and BMIz, with models further adjusted for SES at birth, and SES age 9.
95% CI, 95% confidence interval; SES, socioeconomic status; RWG, rapid weight gain; RT, rapid thrive.

Table 8 Results of unadjusted logistic regression for early life variables and socioeconomic status on overweight/obese

Logistic bivariate regression of variables with OWOB age 9, by cohort				
	NTFS		GMS	
	Unadjusted		Unadjusted	
Variable	OR	95% CI	OR	95% CI
SES at birth				
Least advantaged	Ref		Ref	
2nd to least advantaged	**0.20**	(0.04,0.95)	0.87	(0.44,1.71)
Mid	0.98	(0.47,2.05)	1.01	(0.52,1.99)
2nd to most advantaged	1.05	(0.31,3.53)	1.34	(0.68,2.65)
Most advantaged	0.87	(0.10,7.35)	0.79	(0.38,1.62)
SES at age 9				
Least advantaged	Ref		Ref	
Middle	1.2	(0.63,2.31)	**0.50**	(0.26,0.96)
Most advantaged	1.46	(0.46,4.60)	0.56	(0.29,1.07)
Female	1.02	(0.58,1.80)	0.96	(0.63,1.47)
Birthweight z-score	1.17	(0.90,1.53)	1.28	(1.04,1.57)
Birthweight categories				
SGA	0.75	(0.26,2.15)	0.75	(0.34,1.67)
Normal	Ref		Ref	
LGA	1.17	(0.44,3.08)	1.31	(0.68,2.54)
Maternal age (years)	0.97	(0.92,1.02)	0.98	(0.95,1.02)
Adversity	0.85	(0.18,3.91)	**1.78**	(1.12,2.85)
RWG	1.71	(0.77,3.75)	**1.65**	(1.04,2.60)
RT	**2.24**	(1.01,4.96)	**2.38**	(1.51,3.75)
Breastfeeding categories				
None	Ref		Ref	
<6 weeks	2.36	(0.41,13.46)	0.93	(0.55,1.58)
6 weeks-4 months	2.72	(0.58,12.74)	0.47	(0.21,1.05)
>4 months	2.58	(0.55,12.05)	0.85	(0.48,1.49)
Height (z-score)	1.25	(0.96, 1.63)	**2.25**	(1.77,2.87)

OR. Odds ratio; 95% CI, 95% confidence interval.* $p<0.05$.
SGA, Small for gestational age; LGA, Large-for-gestational age; RWG, rapid weight gain; RT, rapid thrive; SES, socioeconomic status.

Table 9 RWG sensitivity - multivariable regression models for BMIz and OWOB (age 9)

	NTFS (BMIz)		GMS (BMIz)		GMS (OWOB)	
Exposure	Coef	95% CI	Coef	95% CI	OR	95% CI
Female	**-0.22**	(-0.41,-0.02)	-0.17	(-0.40,0.06)	0.71	(0.36,1.38)
RWG	**0.33**	(0.11,0.55)	**0.39**	(0.10,0.69)	2.10	(0.93,4.73)
Birthweight z-score	0.08	(-0.03,0.18)	**0.23**	(0.09,0.37)	**1.54**	(1.03,2.29)
SES at birth					0.71	(0.36,1.38)
Least advantaged	Ref		Ref			
2nd to least advantaged	0.07	(-0.29,0.42)	-0.22	(-0.61,0.16)	1.14	(0.39,3.32)
Mid	0.13	(-0.18,0.44)	-0.32	(-0.71,0.08)	0.66	(0.21,2.08)
2nd to most advantaged	0.06	(-0.43,0.54)	-0.19	(-0.59,0.20)	1.03	(0.35,3.09)
Most advantaged	-0.86	(-1.79,0.08)	-0.22	(-0.63,0.18)	0.86	(0.28,2.64)
SES (age 9)						
Mid	-0.16	(-0.39,0.08)	-0.12	(-0.43,0.18)	**0.37**	(0.15,0.89)
Most advantaged	0.19	(-0.30,0.68)	-0.04	(-0.36,0.29)	**0.36**	(0.15,0.87)
Height-z (age 9)	-0.03	(-0.12,0.06)	**0.28**	(0.15,0.40)	**2.10**	(1.43,3.09)
Adversity	-		**0.30**	(0.04,0.56)	1.63	(0.82,3.24)
Adjusted R^2	0.036		0.183		0.163	
N	313		269		269	

Models also adjusted for maternal age and gestational age (non-significant). Coef, coefficient; OR, Odds ratio; 95% CI, 95% confidence interval; Ref, reference category; N, number of observations. RWG, rapid weight gain; SES, socioeconomic status; SES reference category is least advantaged.

Declarations

Conflict of interest

None.

Ethics approval

Ethics approval for both studies was obtained from the appropriate local research ethics committees and all participants gave their written informed consent.

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