Title: Intergenerational change and familial aggregation of body mass index

Running title: Intergenerational change & familial aggregation of BMI

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Abstract

The relationship between parental BMI and that of their adult offspring, when increased adiposity can become a clinical issue, is unknown**.** We investigated the intergenerational change in body mass index (BMI) distribution, and examined the sex-specific relationship between parental and adult offspring BMI. Intergenerational change in the distribution of adjusted BMI in 1443 complete families (both parents and at least one offspring) with 2286 offspring (1263 daughters and 1023 sons) from the west of Scotland, UK, was investigated using quantile regression. Familial correlations were estimated from linear mixed effects regression models.The distribution of BMI showed little intergenerational change in the normal range (<25 kg/m^2), decreasing overweightness (25–<30 kg/m^2) and increasing obesity (≥30 kg/m^2). Median BMI was static across generations in males and decreased in females by 0.4 (95% CI: 0.0, 0.7) kg/m^2; the 95^{th} percentile increased by 2.2 (1.1, 3.2) kg/m^2 in males and 2.7 (1.4, 3.9) kg/m^2 in females. Mothers' BMI was more strongly associated with daughters' BMI than was fathers' (correlation coefficient (95% CI): mothers 0.31 (0.27, 0.36), fathers 0.19 (0.14, 0.25); p=0.001). Mothers' and fathers' BMI were equally correlated with sons' BMI (correlation coefficient: mothers 0.28 (0.22, 0.33), fathers 0.27 (0.22, 0.33).The increase in BMI between generations was concentrated at the upper end of the distribution. This, alongside the strong parent-offspring correlation, suggests that the increase in BMI is disproportionally greater among offspring of heavier parents. Familial influences on BMI among middle-aged women appear significantly stronger from mothers than fathers.

Keywords: Obesity, body mass index, sex-specific, maternal, paternal.

Introduction

While there is no doubt that westernised populations are becoming more obese[1 2] the distribution of weight change within the population is less well defined. The majority of the published literature in this area uses data from the National Health and Nutrition Examination Survey, based in the United States. Comparison of survey results from 1994 with previous surveys in the late seventies and eighties showed that the greatest absolute increases in body mass index (BMI) were within the already heaviest group; significant upwards change in the entire distribution was only seen in older age groups[3]. However, while such data shows trends in the BMI of the population as a whole, studies describing changes within families are rare.

There has been increasing interest in the effects of parental BMI on childhood BMI, encompassing the influence of genetics, maternal programming and environmental factors; we have previously shown in this same cohort that midparental BMI is a strong determinant of offspring BMI[4]. There is now evidence of a sex-specific association, with one study reporting that childhood obesity is linked to obesity in the same-sex parent[5], and another that both parents' BMI has an effect on offspring BMI, but in female children the influence of mothers' BMI is stronger than fathers'[6]. Those studies focused on an age when the child is still predominantly dependent on their parents for nutrition, allowing potential for family-based interventions. However the sex-specific link between parental obesity and obesity in adult offspring, when any predisposition to obesity, including parity and sedentary lifestyle, are likely to be expressed, and when increased adiposity more commonly becomes a clinical issue, is unknown.

Using a two-generational study of 1443 sets of parents and 2286 adult offspring in the west of Scotland-based Midspan cohort, we examined for potential differences in BMI distribution between parents and offspring within the same population, using generational data gathered 20 years apart. The familial influences on BMI were examined by parent-offspring correlations, allowing the sex-specific relationship between parental and adult offspring BMI to be studied in depth.

Methods

Study populations

The Midspan Renfrew/Paisley Study: In 1972-76, 15402 residents of Renfrew and Paisley (7049 men and 8353 women), comprising 79% of the general population aged 45-64 and including 4064 married couples, completed a questionnaire and attended for a clinical examination[7].

The Midspan Family Study: In 1993-4, current addresses were available for 3445 couples from the Renfrew/Paisley Study (including the death certificate informant when both had died[8]); 2841 responded with information on the names, dates of birth and addresses of offspring. 3202 offspring from 1767 families were identified as living locally (within 30 miles), aged between 30 and 59 and therefore formed the eligible population for this study. In 1996 2338 offspring (1040 sons and 1298 daughters) from 1477 families participated (73% response rate for individuals, 84% for families). In the present study excluding step-children, adopted offspring and families with a missing parental or offspring BMI, reduced the study sample to 1443 complete families (both parents and at least one offspring included) with 2286 offspring (1263 daughters and 1023 sons). The families were ascertained (by self

report) to be full-sibling families with no step-children, adoptees, half-sibs etc. All were white. Details of the study have been described previously[4 8 9].

In addition to the 2338 participants in the Family study, there were 864 eligible offspring who declined to take part. A further 1358 offspring were ineligible only because they no longer lived locally. Sex, age, parental BMI and parental social class were compared across these three groups (participants, local non-participants and migrant non-participants) to investigate the possibility of migration and participation bias.

Physical measurements

Standing height was measured in stockinged feet; in the offspring study a Holtein stadiometer was used recorded to the nearest mm in 1996 and to the nearest cm in 1970s. Weight at both time points was measured to the nearest 0.1 kg in stockinged feet and wearing indoor clothes. BMI was calculated as weight (kg)/ height (m^2), with categories normal weight (<25 kg/m^2), overweight (25-29.9 kg/m^2) and obese (≥30 kg/m^2).

Questionnaire

Parents and offspring completed questionnaires recording marital status, smoking status (never, current or former) and occupation. The offspring questionnaire also asked for number of children. Marital status was recorded on the parent questionnaire as married, single, widowed or other, and on the offspring questionnaire as married, living with a partner, single, widowed, divorced or separated. Respondents who identified themselves as married were classed as “married”; all others were classed as

"not married". Social class was coded from occupation, using the Registrar General's classification of occupation[10 11]. Social classes I, II, or III-nonmanual were defined as nonmanual, while III-manual, IV and V were defined as manual. Women's social class was based on their own occupation or previous occupation, except housewives, where their husband's or father's occupation was used [9].

Statistical analyses

To allow comparison between parents and offspring, who differed in their distributions of age, marital status, number of children, smoking status and social class, all analyses were performed on BMI scores that had been adjusted to remove differences due to these potential confounding factors while preserving intergenerational differences. We used linear regression models to investigate the associations between BMI and potential confounding factors, separately for mothers, fathers, daughters and sons. The outcome was log(BMI) and the explanatory variables were age (as a 3rd-order polynomial) (web figure 1), marital status, number of children (none, 1, 2, 3, ≥ 4), smoking status and social class (web figure 2). The residuals were added to the predicted log(BMI) for a 50-year-old married never-smoker with two children and overall mean social class; taking exponentials gave adjusted BMI (BMI_{adj}).

BMI probability densities were estimated using a Gaussian kernel density estimator with bandwidth chosen by Silverman's rule of thumb[12]. The mean, variance, and 5^{th}, 25^{th}, 50^{th}, 75^{th} and 95^{th} percentiles of BMI_{adj} were estimated to assess intergenerational changes in the location and shape of the BMI distributions. Intergenerational change in percentiles of BMI_{adj} was estimated using quantile regression. Quantile regression models the relationship of the explanatory variables

with a given percentile of the outcome variable, in contrast with linear regression where the relationship with the mean of the outcome is modelled. Unlike linear regression, quantile regression allows us to investigate intergenerational change at specific points along the BMI_{adj} distribution. To illustrate the contribution of familial BMI to the BMI_{adj} distribution in the offspring generation, probability densities were estimated for offspring of normal weight and overweight parents.

Parent-offspring correlations in BMI were estimated from multilevel linear regression models. The standardised residuals from the models used to generate BMI_{adj}, as defined above, were denoted BMI-SDS (BMI standard deviation score). Multilevel models were fitted for BMI-SDS across all family members with separate family-level random intercepts for each family member group (pooled as parents and offspring or separated into mothers, fathers, daughters and sons). Within-family correlations were estimated as the correlation matrix of random intercepts.

The first model fitted assumed a common correlation between parents and offspring. Subsequent models assumed correlations to be sex-specific at the parental level (i.e. separate mother-offspring and father-offspring correlations), at the offspring level (separate parent-daughter and parent-son correlations) and at both levels (four separate correlation coefficients). When adjusting for potential confounders, missing social class for 68 subjects and missing number of children for two subjects were imputed using multiple imputation by additive regression. Statistical analyses were performed using the software packages MLwiN version 1.1[13] and R version 2.10.0[14] with packages Hmisc and quantreg[15]. Multiple imputation was performed using the aregImpute R function[16].

Results

Descriptive

5172 subjects were included, comprising 1443 sets of parents, 1263 daughters and 1023 sons. Table 1 allows intergenerational comparison between equivalent age cohorts by showing mean BMI and obesity prevalence divided into 5-year age bands. The mean (SD) parity was 2.9 (1.7) among the parents and 2.2 (0.9) among the 82% of offspring who were themselves parents. All the parents were married compared with 78% of the offspring. Parents were more likely to be current smokers (49% *vs* 25%) and manual social class (61% *vs* 31%) compared with offspring. Web table 1 describes the nonparticipants, both those living locally and those who migrated; there were no differences in parental BMI between participants and non-participants.

Intergenerational change in BMI distribution

The distribution of BMI_{adj} differed between generations in a number of ways (Table 2, Figure 1). Mean BMI_{adj} was 0.6 kg/m^2 (95% CI 0.3 to 0.9) higher in sons than in fathers, while mothers and daughters did not differ significantly. However median BMI_{adj} did not differ between generations in males, and decreased from mothers to daughters by 0.4 kg/m^2 (95% CI 0.0 to 0.7), suggesting that differences at the extremes of the distributions may be driving the difference between the means in males. Variance in BMI_{adj} increased across generations by 43% in females and 53% in males. In females the distribution of BMI_{adj} spread in both directions, less at the lower end but far more at the extreme upper end, while among males, the lower end and centre of the BMI_{adj} distribution were comparatively static across generations, while the upper end had increased. Since the age effect differed between generations in both sexes (Web Figure 1), the relatively small intergenerational changes detected in the

centre of the distribution (but not the larger increases observed in the upper tail) were sensitive to the choice of 50 years as the age to which to adjust BMI_{adj} (supplementary material).

Familial influences on obesity and BMI

The prevalence of obesity among offspring of normal weight parents (midparental BMI < 25 kg/m^2) was 9%, compared with 24% among the children of overweight and obese parents (midparental BMI ≥ 25 kg/m^2). Intra-familial correlations in BMI are reported in Table 3, derived from multilevel models of BMI-SDS. The parent-offspring correlation was 0.26 (95% CI: 0.23, 0.29). There was no difference between parent-daughter and parent-son correlations (p=0.423), suggesting that parental BMI predicts sons' and daughters' BMI equally well. There was strong evidence for a difference between mother-offspring and father-offspring correlations (p=0.016). However, this effect appears to be specific to daughters (p=0.001 for interaction): a mother's BMI is a better predictor than the father's BMI of their daughter's BMI. Maternal overweight and obesity is associated with a greater rightwards spread in the distribution of daughters' BMI than is paternal overweight and obesity (Figure 2). For sons, there is no evidence of a difference in correlation with mothers' and fathers' BMI (p=0.944): both parents' BMI is equally good at predicting their son's BMI (Web Figure 3).

We hypothesised that propensity for weight gain following childbirth might have contributed to the asymmetry between father-daughter and mother-daughter correlations. To test if parity had a role in weakening the father-daughter relative to the mother-daughter BMI correlation, we re-estimated the correlation coefficients in

Table 3 splitting daughters into those with (N=1065) and without children (N=198). The correlation (95% CI) between fathers and daughters with at least one child remained low at 0.18 (0.12, 0.24), while the correlation with childless daughters was 0.23 (0.11, 0.36), slightly closer to the mother-daughter correlation. There was no significant difference between these correlations (p=0.438), and therefore no evidence for a role for parity, although the wide confidence interval for the difference (-0.08, 0.19) suggests that this test has little power due to the low number of non-parous daughters.

Non-paternity would weaken the portion of father-offspring correlation that is due to shared genetic factors, and therefore could have contributed to the relatively weak father offspring correlations that we have observed. We investigated the impact of non-paternity by adjusting the correlations between mothers, fathers, daughters and sons under highly conservative assumptions of a 15% non-paternity rate and 100% of the father-offspring correlation being genetic[17 18]: the strength of the interaction was not substantially reduced (unadjusted p=0.001, adjusted p=0.003).

Discussion

This study adds to our understanding of the obesity epidemic in three ways. Firstly, it shows a pattern of changing adult body mass within one generation, characterised by the threshold defining the most overweight 5% of the population shifting substantially upwards (2-3 kg/m^2), while the middle and lower portions of the distribution changed little (<1 kg/m^2). Secondly, examination of familial influences on BMI showed that although both parents' BMI have an association with offspring adult BMI, maternal BMI is the significantly stronger influence on daughters' adult BMI, whereas both

parents influence sons' adult BMI equally. Finally, there is a very high prevalence of obesity among adult offspring from overweight and obese parents compared with offspring of normal weight parents (24% vs 9%).

The change in BMI distribution in this study confirms the findings of comparisons of population based cross-sectional studies[19 20]: BMI has not increased evenly across the population as a whole, but rather there has been a sharp increase in BMI at the upper tail of the distribution. Broadly, the proportion of the population with normal BMI is unchanged, while a decrease in overweightness is matched by a corresponding increase in obesity. This pattern contradicts Rose's paradigm[21] of rising obesity driven by a rightward shift in the entire distribution, but agrees with recent US cross-sectional surveys[3] that suggest a "landslip" effect (Figure 1), where the overweight are being replaced by the obese, but there is no corresponding recruitment into the overweight cohort from those of normal weight.

The upward spread of the BMI distribution does not in itself imply that the increase is concentrated among the most overweight families. Detection of such a trend is complicated by regression to the mean, which predicts that the most overweight parents will tend to have less overweight offspring[22]. However, purely artefactual regression to the mean predicts stable variance across generations, while a genuine tendency to divergence predicts increasing variance[23], as observed here. Thus the upward spread of the BMI distribution over one generation, coupled with the positive parent-offspring correlation, is consistent with the increase in BMI being disproportionately among the adult offspring of heavier parents.

The sex-specific correlations observed here point to a substantial influence of shared family environment on BMI, because no known genetic mechanism explains daughters inheriting their BMI preferentially from their mothers. Relatively strong mother-daughter BMI correlations (in this case relative to mother-son rather than father-daughter correlations) were also found in a recent analysis of 4654 seven-year-old children in the large ALSPAC cohort[6].Another recent study of 226 children aged 5-8 years in the EarlyBird cohort[5] found both same-sex parent-offspring correlations in BMI (i.e. both mother-daughter and father-son) but no significant opposite sex correlations. We note that the EarlyBird analysis did not test for a difference between same-sex and opposite-sex correlations, as was done here and in the ALSPAC study, so the failure to find opposite sex correlations may have been a consequence of small sample size rather than an indication of sex-specific inheritance. Nevertheless, BMI category of same-sex parents was a better predictor of offspring BMI than that of opposite sex parents[5]. In our analysis we have also adjusted for potential confounders within both the parents and offspring, such as smoking, marital and socioeconomic status, and number of children. We saw no difference for parental effect on sons' BMI while daughters' were more strongly influenced by mothers' BMI than fathers', and this difference was not explained by parity; however both parents' BMI did have an effect on offspring BMI regardless of sex. Taken together, these data are consistent with a model in which familial influences on daughters' BMI are predominantly maternal in both young childhood and middle age, while familial influences on sons' BMI is likely shared equally between both parents during childhood and middle age.

It is widely accepted that parental BMI is related to offspring BMI[24]. Twin studies have found BMI to be highly heritable[25 26] even in studies conducted during the obesity epidemic[27], with a small environmental effect. However, genetics and environment are closely linked in obesity; known obesity genes are thought to increase susceptibility to obesity through control of food intake and food choice [28 29], hence why obesity has increased far faster than a genetic change would allow, as the environment has changed. As women tend to do the majority of shopping and cooking within a family, they have a strong influence over their children's diet; if they are expressing their genotype by choosing high fat foods to feed the family, this may explain why the mothers' influence is stronger. In this study however the offspring were adults and there was no sex specificity over the sons' BMI; possible reasons for this may include the influence of spouses on food provision and the influence of fathers on sons' participation in sports and exercise. These results fit with the previous findings in this cohort that parental socioeconomic position is more strongly associated with offspring obesity in women than men[7 9 30]; there is a well described socioeconomic gradient of environmental factors such as food choice and availability that could be linked with increased obesity[31 32].

Strengths and limitations

The main strength of this study, in addition to the large sample size and the availability of data on potential confounding factors, is the availability of adult offspring. This unusual aspect of the study allowed familial influences on BMI to be examined at the time when adiposity most often becomes clinically relevant. Another strength is the positioning of the two generations on either side of a period of rapid increase in obesity. However, environmental influences on obesity are likely to have

worsened further since 1996, so further research would be required to discover if the intergenerational patterns we have detected also apply to adults who are currently middle-aged. Other than that men were less likely to participate than females, no biases were found as a result of local offspring not participating in the study. There is a bias in the local eligible population towards the offspring of parents of manual social class and, possibly consequentially, mothers with higher BMI. If the trends in parental-offspring BMI correlations were similar in migrants and participants this BMI difference may have biased the results towards a larger right-shift in the offspring BMI; however, the size of the BMI difference between migrants and participants means the effect size would be very low.

Conclusions

Over one generation, the heaviest parents within our study population have been replaced by still heavier adult offspring while BMI in the remainder of the population has remained relatively unchanged. Strong parent-offspring correlations in BMI, even when the offspring are themselves adults, suggest that a large part of this increase has occurred within the heaviest families, possibly due to a combination of environmental, gestational and genetic influences. Further, we have shown for the first time that mothers appear to more strongly influence daughters' risk of obesity in adulthood than do fathers, indicating an environmental component alongside genetic factors.

COI statement: The authors declare no conflicts of interest.

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Ethics: Not required at the time of the Midspan Renfrew Paisley Study. Approval for the Midspan Family Study was granted from both the Argyll and Clyde, and Greater Glasgow Health Board Local Research Ethics Committees.

All authors contributed to the design of the study. PJ and AMcC analysed the data. PJ and JL wrote the first draft of the manuscript. All authors contributed to the redrafting of the manuscript and approved the final version. GW is the guarantor.

PJ and AMcC had full access to the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. The other authors had full access to all of the results.

Reference List

1 Government Office for Science. Foresight. Tackling obesities: future choices. 2010 Oct 17.

2 Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006 Apr 5;**295**(13):1549-55.

3 Wang Y, Beydoun MA, Liang L, et al. Will all Americans become overweight or obese? estimating the progression and cost of the US obesity epidemic. *Obesity (Silver Spring)* 2008 Oct;**16**(10):2323-30.

4 Abu-Rmeileh NM, Hart CL, McConnachie A, et al. Contribution of Midparental BMI and other determinants of obesity in adult offspring. *Obesity (Silver Spring)* 2008 Jun;**16**(6):1388-93.

5 Perez-Pastor EM, Metcalf BS, Hosking J, et al. Assortative weight gain in mother-daughter and father-son pairs: an emerging source of childhood obesity. Longitudinal study of trios (EarlyBird 43). *Int J Obes (Lond)* 2009 Jul;**33**(7):727-35.

6 Leary S, Davey SG, Ness A. No evidence of large differences in mother-daughter and father-son body mass index concordance in a large UK birth cohort. *Int J Obes (Lond)* 2010 Jul;**34**(7):1191-2.

7 Hawthorne VM, Watt GC, Hart CL, et al. Cardiorespiratory disease in men and women in urban Scotland: baseline characteristics of the Renfrew/Paisley (midspan) study population. *Scott Med J* 1995 Aug;**40**(4):102-7.

8 Upton MN, McConnachie A, McSharry C, et al. Intergenerational 20 year trends in the prevalence of asthma and hay fever in adults: the Midspan family study surveys of parents and offspring. *BMJ* 2000 Jul 8;**321**(7253):88-92.

9 Hart C, McConnachie A, Upton M, et al. Risk factors in the Midspan family study by social class in childhood and adulthood. *Int J Epidemiol* 2008 Jun;**37**(3):604-14.

10 General Register Office. Classification of occupations 1966.London: HMSO, 1966. p. 1-148.

11 General Register Office. Classification of Occupations 1990.London: HMSO, 1990.

12 Silverman BW. *Density Estimation*. Chapman and Hall, 1986.

13 Rasbash J, Brown W, Healy M, et al. MLwiN Version 1.1. Multilevel Models Project. 2011.

14 R Development Core Team. R: A language and environment for statistical computing. 2009.

15 Roger Koenker. quantreg: Quantile Regression. R package version 4.50. 2010.

16 Harrell Jr FE. Hmisc: Harrell Miscellaneous. R package version 3.7-0. 2009.

17 Clemons T. A look at the inheritance of height using regression toward the mean. *Hum Biol* 2000 Jun;**72**(3):447-54.

18 Davey SG, Steer C, Leary S, et al. Is there an intrauterine influence on obesity? Evidence from parent child associations in the Avon Longitudinal Study of Parents and Children (ALSPAC). *Arch Dis Child* 2007 Oct;**92**(10):876-80.

19 Flegal KM, Troiano RP. Changes in the distribution of body mass index of adults and children in the US population. *Int J Obes Relat Metab Disord* 2000 Jul;**24**(7):807-18.

20 Micciolo R, Di F, V, Fantin F, et al. Prevalence of overweight and obesity in Italy (2001-2008): is there a rising obesity epidemic? *Ann Epidemiol* 2010 Apr;**20**(4):258-64.

21 Rose G, Khaw KT, Marmot M. *Rose's Strategy of Preventative Medicine*. Revised Edition ed. Oxford University Press, 2008.

22 Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol* 2005 Feb;**34**(1):215-20.

23 Hotelling H. Review of The triumph of mediocrity in business. *Journal of the American Statistical Association* 1933;**28**:463-5.

24 Davey SG, Sterne JA, Fraser A, et al. The association between BMI and mortality using offspring BMI as an indicator of own BMI: large intergenerational mortality study. *BMJ* 2009;**339**:b5043.

25 Herskind AM, McGue M, Sorensen TI, et al. Sex and age specific assessment of genetic and environmental influences on body mass index in twins. *Int J Obes Relat Metab Disord* 1996 Feb;**20**(2):106-13.

26 Stunkard AJ, Harris JR, Pedersen NL, et al. The body-mass index of twins who have been reared apart. *N Engl J Med* 1990 May 24;**322**(21):1483-7.

27 Wardle J, Carnell S, Haworth CM, et al. Evidence for a strong genetic influence on childhood adiposity despite the force of the obesogenic environment. *Am J Clin Nutr* 2008 Feb;**87**(2):398-404.

28 Cecil JE, Tavendale R, Watt P, et al. An obesity-associated FTO gene variant and increased energy intake in children. *N Engl J Med* 2008 Dec 11;**359**(24):2558-66.

29 Bauer F, Elbers CC, Adan RA, et al. Obesity genes identified in genome-wide association studies are associated with adiposity measures and potentially with nutrient-specific food preference. *Am J Clin Nutr* 2009 Oct;**90**(4):951-9.

30 Power C, Graham H, Due P, et al. The contribution of childhood and adult socioeconomic position to adult obesity and smoking behaviour: an international comparison. *Int J Epidemiol* 2005 Apr;**34**(2):335-44.

31 Shelton NJ. What not to eat: inequalities in healthy eating behaviour, evidence from the 1998 Scottish Health Survey. *J Public Health (Oxf)* 2005 Mar;**27**(1):36-44.

32 Macdonald L, Cummins S, Macintyre S. Neighbourhood fast food environment and area deprivation-substitution or concentration? *Appetite* 2007 Jul;**49**(1):251-4.

Figure Legends

Figure 1. Estimated probability densities of adjusted BMI for parents (including those with no same-sex offspring) and offspring, separately for males and females.

Figure 2. Probability density plots of adjusted BMI in daughters of normal weight and overweight fathers and mothers. Percentiles are indicated by vertical lines.

Web Figure 1. Predicted average BMI given age (black line) ± SE (grey line), in mothers, fathers, daughters and sons. BMI was predicted from a model in which log(BMI) was dependent on age (modelled as a 3rd-order polynomial), married status (married, not married), number of children (none, 1, 2, 3, ≥ 4), smoking status (never, former, current) and social class (manual, non-manual). Predictions were adjusted to a married never-smoker with two children and mean social class (averaged across all subjects). The age-BMI association is also represented by a LOESS smoothing line (thin black line).

Web Figure 2. Predicted average BMI given married status, smoking habits, social class and number of children. Predictions were adjusted as in Web Figure 1 for a 50-year-old subject.

Web Figure 3. Probability density plots of adjusted BMI in sons of normal weight and overweight fathers and mothers. Percentiles are indicated by vertical lines.

Table 1. Mean (SD) BMI and obesity prevalence by 5-year age bands in Midspan Family Study offspring and parents, and in 12,435 participants in the original Renfrew/Paisley Study who were not parents of Midspan Family Study offspring and for whom BMI was available.

			Age (years)							
			All	30-34	35-39	40-44	45-49	50-54	55-59	60-64
Female	N	Daughters	1263	57	170	333	398	219	86	0
		Mothers	1443	0	0	0	436	516	314	177
		Renfrew/Paisley	6866	0	0	0	1585	1764	1723	1794
	Mean (SD) BMI (kg/m^2)	Daughters	25.9 (5.0)	25.5 (6.1)	25.6 (5.2)	25.6 (4.7)	26.2 (4.9)	25.7 (4.9)	26.7 (5.1)	-
		Mothers	25.9 (4.3)	-	-	-	25.4 (4.0)	25.5 (4.2)	26.8 (4.6)	26.8 (4.7)
		Renfrew/Paisley	25.7 (4.5)	-	-	-	25.2 (4.2)	25.4 (4.3)	25.7 (4.6)	26.5 (4.9)
	N (%) Obese (BMI ≥ 30 kg/m^2)	Daughters	229 (18.1%)	12 (21.1%)	33 (19.4%)	63 (18.9%)	68 (17.1%)	37 (16.9%)	16 (18.6%)	-
		Mothers	215 (14.9%)	-	-	-	58 (13.3%)	65 (12.6%)	66 (21.0%)	26 (14.7%)
		Renfrew/Paisley	1042 (15.2%)	-	-	-	188 (11.9%)	228 (12.9%)	265 (15.4%)	361 (20.1%)
Male	N	Sons	1023	56	157	263	317	168	62	0
		Fathers	1443	0	0	0	212	514	385	332
		Renfrew/Paisley	5571	0	0	0	1597	1452	1290	1232
	Mean (SD) BMI (kg/m^2)	Sons	26.5 (4.0)	25.8 (3.9)	25.8 (3.6)	26.5 (4.1)	27.0 (4.2)	26.8 (4.1)	25.9 (3.5)	-
		Fathers	26.0 (3.3)	-	-	-	25.8 (2.6)	26.2 (3.4)	26.0 (3.3)	25.8 (3.5)
		Renfrew/Paisley	25.8 (3.4)	-	-	-	25.9 (3.4)	25.9 (3.5)	25.8 (3.4)	25.8 (3.4)
	N (%) Obese (BMI ≥ 30 kg/m^2)	Sons	183 (17.9%)	9 (16.1%)	16 (10.2%)	48 (18.3%)	72 (22.7%)	29 (17.3%)	9 (14.5%)	-
		Fathers	161 (11.2%)	-	-	-	11 (5.2%)	69 (13.4%)	39 (10.1%)	42 (12.7%)
		Renfrew/Paisley	590 (10.6%)	-	-	-	168 (10.5%)	169 (11.6%)	130 (10.1%)	123 (10.0%)

Table 2. Intergenerational change in characteristics of the distributions of BMI_{adj} in females and males.

		Parent	Offspring	Difference (95% CI)	P-value
Female	N	1443	1263		
	Mean	26.3	26.4	0.2 (-0.2, 0.5)	0.380
	Variance	17.5	24.8	7.3 (5.0, 9.7)	<0.001
	5% percentile	20.5	20.0	-0.5 (-1.0, 0.0)	0.035
	25% percentile (Q1)	23.4	22.9	-0.4 (-0.8, -0.1)	0.021
	50% percentile (median)	25.8	25.5	-0.4 (-0.7, 0.0)	0.039
	75% percentile (Q3)	28.5	28.8	0.3 (-0.2, 0.9)	0.256
	95% percentile	33.5	36.1	2.7 (1.4, 3.9)	<0.001
Male	N	1443	1023		
	Mean	26.6	27.2	0.6 (0.3, 0.9)	<0.001
	Variance	10.7	16.3	5.6 (4.0, 7.2)	<0.001
	5% percentile	21.3	21.4	0.0 (-0.5, 0.6)	0.875
	25% percentile (Q1)	24.5	24.5	0.0 (-0.3, 0.3)	0.998
	50% percentile (median)	26.5	26.6	0.1 (-0.2, 0.5)	0.451
	75% percentile (Q3)	28.6	29.4	0.8 (0.4, 1.3)	0.001
	95% percentile	32.1	34.2	2.2 (1.1, 3.2)	<0.001

Table 3. Correlations (and 95% confidence intervals) between parent and offspring BMI, estimated from multilevel models where the response was BMI-SDS, and family relationships (mother, father, daughter and son) were fitted as random effects.

		Offspring			Daughter-son difference p-value
		Sons and daughters	Daughter	Son	
Parent	Mother and father	0.26 (0.23, 0.29)	0.25 (0.22, 0.29)	0.28 (0.24, 0.32)	0.423
	Mother	0.30 (0.26, 0.34)	0.31 (0.27, 0.36)	0.28 (0.22, 0.33)	
	Father	0.23 (0.19, 0.27)	0.19 (0.14, 0.25)	0.27 (0.22, 0.33)	
	Mother-father difference p-value	0.016	0.001	0.944	

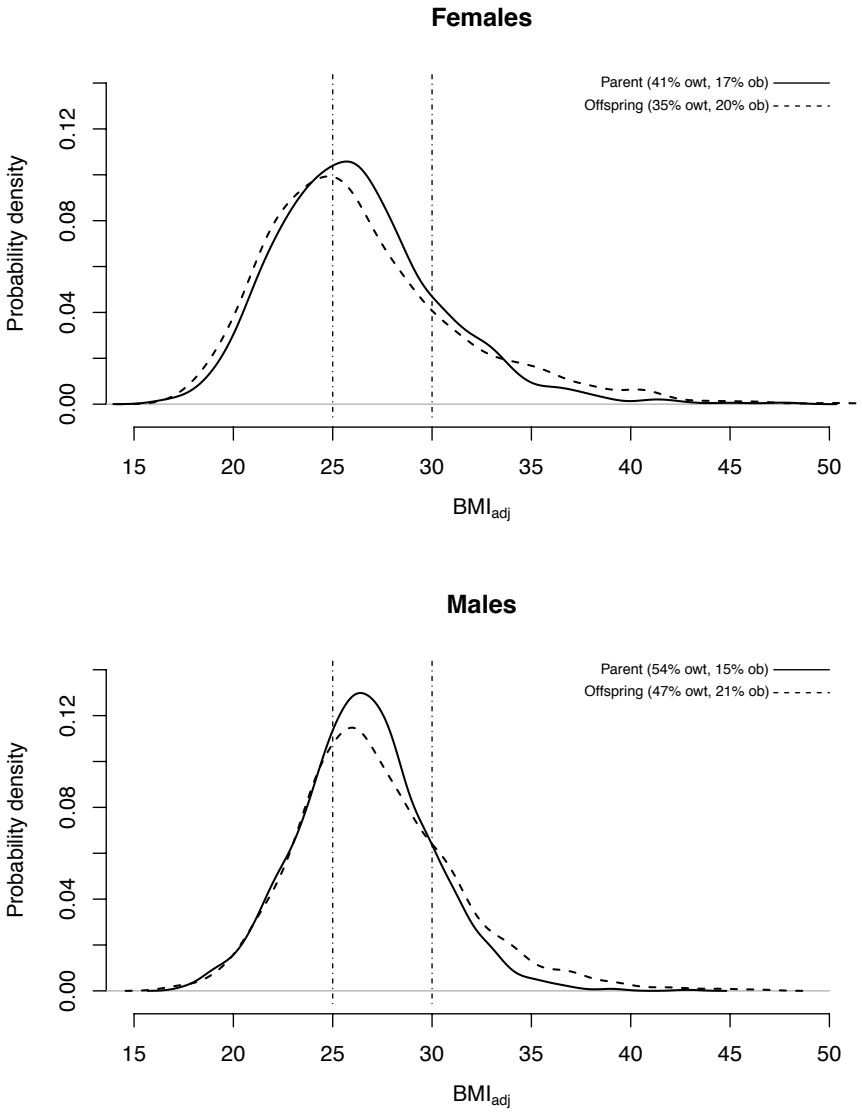

Females
Parent (41% owt, 17% ob)
Offspring (35% owt, 20% ob)
Probability density
0.00
0.04
0.08
0.12
15
20
25
30
35
40
45
50
BMI$_{adj}$
Males
Parent (54% owt, 15% ob)
Offspring (47% owt, 21% ob)
Probability density
0.00
0.04
0.08
0.12
15
20
25
30
35
40
45
50
BMI$_{adj}$

Figure 1

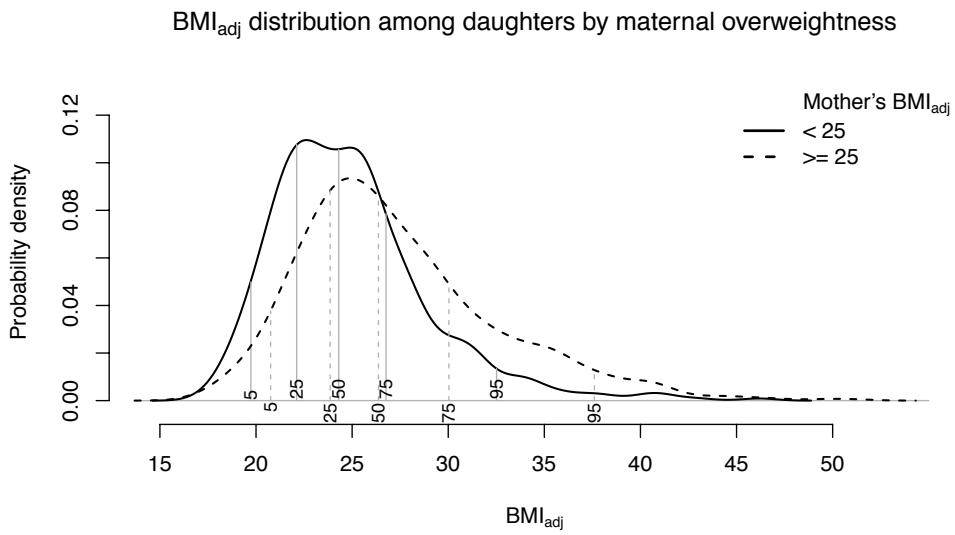

BMIadj distribution among daughters by maternal overweightness
Mother's BMIadj
< 25
>= 25
Probability density
0.00
0.04
0.08
0.12
5
5
25
25
50
50
75
75
95
95
15
20
25
30
35
40
45
50
BMIadj

Figure 2 (top)

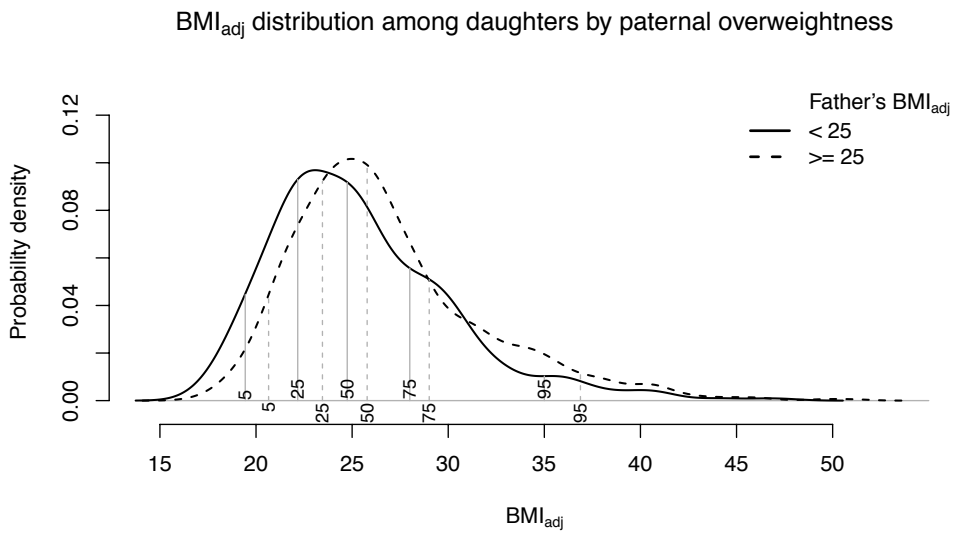
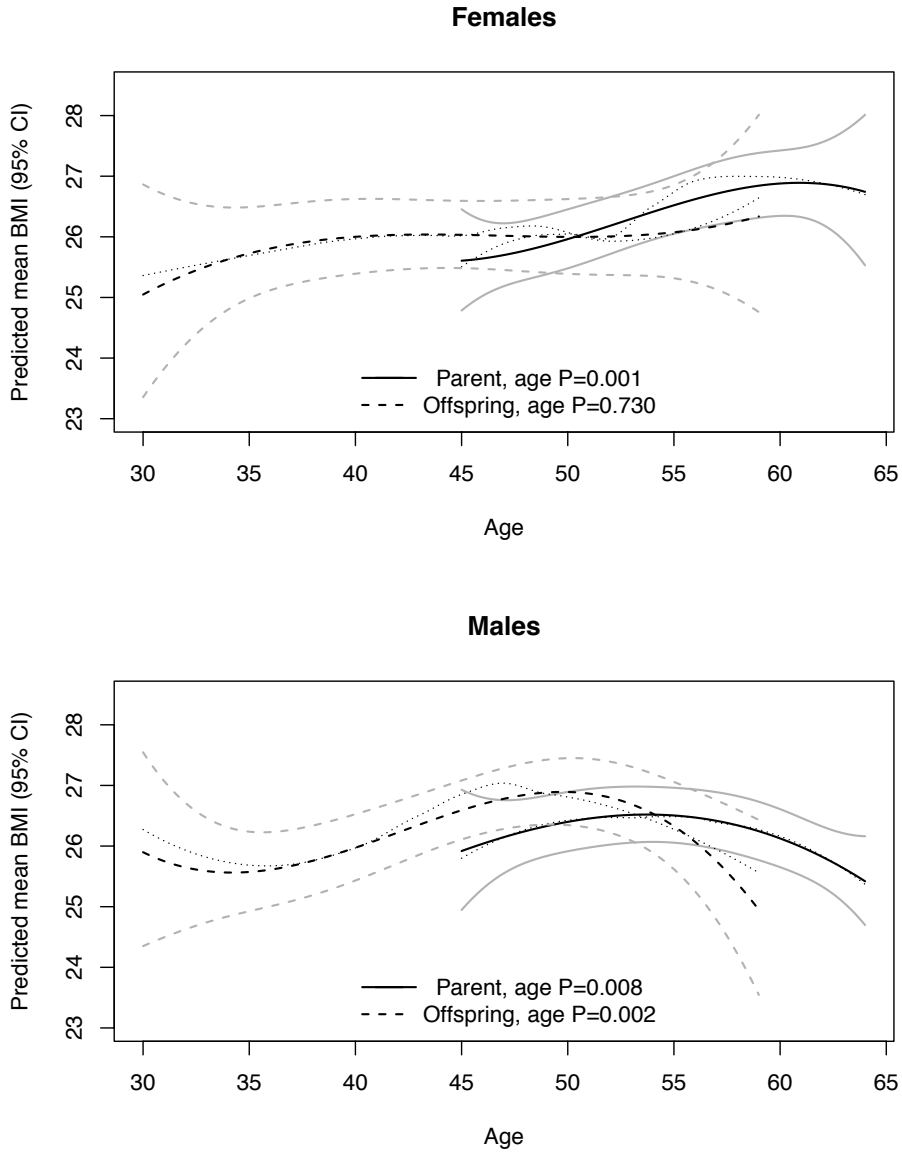
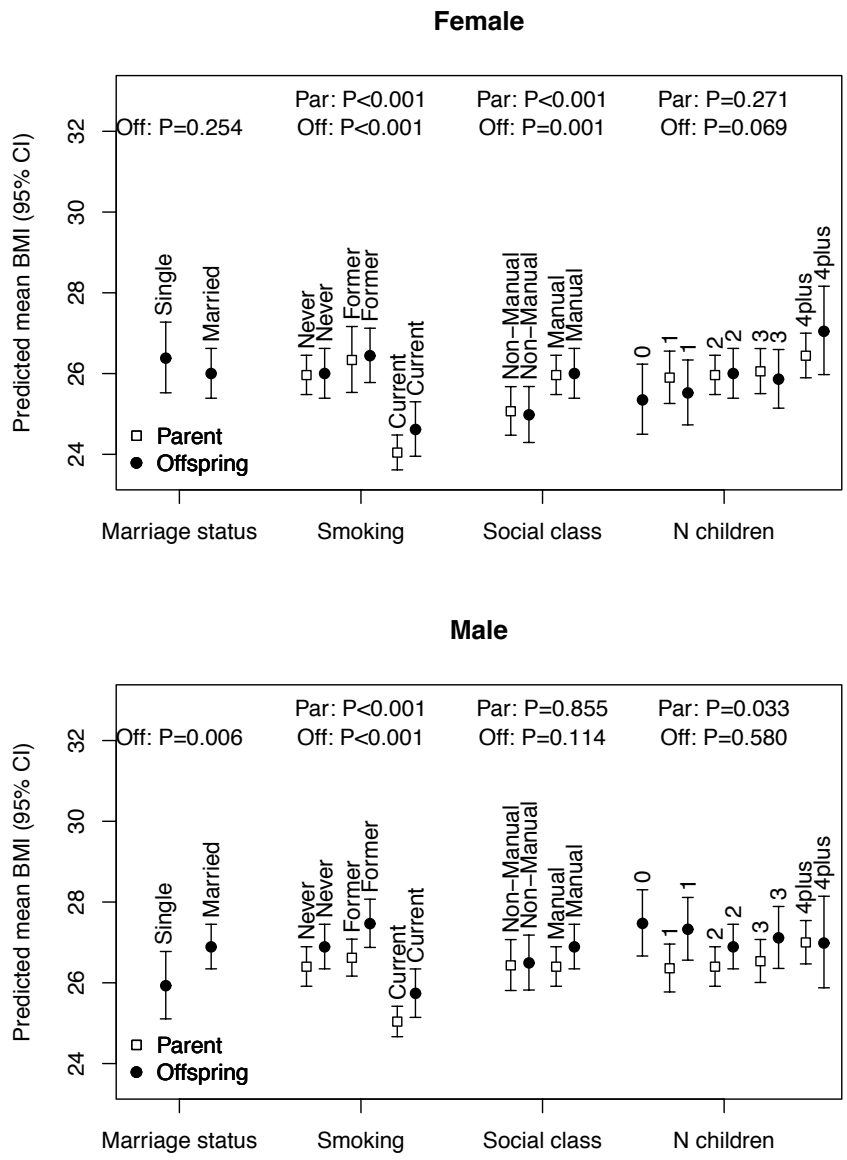


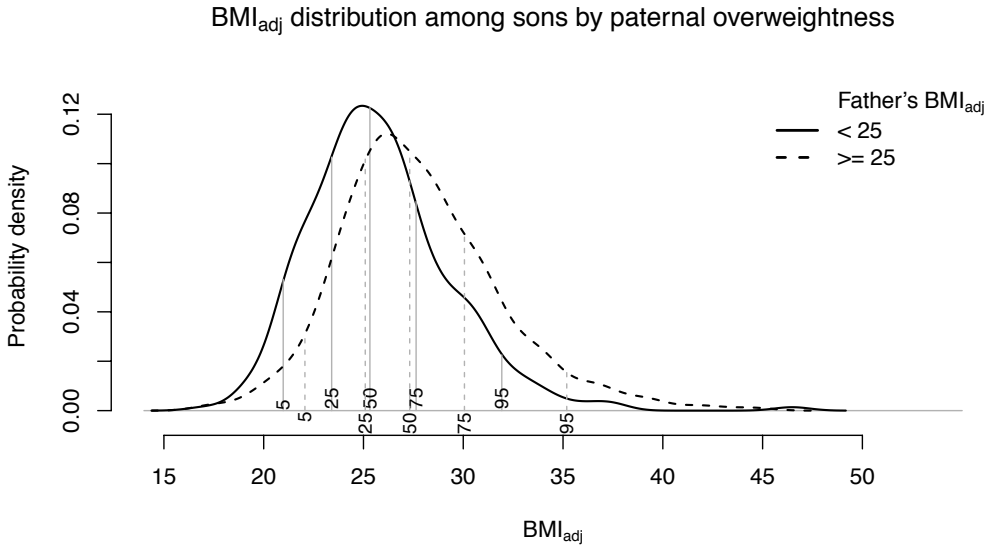
Figure 2 (bottom)


Females
Predicted mean BMI (95% CI)
23
24
25
26
27
28
30
35
40
45
50
55
60
65
Age
Parent, age P=0.001
Offspring, age P=0.730
Males
Predicted mean BMI (95% CI)
23
24
25
26
27
28
30
35
40
45
50
55
60
65
Age
Parent, age P=0.008
Offspring, age P=0.002

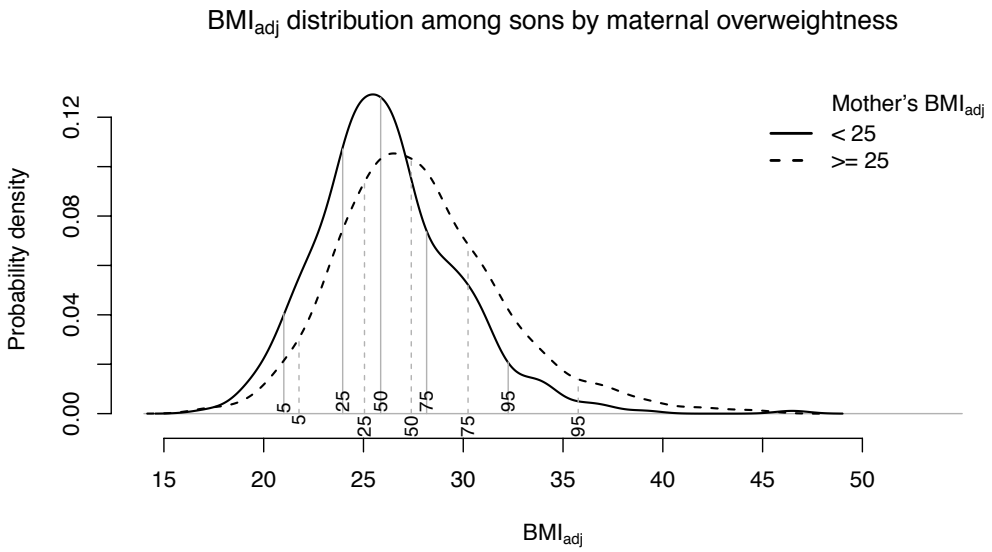
Web Figure 1


Female
Par: P<0.001
Off: P<0.001
Par: P<0.001
Off: P=0.001
Par: P=0.271
Off: P=0.069
Off: P=0.254
Predicted mean BMI (95% CI)
24
26
28
30
32
Single
Married
Never
Never
Former
Former
Current
Current
Non−Manual
Non−Manual
Manual
Manual
0
1
1
2
2
3
3
4plus
4plus
Parent
Offspring
Marriage status
Smoking
Social class
N children
Male
Par: P<0.001
Off: P<0.001
Par: P=0.855
Off: P=0.114
Par: P=0.033
Off: P=0.580
Off: P=0.006
Predicted mean BMI (95% CI)
24
26
28
30
32
Single
Married
Never
Never
Former
Former
Current
Current
Non−Manual
Non−Manual
Manual
Manual
0
1
1
2
2
3
3
4plus
4plus
Parent
Offspring
Marriage status
Smoking
Social class
N children

Web Figure 2



Web Figure 3 (top)



Web Figure 3 (bottom)

Web Table 1. Characteristics of 4560 participant and non-participant offspring, with tests for migration bias (comparing local and migrant offspring) and response bias (comparing local participants and local non-participants). Differences in prevalence were tested using χ^2 tests and differences in means were tested using two sample t-tests.

		Local participant	Local non-participant	Migrant non-participant	$N_{MISSING}$	Migration bias P-value	Response bias P-value
N		2338	864	1358			
Sex	N (%) Male	1040 (44.5%)	475 (55.0%)	699 (51.5%)	0	0.010	<0.001
Age (years)	Mean (SD)	45.0 (6.2)	45.0 (6.8)	45.2 (6.2)	0	0.423	0.846
Maternal BMI (kg/m^2)	Mean (SD)	26.0 (4.4)	26.1 (4.5)	25.6 (4.3)	7	0.001	0.473
Paternal BMI (kg/m^2)	Mean (SD)	26.0 (3.3)	26.0 (3.5)	25.9 (3.2)	4	0.300	0.958
Maternal social class	N (%) Manual	1306 (57.8%)	493 (59.8%)	658 (50.5%)	174	<0.001	0.339
Paternal social class	N (%) Manual	1594 (68.9%)	606 (71.1%)	835 (61.9%)	43	<0.001	0.218

Supplementary Information

Sensitivity analysis for choice of age adjustment

Since the age effect differed between generations in both sexes (Web Figure 1), intergenerational comparisons were sensitive to the choice of 50 years as the age to which to adjust BMI_{adj}. Adjusting instead to 45 years had very little effect on intergenerational differences in male BMI_{adj} distribution, as might be expected by the fact that the age-BMI relationship in males is parallel across this age range (Web Figure 1). However, because there is a positive age effect in the mothers but none in the daughters, reducing the adjustment age to 45 years drew the mothers' distribution down to make the pattern of intergenerational change match closely to that of the fathers: no change in the left hand side of the distribution and a rightward stretch in the right hand side. Adjusting to 55 years had the opposite effect of shifting the BMI_{adj} distributions of both sons and daughters to the left, but not enough to counteract the stretching out of the upper tail. For all three adjustment ages the 95^{th} percentile for BMI was significantly higher in offspring than in parents.