**Modifiable early life risk factors for childhood adiposity and overweight: an analysis of their combined impact and potential for prevention**

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**Running head:** Early life risk factors for childhood obesity

**Abbreviations used:** BMI, body mass index; DXA, dual-energy X-ray absorptiometry; FFQ, food frequency questionnaire; IOTF, International Obesity Task Force; SWS, Southampton Women’s Survey.

**Key words:** childhood obesity, adiposity, early life

**ABSTRACT**

**Background:** Early life may be a ‘critical period’ when appetite and regulation of energy balance are programmed, with lifelong consequences for obesity risk. Insight into the potential impact of modifying early life risk factors on later obesity can be gained by evaluating their combined effects.

**Objective:** To examine the relationship between number of early life risk factors and obesity outcomes among children in a prospective birth cohort (Southampton Women’s Survey).

**Design:** Five risk factors were defined: maternal obesity (pre-pregnant body mass index (BMI) >30kg/m2), excess gestational weight gain (Institute of Medicine, 2009), smoking during pregnancy, low maternal vitamin D status (<64 nmol/l), short duration of breastfeeding (none or < 1 month). Obesity outcomes examined when the children were aged 4 and 6 years were: BMI, dual-energy X-ray absorptiometry-assessed fat mass, overweight or obesity (International Obesity Task Force). Data were available for 991 mother-child pairs, born between 1998 and 2003.

**Results:** 148 (15%) of the children had no early life risk factors, 330 (33%) had one, 296 (30%) had two, 160 (16%) had three, and 57 (6%) had four or five. At both 4 and 6 years, there were positive graded associations between number of early life risk factors and each obesity outcome (all P<0.001). After taking account of confounders, the relative risk of being overweight or obese for children who had 4 or 5 risk factors was 3.99 (95% CI 1.83,8.67) at 4 years and 4.65 (95% CI 2.29,9.43) at 6 years, when compared with children who had none (both P<0.001).

**Conclusions:** Having a greater number of early life risk factors was associated with large differences in adiposity and risk of overweight and obesity in later childhood. These findings suggest that early intervention to change these modifiable risk factors could make a significant contribution to the prevention of childhood obesity.

**INTRODUCTION**

The rapid rise in prevalence of childhood obesity over recent years has prompted widespread research efforts to identify the factors that explain these secular changes [1,2]. However, although children grow up in more ‘obesogenic’ environments than in the past, not all children become overweight. Understanding how individuals interact with their environment, and how these interactions predispose some children to gain excess weight, are key issues in considering future preventive strategies [3]. There is particular interest in understanding the role of environmental factors in early life, as prenatal and early postnatal life may be ‘critical periods’ when appetite and the long-term regulation of energy balance are permanently programmed - with lifelong consequences for risk of excess weight gain [4,5].

A number of early life risk factors have been identified, that include maternal obesity, excess gestational weight gain, smoking in pregnancy and short duration of breastfeeding [3,5,6,7]. These factors are often socially patterned, and they co-exist. For example, excess gestational weight gain and shorter duration of breastfeeding are more common in obese mothers [7-9]. The clustering of risk factors has been used as the basis of scoring algorithms, with a view to identifying individual children, for whom targeted preventive interventions may be appropriate. In an analysis of data from Europe and the United States, Morandi et al showed the best predictors of childhood obesity were parental body mass index (BMI), birth weight, smoking in pregnancy, number of household members and maternal occupation [10], whilst in analyses of data from the Millenium cohort in the United Kingdom (UK), the risk factors used were child’s gender, parental BMI, birth weight, smoking in pregnancy, infant weight gain and breastfeeding status [11]. But to understand the potential public health impact, the combined effects of modifiable factors must be evaluated. This approach was first used in Project Viva, where Gillman and colleagues showed that preschool children, whose mothers had excess gestational weight gain and smoked in pregnancy, who were breastfed for less than 12 months and who slept for less than 12 hours per day in infancy, had a predicted obesity prevalence (BMI >95th centile) of 29%, compared with 6% of children who had none of these risk factors [12]. Importantly, these marked differences have been shown to persist (28% vs 4%) in later childhood, when the children were aged 7 to 10 years [13].

BMI is a surrogate marker for adiposity and, to our knowledge, the combined effects of early modifiable risk factors on direct measures of adiposity in childhood have not been evaluated. Using data from a UK birth cohort, we examine the role of five factors acting in prenatal and early postnatal life. We chose factors that have been shown to be independent predictors of greater adiposity in children either in this cohort or in other studies, and that are potentially modifiable through behaviour change interventions: maternal obesity before pregnancy [14,15], excess gestational weight gain [7,16], maternal smoking in pregnancy [6], low vitamin D status in pregnancy [17,18], and short duration of breastfeeding [19,20,21]. We examine their combined effects in relation to three outcomes determined at 4 and 6 years of age: BMI, adiposity (DXA-assessed fat mass) and overweight or obesity (defined according to the International Obesity Task Force (IOTF)) BMI cut-offs [22]).

**SUBJECTS AND METHODS**

**The Southampton Women’s Survey**

The Southampton Women’s Survey (SWS) is a prospective birth cohort in which the diet, body composition, physical activity and social circumstances of a general population sample of non-pregnant women, aged 20 to 34 years, living in Southampton, were characterised. Detail of the study has been published previously [23]. Women were recruited through General Practices across the city between April 1998 and December 2002. Each woman was invited to take part by letter, followed by a telephone call, when an interview date was arranged. 12,583 women agreed, representing 75% of all women contacted. Trained research nurses visited each woman at home and collected information about her health, diet and lifestyle, as well as taking anthropometric measurements. Women who subsequently became pregnant were followed throughout pregnancy; detailed interviews were conducted at 11 and 34 weeks’ gestation. The growth and development of the SWS children have been assessed at a number of stages in infancy and childhood, and continued follow-up is ongoing. The SWS was approved by the Southampton and South West Hampshire Local Research Ethics Committee (307/97, 153/99w, 005/03/t and 06/Q1702/104); written informed consent was obtained from all participants.

**Maternal data**

Details of the mothers’ sociodemographic background were obtained during the pre-pregnant interviews; educational attainment was categorised in six groups according to highest academic qualification obtained (increasing from none to university degree or higher). Height was measured with a portable stadiometer (Harpenden; CMS Weighing Equipment Ltd, London, UK) to the nearest 0.1 cm with the head in the Frankfort plane. Weight was measured with calibrated electronic scales (Seca, Hamburg, Germany) to the nearest 0.1 kg (after removal of shoes and heavy clothing or jewellery). These measurements were used to calculate BMI (kg/m2). Amongst women who became pregnant, smoking status in pregnancy was ascertained at the 11- and 34-week interviews. At 34 weeks’ gestation, a venous blood sample was taken and an aliquot of maternal serum was frozen at -80°C. Serum 25-hydroxyvitamin D concentrations were analyzed by radioimmunoassay (Diasorin, Stillwater, Minnesota, USA). This assay measures both 25-hydroxyvitamin D2 and D3. The assay met the requirements of the UK National Vitamin D External Quality Assurance Scheme; intra-assay and inter-assay coefficients of variation were less than 10%. At 34 weeks, the research nurses weighed the women again; pregnancy weight gain from before pregnancy to 34 weeks’ gestation was defined as excessive according to the Institute of Medicine (IOM) 2009 recommendations [24], as described previously (weekly gains in 2nd and 3rd trimesters: more than 0.51 kg/week in underweight women, 0.42kg/week in normal weight women, 0.28kg/week in overweight women, or 0.22kg/week in obese women) [7]. Gestational age at birth was determined using a computerised algorithm based on menstrual data or, when these were uncertain (34% of women), with ultrasound assessment of fetal anthropometry in early pregnancy.

**Infancy and childhood data**

For infants who were breastfed, the date of the last breastfeed was recorded at 6, 12 or 24 months, and was used to define duration of breastfeeding. When the children reached 4 and 6 years of age, subsets were invited to have an assessment of body composition. Children’s height was measured using a Leicester height measurer (Seca Ltd., Birmingham, UK), and weight was measured using calibrated digital scales (Seca Ltd.). These data were used to calculate BMI at 4 and 6 years. Dual-energy X-ray Absorptiometry (DXA) using a Hologic Discovery instrument (Hologic Inc., Bedford, MA, USA) was used to assess body composition. Fat mass was derived from the whole body scan, using paediatric software. The total X-ray dose for the whole body scans was approximately 10.5 microsieverts (paediatric scan mode), equivalent to around 1-2 days background radiation. All scan results were checked independently by two trained operators, and agreement reached as to their acceptability; scans showing unacceptable movement artefact were excluded. Physical activity level at 4 years was determined according to the child’s average number of hours spent ‘on the move’ and time spent watching television each day, as reported by their parent [25]. Diet was assessed when the children were aged 3 and 6 years using an 80-item food frequency questionnaire (FFQ) [26,27]. In principal component analyses of the FFQ data, the first component at each age (that explains the greatest variance in the dietary data) described a ‘healthy’ dietary pattern, characterised by frequent consumption of fruit, vegetables and wholegrain cereals [26]. We called this a prudent dietary pattern to be consistent with other studies [28,29]. Prudent diet scores at 3 and 6 years of age were calculated using the prudent dietary pattern coefficients for every food/group on the FFQ and their reported frequency of consumption at the respective ages. The score describes compliance with the prudent dietary pattern, and was used as an indicator of the quality of the children’s diets at 3 and 6 years.

**Study population**

A total of 1981 women became pregnant and delivered a live-born singleton infant before the end of 2003. Six infants died in the neonatal period and two had major congenital growth abnormalities. Of the 1973 mother-offspring pairs who were available for follow-up, 121 mothers delivered before 37 weeks’ gestation and were excluded. A further 861 mother-child pairs were not included in the analysis as they did not have complete data either on outcome measurements (n=693 without BMI or fat mass at either 4 or 6 years of age) or on early life risk factors (n=168) . Data for the remaining 991 children are presented in this paper.

**Statistical analysis**

We selected five early life risk factors, on the basis of previous analyses from the cohort that showed they were independently associated with greater childhood adiposity (excess gestational weight gain [7], low vitamin D status [17], short duration of breastfeeding [20]), or were factors that have well-established links to obesity in children (maternal obesity [2,4,15], smoking in pregnancy [6]). They were defined as follows: maternal obesity before pregnancy (>30kg/m2), excess gestational weight gain (according to IOM categorisation [7]), smoking in pregnancy according to maternal report, low vitamin D status (<64nmol/L) as defined previously in this population [17], short duration of breastfeeding (never or less than one month). Age at introduction of solid foods was not considered as, consistent with recent systematic reviews [30,31], we have not found independent associations with adiposity in SWS children [20].

Children’s fat mass and BMI data were positively skewed at 4 and 6 years of age, and thus were log-transformed and converted to have a mean of 0 and a standard deviation of 1. All outcomes at 4 and 6 years were adjusted for sex and age at measurement, fat mass was also adjusted for height to ensure that any associations were independent of children’s stature. Overweight and obesity at 4 and 6 years of age were defined according to the International Obesity Task Force (IOTF) categorisation of BMI [22]. For BMI and fat mass outcomes, linear regression models were fitted with the risk factor score as a categorical predictor; zero risk factors was used as the baseline. To assess the effect of the trend in risk factor score, the same models were fitted but with risk factor as a continuous variable. Poisson regression models with robust variance were used to calculate the relative risk of being overweight or obese (defined using IOTF cut-offs) for each number of factors, compared to the baseline of zero risk factors [32]. Additional adjustments were made for potential confounding factors: maternal height, parity, age at child’s birth, level of educational attainment, and gestational age of the child at birth. In a final analysis, values were imputed for 861 children with missing data by multiple imputation using chained equations (MICE), generating 20 imputed datasets. We then re-ran the models that examined the associations between number of risk factors and obesity outcomes at 4 and 6 years of age.

Because the risk factors considered could be acting as markers of the nature of the child’s postnatal environment, final models further adjusted for childhood level of physical activity (assessed at 4 years) and quality of childhood diet (prudent diet scores determined at 3 years and 6 years). Comparisons between the participants studied and those not included were made using t-tests for normally distributed continuous variables, Mann-Whitney rank-sum tests for non-normally distributed continuous variables, and chi-squared tests for categorical variables. All statistical analyses were performed using Stata version 13.1 (Statacorp LP, College Station, TX, USA).

**RESULTS**

The characteristics of the SWS mothers and children studied are shown in **Table 1**. The median ages at the two DXA assessments were 4.11 (interquartile range (IQR) 4.08-4.16) and 6.65 (IQR 6.47-6.85) years. When compared with other 861 mothers in the SWS cohort who had term babies born before the end of 2003, those included in the analyses were slightly taller and older; they had higher levels of educational attainment and were more likely to be of white ethnicity, primiparous and a non-smoker in pregnancy. However, there were no differences in BMI before pregnancy or in their pattern of gestational weight gain. The SWS children who were included in the analyses had comparable BMI at 6 years to the remaining children (Table 1), but were more likely to have been breastfed for longer (P<0.001).

The prevalence of each of the five early life risk factors examined in the analyses is shown in **Table 2**. BMI and fat mass at 4 and 6 years of age are shown in relation to the individual risk factors in **Supplementary Table 1**. When the children were considered in terms of the number of risk factors that they had, 148 (15%) of the children studied had none; 330 (33%) had one; 296 (30%) had two; 160 (16%) had three; 52 (5%) had four; 5 (1%) had all five. The children who had four or five risk factors were therefore combined in one group for all subsequent analyses.

**Table 3** shows the children’s BMI at 4 years and 6 years, according to the number of early life risk factors. After taking account of a range of potential confounding influences, there was a clear graded increase in BMI at both ages, in association with increasing number of risk factors. Further adjustment for childhood level of physical activity and prudent diet score made little difference to the patterns of association (adjusted βtrend=0.21SD (95% CI 0.14,0.28) at 4 years; βtrend=0.25SD (95% CI 0.17,0.33) at 6 years; both P<0.001). The associations between number of early life risk factors and adiposity, using DXA-assessed fat mass, in childhood were very similar to those observed with BMI (**Table 4**); clear graded increases in adiposity were found with increasing number of risk factors. Further adjustment for level of physical activity and prudent diet score did not change the associations (adjusted βtrend=0.17SD (95% CI 0.10,0.25) at 4 years; βtrend=0.22SD (95% CI 0.14,0.30) at 6 years, both P<0.001). To estimate the difference in fat mass between children with 4 or 5 risk factors and those with none, the logged data (Table 4) were used as follows: at 4 years the fat mass of children who had 4 or 5 risk factors was 0.71 SDs higher than those with no risk factors.  Since the SD of the log fat mass was 0.24, this equates to an increase of 0.17 (=0.71\*0.24) log kg, which is equivalent to a multiplicative change in fat mass of 1.19 (exp(0.17)) (a difference of 19%).  Doing the same calculation using the 6-year data, the difference in fat mass amounted to 47%. .

Using the IOTF BMI cut-offs, 77 (11.2%) of children were defined as overweight and 19 (2.8%) were obese at 4 years; the figures at 6 years were 97 (12.9%) and 25 (3.3%) respectively. The relative risk of being overweight or obese at 4 or 6 years of age, according to number of early life risk factors, is shown in **Figure 1**. At both ages studied, there was a graded increase in risk, such that, after taking account of the effects of confounders, the relative risk for children who had 4 or 5 risk factors was 3.99 (95% CI 1.83,8.67) at 4 years and 4.65 (95% CI 2.29,9.43) at 6 years, when compared with the children who had none (P<0.001 at both ages). Further adjustment for level of physical activity in childhood and prudent diet score attenuated the associations but a four-fold difference in relative risk remained (relative risk for children who had 4 or 5 risk factors, 3.51 (95% CI 1.55,7.92) at 4 years, 3.52 (95% CI 1.56,7.95) at 6 years).

In our final analyses we examined the robustness of the associations, firstly by changing the categorisation of two risk factors, and secondly by conducting a multiple imputation to address the missing data for 861 children. In the first of these steps, overweight in mothers before pregnancy was defined as a BMI above 25kg/m2 (instead of 30kg/m2) and short duration of breastfeeding was defined as less than 6 months (instead of 1 month). The models presented in Tables 3 and 4 were rerun firstly using each of the new categorisations separately, and then both together. For BMI and fat mass at 4 and 6 years, the models were comparable to the original models, although in some cases the associations were slightly attenuated. For example, in the model that predicted fat mass at 6 years, when both categories were changed (such that 6% of children had no risk factors and 17% had 4 or 5) the βtrend was 0.17SD (95% CI 0.12,0.23, P<0.001), compared with 0.22SD (95% CI 0.16,0.28 P<0.001) in the original model, shown in Table 4. However, the effects of changing the definitions of maternal overweight, or short breastfeeding duration, on the models were small and the clear positive graded increases in obesity outcomes, in association with increasing number of early life risk factors, remained; in all models the positive trends were significant (all P<0.001, data not shown). In the second step we ran a multiple imputation to impute values for children with missing data, and then re-ran the models that examined the association between number of risk factors and BMI and fat mass at 4 and 6 years. Inclusion of data for these children (n=861) in the models made little difference to the findings, and the pattern of association and size of effects were largely unchanged (data not shown).

**DISCUSSION**

We examined five early life risk factors for obesity in childhood (maternal obesity, excess gestational weight gain, smoking in pregnancy, low maternal vitamin D status, short duration of breastfeeding) that are potentially modifiable through behaviour change interventions. Using the categorisations we defined *a priori*, 15% of the children studied had none of these risk factors, whilst half (52%) had at least two. We considered BMI, DXA-assessed fat mass and risk of overweight and obesity as outcomes when the children were aged 4 and 6 years. In each case we found positive graded associations with the number of early life risk factors - and the differences were large. For example, there was a four-fold increase in risk of being overweight or obese for the children who had four or more risk factors, when compared with children who had none, and a difference in fat mass between these groups of 19% at 4 years and 47% at 6 years. The associations were still evident after taking account of a range of potential confounding factors, including childhood level of physical activity and diet quality.

To our knowledge, an evaluation of the combined effects of early life risk factors on adiposity, using direct measures of fat mass, has not been conducted before. The four-fold difference in relative risk of being overweight that we observed, when comparing children who had at least four early life risk factors with those who had none, is comparable to data from Project Viva [12]. In that study, a five-fold difference in predicted obesity prevalence in preschool children was described in children whose mothers had excess gestational weight gain, smoked in pregnancy, who were breastfed for less than 12 months and slept for less than 12 hours per day in infancy (29% vs 6%). Although some of the risk factors differed between studies (Project Viva included duration of sleep in infancy, but did not consider maternal vitamin D status or BMI as individual risk factors), the analyses from both cohorts point to the potential importance of early life influences for later obesity risk, and are suggestive of the public health impact that interventions to change levels of risk factors in early life might achieve.

More recent follow-up of the children in Project Viva has shown that the differences in obesity risk persist, with a seven-fold difference in predicted prevalence between children with all four risk factors and those with none, when aged 7 to 10 years [13]. Consistent with this finding, we observed a slightly greater relative risk of overweight or obesity, and a larger difference in fat mass, at 6 years, suggesting that the differences may widen in later childhood. Such an effect has been described in other studies [33,34]. For example, in an analysis of data from the National Longitudinal Study of Youth, an increasing influence of maternal prepregnancy obesity on child overweight was seen at each follow up (adjusted OR 1.37 (95% CI 1.02,1.84) age 2-3years; OR 1.69 (95% CI 1.22,2.34) age 4-5years; OR 2.91 (95% CI 2.09,4.03) age 6-7years) [34]. The authors suggested that maternal obesity may affect both the propensity to gain excess weight in childhood, and the dynamics of the process. This could be explained by a combination of programmed effects of prenatal exposure to maternal obesity, together with exposure to a more obesogenic postnatal environment. In the present study we took account of diet quality in childhood and level of physical activity, which slightly attenuated, but did not remove, the associations. In the continued follow-up of the SWS children, it will be important to address the potential amplification of effects of early life factors on later childhood obesity, and contributions made by factors, such as diet and exercise, to its development in high-risk children.

The SWS provides data from a large contemporary cohort of women and children. A strength of our analyses is that the children and mothers have been characterized in detail, enabling us to take account of effects of a number of potential confounding influences. However, it is a significant limitation that we examined subsets of SWS children at 4 and 6 years of age, and that data were not available for all children. The children included in our analyses came from a wide variety of social backgrounds but differed in some characteristics from other SWS children (Table 1). However, maternal BMI and children’s BMI at the age of 6 years did not differ between the groups, and multiple imputation to include children with missing risk factor data in the analyses did not change the nature of the associations described. Unless associations differ in the remainder of the cohort, we think it unlikely that selection bias could be the explanation for the findings. We examined both BMI and DXA-assessed fat mass as outcomes in childhood. DXA provides a direct measure of fat mass, and its use is well-validated in adults, but there may be challenges with its use in children. To address these, we used specific paediatric software and movement artifact was modest; the few individuals with excessive movement were excluded from our analyses.

In an observational study it is not possible to determine whether associations are causal, and there is continuing debate regarding the possibility that early life factors, such as breastfeeding duration, are acting as markers of the postnatal environment [35,36]. We therefore took account of a range of confounding influences, although there may be other factors, that are associated both with the early life risk factors and with childhood adiposity, that we did not consider. However, while we cannot rule out the possibility of residual confounding, we would not expect it to explain the strong associations we observed.

The size of the differences in adiposity, and the risk of being overweight or obese, between children who had a number of early life risk factors, and those who had none, is an indication of the potential public health significance of early influences on obesity. Body composition ‘tracks’ from early childhood [37,38], suggesting that these differences will persist into adult life. While early preventive interventions in childhood are recognised as being of importance [39], much of the existing evidence of benefit is from school-aged children [40]. The SWS data together with findings from other cohorts [10-13] make a clear case for interventions earlier in the lifecourse, although more evidence is needed. Pregnancy and early infancy have both been considered, not least as times when women will be receptive to health promotion messages [4,13,41], and interventions to limit gestational weight gain [42] and promote breastfeeding have been successful [43] . But earlier interventions, to change levels of risk factors before conception, may be a more effective preventive strategy. Two of the risk factors we examined (obesity, smoking) are present before pregnancy. Importantly, they have been shown to co-exist with other risk factors in SWS women, such that maternal obesity is associated with greater risk of excess gestational weight gain and shorter duration of breastfeeding [7,44], and maternal smoking is linked to lower vitamin D status in late pregnancy [17]. If these are causally related, interventions that address obesity and smoking behaviours before pregnancy will also impact on the other risk factors we considered.

Health behaviours are socially patterned, and so predict future social inequalities [45]. Evidence from the SWS shows there is little preparation for pregnancy in terms of changes in health behaviours, and this is more marked among disadvantaged women [46]. Interventions and policies to encourage behaviour change need to include recognition of the influence of the wider social and economic environment [47], as well as consideration of how best to support individuals [48]. Thechallenges of changing behaviour, to achieve a healthy body weight and stop smoking, are considerable [49,50]. But for women who go on to become pregnant, our findings suggest that the impact of these changes could be significant.

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|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Mother-child pairs studied** |  | **Remaining mother-child pairs** |  |
|  | **n** |  | **n** |
| ***Mother*** |  |  |  |  |  |  |  | **P-value1** |
|  |  |  |  |  |  |  |  |  |
| Height (cm)2 | 991 | 163.6 | (6.4) |  | 852 | 162.8 | (6.5) | 0.003 |
|  |  |  |  |  |  |  |  |  |
| BMI (kg/m2)3 | 991 | 24.3 | (22.0-27.5) |  | 845 | 24.2 | (22.0-28.1) | 0.62 |
|  |  |  |  |  |  |  |  |  |
| Age at child’s birth (years)2 | 991 | 30.4 | (3.8) |  | 859 | 29.7 | (3.8) | < 0.001 |
| Serum vitamin D concentration (nmol/l)3 | 991 | 61.0 | (41.7-87.0) |  | 705 | 57.0 | (40.2-82.4) | 0.07 |
|  |  |  |  |  |  |  |  |  |
|  |  | **n** | **%** |  |  | **n** | **%** |  |
| Educational attainment; qualifications $>$ A-level4 | 988 | 293 | 29.7 |  | 859 | 228 | 26.5 | 0.005 |
|  |  |  |  |  |  |  |  |  |
| Multiparous | 991 | 524 | 52.9 |  | 860 | 518 | 60.2 | 0.001 |
|  |  |  |  |  |  |  |  |  |
| Smoked in pregnancy | 991 | 140 | 14.1 |  | 852 | 184 | 21.6 | < 0.001 |
|  |  |  |  |  |  |  |  |  |
| Pregnancy weight gain5 | 991 |  |  |  | 703 |  |  | 0.68 |
| Inadequate |  | 216 | 21.8 |  |  | 165 | 23.5 |  |
| Adequate |  | 301 | 30.4 |  |  | 204 | 29.0 |  |
| Excessive |  | 474 | 47.8 |  |  | 334 | 47.5 |  |
|  |  |  |  |  |  |  |  |  |
| White ethnicity | 991 | 953 | 96.2 |  | 861 | 800 | 92.9 | 0.002 |
|  |  |  |  |  |  |  |  |  |
| ***Child*** |  |  |  |  |  |  |  |  |
| Gestation at birth (weeks)3 | 991 | 40.2 | (39.3-41.0) |  | 859 | 40.1 | (39.1-41.0) | 0.29 |
|  |  |  |  |  |  |  |  |  |
| Duration breastfeeding(weeks)3 | 991 | 13.0 | (1.0-30.4) |  | 758 | 6.0 | (0.1-24.7) | < 0.001 |
|  |  |  |  |  |  |  |  |  |
| BMI at 6 years (kg/m2)3 | 750 | 15.8 | (14.9-16.9) |  | 124 | 15.5 | (14.9-16.5) | 0.21 |
|  |  |  |  |  |  |  |  |  |
|  |  | **n** | **%** |  |  | **n** | **%** |  |
| Overweight/obese at 6 years6  | 750 | 122 | 16.3 |  | 124 | 18 | 14.5 | 0.62 |
|  |  |  |  |  |  |  |  |

**Table 1. Characteristics of 991 mothers and children studied, compared with the rest of the SWS cohort, born before the end of 2003**

1P-values determined according to t-test for normally distributed continuous variables, Mann-Whitney rank-sum tests for non-normally distributed continuous variables, and chi-squared tests for categorical variables; 2Mean (Standard deviation); 3Median (Interquartile range) concentration determined in late pregnancy; 4Educational qualification awarded at 18 years of age; 5Institute of Medicine 2009 categorisation [7,24]; 6International Obesity Task Force categorisation [17]

**Table 2. Definition and prevalence of early life risk factors**

|  |  |  |
| --- | --- | --- |
| **Risk factor** | **n** |  **Prevalence** |
|  |  |  |  |
| Maternal obesity before pregnancy1 |  | 135 | 14% |
| Excessive gestational weight gain2 |  | 474 | 48% |
| Smoked in pregnancy |  | 140 | 14% |
| Low vitamin D status in pregnancy3 |  | 531 | 54% |
| Not breastfed or short duration of breastfeeding4 |  | 355 | 36% |

1BMI>30 kg/m2

2Institute of Medicine 2009 categorisation [7,24]

3Serum vitamin D concentration in late pregnancy <64nmol/l [17]

4Never breastfed or less than 1 month completed breastfeeding

**Table 3. Levels of body mass index in childhood (SD) according to number of early life risk factors**

|  |  |  |  |
| --- | --- | --- | --- |
| **Number of early life risk factors** | **BMI at 4 years1 (SD)** |  | **BMI at 6 years1 (SD)** |
|  |  |  |  |  |  |  |  |  |  |
| **n** | **β** | **(95% CI)** | **P-value2** |  | **n** | **β** | **(95% CI)** | **P-value2** |  |
|  |  |  |  |  |  |  |  |  |  |  |
| 0 | 116 | 0 | -- | -- |  | 109 | 0 | -- | -- |  |
| 1 | 233 | -0.02 | (-0.23,0.20) | 0.89 |  | 251 | 0.05 | (-0.16,0.27) | 0.63 |  |
| 2 | 200 | 0.21 | (-0.02,0.43) | 0.07 |  | 224 | 0.28 | (0.06,0.50) | 0.01 |  |
| 3 | 102 | 0.54 | (0.27,0.81) | <0.001 |  | 119 | 0.55 | (0.30,0.81) | <0.001 |  |
| 4 or 5 | 37 | 0.79 | (0.42,1.16) | <0.001 |  | 46 | 1.16 | (0.82,1.50) | <0.001 |  |
|  |  |  |  |  |  |  |  |  |  |  |
| β for trend3 | 688 | 0.20 | (0.13,0.27) | <0.001 |  | 749 | 0.25 | (0.19,0.32) | <0.001 |  |

1Adjusted for child’s sex, gestational age at birth, age at measurement; maternal height, education, parity and age at child’s birth; 2P-values were determined by linear regression models of BMI (z-score) on risk factor score (zero risk factors as baseline); 3P for trend were determined by linear regression models of BMI (z-score) on continuous risk factor score.

**Table 4. Levels of fat mass in childhood (SD) according to number of early life risk factors**

|  |  |  |  |
| --- | --- | --- | --- |
| **Number of early life risk factors** | **Fat mass at 4 years1(SD)** |  | **Fat mass at 6 years1(SD)** |
|  |  |  |  |  |  |  |  |  |  |
| **n** | **β** | **(95% CI)** | **P-value2** |  | **n** | **β** | **(95% CI)** | **P-value2** |  |
|  |  |  |  |  |  |  |  |  |  |  |
| 0 | 92 | 0 | -- | -- |  | 99 | 0 | -- | -- |  |
| 1 | 169 | -0.08 | (-0.30,0.13) | 0.45 |  | 217 | 0.06 | (-0.13,0.24) | 0.54 |  |
| 2 | 141 | 0.14 | (-0.08,0.37) | 0.21 |  | 176 | 0.25 | (0.06,0.44) | 0.01 |  |
| 3 | 75 | 0.41 | (0.14,0.69) | 0.003 |  | 99 | 0.48 | (0.26,0.70) | <0.001 |  |
| 4 or 5 | 28 | 0.71 | (0.34,1.08) | <0.001 |  | 31 | 1.14 | (0.82,1.46) | <0.001 |  |
|  |  |  |  |  |  |  |  |  |  |  |
| β for trend3 | 505 | 0.17 | (0.10,0.24) | <0.001 |  | 622 | 0.22 | (0.16,0.28) | <0.001 |  |

1Adjusted for child’s sex, gestational age at birth, age at DXA assessment, height; maternal height, education, parity and age at child’s birth; 2P-values were determined by linear regression models of fat mass (z-score) on risk factor score (zero risk factors as baseline for categorical analysis); 3P for trend were determined by linear regression models of fat mass (z-score) on continuous risk factor score.

**Figure 1**. Relative risk (95% CI) of being overweight or obese at 4 and 6 years of age (defined using International Obesity Task Force cut-offs [22]), according to number of early life risk factors (number of children:116 at 4 years and 109 at 6 years with no risk factors; 233 at 4 years and 251 at 6 years with one risk factor; 200 at 4 years and 224 at 6 years with two risk factors; 102 at 4 years and 119 at 6 years with three risk factors; 37 at 4 years and 46 at 6 years with four or five risk factors). Data are adjusted for child’s gestational age at birth; maternal height, education, parity and age at child’s birth. P-values were determined by Poisson regression models with robust variance of IOTF overweight/obese on continuous risk factor score.