Maternal smoking in pregnancy association with childhood adiposity and blood pressure

Leah Li, PhD[1], Helen Peters, MSc[1], Augusta Gama, PhD[2,4], Maria Isabel Mourao Carvalhal, PhD[3], Helena Guilhermina Marques Nogueira, PhD[4,5], Vítor Rosado-Marques, PhD[4,6], Cristina Padez, PhD[4]

Affiliations:
[1]Life Course and Statistics, Population, Policy, and Practice Programme, Institute of Child Health, University College London, UK;
[2]Departamento de Biologia Animal, Faculdade de Ciências, University of Lisbon, Portugal;
[3]University of Tras-os-Montes and Alto Douro, Portugal;
[4]Research Centre for Anthropology and Health, Department of Life Sciences, University of Coimbra, Portugal;
[5]Department of Geography, University of Coimbra, Portugal;
[6]Tropical Research Institute of Lisbon, Portugal

Correspondence Author: Dr Leah Li, Population, Policy, and Practice Programme, UCL Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK. Email: leah.li@ucl.ac.uk

Running title: Maternal smoking associations with child adiposity and blood pressure

Abbreviations: BMI-body mass index; BP-blood pressure; DBP-diastolic blood pressure; SBP-systolic blood pressure

Key Words: maternal smoking in pregnancy, adiposity, blood pressure, children

Word count: abstract=218 words; text=3310 words

Tables: 2

Supplementary tables: 3

What is already known about this subject

- Maternal smoking during pregnancy has been associated with increased risk of overweight/obesity defined by BMI.
- Less is known about its relation with other adiposity measures or cardiovascular indicators in children.

What this study adds

- Maternal smoking during pregnancy was associated with increased childhood BMI, waist circumferences, and skinfold thickness, particularly among older children.
- While maternal smoking was not consistently associated with blood pressure and resting pulse rate, its association with increased levels of adiposity may have implications on cardiovascular risk over the life-course.

Abstract

Background: Maternal smoking during pregnancy has been associated with increased risk of childhood overweight/obesity defined by BMI. We examined its association with a range of adiposity measures and cardiovascular indicators in children aged 3-10y.

Methods: We used data from a cross-sectional study of school children across mainland Portuguese districts (2009-10). We applied quantile regressions to examine maternal smoking associations with adiposity (n=17,286) and blood pressure (BP), and resting pulse rate (RPR) (n≈2500) measures across the age range, adjusting for pre-natal and early life factors.

Results: Maternal smoking during pregnancy was associated with increases in offspring adiposity levels. The difference in median BMI between children of smokers and non-smokers was 0.39kg/m^2(95% CI: 0.25,0.53) in boys and 0.46kg/m^2(0.31,0.62) in girls, 0.55cm(0.24,0.87) and 0.82cm(0.45,1.19) respectively in median waist circumference, and 0.94mm(0.49,1.40) and 1.47mm(0.87,2.07) in median sum of (triceps, subscapular, suprailiac) skinfolds. The associations appeared to be stronger with increasing age. The differences in the 90th centile tended to be greater than those in median. There was no consistent association of maternal smoking with BP and RPR.

Conclusions: Children whose mother smoked during pregnancy had higher adiposity levels than children of non-smokers, across several measures, particularly among older children. While there was no consistent association with cardiovascular indicators, maternal smoking association with childhood obesity may have implications for cardiovascular risk factors over the life-course.

Introduction

There is increasing evidence to suggest that maternal smoking during pregnancy is associated with increased adiposity levels and risk of overweight and obesity in offspring. The associations persist with the adjustment for birth size and socio-economic factors(1-4). Research into maternal smoking and offspring adiposity tends to focus mainly on body mass index (BMI) as an indicator of total adiposity at one age in childhood (1;2;4;5). Less is known whether the maternal smoking/adiposity association differs by age. A recent study found little or no association with BMI or overweight/obesity in infancy(6), while some show that a greater BMI and risk of overweight are evident by 2-3y(7;8) and perpetuates as the child ages(8). A longitudinal cohort study shows that the association is stronger with adult BMI than childhood BMI(9).

Limited evidence is available for the association of maternal smoking in pregnancy with other adiposity measures and findings are less consistent. One study shows that maternal smoking is not associated with childhood overweight/obesity defined by skinfolds(10), whereas another study found an association with increased sum of triceps and subscapular skinfolds, a proxy for fat mass, but no relationship with central adiposity(7). It has been suggested that skinfold thickness is more strongly associated with body fatness than is BMI, as estimated by various reference methods(11;12). Because of these stronger associations with body fatness, it is frequently assumed that skinfold thickness would be a better predictor of adverse health outcomes than BMI. Waist circumference, a measure for central adiposity, has been found to be a better predictor of cardiovascular risk factors in children than BMI(13) and the association with HDL-cholesterol and systolic blood pressure (SBP) is independent of BMI(14).

Furthermore, maternal smoking in pregnancy has been associated with adverse cardiovascular risk factors in offspring, although this evidence is scant and inconsistent. Studies reported an increase in mean SBP by about 1mmHg in 5-6y children whose mothers smoked in pregnancy compared those of non-smokers(15;16), whereas others found no association among children of similar ages(17;18).

The associations of maternal smoking with adiposity and cardiovascular indicators in contemporary children are of particular interest in the light of substantial increases in the level of child obesity. Our aims were to examine (1) whether maternal smoking in pregnancy was associated with adiposity measures (including BMI, waist circumference, and skinfold thickness), cardiovascular indicators (BP and resting pulse rate) in children and (2) whether the associations differed by the age of the child.

Methods

We used data from the Portuguese Prevalence Study of Obesity in childhood, a cross-sectional study carried out in public and private schools across all mainland Portuguese districts between March 2009 and January 2010. The regions of Madeira and Azores (Portuguese Archipelagos) were not included. The study population was selected based on a proportionate stratified random sampling design taking into account the number of children by age and sex in each district and was designed to provide a national representative survey of 3-10y children in Portugal. In each district, schools were randomly selected from the central database of schools of the Ministry of Education until the established number of subjects was reached. A total of 17,509 children aged 2-11y were included. Participation rate was 57.4% (49.3% in preschool children and 63.6% in school children). Parents were asked to fill out a questionnaire about family characteristics including sedentary and physical activity behaviours of the child. There were few (<1%)

children under 3y or over 10y. We restricted our analysis to children between 3-10y (mean 7.0y). The study protocol was approved by Direcção Geral de Inovação e Desenvolvimento Curricular and informed consent was obtained from all the children's parents.

Adiposity measures

In each school two trained technicians performed anthropometric measurements using a standardized procedure, with children lightly dressed without shoes. Height (to the nearest mm) was measured with a portable stadiometer and weight (0.1kg) was measured with an electronic portable scale. BMI (kg/m^2) was calculated for each child. Waist circumference (mm) was measured with a flexible non-elastic tape (SECA) midway between the tenth rib and the iliac crest. Triceps, subscapular, and suprailiac skinfold thickness (mm) were all measured twice with a skinfold calliper (Holtain Ltd) and the average of two readings was used for each skinfold thickness. The sum of three skinfolds was derived.

BP and resting pulse rate

During the survey, one district was chosen from one large region in Northern, Central and Southern Portugal in order to select children from different socio-economic backgrounds. Clinic measurements were obtained for children recruited in the sub-sample. SBP, diastolic BP (DBP, mmHg), and resting pulse rate (RPR, bpm) were measured three times by trained technicians using an Omron M7 BP monitor, with the child seated after at least five minutes rest. We used the average of three measurements for children aged 3-10y in the analysis (n= 2,492).

Maternal smoking during pregnancy

Maternal smoking was reported in the questionnaire as whether or not the mother smoked during pregnancy and number of cigarettes smoked per day. Mothers were categorised as non-smokers (<1 cigarette/day) or smokers (≥1 cigarette/day).

Covariates

Several covariates were examined, including potential confounding factors and known risk factors for the outcomes, including maternal BMI, prenatal factors (maternal age at child birth, birthweight, gestational age, and parity), and childhood factors (infant feeding, maternal education, maternal employment, lone mother family, TV viewing time), and these were obtained from a questionnaire completed by the parent (mostly the mother). Maternal BMI (kg/m^2) was calculated from reported height and weight. Parity was coded as first, second, and third or higher birth order. Infant feeding was classified as 'never' or 'ever' breastfed. Maternal education was classified as 'primary', 'secondary', and 'university or higher', and where missing was supplemented with paternal education (1.1% of cases). Parents reported the average number of hours (i.e. none, ≤1, 1, 2, 3, 4, and ≥5 hours) per day that the child spent watching TV on a weekday, a Saturday, and a Sunday. TV viewing time was classified as '<1', '1-2', or '≥2' hours per day.

Statistical analysis

Some outcome measures (e.g. BMI, waist circumference, and skinfold thickness) had a skewed distribution. We thus applied quantile regression models to each outcome (adiposity, BP, and RPR measure), separately for boys and girls. To capture the non-linear trends of these measures for the age range (3-10y) we adopted a second degree fractional polynomial function of age(19). The goodness of fit was based on the residual mean square errors and also AIC and BIC. For all the outcome measures, the best fitting fractional polynomials were $a + b \cdot age + c \cdot \ln(age)$ for boys and $a + b \cdot age + c \cdot age^2$ for girls. The unadjusted models included the gender-specific age function and maternal smoking. The models for waist circumference and skinfold thickness also included height as a covariate, as it has be shown to be positively associated with these measures in our study and elsewhere(20). We estimated the difference in 50^{th} (median) and in 90^{th} (top 10%) centiles of each measure between children whose mothers smoked in pregnancy and those of non-smokers. The models were adjusted first for maternal BMI and pre-natal factors (i.e. maternal age, parity, birthweight, and gestational age), and further for early life factors (infant feeding, maternal education, maternal employment, lone mother family, and TV viewing time). The adjusted models for BP and RPR measures also included BMI, which might be on the causal pathway between maternal smoking and cardiovascular indicators. For each outcome measure, the age interaction with maternal smoking was tested to assess whether the association differed with increasing age.

To illustrate the relative scale of the association between maternal smoking in pregnancy and each adiposity measure, we estimated differences in median and 90^{th} centile for each measure in terms of standard deviation scores (i.e. internally derived SDS). We performed additional analysis by grouping children according to mothers smoked (1) ‘<10’ and ‘≥10’ cigarettes/day to assess whether there was a dose effect and (2) during/before pregnancy, only before pregnancy, and never smoked, and (3) by excluding children whose mother smoked only before pregnancy to assess whether it had a similar effect as smoking during pregnancy on offspring adiposity.

Analysis for adiposity measures was based on participants aged 3-10y with adiposity measures (n=17,287). Among them 16,671 children had data on maternal smoking and

11,478 also had complete data on covariates. Analysis for cardiovascular indicators was based on 2492 children with information on BP and RPR measures (n=1832 with complete data). We applied multiple imputation to impute missing covariates to the sample of 17,287 children with adiposity and 2492 with BP/RPR measures. The imputation model included factors predicting non-response (i.e. sex, age, maternal and paternal education, family size, parity, shared bedroom or overcrowding, and lone-parenthood), maternal smoking, measures of adiposity and cardiovascular indicators, and all covariates in the analysis models. We used SPSS (version 20, IBM) to create 10 imputed datasets(21) assuming missing is at random given observed values of other variables. The MIM command in STATA v12 was used to analyze these datasets using quantile regression and parameters estimated were combined to obtain overall estimates using Rubin's rules(22). Analyses were repeated using children with available data. Conclusions were unaltered and hence, we present results based on imputation.

Results

Mothers who smoked during pregnancy (13.7%) tended to be younger at child birth (by 0.7y), have a lower mean BMI (by 0.78kg/m^2) and lower education levels (primary school education 24.1% versus 17.7%), compared to those did not. Maternal smoking in pregnancy was also associated with higher birth order (third or higher 14% versus 8.6%), lower mean birthweight (by 163g), premature births (<32 weeks gestation 1.4% versus 0.9%, no difference in mean gestational age), non-breastfed (18.9% versus 12.5%), and more TV time (≥2 hours/day 39.1% versus 31.5%) (**Table 1**).

Maternal smoking during pregnancy was associated with increased adiposity measures (**Table 2**). The associations tended to strengthen after adjusting for maternal BMI and pre-natal factors, and persist when further including early life factors in models. The adjusted difference in median BMI was 0.39kg/m^2(95% CI:0.25,0.53) in boys and 0.46kg/m^2(0.31,0.62) in girls. The respective difference in median waist circumference was 0.55cm(0.24,0.87) and 0.82cm(0.45,1.19), and in median sum of skinfold thickness was 0.94mm(0.49,1.40) and 1.47mm(0.87,2.07). Maternal smoking was also positively associated with individual measure of skinfold (**Table 2**).

Maternal smoking during pregnancy was associated with the upper end of the distribution for each adiposity measure. The adjusted difference in the 90th centile was 0.84kg/m^2(0.43,1.25) in boys and 0.63kg/m^2(0.27,1.00) in girls for BMI, 1.59cm(0.86,2.33) and 1.14cm(0.36,1.92) respectively for waist circumference, and 2.43mm(0.68, 4.18) and 1.33mm(-0.33, 3.75) for sum of skinfolds (**Table 2**).

There was a positive interaction between maternal smoking in pregnancy and age of the children for median BMI (p=0.06 for boys and 0.04 for girls), waist circumference (p=0.02 for boys and 0.06 for girls), and sum of skinfolds in girls (p=0.03), indicating that the association between maternal smoking and adiposity measures was stronger among older than younger children. For example, the adjusted difference in median BMI was 0.80kg/m^2(0.55,1.21) for boys aged 8-10y, compared to 0.26kg/m^2(0.02,0.54) for boys aged 3-5y, and 0.55kg/m^2(0.19,0.88) versus 0.20kg/m^2(0.08,0.50) for girls (data not shown). There was no interaction between maternal smoking and age for the 90th centile of each adiposity measure.

There was no consistent evidence that the difference in median of each adiposity measure was greater for children whose mother smoked ‘≥10’ (vs those of non-smokers) than children whose mother smoked ‘<10’ cigarettes/day (supplementary **Table S1**).

Furthermore, relative to children of non-smokers, the differences in median BMI and waist circumference (not skinfolds) were greater for offspring whose mother smoked during pregnancy than those whose mother smoked only before pregnancy (Supplementary **Table S2**). In addition, findings did not change substantially when excluding children whose mother smoked before (not during pregnancy) (supplementary **Table S3**).

There was no consistent association between maternal smoking in pregnancy and the median or 90th centile of SBP, DBP, and RPR (**Table 2**).

Discussion

In this population sample of Portuguese children aged 3-10y, we found that maternal smoking during pregnancy was associated with increased levels of adiposity across all measures after adjusting for pre-natal and childhood factors. The difference was 0.4-0.5kg/m^2 in median BMI (equivalent to 0.18-0.20 SDS), 0.6-0.8cm in median waist circumference (0.11-0.16 SDS), and 0.9-1.5mm in median sum of skinfolds (0.09-0.11 SDS), and appeared to be greater with increasing age. The difference in the 90th centiles was 0.6-0.8kg/m^2 (0.29-0.40 SDS), 1.1-1.6cm (0.19-0.25 SDS), 1.3-2.4mm (0.18-0.24 SDS) respectively, greater than those in medians. There was no consistent evidence of an association between maternal smoking and offspring BP or RPR.

Strengths and limitations

The strengths of our study are the large national sample of contemporary Portuguese children with a range of adiposity measures, which although are inter-related, indicate different aspects of adiposity. While BMI reflects overall adiposity, waist circumference measures central adiposity and skinfold thickness is a proxy for fat mass. Measures were collected on children aged between 3-10y, allowing us to compare the association between maternal smoking in pregnancy and adiposity measures by age. Limitations include the cross-sectional design, thus we cannot explore growth trajectories. Maternal BMI and birthweight are subject to report bias. Maternal smoking during pregnancy was ascertained retrospectively from parental report. It has been suggested that retrospective reports of maternal pre-natal smoking are acceptable to be used to identify its potential associations with later child outcomes(23). In a meta-analysis, the estimated association of maternal smoking with increased offspring adiposity did not change when excluding studies in which mother reported pre-natal smoking at the same time outcomes were measured(24). The timing of smoking during pregnancy was not available in our study. It has been suggested that the greatest risk of overweight was associated with smoking later in pregnancy(25). Only a sub-sample of children had BP and RPR measures. The sub-sample remained broadly representative of the population sample; the associations between maternal smoking and adiposity measures found in the sub-sample was similar to those in the population sample, although some groups were overrepresented, e.g. older mothers (mean age 30.1y versus 29.3y) and mothers with high education (university degree 45.2% versus 34.5) (data not presented). The smaller sample size would reduce the power to assess their association with maternal smoking. For example, the reduction in the 90^{th} centile of SBP (p>0.05) found in girls of smokers is likely to be chance finding due to the small number of girls with BP measures born to smokers.

Comparison with other studies

We found a positive association of maternal smoking in pregnancy with BMI, waist circumference and sum of skinfolds of offspring aged 3-10y. Children of smokers had a higher median BMI by 0.4-0.5kg/m^2 than those of non-smokers. A US study showed a difference in mean BMI of 0.1kg/m^2 at 4y and 0.15-0.3kg/m^2 at 8y(25). Our results indicate that the difference was greater among older than younger children across adiposity measures. As our findings were based on cross-sectional data, we could not conclude that the maternal smoking/adiposity association strengthened with age. However, a stronger association with mean BMI with increasing age has been found in a study of US children. Although the explanation is not clear, it could be the result of the accumulation of a small change of metabolism or behaviour that becomes detectable over time(25) or it might reflect different postnatal risk factors at different childhood ages. A stronger association of maternal prenatal smoking with BMI in adulthood than in childhood has been found A British birth cohort study(9).

In our study, the association was evident with both the central tendency and the upper end of the distribution for these adiposity measures. An association between maternal smoking and a greater 90th centile of BMI distribution (by 0.6-0.8kg/m^2) is consistent with previous studies showing an association with increased risk of overweight and obesity, defined by age- and gender-specific BMI cut-offs. A number of studies have shown an increased risk of being overweight in offspring of smokers compared to those of non-smokers, with odds ratios ranging from 1.1 to 2.5(1;2;4-6;9;10;25-30). Two recent meta-analyses also show that offspring whose mothers smoked in pregnancy were at elevated risk for overweight at ages 3-33y, compared with those of non-smokers(24;31).

We found an association of maternal smoking during pregnancy with increased waist circumference and skinfolds thickness. Subscapular and triceps skinfolds(30) and the sum of these two skinfolds at 5y(3) were found to be higher for children of smokers, compared to those of non-smokers. It has also been shown that children exposed to maternal smoking in pregnancy had higher values of total fat mass and also lean mass at mean age 9.9y than those were not-exposed(32;33). Another study found an association of maternal pre-natal smoking with increased sum of (triceps and subscapular) skinfolds, but not with central adiposity(7).

Childhood cardiovascular indicators

We found no consistent association between maternal smoking during pregnancy and BP or RPR. Results from previous studies have been inconsistent. Some studies showed an increase in BP in children whose mother smoked in pregnancy(15;16). A study into the effect of intrauterine exposure to nicotine on BP in rats suggests that nicotine has a direct effect on the development cardiovascular systems(34). However, other studies reported no association between maternal smoking and offspring BP(17;18;35;36). A similar association of parental pre-natal smoking with offspring BP found in a study suggests that the association of maternal smoking with BP may not be a biological influence on the intrauterine environment(35). There is little evidence on the association between maternal smoking and RPR. Only one study showed a reduction in RPR in smoke-exposed infants at 10-16 weeks(37).

Potential explanation for the maternal smoking/adiposity association

Our data provided little evidence of a dose-response effect. However, there were only a small number of heavy smokers in pregnancy (i.e. ≈3% mothers smoked ≥10 cigarettes per day). Maternal smoking during pregnancy is a well-established risk factor for intrauterine growth retardation, including reduced birthweight(30). The majority of studies have shown a positive relationship between birthweight and later adiposity indices(38). Like several other studies (3;9;26), we found that the association between maternal smoking and levels of adiposity in children strengthens with adjustment of birthweight. This suggests that the risk of childhood overweight and obesity associated with smoking during pregnancy was independent of birthweight and intrauterine growth retardation.

The mechanisms for the association between smoking in pregnancy and offspring adiposity are not fully understood. While offspring of smokers had higher adiposity levels than those of non-smokers, mothers who smoked during pregnancy had a lower BMI than those did not. In adults, nicotine is associated with increased energy expenditure (39) and could also reduce appetite and weight in short term(40). One possible explanation for the association with high adiposity levels in offspring which has been suggested is that fetal exposure to nicotine may affect the in-utero development of the hypothalamic function, exerting an impact on appetite control and energy expenditure throughout the life-course(41-44). A recent study suggests that pre-natal exposure to maternal cigarette smoking may promote obesity by enhancing dietary preference for fat through neural mechanism involving in the amygdala(45).

The association between maternal smoking and offspring adiposity could also be due to maternal factors such as maternal diet, lifestyle, obesity and socio-economic status, and infant feeding(3;29). In our study, BMI and waist circumference of offspring whose mothers smoked before pregnancy only (14.9%) differed little from those whose mothers never smoked, whereas adiposity levels of children whose mother smoked in pregnancy were higher. It is likely that women who continued to smoke in pregnancy may have poor valuation of the future, self-control, risk aversion, and family nutritional environment than those who did not. Thus maternal BMI may act as a proxy for these maternal influences as well as genetic predisposition. We found the association with adiposity measures remained after adjusting for maternal BMI, pre-natal and early life factors, although we cannot rule out residual confounding such as maternal health behavior. Maternal smoking has been associated with unhealthy diet (i.e. higher intakes of energy, total and saturated fat, cholesterol, and alcohol)(46;47) and their children are likely to share a similar diet, and these behavioural factors could be important determinants for childhood overweight.

Summary

Maternal smoking during pregnancy was associated with increased levels of adiposity in contemporary Portuguese children. The association with the median, and more evidently with upper end of the distribution across several adiposity measures remained after adjusting for pre-natal and early life factors. The findings highlight that tackling childhood obesity should not only focus on policies targeting eating behaviors and physical activity of children, but also on early interventions of behaviors of pregnant women to effectively reduce the incidence of child obesity. While there was no consistent evidence of an association between maternal smoking and offspring cardiovascular indicators, the underlying role of maternal smoking in childhood obesity may have implications on cardiovascular risk factors over the life-course.

Conflict of Interest: None declared.

Acknowledgements

This study was supported by the Fundação para a Ciência e Tecnologia (Grant: FCOMP-01-0124-FEDER-007483). LL was supported by a Medical Research Council (MRC) Career Development Award in Biostatistics (Grant G0601941). HP was supported by the MRC Centre of Epidemiology for Child Health Small Project Grant (MRC Centre Grant G0400546) and was undertaken at UCL Institute of Child Health, which received a portion of its funding under the UK Department of Health's National Institute for Health Research (NIHR) Biomedical Research Centres funding scheme.

LL conceptualized the study, designed the analysis, drafted the initial manuscript, and approved the final manuscript as submitted.

HP carried out the analyses, drafted sections of the manuscript, reviewed and revised the manuscript, and approved the final manuscript as submitted.

AG, MIMC, HGMN, VRM: contributed to the data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted.

CP designed the data collection instruments, and coordinated data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Legends

Table 1 Mean (SD) and frequency (%) for parental and child characteristics in Portuguese children by maternal smoking during pregnancy

Table 2: Differences measures for adiposity and cardiovascular indicators by maternal smoking in pregnancy

Reference List

(1) von KR, Toschke AM, Koletzko B, Slikker W, Jr. Maternal smoking during pregnancy and childhood obesity. Am J Epidemiol. 2002 Nov 15;156(10):954-61.

(2) Adams AK, Harvey HE, Prince RJ. Association of maternal smoking with overweight at age 3 y in American Indian children. Am J Clin Nutr. 2005 Aug;82(2):393-8. doi: 82/2/393 [pii].

(3) Wideroe M, Vik T, Jacobsen G, Bakketeig LS. Does maternal smoking during pregnancy cause childhood overweight? Paediatr Perinat Epidemiol. 2003 Apr;17(2):171-9. doi: 481 [pii].

(4) Toschke AM, Montgomery SM, Pfeiffer U, von KR. Early intrauterine exposure to tobacco-inhaled products and obesity. Am J Epidemiol. 2003 Dec 1;158(11):1068-74.

(5) Toschke AM, Koletzko B, Slikker W, Jr., Hermann M, von KR. Childhood obesity is associated with maternal smoking in pregnancy. Eur J Pediatr. 2002 Aug;161(8):445-8. doi: 10.1007/s00431-002-0983-z [doi].

(6) Durmus B, Ay L, Hokken-Koelega AC, Raat H, Hofman A, Steegers EA, et al. Maternal smoking during pregnancy and subcutaneous fat mass in early childhood. The Generation R Study. Eur J Epidemiol. 2011 Apr;26(4):295-304. doi: 10.1007/s10654-010-9544-3 [doi]. Pubmed PMID: PMC3088815.

(7) Oken E, Huh SY, Taveras EM, Rich-Edwards JW, Gillman MW. Associations of maternal prenatal smoking with child adiposity and blood pressure. Obes Res. 2005 Nov;13(11):2021-8. doi: 13/11/2021 [pii];10.1038/oby.2005.248 [doi]. Pubmed PMID: PMC1483219.

(8) Salsberry PJ, Reagan PB. Dynamics of early childhood overweight. Pediatrics. 2005 Dec;116(6):1329-38. doi: 116/6/1329 [pii];10.1542/peds.2004-2583 [doi]. Pubmed PMID: PMC1479091.

(9) Power C, Jefferis BJ. Fetal environment and subsequent obesity: a study of maternal smoking. Int J Epidemiol. 2002 Apr;31(2):413-9.

(10) Bergmann KE, Bergmann RL, von KR, Bohm O, Richter R, Dudenhausen JW, et al. Early determinants of childhood overweight and adiposity in a birth cohort study: role of breast-feeding. Int J Obes Relat Metab Disord. 2003 Feb;27(2):162-72. doi: 10.1038/sj.ijo.802200 [doi];802200 [pii].

(11) Steinberger J, Jacobs DR, Raatz S, Moran A, Hong CP, Sinaiko AR. Comparison of body fatness measurements by BMI and skinfolds vs dual energy X-ray absorptiometry and their relation to cardiovascular risk factors in adolescents. Int J Obes (Lond). 2005 Nov;29(11):1346-52. doi: 0803026 [pii];10.1038/sj.ijo.0803026 [doi].

(12) Freedman DS, Wang J, Ogden CL, Thornton JC, Mei Z, Pierson RN, et al. The prediction of body fatness by BMI and skinfold thicknesses among children and adolescents. Ann Hum Biol. 2007 Mar;34(2):183-94. doi: 779267900 [pii];10.1080/03014460601116860 [doi].

(13) Savva SC, Tornaritis M, Savva ME, Kourides Y, Panagi A, Silikiotou N, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord. 2000 Nov;24(11):1453-8.

(14) Maffeis C, Pietrobelli A, Grezzani A, Provera S, Tato L. Waist circumference and cardiovascular risk factors in prepubertal children. Obes Res. 2001 Mar;9(3):179-87.

(15) Blake KV, Gurrin LC, Evans SF, Beilin LJ, Landau LI, Stanley FJ, et al. Maternal cigarette smoking during pregnancy, low birth weight and subsequent blood pressure in early childhood. Early Hum Dev. 2000 Feb;57(2):137-47. doi: S0378-3782(99)00064-X [pii].

(16) Lawlor DA, Najman JM, Sterne J, Williams GM, Ebrahim S, Davey SG. Associations of parental, birth, and early life characteristics with systolic blood pressure at 5 years of age: findings from the Mater-University study of pregnancy and its outcomes. Circulation. 2004 Oct 19;110(16):2417-23. doi: 01.CIR.0000145165.80130.B5 [pii];10.1161/01.CIR.0000145165.80130.B5 [doi].

(17) Whincup PH, Cook DG, Papacosta O. Do maternal and intrauterine factors influence blood pressure in childhood? Arch Dis Child. 1992 Dec;67(12):1423-9. Pubmed PMID: PMC1793969.

(18) Bergel E, Haelterman E, Belizan J, Villar J, Carroli G. Perinatal factors associated with blood pressure during childhood. Am J Epidemiol. 2000 Mar 15;151(6):594-601.

(19) Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. Int J Epidemiol. 1999 Oct;28(5):964-74.

(20) Yabanci N, Kilic S, Simsek I. The relationship between height and arm span, mid-upper arm and waist circumferences in children. Ann Hum Biol. 2010 Jan;37(1):70-5. doi: 10.3109/03014460903198517 [pii];10.3109/03014460903198517 [doi].

(21) Royston P. Multiple imputation of missing values: Update of ice. Stata Journal. 2005;5(4):527-36.

(22) Schafer JL. Multiple imputation: a primer. Stat Methods Med Res. 1999 Mar;8(1):3-15.

(23) Heath AC, Knopik VS, Madden PA, Neuman RJ, Lynskey MJ, Slutske WS, et al. Accuracy of mothers' retrospective reports of smoking during pregnancy: comparison with twin sister informant ratings. Twin Res. 2003 Aug;6(4):297-301. doi: 10.1375/136905203322296656 [doi].

(24) Oken E, Levitan EB, Gillman MW. Maternal smoking during pregnancy and child overweight: systematic review and meta-analysis. Int J Obes (Lond). 2008 Feb;32(2):201-10.

(25) Chen A, Pennell ML, Klebanoff MA, Rogan WJ, Longnecker MP. Maternal smoking during pregnancy in relation to child overweight: follow-up to age 8 years. Int J Epidemiol. 2006 Feb;35(1):121-30. doi: dyi218 [pii];10.1093/ije/dyi218 [doi].

(26) Al Mamun A., Lawlor DA, Alati R, O'Callaghan MJ, Williams GM, Najman JM. Does maternal smoking during pregnancy have a direct effect on future offspring obesity? Evidence from a prospective birth cohort study. Am J Epidemiol. 2006 Aug 15;164(4):317-25. doi: kwj209 [pii];10.1093/aje/kwj209 [doi].

(27) Huang RC, Burke V, Newnham JP, Stanley FJ, Kendall GE, Landau LI, et al. Perinatal and childhood origins of cardiovascular disease. Int J Obes (Lond). 2007 Feb;31(2):236-44. doi: 0803394 [pii];10.1038/sj.ijo.0803394 [doi].

(28) Mizutani T, Suzuki K, Kondo N, Yamagata Z. Association of maternal lifestyles including smoking during pregnancy with childhood obesity. Obesity (Silver Spring). 2007 Dec;15(12):3133-9. doi: 15/12/3133 [pii];10.1038/oby.2007.373 [doi].

(29) Suzuki K, Ando D, Sato M, Tanaka T, Kondo N, Yamagata Z. The association between maternal smoking during pregnancy and childhood obesity persists to the age of 9-10 years. J Epidemiol. 2009;19(3):136-42. doi: JST.JSTAGE/jea/JE20081012 [pii].

(30) Vik T, Jacobsen G, Vatten L, Bakketeig LS. Pre- and post-natal growth in children of women who smoked in pregnancy. Early Hum Dev. 1996 Jul 19;45(3):245-55.

(31) Ino T. Maternal smoking during pregnancy and offspring obesity: meta-analysis. Pediatr Int. 2010 Feb;52(1):94-9. doi: PED2883 [pii];10.1111/j.1442-200X.2009.02883.x [doi].

(32) Leary SD, Smith GD, Rogers IS, Reilly JJ, Wells JC, Ness AR. Smoking during pregnancy and offspring fat and lean mass in childhood. Obesity (Silver Spring). 2006 Dec;14(12):2284-93. doi: 14/12/2284 [pii];10.1038/oby.2006.268 [doi]. Pubmed PMID: PMC1890311.

(33) Leary S, Davey-Smith G., Ness A. Smoking during Pregnancy and Components of Stature in Offspring. Am J Human Biol. 2006;18(4):502-12.

(34) Pausova Z, Paus T, Sedova L, Berube J. Prenatal exposure to nicotine modifies kidney weight and blood pressure in genetically susceptible rats: a case of gene-environment interaction. Kidney Int. 2003 Sep;64(3):829-35. doi: kid172 [pii];10.1046/j.1523-1755.2003.00172.x [doi].

(35) Brion MJ, Leary SD, Smith GD, Ness AR. Similar associations of parental prenatal smoking suggest child blood pressure is not influenced by intrauterine effects. Hypertension. 2007 Jun;49(6):1422-8. doi: HYPERTENSIONAHA.106.085316 [pii];10.1161/HYPERTENSIONAHA.106.085316 [doi].

(36) Law CM, Barker DJ, Bull AR, Osmond C. Maternal and fetal influences on blood pressure. Arch Dis Child. 1991 Nov;66(11):1291-5. Pubmed PMID: PMC1793274.

(37) Viskari-Lahdeoja S, Hytinantti T, Andersson S, Kirjavainen T. Heart rate and blood pressure control in infants exposed to maternal cigarette smoking. Acta Paediatr. 2008 Nov;97(11):1535-41. doi: APA966 [pii];10.1111/j.1651-2227.2008.00966.x [doi].

(38) Whitaker RC, Dietz WH. Role of the prenatal environment in the development of obesity. J Pediatr. 1998 May;132(5):768-76.

(39) Hofstetter A, Schutz Y, Jequier E, Wahren J. Increased 24-hour energy expenditure in cigarette smokers. N Engl J Med. 1986 Jan 9;314(2):79-82. doi: 10.1056/NEJM198601093140204 [doi].

(40) Jo YH, Talmage DA, Role LW. Nicotinic receptor-mediated effects on appetite and food intake. J Neurobiol. 2002 Dec;53(4):618-32. doi: 10.1002/neu.10147 [doi]. Pubmed PMID: PMC2367209.

(41) Kane JK, Parker SL, Matta SG, Fu Y, Sharp BM, Li MD. Nicotine up-regulates expression of orexin and its receptors in rat brain. Endocrinology. 2000 Oct;141(10):3623-9.

(42) Li MD, Kane JK, Parker SL, McAllen K, Matta SG, Sharp BM. Nicotine administration enhances NPY expression in the rat hypothalamus. Brain Res. 2000 Jun 9;867(1-2):157-64. doi: S0006-8993(00)02283-6 [pii].

(43) Eliasson B, Smith U. Leptin levels in smokers and long-term users of nicotine gum. Eur J Clin Invest. 1999 Feb;29(2):145-52.

(44) Slotkin TA. Fetal nicotine or cocaine exposure: which one is worse? J Pharmacol Exp Ther. 1998 Jun;285(3):931-45.

(45) Haghighi A, Schwartz DH, Abrahamowicz M, Leonard GT, Perron M, Richer L, et al. Prenatal exposure to maternal cigarette smoking, amygdala volume, and fat intake in adolescence. JAMA Psychiatry. 2013 Jan;70(1):98-105. doi: 1356544 [pii];10.1001/archgenpsychiatry.2012.1101 [doi].

(46) Trygg K, Lund-Larsen K, Sandstad B, Hoffman HJ, Jacobsen G, Bakketeig LS. Do pregnant smokers eat differently from pregnant non-smokers? Paediatr Perinat Epidemiol. 1995 Jul;9(3):307-19.

(47) Dallongeville J, Marecaux N, Fruchart JC, Amouyel P. Cigarette smoking is associated with unhealthy patterns of nutrient intake: a meta-analysis. J Nutr. 1998 Sep;128(9):1450-7.

Table 1 Mean (SD) and frequency (%) for parental and child characteristics in Portuguese children by maternal smoking during pregnancy

Characteristics	N†	All (16680)	Non-Smoker (14397, 86.3%)	Smoker (2283, 13.7%)	Difference*
Maternal BMI (kg/m^2)	15633	24.0(4.0)	24.1(3.9)	23.3(4.0)	<0.001
Maternal age	16300	29.3 (5.3)	29.4 (5.3)	28.7 (5.8)	<0.001
Birthweight (g)	15965	3213(524)	3235 (521)	3072(519)	<0.001
Gestational age (week)	14672	38.7 (2.0)	38.7 (2.0)	38.7 (2.2)	0.40
Breastfeeding (month)	15958	4.4 (4.9)	4.6 (5.0)	3.5 (4.6)	<0.001
Yes (%)		13822 (86.6%)	12044 (87.5%)	1778 (81.1%)	<0.001
Parity	16198				
First		9008 (55.6%)	7842 (56.0%)	1166 (53.2%)	<0.001
Second		5679 (35.1%)	4959 (35.4%)	720 (32.8%)	
Third or higher		1511 (9.3%)	1205 (8.6%)	306 (14.0%)	
Maternal education	16318				<0.001
Primary		3032 (18.6%)	2499 (17.7%)	533 (24.1%)	
Secondary		7661 (46.9%)	6513 (46.2%)	1148 (52.0%)	
University		5625 (34.5%)	5098 (36.1%)	527 (23.9%)	
Maternal employment	16067	13516 (84.1%)	11889 (85.4%)	1627 (75.9%)	<0.001
Lone mother	16317	2313 (14.2%)	1733 (12.3%)	580 (26.0%)	<0.001
TV viewing time	14939				<0.001
<1hr/day		3619 (24.2%)	3232 (26.0%)	387 (19.5%)	
1-2hr/day		6470 (43.3%)	5645 (43.6%)	825 (41.5%)	
≥2hr/day		4850 (32.5%)	4073 (31.5%)	777 (39.1%)	

† Children (3-10y) with adiposity measures;
*p<0.05 for difference by maternal smoking based on t-test for continuous variables and on chi-squared test for categorical variables

Table 2: Differences in measures for adiposity and cardiovascular indicators by maternal smoking in pregnancy

	Boys			Girls		
Difference in median	**Model 1**	**Model 2**	**Model 3‡**	**Model 1**	**Model 2**	**Model 3‡**
BMI(kg/m^2)	0.19(0.05,0.33)	0.39(0.26,0.58)	0.39(0.25,0.53)	0.22(0.05,0.39)	0.47(0.32,0.62)	0.46(0.31,0.62)
Waist(cm)	0.40(0.10,0.70)	0.50(0.20,0.81)	0.55(0.24,0.87)	0.59(0.25,0.93)	0.86(0.54,1.19)	0.82(0.45,1.19)
Sum skinfolds(mm)	0.86(0.44,1.28)	1.02(0.57,1.46)	0.94(0.49,1.40)	1.10(0.49,1.71)	1.49(0.88,2.10)	1.47(0.87,2.07)
Triceps	0.30(0.08,0.52)	0.36(0.11,0.61)	0.34(0.08,0.60)	0.26(-0.03,0.55)	0.53(0.24,0.82)	0.57(0.27,0.86)
Subscapular	0.26(0.14,0.38)	0.27(0.15,0.39)	0.24(0.13,0.36)	0.34(0.16,0.52)	0.47(0.29,0.66)	0.40(0.22,0.58)
Suprailiac	0.21(0.57,0.36)	0.25(0.10,0.40)	0.22(0.08,0.37)	0.44(0.22,0.66)	0.54(0.33,0.75)	0.49(0.27,0.71)
SBP(mmHg)	-1.20(-2.90,0.50)	-0.99(-3.00,1.03)	-1.61(-3.58,0.36)	-1.44(-3.64,0.77)	-1.39(-3.64,0.85)	-1.68(-4.61,1.25)
DBP(mmHg)	-1.63(-3.12,-0.14)	-1.59(-3.10,0.08)	-1.65(-2.98,0.31)	-0.40(-2.00,1.20)	-0.35(-2.02,1.31)	-0.26(-1.88,1.35)
RPR(bpm)	-0.65(-3.07,1.77)	-0.46(-3.06,2.14)	-0.55(-3.05,1.96)	-0.47(-2.54,1.61)	-0.33(-2.61,1.96)	-0.42(-2.68,1.84)
Difference in 90th centile						
BMI(kg/m^2)	0.82(0.46,1.18)	1.04(0.64,1.44)	0.84(0.43,1.25)	0.39(0.02,0.75)	0.63(0.28,0.98)	0.63(0.27,1.00)
Waist(cm)	1.56(0.89,2.21)	1.55(0.87,2.22)	1.59(0.86,2.33)	0.73(-0.05,0.35)	1.39(0.71,2.10)	1.14(0.36,1.92)
Sum skinfolds(mm)	2.94(1.38,4.50)	2.43(1.10,3.76)	2.43(0.68,4.18)	1.85(0.25,3.45)	3.01(1.11,3.90)	1.33(-0.33,3.75)
Triceps	0.64(0.13,1.14)	0.63(0.01,1.25)	0.57(-0.05,1.18)	0.06(-0.45,0.55)	0.34(-0.20,0.89)	0.35(-0.17,0.87)
Subscapular	1.31(0.73,1.89)	1.23(0.58,1.88)	1.16(0.50,1.81)	0.77(-0.02,1.56)	1.05(0.33,1.77)	0.79(0.06,1.52)
Suprailiac	1.13(0.44,1.81)	0.97(0.35,1.60)	0.84(0.25,1.43)	0.30(-0.36,0.97)	0.86(0.18,1.54)	0.75(0.02,1.48)
SBP(mmHg)	0.37(-3.27, 4.02)	0.03(-4.00,4.07)	-0.12(-4.64,4.61)	-3.88(-7.41,-0.33)	-4.54(-7.97,-1.12)	-3.92(-7.60,-0.24)
DBP(mmHg)	-2.66(-6.04,0.72)	-3.01(-6.21,0.18)	-3.40(-6.87,0.07)	-0.10(-3.30,3.10)	0.39(-3.01,3.80)	0.65(-2.57,3.86)
RPR(bpm)	-0.56(-3.30,2.17)	-0.43(-3.13,2.26)	-0.63(-3.31,2.06)	-0.62(-3.15,1.92)	-0.43(-3.00,2.15)	-0.33(-3.08,2.43)

† Model 1 included age (t) trends (t+t^2 for girls; t+ln(t) for boys) and height (for waist circumference and skinfolds). Model 2 added maternal BMI, maternal age, birthweight, gestation, parity. Model 3 further added infant feeding, maternal education, maternal employment, lone mother, TV time, and BMI (for BP and RPR). Models were fitted using multiple imputation. Sample size differed by adiposity measure (n=17,286 for BMI; 16,568 for waist circumference; 15,329 for skinfold thickness) and for BP and RPR (n=2492).

‡ *p*-value for age interaction with maternal smoking: for median 0.06 (boys) and 0.04 (girls) for BMI, 0.02 and 0.06 for waist circumference, 0.24 and 0.03 for sum of skinfolds; *p-values* >0.10 for BP and RPR and 90^{th} centiles of all adiposity measures.

Table 2a (same models in Tab 2, observed data only): Differences (95% CI) in measures for adiposity and cardiovascular indicators by maternal smoking in pregnancy-old-to be deleted

	Boys			Girls		
50th centile (median)	**Model 1**	**Model 2**	**Model 3‡**	**Model 1**	**Model 2**	**Model 3‡**
BMI(kg/m^2)	0.19(0.05,0.33)	0.37(0.26,0.55)	0.42(0.30,0.59)-**0.18**	0.21(0.08,0.37)	0.47(0.30,0.60)	0.38(0.23,0.57)-**0.18**
Waist(cm)	0.43(0.11,0.70)	0.74(0.36,1.02)	0.84(0.51,1.15)-**0.14**	0.58(0.32,0.85)	0.60(0.36,0.99)	0.67(0.32,0.95)-**0.13**
Sum skinfolds(mm)	0.77(0.39,1.19)	0.96(0.65,1.47)	0.82(0.36,1.38)-**0.08**	0.91(0.46,1.36)	1.23(0.67,1.70)	0.96(0.27,1.60)-**0.09**
Triceps	0.31(0.10,0.52)	0.39(0.13,0.71)	0.25(-0.04,0.59)	0.24(0.04,0.48)	0.62(0.27,0.85)	0.53(0.19,0.77)
Subscapular	0.27(0.19,0.38)	0.34(0.20,0.46)	0.29(0.14,0.47)	0.35(1.66,0.53)	0.50(0.26,0.68)	0.36(0.17,0.56)
Suprailiac	0.22(0.07,0.36)	0.26(0.16,0.39)	0.21(0.09,0.38)	0.45(0.31,0.60)	0.46(0.28,0.67)	0.36(0.18,0.69)
SBP(mmHg)	1.18(-1.66,3.01)	-1.49(-2.99,0.88)	-2.04(-3.15,0.43)	-0.30(-2.53,2.09)	-1.18(-2.77,0.95)	-0.27(-3.13,1.07)
DBP(mmHg)	0.10(-0.91,1.84)	-0.56(-2.05,0.64)	-1.61(-2.56,0.10)	-0.32(-1.34,1.39)	0.08(-1.80,1.45)	0.52(-1.54,1.23)
RPR(bpm)	-0.15(-1.74,1.66)	-1.47(-4.59,1.37)	-1.84(-4.21,1.39)	0.43(-1.24,1.92)	1.01(-0.70,2.77)	1.14(-1.39,2.77)
90th centile						
BMI(kg/m^2)	0.80(0.39,1.06)	0.93(0.64,1.24)	0.77(0.36,1.28)-**0.41**	0.40(0.05,0.73)	0.67(0.40,0.87)	0.57(0.12,0.91)-**0.23**
Waist(cm)	1.59(0.84,2.41)	1.20(0.47,2.40)	0.86(0.10,2.24)-**0.18**	0.63(0.18,1.54)	1.24(0.65,1.81)	0.93(0.29,1.51)-**0.17**
Sum skinfolds(mm)	2.66(1.13,4.25)	2.97(1.30,5.69)	1.97(0.17,4.18)-**0.20**	1.80(0.31,2.99)	2.58(0.66,4.81)	1.33(-0.33,3.75)-**0.16**
Triceps	0.59(0.09,0.91)	0.84(0.08,1.64)	0.34(-0.13,1.28)	0.06(-0.31,0.65)	0.23(-0.23,0.57)	0.11(-0.55,0.52)
Subscapular	1.33(0.55,1.98)	1.29(0.59,2.26)	0.83(0.09,1.75)	0.81(0.11,1.54)	0.81(0.09,1.39)	0.50(-0.12,1.11)
Suprailiac	1.15(0.44,1.90)	0.96(0.39,1.69)	0.69(0.08,1.54)	0.25(-0.23,1.03)	0.81(0.03,1.34)	0.09(-0.27,0.79)
SBP(mmHg)	-1.05(-2.27, 1.55)	0.97(-1.80,2.52)	0.85(-2.38,3.31)	-1.62(-5.82,-0.59)	-3.39(-5.93,-1.54)	-2.59(-6.03,5.19)
DBP(mmHg)	-1.31(-2.49,0.66)	-2.41(-3.88,2.32)	-2.59(-5.75,3.11)	0.59(-3.26,3.27)	-0.06(-5.28,3.03)	1.25(-3.58,3.18)
RPR(bpm)	-0.28(-3.59,3.90)	-1.24(-3.54,2.69)	-2.21(-4.54,1.57)	-1.42(-3.00,1.03)	0.08(-1.73,4.55)	0.81(-2.34,5.35)

† Model 1 included age (*t*) trends (t+t^2 for girls; t+ln(t) for boys) and height (for waist circumference and skinfolds). Model 2 added maternall BMI, maternal age, birthweight, gestation, parity. Model 3 further added infant feeding, maternal education, maternal employment, lone mother, TV time, and BMI (for BP and RPR only). Sample size differed by adiposity measure (n=17,286 for BMI; 16,568 for waist circumference; 15,329 for skinfold thickness) and for BP and RPR (n=2492).

‡ *p*-value for age interaction with maternal smoking: for median 0.06 (boys) and 0.04 (girls) for BMI, 0.02 and 0.06 for waist circumference, 0.24 and 0.03 for sum of skinfolds; *p-values* >0.10 for BP and RPR and 90th centiles of all adiposity measures.

Table a: Differences in Z-scores for adiposity and CV indicators by maternal smoking in pregnancy-to be deleted

	Imputed samples		Observed samples	
50th centile (median)	**Boys**	**Girls**	**Boys**	**Girls**
BMI(kg/m^2)	**0.18**(0.12,0.24)	**0.20**(0.13,0.26)	**0.18**	**0.18**
Waist(cm)	**0.11**(0.05,0.16)	**0.16**(0.10,0.22)	**0.14**	**0.13**
Sum skinfolds(mm)	**0.09**(0.03,0.14)	**0.11**(0.05,0.17)	**0.08**	**0.09**
90th centile				
BMI(kg/m^2)	**0.40**(0.22,0.58)	**0.29**(0.15,0.43)	**0.41**	**0.23**
Waist(cm)	**0.25**(0.10,0.39)	**0.19**(0.06,0.32)	**0.18**	**0.17**
Sum skinfolds(mm)	**0.24**(0.06,0.40)	**0.18**(0.02,0.34)	**0.20**	**0.16**

† Model included age (t) trends ($t+t^2$ for girls; $t+\ln(t)$ for boys) and height (for waist circumference and skinfolds), also included maternall BMI, maternal age, birthweight, gestation, parity, infant feeding, maternal education, maternal employment, lone mother, TV time, and BMI (for BP and RPR only).

Table b. Adjusted difference in median BMI was 0.75kg/m^2(0.38,1.12) for boys aged 8-10y, compared to 0.25kg/m^2(0.05,0.45) for boys aged 3-5y, and 0.67kg/m^2(0.36,0.98) versus 0.19kg/m^2(-0.01,0.39) for girls (data not shown).

Difference in median BMI	**Observed samples**	
	Boys	**Girls**
3-5y	0.26(0.02,0.54)	0.20(0.08,0.50)
6-7y	0.45(0.18,0.73)	0.55(0.18,0.80)
8-10y	0.80(0.55,1.21)	0.55(0.19,0.88)
9-10y	0.83(0.48,1.42)	0.70(0.27,1.41)

Table 2c: Differences in 50th (median) and 90th centiles (95% CI) of measures for adiposity and cardiovascular indicators by maternal smoking in pregnancy-old to be deleted

	Boys			Girls		
50th centile (median)	**Model 1**	**Model 2**	**Model 3‡**	**Model 1**	**Model 2**	**Model 3‡**
BMI(kg/m^2)	0.18(0.04,0.32)	0.41(0.25,0.57)	0.44(0.30,0.58)	0.21(0.05,0.37)	0.43(0.27,0.59)	0.43(0.27,0.59)
Waist(cm)	0.37(0.06,0.68)	0.56(0.21,0.91)	0.61(0.26,0.96)	0.59(0.26,0.92)	0.85(0.52,1.18)	0.79(0.44,1.14)
Sum skinfolds(mm)	0.27(-0.10,0.38)	0.89(0.03,0.51)	0.90(0.04,0.58)	0.77(-0.10,0.48)	1.43(0.11,0.73)	1.37(0.20,0.82)
Triceps	0.14(0.07,0.35)	0.27(0.14,0.42)	0.31(0.13,0.41)	0.19(0.05,0.49)	0.42(0.24,0.64)	0.51(0.20,0.60)
Subscapular	0.21(0.07,0.35)	0.28(0.14,0.42)	0.27(0.13,0.41)	0.27(0.05,0.49)	0.44(0.24,0.64)	0.40(0.20,0.60)
Suprailiac	0.11(-0.05,0.27)	0.30(0.18,0.42)	0.28(0.14,0.42)	0.32(0.10,0.54)	0.56(0.32,0.80)	0.47(0.23,0.71)
SBP(mmHg)	1.18(-1.00,3.36)	0.98(-1.29,3.25)	-0.80(-2.76,1.16)	-0.31(-3.11,2.49)	-0.44(-2.65,1.77)	-0.78(-3.39,1.83)
DBP(mmHg)	-0.01(-1.68,1.66)	0.08(-1.72,1.88)	-0.05(-1.95,1.85)	-0.18(-1.71,1.35)	-0.01(-1.64,1.62)	-0.10(-1.75,1.55)
RPR(bpm)	-0.32(-1.22,0.58)	-0.05(-2.50,2.40)	0.29(-2.36,2.94)	0.32(-2.29,2.93)	0.62 (-1.67,2.91)	-0.01(-2.48,2.46)
90th centile						
BMI(kg/m^2)	0.79(0.46,1.12)	1.20(0.87,1.53)	1.05(0.72,1.38)	0.45(0.10,0.80)	0.79(0.46,1.12)	0.75(0.46,1.04)
Waist(cm)	1.47(0.73,2.21)	1.31(0.53,2.09)	1.14(0.40,1.88)	0.79(0.06,1.52)	1.61(0.88,2.34)	1.17(0.31,2.03)
Sum skinfolds(mm)	3.28(1.44,5.12)	4.05(2.38,5.72)	4.01(2.19,5.83)	2.45(0.14,4.76)	3.66(1.78,5.54)	2.48(0.60,4.36)
Triceps	0.55(0.02, 1.08)	0.87(0.30, 1.44)	0.81(0.26, 1.36)	-0.53(-1.16, 0.10)	0.47(0.16, 0.78)	0.18(-0.43, 0.79)
Subscapular	1.08(0.49,1.67)	1.77(1.12,2.42)	1.49(0.94,2.04)	0.44(-0.50,1.38)	1.50(0.83,2.17)	1.36(0.56,2.16)
Suprailiac	1.28(0.50, 2.06)	1.47(0.80, 2.14)	1.21(0.58, 1.84)	0.31(-0.59, 1.21)	1.32(0.58, 2.06)	1.02(0.28, 1.76)
SBP(mmHg)	0.21(-3.87, 4.29)	0.02(-1.63, 1.67)	0.74(-2.94, 4.42)	-3.58(-7.60, 0.44)	-4.62(-8.48,-0.76)	-3.32(-7.06,0.42)
DBP(mmHg)	-1.65(-4.69,1.39)	-0.95(-3.97,2.07)	-1.22(-4.92,2.48)	0.98 (-2.47,4.43)	0.38(-3.17,3.93)	0.66(-2.85,4.17)
RPR(bpm)	-0.50(-4.97,3.97)	-0.58(-4.32,3.16)	-1.66(-5.42,2.10)	-1.28(-5.22,2.66)	-0.67(-4.32,2.98)	-1.73(-6.73,3.27)

† Model 1 included age (t) trends ($t+t^2$ for girls; $t+\ln(t)$ for boys) and height (for waist circumference only). Model 2 added parental BMI, birthweight, gestation, parity. Model 3 further added infant feeding, maternal age and education, TV time, frequency of sweet drinks, and BMI (for BP and RPR only). Models were fitted using multiple imputation. Sample size differed by adiposity measure (n=17,286 for BMI; 16,568 for waist circumference; 15,329 for skinfold thickness) and for BP and RPR (n=2492).

‡ *p*-value for age interaction with maternal smoking: for median 0.06 (boys) and 0.04 (girls) for BMI, 0.02 and 0.06 for waist circumference, 0.24 and 0.03 for sum of skinfolds; *p-values* >0.10 for BP and RPR and 90^{th} centiles of all adiposity measures.