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Maternal smoking during pregnancy and child overweight:

systematic review and meta-analysis

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Abstract

Objective—Perform a systematic review of studies reporting on the association between maternal prenatal cigarette smoking and child overweight.

Design—Meta-analysis of observational studies.

Data sources—Medline search and review of reference lists among studies published through June 2006.

Review methods—Included studies reported an association between maternal smoking during pregnancy and risk of overweight among children at least 2 years of age. We did not include in the meta-analysis studies that provided only a continuous measure of adiposity, although those studies are discussed separately.

Results—Based on results of 84 563 children reported in 14 observational studies, children whose mothers smoked during pregnancy were at elevated risk for overweight (pooled adjusted odds ratio (OR) 1.50, 95% CI: 1.36, 1.65) at ages 3–33 years, compared with children whose mothers did not smoke during pregnancy. The pooled estimate from unadjusted odds ratios (OR 1.52, 95% CI: 1.36, 1.69) was similar to the adjusted estimate, suggesting that sociodemographic and behavioral differences between smokers and nonsmokers did not explain the observed association. Although we observed evidence for publication bias, simulating a symmetric set of studies yielded a similar estimate (OR 1.40, 95% CI: 1.26, 1.55).

Conclusions—Prenatal smoking exposure appears to increase rates of overweight in childhood. In parts of the world undergoing the epidemiologic transition, the continuing increase in smoking among young women could contribute to spiraling increases in rates of obesity-related health outcomes in the 21st century.

Keywords

smoking; pregnancy; overweight; meta-analysis; systematic review

Introduction

Despite decades of research, press, counter-advertising, and litigation regarding its adverse effects, tobacco use remains a major cause of preventable morbidity and mortality world-wide.

¹ Although fewer women in the US and Britain now smoke than in past decades, an increasing number of teenage girls are initiating smoking, and smoking rates are declining less rapidly among women than among men, so cigarette smoking remains common among women who are of childbearing age, pregnant, or breastfeeding.¹⁻⁴ In the developing world, a small but rapidly expanding proportion of women smoke.⁵

Exposure to cigarette smoke *in utero* puts a fetus at increased risk for a number of adverse health outcomes, including growth restriction.^{2,6} Whereas smaller size at birth is generally associated with reduced later risk for overweight,⁷ recent research suggests that mothers who smoke during pregnancy have children at increased risk for later obesity. The combination of small size at birth and overweight in later life is not only characteristic of the epidemiologic transition from acute to chronic disease, but also confers a high risk of cardiovascular outcomes in adulthood.⁷⁻⁹

The magnitude of the association between prenatal smoking and childhood overweight and independence from social influences are not clear. In this paper, we review the evidence from both human and animal studies linking prenatal nicotine or tobacco exposure with offspring adiposity. We hypothesized that exposure prenatal smoking would predispose offspring to elevated risk for overweight. We performed a meta-analysis of published observational cohort studies to obtain a pooled estimate of the risk for overweight associated with maternal smoking during pregnancy, using unadjusted estimates and estimates adjusted for factors that may confound the association. We chose to evaluate a dichotomous outcome for weight because overweight is a routinely used measure and has established public health impact. We discuss possible mechanisms by which intrauterine tobacco exposure might program child weight. Finally, we discuss the potential of increasing rates of smoking during pregnancy to fuel the epidemiologic transition to obesity-related adverse health outcomes in the developing world.

Search strategy

To find studies of prenatal smoking and risk for offspring overweight, we performed online searches of the published literature using Pub Med online (1966 to June 2006) with the keywords 'smoking', 'pregnancy', and 'overweight or obesity', yielding 416 references. We also searched using Ovid, with the same terms, each exploded and searched both as a keyword and as a subject heading, yielding 308 references, all of which were also obtained via Pub Med. One of us (EO) reviewed all titles for studies with potential information about smoking during pregnancy and child overweight. We then obtained the full text of candidate articles, and reviewed reference lists from all relevant papers and reviews to identify additional candidates. We performed a full text review on 69 papers. We excluded 13 studies that did not have information on prenatal smoking exposure, and 38 without information on overweight as an outcome, or with outcome prior to age 3 years (Figure 1). Of the 18 remaining studies, 2 did not provide data regarding the multivariable association between prenatal smoking and child overweight, and we were unable to obtain these data by contacting the authors.^{10,11} We also excluded two studies that presented data wholly presented in another publication.^{12,13} We did not contact authors or otherwise attempt to obtain unpublished data. None of the candidates were published in a language other than English, and we identified no data that were published only in abstract form. We thus included in our meta-analysis the 14 studies that met our *a priori* inclusion criteria. We obtained unadjusted estimates from authors of four studies (Table 1).

Methods

Two authors (EO and EL) performed independent data extractions of the eligible studies, in accordance with the 'MOOSE' guidelines.²⁸ We used random-effects models weighted by the inverse of the variance of each study²⁹ to calculate pooled odds ratios across studies. We tested

for heterogeneity between studies and calculated the proportion of the total variability attributable to between-study heterogeneity (I^2).³⁰ To assess potential publication bias, we plotted the natural logarithm of the published odds ratio versus its standard error, and performed a rank correlation test.³¹ When we observed evidence for a publication bias, we used the trim and fill method of Duval and Tweedie³² to impute 'missing' studies and simulate an unbiased dataset. With this method, we removed the most extreme studies one by one, and tested the remaining studies for symmetry. Once the group was no longer asymmetrical, we mirrored the studies that were removed, and included both the published studies and the simulated mirrored studies in the analysis.

We included studies that presented results as an odds ratio for overweight or obesity associated with smoking at some point during pregnancy. We used the final fully adjusted model presented by study authors, although the covariates they included differed across studies. For studies with outcome assessment at multiple ages, we chose the oldest age. When study authors presented multiple outcomes, we chose for the primary analysis overweight, which we defined as BMI $\geq$ 85th percentile or $\geq$ 90th percentile for age and sex. When study authors reported multiple exposures, we selected the lowest smoking dose, and smoking in early pregnancy as opposed to later in pregnancy or throughout pregnancy. We performed secondary analyses (1) using unadjusted estimates, (2) excluding studies in which exposure and outcome were assessed simultaneously, and (3) including obesity (BMI $\geq$ 95th percentile or $\geq$ 97th percentile) as the outcome instead of overweight. We additionally examined the effect of replacing endpoints measured at age 33 years in the 1958 British birth cohort²⁰ with those measured at age 7 years, closer to endpoints for the other studies.

Results

Prenatal smoking and child overweight

Our literature review yielded 14 studies eligible for inclusion in the meta-analysis of smoking and overweight risk^{14–27} (Table 1). These studies included 84 563 children, and represent pregnancies that occurred from 1958 to 2002 in low and non-low income populations in Australia, North America, and Europe. The prevalence of smoking during pregnancy in the studied populations ranged from 7.5 to 51%. We did not include in the meta-analysis studies that presented results as a continuous measure of adiposity or as height and weight individually, although we discuss them below.

Based on our meta-analysis, children whose mothers smoked during pregnancy were at elevated risk for overweight (pooled adjusted odds ratio (OR) 1.50, 95% CI: 1.36, 1.65, P for heterogeneity = 0.02, I^2 = 49%, 95% CI: 8, 71%) compared with children whose mothers did not smoke during pregnancy (Figure 2). The study by Wideroe *et al.*²⁷ had the largest effect on the pooled estimate, but excluding that study only slightly influenced the pooled odds ratio (OR 1.44, 95% CI: 1.33, 1.56, P for heterogeneity = 0.13, I^2 = 30%, 95% CI: 0, 62%). Excluding studies in which mothers were asked about prenatal smoking at the same time outcomes were assessed^{23–25} did not change the pooled estimate (OR 1.51, 95% CI: 1.35, 1.70, P for heterogeneity = 0.005, I^2 = 57%, 95% CI: 21, 77%). Including the age 7 endpoint, rather than that at age 33, from the paper by Powers *et al.*,²⁰ resulted in a somewhat lower pooled odds ratio (OR 1.44, 95% CI: 1.29, 1.60, P for heterogeneity < 0.001, I^2 = 63, 37, 78%). Using obesity cut points, where available, the pooled estimate (OR 1.52, 95% CI: 1.36, 1.69, P for heterogeneity = 0.07, I^2 = 40%, 95% CI: 0, 69%) was similar to that for overweight cut points.

Mothers who smoked during pregnancy tended to be substantially different from nonsmokers in ways that also predict child obesity risk. In general, smokers had lower income, were less educated, heavier, and less likely to breastfeed, and their children had more rapid infancy weight gain and were more inactive.^{19,24,25} However, in older US cohorts and in European

populations in which smoking was more common, smokers differed from nonsmokers less than among populations in which smoking was more rare. The published studies evaluated and included different covariates, although most accounted for maternal weight, fetal growth, and some measure of socioeconomic status (Table 1). In most studies the association between prenatal smoking exposure and child overweight was either unaffected or slightly attenuated by confounder adjustment (Table 1), with a few exceptions^{16,21,26} though authors generally did not report which factors accounted for the change in risk. In one study, adjustment for breastfeeding substantially strengthened the risk of overweight associated with maternal smoking.²⁷ The pooled estimate from the unadjusted odds ratios (OR 1.52, 95% CI: 1.36, 1.69, P for heterogeneity <0.001 , $I^2=67$, 45, 81%) was similar to the adjusted estimate.

We observed evidence for a small study effect suggestive of publication bias, based on asymmetry of the funnel plot (Figure 3) and by rank correlation testing ($P<0.001$). We then imputed 'missing' studies to simulate a dataset without publication bias (Figure 3). The resulting pooled odds ratio (OR 1.40, 95% CI: 1.26, 1.55) was somewhat lower, but still indicated a substantial detrimental effect of prenatal smoking.

Several studies reported associations of prenatal smoking with continuous measures of adiposity. As these studies used a number of different outcome measures, including BMI, BMI z-score, weight-for-height z-score, ponderal index, and skinfold thicknesses, assessed at different ages, we did not pool the continuous outcomes. Consistent with the dichotomous overweight outcome, most estimated greater adiposity in offspring of mothers who had smoked during pregnancy.^{14,15,17,19,20,27,33–36} Two studies reported associations that were not statistically significant, although they did not provide adjusted estimates.^{37,38} No study reported less adiposity. A recent study evaluated children at age 7 with DXA scanning, and reported substantially higher over all body fat, but not truncal distribution of fat, and to a lesser extent higher lean body mass, in children exposed to prenatal smoking.³⁹ Several other publications reporting continuous measures of adiposity were interim analyses of longitudinal cohort studies, including the National Child and Development Study,^{40–42} the Collaborative Perinatal Project,^{43,44} and the ALSPAC cohort^{45,46} for which later publications included a measure of overweight and thus were included in our meta-analysis.^{17,20,21}

A few studies provided information on weight and height individually. Three recent studies reported higher weight but no difference in height in children exposed to prenatal smoking.^{14,19,33} Others have found that prenatally exposed children were both shorter and heavier^{17,34,35,44,47} with shorter leg length.⁴⁸ Additional older studies with no information on weight found that children of smokers were shorter.^{40–42,49,50}

Despite considerable differences in the study populations and exposure metrics, some general patterns were evident that add further detail to the association between prenatal smoking and child overweight. Among studies with information on the amount of maternal smoking, all found evidence for a dose-response.^{19–21,25,27,33,39} Two studies with repeated outcome measurements found that obesity risk increased with increasing child age.^{17,20} Associations between smoking and child overweight were present in studies using never smokers as a reference group and in those that used women not smoking during the index pregnancy, that is, including former smokers, as a reference group.

The timing of smoking exposure was important. In general, smoking throughout pregnancy was associated with a greater risk for child overweight than was smoking in early pregnancy only^{17,20,23} although other studies reported similar estimates for smoking regardless of time during pregnancy.^{24,39} One study found an increased risk of overweight among children whose mothers reported having quit smoking prior to pregnancy,²³ although this finding was

not supported elsewhere.^{15,17,19} Maternal smoking limited to after pregnancy did not appear to increase risk for offspring overweight.²³

Two publications report follow-up of children whose mothers participated in a randomized controlled trial of smoking cessation during pregnancy. MacArthur *et al.*⁵¹ reported on 9-year follow-up of an antismoking intervention consisting of an educational leaflet and a one-time clinician-led discussion and advice to quit, compared with usual care. The intervention resulted in reduced maternal smoking and higher birth weight.⁵² At age 9 years, children whose mothers were randomized to usual care were slightly shorter (0.3 cm) and lighter (0.3 kg), although differences were not statistically significant. When the authors analyzed data according to whether mothers quit smoking or continued smoking, regardless of group assignment, children of persistent smokers were significantly shorter (1.0 cm) but 'not different' in weight (0.6 kg lighter).⁵¹ Fox *et al.*⁵³ did not provide results according to randomization, but similarly found that 3-year-old children of persistent smokers were significantly shorter (1.04 cm) but not different in weight (0.32 kg lighter) compared with children of women who quit during pregnancy. Neither study reported weight-for-height or BMI.

Discussion

Our systematic review suggests that exposure to prenatal smoking increases risk for overweight in childhood. The association was unaffected by adjustment for parental sociodemographic factors and body size, gestational weight gain, infant feeding, and child behaviors, indicating that social and behavioral differences between smokers and nonsmokers are not likely to account for the observed differences in overweight risk. In all of the studies, smoking during pregnancy was associated with increased overweight in offspring, despite a wide range of populations, smoking habits, birth years, and overweight prevalence. Compared with children of nonsmokers, children exposed to prenatal smoking may be heavier, shorter or both.

Publication bias likely exists, as smaller studies reported stronger effects than larger ones, and no published studies were null or reported an inverse association. The data in our review come from observational studies rather than registered clinical trials, so we cannot determine the number of unpublished null studies. We did not contact authors to obtain unpublished effect estimates. However, our efforts to impute the unpublished data suggest that the observed association does not entirely derive from a publication bias.

Other studies have evaluated additional endpoints related to overweight. Single studies have suggested that individuals exposed to prenatal smoking may have greater weight gain from birth to age 2 years,⁴⁵ earlier puberty,³³ elevated risk for diabetes mellitus,⁵⁴ and exhibit a high-risk cluster of low birth weight and higher attained BMI,⁵⁵ or of higher BMI, blood pressure, lipids, and glucose levels.⁵⁶ Several investigators have studied associations between prenatal smoking exposure and blood pressure in childhood. In the studies that accounted for sociodemographics and other characteristics including child size, systolic blood pressure was consistently about 1 mm Hg higher among children who were exposed to prenatal maternal smoking.^{19,36,57,58}

A growing body of epidemiologic and experimental evidence indicates that the prenatal period is a sensitive period for later health outcomes.⁵⁹ Early research in the field considered birth weight as a marker for intrauterine nutrition. The example of maternal smoking highlights the importance of looking at more refined measures, such as body composition, rather than birth weight alone in studying prenatal influences on later size and disease risk. Maternal smoking may result in lower fetal growth but more rapid postnatal weight gain, yet both fetal growth and weight gain in early infancy are directly associated with weight in later life.⁷ In our meta-analysis, associations of smoking with child overweight were independent of birth weight or

fetal growth and postnatal weight gain. These apparently incongruous relationships may be explained by reports that even at birth, infants born to mothers who smoked in pregnancy have a preserved ponderal index⁶⁰ (a measure of weight for length) compared with infants of nonsmokers, and have relatively more body fat but less lean body mass.^{61,62} These findings also reinforce the need for research aimed at understanding pathways independent of early growth by which early life experiences may influence later health and disease risk.⁵⁹

Mechanisms by which maternal smoking may program child weight are not yet well characterized. Likely culprits for the physiologic effects of cigarette smoking during pregnancy are nicotine, which is transported across the placenta, and carbon monoxide, which may influence placental vascular function and cause fetal hypoxia. In both humans and animals, nicotine acts both centrally and peripherally to reduce appetite and body weight, and nicotine withdrawal results in hyperphagia and weight gain.^{63–65} Children of smokers tend to be less physically active and have poorer diet quality.^{66–68} In one study, adults with prenatal smoking exposure were more likely to report having a ‘poor appetite’, although dietary intake was not measured; since they were also heavier, appetite perception might have been influenced rather than appetite itself.^{20,69}

In animal studies, administration of nicotine to pregnant mothers resulted in offspring that were smaller at birth but had increased body fat.^{70–73} In other studies, rats prenatally exposed to low doses of nicotine were not smaller at birth but became heavier by 5–10 weeks of age^{74, 75} and had higher overall body fat as well as increased perivascular adipose tissue, resulting in decreased vascular relaxation.⁷⁵ In another protocol, prenatal nicotine exposure did not influence body weight, but caused higher blood pressure only among genetically susceptible rats.⁷⁶ Among humans, some researchers have studied whether hormones such as leptin may mediate associations of smoking with offspring size. Maternal smoking throughout pregnancy may be associated with lower cord blood leptin^{77,78} though other studies have not suggested an association.^{79,80} Investigations of other possible mediators, including growth hormone and IGF-1, have not been as well studied,⁸⁰ and no data exist regarding levels of any of these hormones beyond the newborn period.

A recent systematic review of prenatal programming of childhood overweight and obesity also considered prenatal smoking, concluding that strong evidence linked maternal smoking with childhood obesity.⁸¹ However, those authors included only 8 studies of the 14 that we evaluated, primarily those with simultaneous collection of exposure and outcome data and with clinical height and weight measurement, did not calculate a pooled effect size, and did not consider publication bias. This present study overcomes these limitations and allows for an estimation of the public health impact on overweight risk resulting from maternal prenatal smoking.

All of the studies included in the present meta-analysis relied upon maternal self-report of smoking behaviors without biochemical validation. However, self-report of smoking during pregnancy has reasonable validity,⁸² and any under-reporting would likely bias results towards the null. Although some studies collected information on prenatal smoking at the same time that child outcomes were assessed, we doubt recall bias as exclusion of these studies did not substantially change estimates. All studies used measured height and weight as the endpoint, none relied on self-report. Sufficient data do not exist to determine whether quitting smoking would lower the risk of child overweight to the same degree as never having smoked.

In addition to demographic differences such as education and income, smokers and their children also tend to have less healthy lifestyle habits, including diet and physical activity.^{66–68,83} Residual confounding may explain the observed higher risk for overweight in exposed children. The similar pooled estimates for unadjusted and adjusted associations

suggest that sociodemographic, behavioral, and dietary differences between smokers and nonsmokers did not explain the observed association. A recent publication found that associations of maternal prenatal smoking with child body fat were only slightly stronger than associations of paternal prenatal smoking, and concluded that residual confounding may explain the observed association.³⁹ However, the evidence for dose-effect, the lack of association with smoking before or after pregnancy, the support from animal studies, and the consistency of results across populations with markedly different demographic profiles and confounding structures make it more likely that a causal association exists. Future studies following children whose mothers participated in randomized trials of smoking cessation during pregnancy might help further elucidate the role of confounding.

In conclusion, available evidence suggests that maternal smoking during pregnancy increases risk for overweight in childhood. These findings add to the recognized health burden from tobacco, already estimated at almost 5 million deaths per year.⁵ The overall population impact of a 50% increased risk of overweight is likely to be large. In the US, where 11% of pregnant women currently smoke⁴ and child overweight is highly prevalent,⁸⁴ about 715 000 US children may be overweight because their mothers smoked. Individuals who are born small and later become obese are at highest risk for developing cardiovascular disease.⁷ This phenotype, typical of exposure to maternal prenatal smoking, is also characteristic of parts of the world undergoing the nutritional transition to high fat diets and sedentary lifestyle and the accompanying epidemiologic transition to chronic diseases associated with obesity.⁸ In such populations, the combination of poor maternal nutrition, lower birth weight, and increasing adoption of a western lifestyle heralds an explosion in obesity and cardiovascular disease that may well intensify if young women respond to tobacco companies' advertisements targeting them.^{8,85}

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Figure 1.
Flow diagram showing the number of studies included in and excluded from the meta-analysis.

Figure 2. Results of meta-analysis of maternal smoking during pregnancy and child overweight. Individual study estimates are indicated by boxes with 95% CIs indicated by lines. The size of the box is inversely proportional to the variance. The pooled estimate is represented by the diamond, with the width of the diamond representing the pooled CI (pooled OR 1.50, 95% CI: 1.36, 1.65).

Figure 3.

Begg's funnel plot with pseudo 95% CIs. Filled circles indicate observed data, and open squares indicate simulated data.

Table 1
Studies included in meta-analysis of maternal smoking during pregnancy and child overweight

<i>Study, 1st author (year), population</i>	<i>N in analysis (cohort)</i>	<i>Child age in years at outcome</i>	<i>Smoking exposure (prevalence)</i>	<i>Covariates</i>	<i>Outcome (prevalence)</i>	<i>Unadjusted OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>
Adams (2005) ¹⁴	252	3	At initial WIC visit—'most 1st or 2nd trimester' (42.5%)	Maternal: age, BMI, education, income Child: birthweight, ever breastfed	BMI≥85th percentile (40.9%)	1.74 (1.05, 2.90) ^d	2.16 (1.05, 4.47)
American Indians in Wisconsin enrolled in the Supplemental Program for Women, Infants, and Children (WIC) ¹⁵	(3015)		Maternal report at prenatal WIC visit		Height and weight measured at WIC visit		
AI Mamun (2006) ¹⁵	3253 (7223)	14	During pregnancy (36.6%)	Maternal: age, marital status, income Child: age, sex, breastfeeding, consumption of fast food, salad, soft drinks, red meat, TV viewing, participation in sports and exercise	85th ≤BMI <95th percentile (19.3%)	1.30 (1.07, 1.58)	1.30 (1.05, 1.60)
Mater University Study of Pregnancy and its Outcomes, Australia			Maternal report during pregnancy and at birth	Child: age, sex, breastfeeding, consumption of fast food, salad, soft drinks, red meat, TV viewing, participation in sports and exercise	BMI≥95th percentile (6.2%) Research measurement of height and weight	1.41 (1.04, 1.91)	1.40 (1.01, 1.94)
Bergmann (2003) ¹⁶	480 (1314)	6	During pregnancy (19.6%) Not reported how assessed	Maternal: social status, overweight in pregnancy Child: breastfeeding	BMI≥90th percentile (9.5%) BMI≥97th percentile (9.5%) Research measurement of height and weight	1.78 (1.21, 2.64)	2.08 (1.19, 3.63) 2.30 (1.15, 4.60)
Chen (2006) ¹⁷	34 866 (44 213)	8	During pregnancy (51.4%)	Maternal: age, race, pre-pregnancy BMI, marital status, education, socioeconomic index, gestational age at recruitment, recruitment site Child: age, birth order, breastfeeding	BMI≥85th percentile (11%)	1.23 (1.08, 1.39) M ^d 1.29 (1.14, 1.47) F ^{da}	1.21 (1.05, 1.39) M 1.37 (1.19, 1.58) F
Collaborative Perinatal Project			Maternal report during pregnancy		BMI≥95th percentile (4%) Research measurement of height and weight	1.17 (0.96, 1.43) M ^d 1.20 (0.99, 1.44) F	1.21 (0.96, 1.51) M 1.31 (1.06, 1.61) F
Dubois (2006) ¹⁸	1550 (2103)	4.5	During pregnancy (25.2%) Maternal report at 5 months postpartum	Maternal: overweight, Child: birth weight, gestational age, weight gain birth to 5 months Other: paternal overweight, household income	BMI≥95th percentile (8.5%) Not reported how height and weight measured	1.6 (1.1, 2.4)	1.8 (1.2, 2.8)

Study, 1st author (year), population	N in analysis (cohort)	Child age in years at outcome	Smoking exposure (prevalence)	Covariates	Outcome (prevalence)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Oken (2005) ¹⁹ Project Viva, US	746 (2128)	3	Early pregnancy (10%) Maternal report during pregnancy	Maternal: pre- pregnancy BMI, gestational weight gain, education, race/ ethnicity, parity Child: age, sex, fetal growth, gestation length Other: Paternal BMI, household income	BMI≥85th percentile (27%) Research measurement of height and weight	2.5 (1.5, 4.1) ^d	2.2 (1.2, 3.9)
Power (2002) ²⁰ National Child and Development Study, UK	5839 (17 414)	33	After the 4th month of pregnancy (33.5%) Maternal report at birth	Maternal: BMI, Child: social class at birth, age 7, and age 33, birthweight, infant feeding, physical inactivity age 23, diet age 33 (fried foods, chips, biscuits, sweets, chocolates), attained education age 33 Maternal: age, parity, obesity Child: birth weight, sex, season at birth, gestational age, plurality, breast feeding, introduction of solids, number of siblings, ethnicity, in childhood time spent watching TV, in car, sleeping. Dietary pattern in childhood. Other: paternal obesity	BMI≥30 Research measurement of height and weight	1.56 (1.22, 2.00) M 1.41 (1.12, 1.79) F	1.55 (1.19, 2.00) M 1.45 (1.13, 1.87) F
Reilly (2005) ²¹ Avon Longitudinal Study of Parents and Children, UK	5493 (13 971)	7	During pregnancy 1-9 cigs/day vs 0 (5.5%) (in total 14% smoked) Maternal report during pregnancy		BMI≥95th percentile (8.6%) Research measurement of height and weight	1.60 (1.17, 2.18)	1.76 (1.21, 2.52)
Salsberry (2005) ²² National Longitudinal Survey of Youth, US	3022 (6615)	6-7	During pregnancy (29%) Maternal report -not reported when assessed	Maternal: Age, parity, race/ ethnicity, pre- pregnancy BMI, education, marital status	BMI≥95th percentile (12%) Not reported how height and weight measured	1.43	1.74 (1.32, 2.29)

Study, 1st author (year), population	N in analysis (cohort)	Child age in years at outcome	Smoking exposure (prevalence)	Covariates	Outcome (prevalence)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Toschke (2002) ²³ Bavarian schoolchildren, Germany	8765 (13 345)	5–6.9	Throughout pregnancy (7.5%) Maternal report at outcome assessment	Child: sex, age, birth year, breast feeding, height and weight measured Child: low birth weight, prematurity, breastfeeding Other: parental education Maternal: education, obesity Child: breastfeeding, TV viewing, video games, physical activity, high infant weight gain Other: paternal obesity	BMI≥90th percentile (10%) BMI≥97th percentile (3%) Clinical measurement of height and weight	1.85 (1.47, 2.33) 2.32 (1.63, 3.30)	1.58 (1.23, 2.04) 1.92 (1.29, 2.86)
Toschke (2003) ²⁴ Bavarian schoolchildren, Germany	4974 (7026)	5–6.9	Early pregnancy (10.9%) Maternal report at outcome assessment	Maternal: education, obesity Child: breastfeeding, TV viewing, video games, physical activity, high infant weight gain Other: paternal obesity	*Overweight* (10.4%) *Obesity* (2.7%) Clinical measurement of height and weight	1.66 (1.27, 2.18) 2.41 (1.41, 3.91)	1.52 (1.14, 2.01) 2.22 (1.33, 3.69)
Von Kries (2002) ²⁵ Bavarian schoolchildren, Germany	6483 (9731)	5–6.9	During pregnancy (9.8%) Maternal report at outcome assessment	Maternal: education, overweight Child: birth weight > 90th percentile, any breastfeeding, TV/video game > 1 h daily, eating snacks in front of TV Other: paternal education overweight Maternal: age, BMI, race/ ethnicity, parity, pregnancy weight gain, education, marital status Child: fetal growth, sex, year of birth	BMI≥90th percentile (10%) BMI≥97th percentile (3%) Clinical measurement of height and weight	1.97 (1.52, 2.56) 2.96 (1.97, 4.46)	1.43 (1.07, 1.90) 2.06 (1.31, 3.23)
Whitaker (2004) ²⁶ Ohio children enrolled in WIC, US	8494	2–4	During pregnancy (32.9%) Birth certificate data	Maternal: age, BMI, race/ ethnicity, parity, pregnancy weight gain, education, marital status Child: fetal growth, sex, year of birth	BMI≥95th percentile age 2 (9.5%) BMI≥95th percentile age 3 (12.5%) BMI≥95th percentile age 4 (14.8%) Height and weight measured at WIC visit	1.20 (1.02, 1.42) ^a 1.09 (0.93, 1.28) ^a 1.06 (0.90, 1.24) ^a	1.43 (1.19, 1.72) 1.25 (1.05, 1.49) 1.21 (1.01, 1.45)
Wideroe (2003) ²⁷ Population based pregnancy cohort in Norway and Sweden	346 (5722)	5	At week 17 (31.3%) Maternal report during pregnancy	Maternal: age, skinfold thickness, education, total energy intake	BMI≥85th percentile (15%) Research measurement of height and weight	3.0 (1.6, 5.6)	3.8 (2.0, 7.2)

<i>Study, 1st author (year), population</i>	<i>N in analysis (cohort)</i>	<i>Child age in years at outcome</i>	<i>Smoking exposure (prevalence)</i>	<i>Covariates</i>	<i>Outcome (prevalence)</i>	<i>Unadjusted OR (95% CI)</i>	<i>Adjusted OR (95% CI)</i>
				week 17, fat and carbohydrate intake week 33 Child: birth weight, breastfeeding duration Other: paternal education			

^aUnadjusted estimate provided by personal communication from study authors.