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Effect of the exposure to maternal smoking during pregnancy and childhood on the body mass index until adolescence

ABSTRACT

OBJECTIVE: Investigate the effect of exposure to smoking during pregnancy and early childhood on changes in the body mass index (BMI) from birth to adolescence.

METHODS: A population-based cohort of children (0-5 years old) from Cuiabá, Midwest Brazil, was assessed in 1999-2000 (n = 2,405). Between 2009 and 2011, the cohort was re-evaluated. Information about birth weight was obtained from medical records, and exposure to smoking during pregnancy and childhood was assessed at the first interview. Linear mixed effects models were used to estimate the association between exposure to maternal smoking during pregnancy and preschool age, and the body mass index of children at birth, childhood and adolescence.

RESULTS: Only 11.3% of the mothers reported smoking during pregnancy, but most of them (78.2%) also smoked during early childhood. Among mothers who smoked only during pregnancy (n = 59), 97.7% had smoked only in the first trimester. The changes in body mass index at birth and in childhood were similar for children exposed and those not exposed to maternal smoking. However, from childhood to adolescence the rate of change in the body mass index was higher among those exposed only during pregnancy than among those who were not exposed.

CONCLUSIONS: Exposure to smoking only during pregnancy, especially in the first trimester, seems to affect changes in the body mass index until adolescence, supporting guidelines that recommend women of childbearing age to stop smoking.

DESCRIPTORS: Pregnant Women. Smoking, adverse effects. Child Development. Body Mass Index. Cohort Studies.

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INTRODUCTION

The prevalence of overweight and obesity in childhood and adolescence is increasing mainly among low-middle income countries,[17] challenging health systems in areas of limited resources. It is well-established that maternal smoking during pregnancy is associated with low birth weight and size of offspring;[a] however, the long term effects of smoking during pregnancy on growth and gain of weight have not been established. Some studies, including systematic review and meta-analysis, report an association between maternal smoking during pregnancy and overweight in later life.[14,23] Studies also confirmed a dose-dependence relationship between the number of cigarettes smoked during pregnancy and overweight[13,15] and independence of intrauterine growth restriction.[28] Most studies were performed in high-income countries and approached the effects of maternal smoking during pregnancy on the risk of overweight and adiposity in childhood, and the effects of these factors in adolescence have also been reported.[2,13] The underlying mechanisms of this association are not well understood. Thus, it is not clear how the period of exposure to maternal smoking affects the risk of obesity in offspring. Furthermore, exposure after birth is highly correlated with prenatal exposure and also appears to be associated with overweight in childhood.[9,18,24] However, few studies have considered the prenatal period in their analyses.

This study aimed to analyze if exposure to maternal smoking during pregnancy and early childhood affects the body mass index (BMI) from birth to adolescence.

METHODS

A cohort of 2,405 children born between 1994 and 1999 was assessed in randomly selected 10 primary care centers of Brazil, in the Cuiabá, MT, Midwest Brazil, from May 1999 to January 2000. According to the National Census of 2000, Cuiabá had 483,346 inhabitants and 8.4% (43,197) were under five years of age.[b] The sampling and research protocols used in this study were previously described.[12] Of the children randomly selected in one of the 10 primary care centers, 94.6% were interviewed. We applied face-to-face interviews using a standardized questionnaire to collect data on socioeconomic and demographic characteristics of households, smoking during pregnancy (including information about on which trimester mothers have smoked), child exposure to parents and any household member smoking, and breastfeeding.

After approximately 11 years, the population was between 10 and 17 years old and the study subjects were located by the 2009, 2010, and 2011 censuses carried out in public and private schools all over the country. The census is conducted on an annual basis under the coordination of the *Instituto Nacional para Estudos Educacionais Anísio Teixeira* (INEP – National Institute for Educational Studies), with the support of the State Education Department. Further details about the search and location of the adolescents were previously described.[12] Children's names, date of birth, and name of mothers were used to identify 86.8% of the adolescents and their schools. For the few cases of more than one child with same name and date of birth, the school census used the name of the mother to confirm the identity of the child participating in the study. Adolescents were also located based on the National Mortality Information System.

Data on birth length and weight were obtained from hospital records; other parameters of the child at ages between zero and five years old (preschool age) and between 10 and 17 years of age were measured or assessed using questionnaires applied by the researchers. At adolescence, data collection was carried out from October 2009 to August 2011 in Cuiabá, Várzea Grande (city geographically and economically integrated to Cuiabá), and 17 other cities in the state of Mato Grosso near the capital, and five Brazilian capitals (Campo Grande, MS; Brasilia, DF; Sao Paulo, SP; Rio de Janeiro, RJ; and Goiania, GO). Figure 1 shows that, from all children evaluated at preschool age (2,405), 0.4% with disabling health conditions were excluded from the interview, the parents or guardians of 2.9% have not authorized their participation in the survey, 2.6% did not come to school on the three attempts to measure them, 0.2% adolescents refused to participate, and 9.0% adolescents could not be evaluated due, for example, to living in distant cities.

Exposure to maternal smoking during pregnancy and early childhood was classified as follows: no exposure (those who were not exposed during neither periods); exposed only during pregnancy (those whose mothers reported having smoked during pregnancy but not during early childhood); exposed only during childhood (when mothers reported not having smoked during pregnancy but smoked during childhood); and exposed to maternal smoking during both periods.

In the first interview, children under two years of age were weighed without clothes in a pediatric scale with

[a] U.S. Department of Health and Human Services The Health Consequences of Smoking. In. Edited by National Institutes of Health NCI, Dept. of Health and Human Services. Rockville: Centers for Disease Control and Prevention; 2004.
[b] Instituto Brasileiro de Geografia e Estatística. Demographic Census 2000: population and household characteristics – universe results. Brasília (DF); 2001 [cited 2013 Dec]. Available from: http://www.ibge.gov.br/english/estatistica/populacao/censo2000/

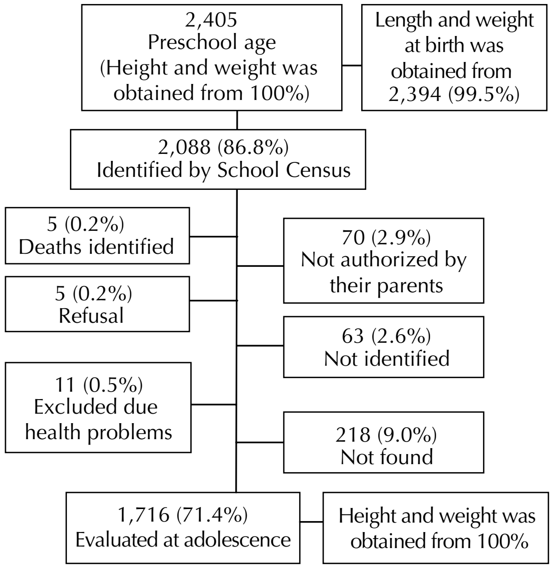

Figure 1. Flow chart of study population.

maximum capacity of 20 kg and accuracy of 10 g. An anthropometric wooden ruler was used to measure length with a fixed vertical piece applied to the head and another mobile piece on the feet, with the child in a supine recumbent position on a firm surface with knees extended. Children of two years or older were weighed on a digital scale with maximum capacity of 150 kg and variation of up to 100 g, minimal clothing and without shoes. Height was measured using a metallic tape attached to a wooden pole mounted on a wall without baseboard molding.

At adolescence (2009-2011), weight was assessed using an electronic scale (Tanita model A-080) with variation of up to 100 g and capacity for 150 kg. The same electronic scale was used to estimate the percentage of body fat using the bioelectrical impedance technique. Height was measured using a portable anthropometer (Sanny), with accuracy of 1 mm and length capacity of up to 2.10 m. Measurements were performed with the subject wearing minimal clothing and no shoes, standing fully erect with feet together, head on the Frankfurt plane, and shoulders relaxed with arms freely hanging during measurements. Two height measurements were performed, assuming maximum variation of 0.5 cm, and average was used for the analysis; the procedure was repeated if the variation limit was exceeded.

For the analysis, BMI and height according to age and sex were calculated using the growth curves published by the World Health Organization (WHO) and expressed as z-scores.[30,31] Scores were calculated using the WHO Anthro program, version 3.1. The cutoff for deficit in height (stunting) was a z-score below -2 of the reference distribution. For BMI-for-age, a z-score < -2 was considered as thin, between -2 and 1 as adequate, between 1 and 2 as overweight, and > 2 as obesity, according to the WHO recommendations.[29]

The socioeconomic level of the families at preschool age and adolescence was determined based on the number of home appliances, cars, remunerated maids, and the educational level of the household head according to the Brazilian Marketing Research Association criteria.[c,d] Birth weight was classified into four categories according to the WHO criteria[29] as follows: low birth weight (< 2,500 g), underweight (2,500-2,999 g), appropriate weight (3,000-3,999 g), and overweight (≥ 4,000 g). Breastfeeding was classified as "any breastfeeding" when a mother reported that her child received breast milk with or without other drink, formula, or infant food.

The distribution of BMI-for-age z-scores in childhood and adolescence according to demographic and socioeconomic characteristics, birth weight, and exposure to passive smoking were compared using the Student's t-test and analysis of variance (ANOVA).

For the longitudinal analysis, the outcome was the BMI itself rather than the BMI-for-age because studies have shown that the BMI z-score is optimal only for assessing adiposity on a single occasion.[4] The effect of exposure to maternal smoking during pregnancy and in childhood was examined using linear mixed effects models in PROC MIXED in the SAS program based on three measurements of log-transformed BMI: BMI at birth, in preschool age (0-5 years), and in school age (10-17 years).

These models account for the correlation between repeated measurements and allow for incomplete outcome data.[8] Time in the models is the age of the child as a continuous variable (years) in each measurement, and piecewise analysis allowed the evaluation of two different periods: between birth and preschool age (st1) and between preschool age and adolescence (st2). Models were tested for random effects (G matrix) of intercept and slope and both were included in the models. The structure chosen for G matrix was the unstructured type as suggested by Fitzmaurice et al.[8]

The interaction terms (st1*maternal smoking and st2*maternal smoking) were used to compare the BMI change over time between children exposed to maternal smoking during pregnancy and childhood and those

[c] Associação Brasileira de Empresas de Pesquisa. Critério de Classificação Brasil 2003. São Paulo (SP); 2003 [cited 2008 Dec]. Available from: http://www.abep.org/codigosguias

[d] Associação Brasileira de Empresas de Pesquisa. Critério de Classificação Brasil. São Paulo (SP); 2008 [cited 2008 Dec]. Available from: http://www.abep.org/codigosguias

who were not exposed. The null hypothesis assumed the mean difference of BMI between the groups as constant over time. Models were adjusted for all variables with $p < 0.20$ at bivariate analyses, retaining in the analysis those variables that change the effect of maternal smoking exposure on growth. The linear mixed effects final model was adjusted for sex, economic class in childhood, and breastfeeding.

The fitness of the models was examined graphically to assess normality of residuals and regression requirements. Analyses were performed with the Statistical Analysis Systems software, version 9.3 (SAS Institute, Cary, NC, USA).

The project was approved by the Ethics Committee of the Hospital Universitário Júlio Müller, Universidade Federal de Mato Grosso (Protocol 651/CEP-HUJM/2009). Parents or guardians of the participating adolescents have signed an informed consent form.

RESULTS

Among 2,405 children evaluated in childhood (1999/2000), length and weight at birth was obtained from 99.5%; in preschool age the height and weight of all children were measured, and 71.4% of them were evaluated in adolescence (2009-2011) at ages between 10 and 17 years old. The mean age of children was 1.5 years at the first interview and 12.2 years at follow-up. The mean age does not vary by maternal smoking status.

As previously reported,[21] loss to follow-up was higher among adolescents with low height-for-age at preschool age, mothers with lower education level and among those exposed to maternal smoking during pregnancy. On the other hand, no differences were observed regarding age, birth weight, sex, socioeconomic status and BMI-for-age (z-score) at preschool age among the children included in the analyses compared to those lost to follow-up.

Among mothers who smoked only during pregnancy, 97.7% smoked only in the first trimester, whereas for those smoking in pregnancy and childhood, 61.8% smoked throughout pregnancy (Table 1).

Results were similar between sexes; thus, data were analyzed in combination. Children from mothers who smoked during pregnancy showed lower weight at birth than children from non-smoking mothers. In childhood and adolescence, the average BMI-for-age z-score was lower in subjects displaying lower birth weight and lower length-for-age z-score at birth. We also observed a positive association between BMI-for-age z-score at adolescence and economical class, maternal schooling, and BMI-for-age z-score at preschool age (Table 1). The BMI-for-age z-score between childhood and adolescence was not associated with exposure to maternal smoking during pregnancy and preschool age. Paternal smoking in childhood was associated with higher z-score of BMI-for-age only at preschool age, but the information of paternal smoking stood for more than 10.0% of the missing data (Table 1).

Therefore, the linear models indicated that in adolescence children exposed to smoking only during pregnancy showed a greater increase of the BMI, and this association was maintained even after adjusting for sex, economic class in childhood, and breastfeeding (Table 2). Furthermore, children exposed to maternal smoking during pregnancy and early childhood showed lower increase of the BMI between childhood and adolescence than children not exposed (Figure 2), with borderline statistical significance ($p = 0.09$). Due to the shortage of information on the paternal smoking variable, it was not included in the main analysis, but a sensitivity analysis including paternal smoking into the multivariate model did not change the regression coefficient of association between maternal smoking and growth.

DISCUSSION

In the present study, children exposed to maternal smoking during pregnancy but not during childhood showed higher rate of change in the BMI between childhood and adolescence. This result is consistent with other studies that reported greater risk of overweight in children exposed to maternal smoking during the prenatal period.[23] Unexpectedly, in our cohort the lowest increase in the BMI occurred among children exposed to maternal smoking during pregnancy and early childhood.

Most studies have evaluated smoking exposure at any time during pregnancy, with no distinction between different periods. However, the gestational period of exposure may be relevant to the risk of overweight and obesity. Our results showed that 97.7% of mothers who reported smoking only during pregnancy have smoked only in the first trimester of pregnancy, and their children showed greater rate of change of the BMI between childhood and adolescence. This result was consistent with prior reports showing that smoking only in the first trimester of pregnancy presented stronger positive association with the risk of overweight and obesity in childhood if compared with exposure in the second or third trimesters.[20,22,27] However, smoking only in the first trimester of pregnancy was not associated with birth weight or length in a hospital-based cohort in Boston, USA.[16] Recently, in another study with participants of the Nurses' Health Study II,[13] the risk of adiposity was not increased among daughters whose mothers stopped smoking during the first trimester.

A possible explanation for greater adiposity among children of mothers who stopped smoking in the

Table 1. Body mass index z-score in childhood and adolescence, according to characteristics in childhood.

Variable	n	%	BMI-for-age z-score 0 to 5 years old		p	BMI-for-age z-score 10 to 17 years old		p
			Mean	95%CI		Mean	95%CI	
Sex					0.92			0.15
Male	1,224	50.9	0.14	0.08;0.21		0.19	0.09;0.22	
Female	1,181	49.1	0.15	0.09;0.22		0.28	0.20;0.36	
Birth weight (g)					< 0.01			< 0.01
≥ 4,000	143	6.9	0.56	0.39;0.73		0.47	0.26;0.69	
3,000-3,999	1,619	67.6	0.22	0.17;0.28		0.30	0.23;0.38	
2,500-2,999	483	20.1	-0.05	-0.14;0.03		0.01	-0.12;0.15	
< 2,500	160	6.4	-0.37	-0.59;-0.15		-0.00	-0.26;0.25	
Length-for-age at birth (z-score)[a]					< 0.01			0.01
< -2 z-score	270	11.3	0.17	0.12;0.22		0.26	0.20;0.32	
≥ -2 z-score	2,124	88.7	-0.06	-0.21;0.08		0.03	-0.15;0.22	
BMI-for-age (z-score) - preschool age								< 0.01
Thinness (< -2 z-score)	69	2.8				-0.44	-0.88;0.00	
Adequate (≥ -2 to ≤ 1 z-score)	1,857	77.2				0.08	0.02;0.15	
Overweight (> 1 to ≤ 2 z-score)	371	15.4				0.72	0.58;0.86	
Obesity (> 2 z-score)	108	0.45				1.40	1.13;1.67	
Height-for-age (z-score) - preschool age					0.21			0.11
< -2 z-score	2,258	93.9	0.13	0.09;0.18		0.32	-0.04;0.60	
≥ -2 z-score	146	6.1	0.31	0.04;0.60		0.14	0.09;0.18	
Economic class[b]					< 0.01			< 0.01
A (high-income)	86	3.6	0.34	0.11;0.58		0.79	0.48;1.11	
B	289	12.0	0.12	-0.02;0.26		0.44	0.25;0.62	
C	1,019	42.4	0.25	0.18;0.32		0.26	0.17;0.35	
D	807	33.5	0.04	-0.03;0.12		0.17	0.07;0.28	
E (low-income)	204	8.5	0.02	-0.12;0.16		-0.17	-0.35;0.02	
Maternal schooling (years)[c]					0.22			< 0.01
≥ 12	206	8.6	0.17	0.03;0.31		0.60	0.40;0.81	
9 to 11	638	26.5	0.16	0.06;0.25		0.30	0.19;0.41	
5 to 8	1,363	56.7	0.16	0.10;0.22		0.15	0.07;0.23	
0 to 4	177	7.4	-0.02	-0.18;0.14		0.18	-0.05;0.41	
Breastfeeding					< 0.01			< 0.01
Any	1,945	80.9	0.17	0.14;0.20		0.26	0.22;0.30	
Never	460	19.1	0.05	-0.01;0.11		0.13	0.04;0.21	
Maternal smoking during pregnancy and at childhood					0.75			0.13
During both periods	212	8.9	0.14	-0.03;0.31		0.11	-0.07;0.29	
Only during pregnancy	59	2.5	0.18	-0.14;0.50		0.70	0.19;1.22	
Only during childhood	76	3.1	0.29	0.03;0.55		0.27	-0.02;0.56	
No smoking	2,042	85.5	0.15	0.10;0.19		0.24	0.17;0.30	
Paternal smoking at childhood[c]					0.03			0.49
Yes	501	25.6	0.25	0.14;0.35		0.21	0.07;0.34	
No	1,456	76.8	0.12	0.07;0.18		0.28	0.20;0.35	

[a] No information for 11 children.
[b] According to the criteria of the Brazilian Marketing Research Association (2003): based on the number of home appliances, cars and paid maids, and education level of the head of household.
[c] In 1999, 21 mothers and 448 fathers did not live with their children.

first trimester of pregnancy is the excessive gain of weight associated with quitting smoking during pregnancy.[1] Indeed, excessive gain of weight during pregnancy is positively associated with adiposity in children.[7] Furthermore, quitting smoking can cause a great deal of stress to the body, and prenatal exposure to maternal stress or anxiety is associated with elevated maternal cortisol,[25] which can potentially

Table 2. Regression coefficient* of log-transformed body mass index according to exposure to maternal smoking during pregnancy and childhood.

Variable	Coefficient	Standard error	p
Rate of change of body mass index			
Childhood	0.18	0.003	< 0.01
Adolescence	0.15	0.004	< 0.01
BMI at birth (intercept) according maternal smoking during pregnancy and childhood			
During both periods	0.03	0.019	0.09
Only during pregnancy	-0.07	0.036	0.03
Only during childhood	0.01	0.029	0.60
No smoking	–	–	–
Rate of change of BMI between preschool age and adolescence according maternal smoking during pregnancy and childhood			
During both periods	-0.03	0.017	0.09
Only during pregnancy	0.07	0.033	0.03
Only during childhood	-0.01	0.03	0.72
No smoking	–	–	–

* Linear mixed effects model adjusted for sex, economic class in childhood and breastfeeding.
Significant values are presented in bold.

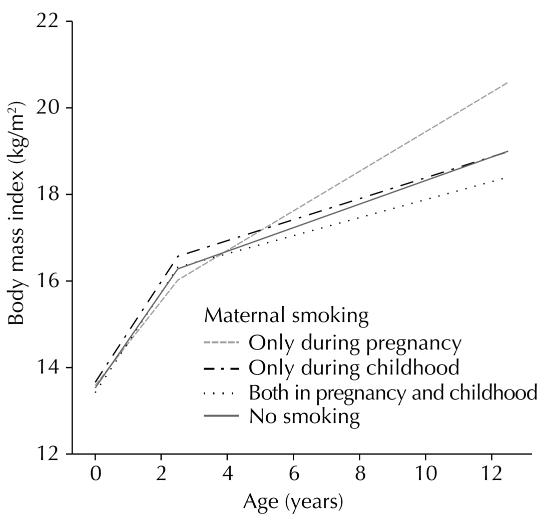

Figure 2. Predicted means of body mass index from birth to adolescence, for exposure to maternal smoking adjusted for gender, socioeconomic position at preschool age, and breastfeeding.

lead to altered metabolism in later life, associated with adiposity and diabetes.[5]

In Brazil, analyses comprising children aged 8-10 years from a cohort of Ribeirao Preto (born between 1987-1989) showed no association between exposure to smoking during pregnancy and overweight in childhood.[26] In the same cohort (born between 1978-1979), however, adolescents whose mothers had smoked during pregnancy reported higher mean BMI at the age of 18 years.[10] Another Brazilian cohort (the Pelotas cohort) showed that children younger than four years exposed to maternal smoking during pregnancy had higher BMI z-scores for age in childhood.[19]

The present study indicates that the period of exposition to maternal smoking affects the risk of gain of weight. However, the challenge is the high correlation observed between smoking in pregnancy and post-pregnancy, which may also have an impact on the nutritional status of children.[25] The results presented herein suggest that changes in the BMI between childhood and adolescence differed between offspring of mothers who smoked during pregnancy and childhood, and those of non-smokers, with lower increase in the BMI among children exposed to both periods; however, but differences were small and could be explained by chance. This result differs from those according to which exposure to tobacco smoke in early life contributes to overweight in later life. Raum et al[24] analyzed the risk of overweight at six years old associated with exposure to maternal smoking before, during, and after pregnancy and showed positive association with overweight only for exposure early in life. Likewise, Mangrio et al[18] suggested that not only smoking during pregnancy, but also secondhand tobacco smoke in early life is a risk factor for overweight in childhood. However, in a recent study, Yang et al[32] concluded that the association between postnatal smoking of both parents and adiposity in children of 6.5 years old was more likely to reflect residual confounding by genetic, family, and environmental factors.

Smoking prevalence is higher among lower-income families and individuals with low education level in Brazil,[e] while socioeconomic levels, in turn, are positively associated with overweight among the Brazilian population.[f] In a previous analysis of this cohort, a higher exposure to household smoking was observed among families of lower socioeconomic level.[11] For this reason, our analysis was adjusted to the socioeconomic level of the family at the first evaluation (when children were up to five years of age). Additional adjustments for socioeconomic level during adolescence did not change the associations with maternal smoking (main exposure of interest).

Despite the well-known harmful effects of smoking, many women continue smoking throughout pregnancy. In Brazil, we observed a decreasing trend in the prevalence of smoking; this trend is stronger among men

[e] Ministério da Saúde. VIGITEL Brasil 2009: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Brasília (DF); 2009.
[f] Instituto Brasileiro de Geografia e Estatística. National Household Budget Survey 2002-2003: anthropometry and nutritional status of children, adolescents and adults in Brazil. Brasília (DF); 2010.

than among women. The prevalence of smoking among women is 12.4% and for men it is18.4%.[3]

Our study evaluated socioeconomic status in childhood, thus we were able to control the possible influence this factor might have since early life on the BMI change. We have used statistical analysis methods for repeated measurements, resulting in incomplete outcome data. We have classified children based on pre- and postnatal exposure to maternal smoking assessed by a questionnaire that appears to be an accurate measure.[6] In addition, the non-reduction of BMI at birth for the offspring of mothers who reported having not smoked during pregnancy but who started smoking again after delivery, supports the validity of self-reported smoking data.

This study has limitations such as the lack of information on pre-pregnancy nutritional status, length and weight at birth obtained from hospital records, gestational weight gain, nutritional habits of children in preschool age, maternal alcohol or other drug use, and number of cigarettes smoked by the mother. Furthermore, the follow-up rate of 72.0% with selective loss of children exposed to maternal tobacco smoke may have biased the study;[21] however, the selective loss to follow-up may have biased findings toward the null hypothesis.

In conclusion, our longitudinal analyses of children from a Brazilian cohort showed that maternal smoking during pregnancy, but not in childhood, affects the rate of change of the BMI until adolescence. Children exposed to maternal smoking during pregnancy reported lower birth weight; however, between childhood and adolescence, the rate of change of the BMI in children exposed to maternal smoking was higher than among those not exposed. Because most of the mothers who smoked only during pregnancy smoked exclusively during the first trimester, our findings support the guidelines of recommending smoking cessation among women of childbearing age.

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