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Is grand-parental smoking associated with adolescent obesity? A three-generational study

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Abstract

Background/Objectives—Data from previous studies consistently suggest that maternal smoking is positively associated with obesity later in life. Whether this association persists across generations is unknown. We examined whether grand-parental smoking was positively associated with overweight status in adolescence.

Subject/Methods—Participants were grandmother-mother-child triads in the Nurses' Health Study II (NHS II), the Nurses Mothers' Cohort Study, and the Growing up Today Study (GUTS). Grandmothers provided information on their and their partner's smoking during pregnancy with the child's mother. Information on child's weight and height at ages 12 (N = 3094) and 17 (N =

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3433) was obtained from annual or biennial GUTS questionnaires. We used logistic regression to estimate ORs of being overweight or obese, relative to normal weight.

Results—Grand-maternal smoking during pregnancy was not associated with overweight status in adolescence. After adjusting for covariates, the OR of being overweight or obese relative to normal weight at age 12 years in girls whose grandmothers smoked 15+ cigarettes daily during pregnancy was 1.21 (95% CI 0.74–1.98; p_{trend} = 0.31) and 1.07 (0.65–1.77; p_{trend} = 0.41) in boys. Grand-paternal smoking during pregnancy was associated with being overweight or obese at age 12 in girls only, but not at age 17 for either sex: the OR for being overweight or obese at age 12 was 1.38 (95% CI 1.01–1.89; p_{trend} = 0.03) in girls, and 1.31 (95% CI 0.97–1.76; p_{trend} = 0.07) in boys. Among children of non-smoking mothers, the OR for granddaughter obesity for grand-paternal smoking was attenuated and no longer significant [OR 1.28 (95% CI 0.87–1.89; p_{trend} = 0.18)].

Conclusions—Our findings suggest that the association between maternal smoking and offspring obesity may not persist beyond the first generation. However, grand-paternal smoking may affect overweight status of the granddaughter, likely through the association between grand-paternal smoking and maternal smoking.

INTRODUCTION

Childhood and adolescent overweight and obesity continue to be a major public health concern in the United States and worldwide. Consequences of childhood and adolescent obesity include increased risk of metabolic diseases ([1], [2]), cardiovascular disease ([3], [4]), and some cancers ([5], [6]). While there has been an appreciable decline in prevalence of overweight and obesity among children aged 2–5 in recent years, there has been little change in older children and adolescents ([7]). Recent data from the United States suggest that 35% of adolescents were overweight or obese in 2011–2012 ([7]), compared to 11% just two decades earlier ([8]).

Determinants of adolescent obesity include physical inactivity ([9], [10]) and diet ([11], [12]); however, the intra-uterine environment may also play a role in the development of obesity ([13]). Data from previous studies consistently suggest that exposure to maternal smoking *in utero* is associated with a 40–60% increased odds of obesity in the offspring ([14]–[16]). Whether this association persists in subsequent generations is unknown.

Female oocytes develop *in utero* and the process is complete prior to birth. Prenatal exposure to smoking may affect the development of these oocytes as the vaso-constrictive effects of nicotine and cotinine may impair blood flow to the developing fetal ovary ([17], [18]). This may lead to phenotypic or inherited maladaptations that could influence the development of obesity in the second generation. In animal models, perturbations during pregnancy such as protein or caloric restriction have been linked to obesity and other metabolic diseases in the second and subsequent generations ([19]–[21]), but data in humans are sparse.

Grand-maternal smoking has been previously examined in relation to birth weight and childhood asthma. Findings from studies on the association between grand-maternal smoking and birth weight suggest that any association may be modest ([22]–[25]). For

childhood asthma, a positive association was reported in a study where only maternal *in utero* exposure was assessed ([26]), whereas in another study ([27]), a positive association was observed among offspring of men who were exposed *in utero*, but not among offspring of women. To our knowledge, the association between grand-maternal smoking and body size during adolescence has not been previously studied.

Understanding whether a link exists between grand-maternal smoking and body size can further elucidate our understanding of the development of obesity, and suggest potential pathways for interrupting this process. About 12% of all women continue to smoke into their third trimester ([28]), despite all widely available information about the dangers of smoking during pregnancy, making understanding this question important.

Therefore, we examined the association between grand-parental smoking and overweight and obesity in the offspring in a three-generation study, including the Nurses' Mother's Cohort Study, the Nurses' Health Study II, and the Growing Up Today Study.

METHODS

Study population

Participants in this study are grandmother-mother-child triads from the Nurses' Mothers' Cohort Study, the Nurses' Health Study II (NHS II), and the Growing Up Today Study (GUTS). The NHS II is a prospective cohort study that began in 1989 with 116,430 female registered nurses residing in the USA. Participants provided information on health and lifestyle factors in 1989, and then every 2 years thereafter. In 1996, participants of the NHS II were asked if their children could participate in a follow-up study, the Growing Up Today Study (GUTS). After receiving consent, invitation letters were sent to 25,000 children who were aged between 9 and 14 years ([29]). In 2001, participants of the NHS II were asked permission to contact their mothers to invite them to participate in the Nurses' Mothers Cohort Study, a study designed to obtain information about the nurse's early life exposures ([30]).

This study was approved by the Committee on the Use of Human Subjects in Research at Brigham and Women's Hospital and the Harvard Chan School of Public Health (Boston, Massachusetts). Completion of the self-administered questionnaires was taken to imply informed consent.

Assessment of grand-parental smoking during pregnancy

Participants in the Nurses' Mothers' Cohort Study were asked whether they smoked cigarettes during their pregnancy with the nurse, and if so, how many cigarettes they smoked daily, and whether they quit smoking during pregnancy. The nurses' mothers were also asked whether the nurse's father or their partner smoked cigarettes during their pregnancy with the nurse, and how many they smoked daily.

The reliability of self-reported smoking during pregnancy has been previously assessed. Participants of the National Collaborative Perinatal Project were asked to recall pregnancy-related events from 30 or more years previously ([31]). Recall was accurate for smoking

(sensitivity = 0.84, specificity = 0.94), suggesting that long-term maternal recall of smoking is a reliable method of assessing smoking status.

Assessment of Body Mass Index at Ages 12 and 17

Information on weight and height was obtained annually via self-report from participants in GUTS from 1996–2001 and then biennially until 2013. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. For boys and girls who reached age 12 or 17 years during a year in which no questionnaire was completed, we estimated their BMI at that age by averaging the BMI reported in the prior and subsequent years (e.g., at ages 11 and 13).

We used the age and sex-specific cut-offs from the International Obesity Task Force to classify participants as normal weight, overweight, and obese at baseline, age 12, and age 17 ([32]). For girls, the BMI cut points for overweight and obese at age 12 were 21.68 and 26.67 kg/m^2, respectively, and at age 17 were 24.70 and 29.69 kg/m^2, respectively. For boys, the BMI cut points for overweight and obese at age 12 were 21.22 and 26.02 kg/m^2, respectively, and at age 17 were 24.46 and 29.41 kg/m^2, respectively. Self-reported height and weight have been found to be reasonably accurate in children and adolescents ([33]), although reliability increases with age ([34], [35]).

Assessment of covariates

From the Nurses' Mothers' questionnaire, we obtained grand-maternal age at time of mother's birth, grand-maternal pre-pregnancy BMI, and grandmother's education. In a validation study, pre-pregnancy height and weight were found to be recalled with high accuracy (r = 0.95), even after decades ([31]). We obtained information on maternal smoking from the Nurses' Health Study II questionnaire. From the GUTS questionnaires, we obtained Tanner stage of development, weekly hours of vigorous physical activity, and weekly hours of TV viewing. If available, the previous year's covariate information was substituted for information needed for years in which no questionnaire was returned, or if the information was missing. Missing indicators were then used for participants remaining information for any covariates. Less than 8% of participants had missing covariates for any variable, except Tanner stage of development at age 12 in boys (11% missing).

Boys and girls were analyzed separately in this study due to differences in growth patterns in both sexes. A total of 3,960 grandmother-mother-girl and 3,473 grandmother-mother-boy triads participated in all three studies. We excluded children who were adopted (girls: n = 5, boys: n = 4), children whose mothers were adopted (girls: n = 7, boys: n = 3), and children whose grandmothers did not report their smoking behavior (girls: n = 290, boys: n=264) to form the base population.

For the analyses at age 12, we further excluded children missing information on BMI at age 12 (girls: n = 1929; boys: n = 1672). We also excluded children whose BMIs were considered outliers using the extreme studentized deviate (ESD) many outlier procedure([36]) (girls: n = 3, boys: n = 4). To eliminate correlation between siblings, when there was more than one child with the same mother (5% of the cohort), we randomly selected one sibling for participation. Among the girls, there were 1555 single-child groups, 84 two-sibling

groups, and 1 three-sibling group. Among the boys, there were 1382 single-child groups, 72 two-sibling groups and no three-sibling groups. After randomly selecting one child per family, 1640 girls and 1454 boys remained in the Age 12 population.

For the analyses of BMI at age 17, we excluded those with missing information on BMI at age 17 (girls: n = 1466; boys: n = 1619) and those considered outliers (girls: n = 24; boys: n = 10) from the base population. Among the girls, there were 1792 single-child groups, 179 two-sibling groups, and 6 three-sibling groups. Among the boys, there were 1344 single-child groups, 107 two-sibling groups, and 5 three-sibling groups. After randomly selecting one child per family, 1977 girls and 1456 boys remained in the Age 17 population.

Our study population was slightly younger than the original GUTS population. For example, for the Age 12 population, the average age was 10.9 years, compared with 12.2 years in the original population. However, ethnicity (percent white; study population 97% versus 96% for those not included) and household income distribution (percent ≥ $75,000 annually; 63% for both) were similar in both populations.

Statistical Analysis

Follow-up began at GUTS baseline in 1996 and ended in 2004, when all participants were at least 17 years of age. We analyzed the association between grand-parental smoking and offspring BMI at ages 12 and 17 using logistic regression. Exposure was assessed in 3 ways: grand-maternal smoking, grand-paternal smoking, and grand-parental smoking. Grand-maternal smoking during pregnancy was categorized as none, quit during pregnancy, 1–14 cigarettes/day, or ≥ 15 cigarettes/day. Grand-paternal smoking was categorized as none, 1–14 cigarettes/day, or ≥15 cigarettes/day. Grand-parental smoking was categorized as none, one grandparent, or both grandparents. Because of the relatively low proportion of obese children in each population (5% or less), we combined the overweight and obese groups and modeled BMI at ages 12 and 17 as binary outcomes, corresponding to normal weight versus overweight or obese.

The first model was adjusted for the child's age at baseline (1996). The second model was further adjusted for covariates associated with the grandmother, and the third model was further adjusted for covariates related with the grandchild (see footnotes in Tables 2–5).

We also examined the association between grand-parental smoking and body size among boys and girls whose mothers never smoked.

We included all participants of the study population that met our inclusion criteria. Based on a 20% overweight/obese status in the unexposed population, and a 3:1 ratio of unexposed to exposed, we require a minimum sample size of 1351 participants to detect an odds ratio of 1.50 with 80% power (37).

All statistical tests were two-sided. The data distribution meets the standard assumptions underlying logistic regression models.

Code Availability

Specific code cannot be accessed externally.

RESULTS

In the Age 12 study population, 2314 (75%) of grandmothers reported not smoking during pregnancy with their grandchild's mother, 138 (4%) reported quitting during pregnancy, while 411 (13%) smoked 1–14 cigarettes per day, and 231 (7%) smoked 15+ cigarettes per day throughout the pregnancy. With the exception of heavy smokers (i.e. grandmothers who smoked 15 or more cigarettes/day) smokers were more highly educated than non-smokers (Table 1). Grandmothers who were smokers were generally more likely to have daughters who were also smokers. The average age (standard deviation) at baseline (1996) for girls was 11.0 (0.9) years and 10.9 (0.9) years for boys. The average BMI (standard deviation) at baseline for girls was 18.2 (3.1) kg/m^2; 16% were overweight, and 3% were obese. The average BMI at baseline for boys was 18.4 (3.2) kg/m^2; 16% were overweight and 4% were obese. The distribution of participant characteristics in the Age 17 population was similar (data not shown).

At age 12, 18% of girls were either overweight or obese. Exposure to grand-maternal smoking during pregnancy with the mother was not associated with body size at age 12 in the age- or covariate-adjusted analyses (Table 2). After adjusting for grand-parental and child covariates, the odds ratio of being overweight or obese, comparing girls whose grandmothers smoked 15 or more cigarettes per day throughout pregnancy to non-smokers was 1.21 (95% CI 0.74–1.98; $p_{trend} = 0.31$). Results were similar among the subset of girls whose mothers never smoked.

Grand-paternal smoking while the grandmother was pregnancy with the mother was associated with increased odds of being overweight or obese at age 12 (Table 2). After adjusting for grandparent and child covariates, the odds ratio of being overweight or obese for girls whose grandfathers smoked 15 cigarettes or more a day compared to girls whose grandfathers did not smoke was 1.38 (95% CI 1.01–1.89; $p_{trend} = 0.03$). After restricting to the girls whose mothers never smoked, the associations for grand-paternal smoking were attenuated and no longer statistically significant.

In secondary analyses, we also examined the association between grand-paternal smoking and obesity in girls at age 12 among girls whose fathers never smoked. The associations were largely unchanged compared to those observed among all mothers (data not shown).

At age 17, 17% of girls were either overweight or obese. Exposure to grand-parental smoking during pregnancy with the mother was unrelated to weight status at age 17 in girls, in both the crude and adjusted analyses (Table 3). After adjusting for grandparent and child covariates, the OR of being overweight or obese at age 17 for girls whose grandmothers smoked 15 or more cigarettes/day during pregnancy compared to girls whose grandmothers did not smoke during pregnancy was 0.91 (95% CI 0.56–1.48; $p_{trend} = 0.81$). Results were similar among daughters of non-smoking mothers. Grand-paternal smoking and grand-parental smoking overall were also unrelated to overweight or obesity at age 17.

At age 12, 22% of boys were either overweight or obese. Grand-maternal smoking during pregnancy with the mother was not associated with weight status at age 12 (Table 4). After adjusting for child-related covariates, the OR was 1.07 (95% CI 0.65–1.77; $p_{trend} = 0.41$). After restricting the population to boys whose mothers never smoked, grand-maternal smoking remained unrelated to body size at age 12. Similarly, grand-paternal smoking was not associated with being overweight or obese at age 12. After adjusting for child covariates, the OR was 1.31 (95% CI 0.97–1.76; $p_{trend} = 0.07$). After restricting to boys whose mothers never smoked, the association remained non-significant. Similarly, grand-parental smoking was unrelated to body size at age 12.

At age 17, 21% of boys were either overweight or obese. Grand-maternal smoking during pregnancy with the mother was not associated with body size at age 17 (Table 5). After adjusting for grand-parental and child covariates, the OR of being overweight or obese for boys whose grandmothers smoked 15 or more cigarettes daily compared to boys whose grandmothers did not smoke, was 0.79 (95% CI 0.46–1.33; $p_{trend} = 0.47$). Among sons of non-smoking women, grand-maternal smoking remained unrelated to weight status at age 17. Similarly, grand-paternal and grand-parental smoking were unrelated to body size at age 17, in both the crude and adjusted analyses.

DISCUSSION

In this three-generational cohort study, exposure to grand-maternal smoking during pregnancy with the mother was not associated with being overweight or obese at age 12 or age 17 in girls or boys. However, grand-paternal smoking was positively associated with being overweight or obese at age 12 in girls, although the positive association was attenuated when the population was restricted to children of non-smoking women.

To our knowledge, this is the first study to examine grand-parental smoking in pregnancy and body size during adolescence. Four previous studies have examined grand-parental smoking with respect to birth weight in the offspring and the results have been conflicting. In the Michigan Bone Health and Metabolism Study, grand-maternal smoking was associated with a statistically significant but small increase in birth weight, which was limited to grandmothers who were born between 1929 and 1945, suggesting that birth cohort effects may play a role ([25]). In the Baltimore cohort of the National Collaborative Perinatal Project, grand-maternal smoking was associated with a statistically significant, small reduction in birth weight ([24]). In the Avon Longitudinal Study of Parents and Children, grand-maternal smoking was associated with a small increase in birth weight in girls only, and there was no association between grand-paternal smoking and birth weight in boys or girls ([23]). However, in a United Kingdom-based population study, there was no association between grand-maternal smoking and birth weight ([22]). Taken together, these findings suggest that, in the absence of residual confounding, any association between grand-maternal smoking and birth weight is modest.

We also observed that grand-paternal smoking and grand-parental smoking were associated with increased odds of being overweight or obese in early adolescence, in girls but not in boys. Data from studies of the epigenetic changes due to *in utero* exposure to smoking

suggest that these changes can persist over time ([38], [39]), at least from birth through late adolescence in the first generation; however, studies are limited on how these changes manifest in the second or subsequent generations. In a review of the dynamics of epigenetic phenomena across and within generations, Burggren hypothesized that epigenetic effects could persist across one generation, and gradually decline within or across subsequent generations ([40]), which is consistent with our finding that grand-paternal smoking was associated with obesity at age 12 years but not at age 17 in girls. Additional epidemiological studies should be conducted to better elucidate these processes across multiple generations. Nevertheless, this finding was unexpected since grand-maternal smoking was unrelated to adolescent body size at any age. Moreover, after the population was restricted to children of non-smoking mothers, the associations were attenuated and no longer significant, suggesting that the association between grand-paternal smoking and body size may be due to the correlation between grand-paternal smoking and maternal smoking. In some studies ([41], [42]) but not all ([43]), parental smoking was associated with offspring smoking. In our population, grand-maternal and grand-paternal smoking were associated with 40% and 60% increased odds of maternal smoking, respectively.

We may not have observed an association between grand-parental smoking and adolescent obesity overall, if the effect of smoking on obesity in the second filial generation is conveyed via only the father's *in utero* exposure. In a follow-up study of those exposed *in utero* to the Dutch famine in 1941, the offspring of men, but not women, were heavier compared with the unexposed ([44]). Since our study involves the offspring of female participants only, we did not have the opportunity to examine such an association. Therefore, future studies on the effects of grand-parental smoking should also examine outcomes in the second filial generation from paternal exposure to *in utero* smoking.

Our study has some limitations. At around 20%, the proportion of overweight or obese children in our population is significantly less than the 35% in the United States population currently ([7]), limiting generalizability. Differences in ethnicity and socioeconomic status, for example 97% Caucasian and 63% with a family income of ≥$75,000 compared with US population proportions of 78% ([45]) and 35% ([46]) respectively, may explain this disparity in weight status ([7], [47]). Although participants in our sample are on average slightly younger than those in the original population, participant characteristics in our study sample do not differ from the original population with respect to important covariates like family income, and ethnicity. Grand-parental smoking during pregnancy was recalled from up to several decades earlier, introducing the possibility of misclassification. However, although some misclassification is likely, another study that used this measure reported significant associations ([14]). Finally, we may not have detected an association with body size in early adolescence after restricting to non-smoking mothers because of the smaller sample size and subsequently lower power. Therefore, an independent association between grand-paternal smoking and offspring obesity cannot be ruled out.

Strengths of our study include unique three generations' worth of high quality and rarely available data, providing an opportunity to examine exposures and outcomes over an extended time frame. Because we had detailed information on grand-maternal smoking during pregnancy, we were able to evaluate the effect of different levels of smoking. Finally,

to our knowledge, this is the first study to examine the association between grand-parental smoking and obesity in adolescence.

Our findings suggest that grand-maternal smoking during pregnancy with the mother is not associated with obesity in the grandchild, and that trans-generational effects of maternal smoking may not progress beyond the first generation.

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Table 1

Age-standardized characteristics of participants of the Growing Up Today Study (GUTS) according to their grandmother's smoking status during pregnancy

	Grandmother's smoking during pregnancy			
	Age 12 population			
	Non-smoker	Quit during pregnancy	1–14 cigarettes/ day	15+ cigarettes/ day
BOYS				
Total population	1454			
n	1084	68	197	105
Age at baseline, years[1]	10.9 (0.9)	11.1 (0.9)	10.9 (0.9)	11.0 (0.8)
BMI at baseline	18.4 (3.2)	17.9 (2.8)	18.6 (3.2)	18.7 (3.3)
- Normal weight, %	80	88	75	76
- Overweight, %	16	11	20	18
- Obese, %	4	1	5	5
From Grandmother's (Nurses' Mother's Cohort) Questionnaire				
Age at time of nurse's birth, years	26.7 (5.1)	25.7 (4.8)	25.9 (4.4)	25.1 (4.0)
Mean pre-pregnancy BMI, kg/m^2	21.5 (2.7)	21.0 (2.1)	21.2 (2.6)	21.7 (3.1)
Education – some college or graduate, %	38	50	50	38
From Mother's (NHS II) Questionnaire				
Mother ever a smoker, %	27	38	34	41
From Boys' (GUTS) Questionnaire				
Weekly hours of TV viewing	16.5 (10.3)	16.3 (10.4)	16.5 (9.5)	17.1 (9.9)
Weekly hours of vigorous physical activity	16.5 (10.3)	16.3 (10.4)	16.5 (9.5)	17.1 (9.9)
Ever tried cigarettes, %	4	4	4	4
GIRLS				
Total population	1640			
n	1230	70	214	126
Age at baseline, years[1]	11.0 (0.9)	10.9 (1.0)	11.0 (0.9)	10.9 (0.9)
BMI at baseline	18.2 (3.0)	18.0 (2.8)	18.0 (3.4)	18.2 (3.1)
- Normal weight, %	80	83	83	79
- Overweight, %	17	16	12	18
- Obese, %	3	2	2	2
From Grandmother's (Nurses' Mother's Cohort) Questionnaire				
Age at time of mother's birth, years	26.4 (4.9)	25.8 (4.6)	26.1 (4.8)	25.8 (2.4)
Pre-pregnancy BMI, kg/m^2	21.3 (2.5)	21.0 (2.2)	20.7 (2.2)	21.1 (2.4)
Education – some college or graduate, %	38	55	46	38
From Mother's (NHS II) Questionnaire				
Mother ever a smoker, %	27	30	36	30
From Girls'(GUTS) Questionnaire				

	Grandmother's smoking during pregnancy			
	Age 12 population			
	Non-smoker	Quit during pregnancy	1–14 cigarettes/ day	15+ cigarettes/ day
Weekly hours of TV viewing	14.2 (9.4)	14.6 (8.7)	14.1 (8.8)	14.8 (9.2)
Weekly hours of vigorous physical activity	7.8 (5.9)	8.7 (5.8)	8.1 (6.7)	8.2 (6.0)
Ever tried cigarettes, %	3	2	2	2

Values are means (standard deviations) or percentages, and standardized to the age distribution of the population.

[1]Value not age-standardized

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Table 2

Associations (odds ratios and 95% CI) between grand-parental smoking during pregnancy and overweight or obesity among GUTS[1] **girls** at age 12 (1996–2004)

	All Mothers				Non-smoking Mothers Only			
	N	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**	**N**	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**
Grand-maternal smoking								
None	1230	Ref	Ref	Ref	893	Ref	Ref	Ref
Quit during pregnancy	70	1.21	1.31 (0.71–2.43)	1.37 (0.73–2.58)	49	1.00	1.09 (0.49–2.40)	0.99 (0.44–2.24)
1–14 cig/day	214	1.01	1.12 (0.76–1.65)	1.14 (0.76–1.69)	137	0.74	0.82 (0.48–1.42)	0.85 (0.48–1.48)
15+ cig/day	126	1.14	1.16 (0.72–1.86)	1.21 (0.74–1.98)	88	1.14	1.20 (0.67–2.14)	1.33 (0.73–2.43)
P_{trend}		0.63	0.40	0.31		0.78	0.91	0.72
Grand-paternal smoking								
None	732	Ref	Ref	Ref	559	Ref	Ref	Ref
1–14 cig/day	373	1.58	1.68 (1.21–2.34)	1.65 (1.18–2.32)	254	1.33	1.45 (0.97–2.18)	1.35 (0.89–2.06)
15+ cig/day	535	1.35	1.38 (1.02–1.87)	1.38 (1.01–1.89)	354	1.24	1.27 (0.88–1.85)	1.28 (0.87–1.89)
P_{trend}		0.04	0.03	0.03		0.22	0.17	0.18
Grand-parental smoking								
None	638	Ref	Ref	Ref	491	Ref	Ref	Ref
One grandparent	686	1.36	1.39 (1.03–1.87)	1.38 (1.02–1.87)	470	1.23	1.28 (0.90–1.83)	1.28 (0.89–1.84)
Both grandparents	316	1.42	1.55 (1.08–2.22)	1.58 (1.09–2.28)	206	1.12	1.25 (0.79–1.97)	1.24 (0.77–1.98)

[1] GUTS: Growing Up Today Study

[2] Adjusted for age at 1996 baseline

[3] Adjusted for grand-maternal pre-pregnancy BMI [<19.9, 20–22.3, 22.3–24.9, ≥ 25.0 kg/m^2], grandmother's age during pregnancy with nurse [< 25, 25–30, 30–35, ≥ 35 years], grandmother's education at time of pregnancy with nurse [<high school, high school graduate, some college, college graduate] (Model 2)

[4] Model 2 + TV viewing [< 7, 7–<13, 13–<21, ≥21 hours/week], vigorous activity [< 4, 4–<6.5, 6.5–10.4, ≥ 10.4 hours/week], Tanner stage of development [Stage 1 (reference), 2, 3, 4+]

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Table 3

Associations (odds ratios and 95% CI) between grand-parental smoking during pregnancy and overweight or obesity among GUTS[1] **girls** at age 17 (1996–2004)

	All Mothers				Non-smoking Mothers Only			
	N	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**	**N**	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**
Grand-maternal smoking								
None	1484	Ref	Ref	Ref	1086	Ref	Ref	Ref
Quit during pregnancy	97	0.74	0.79 (0.42–1.48)	0.77 (0.41–1.45)	67	0.78	0.83 (0.38–1.78)	0.77 (0.36–1.68)
1–14 cig/day	246	0.96	1.02 (0.70–1.49)	1.04 (0.71–1.53)	158	0.93	0.98 (0.60–1.61)	1.02 (0.62–1.67)
15+ cig/day	150	0.91	0.90 (0.56–1.45)	0.91 (0.57–1.48)	110	0.84	0.87 (0.48–1.57)	0.88 (0.49–1.60)
P_{trend}		0.58	0.74	0.81		0.50	0.66	0.73
Grand-paternal smoking								
None	882	Ref	Ref	Ref	674	Ref	Ref	Ref
1–14 cig/day	451	1.13	1.10 (0.80–1.51)	1.10 (0.80–1.52)	314	1.05	1.01 (0.68–1.50)	1.03 (0.69–1.54)
15+ cig/day	644	1.29	1.23 (0.93–1.64)	1.25 (0.94–1.67)	443	1.22	1.12 (0.79–1.59)	1.14 (0.80–1.62)
P_{trend}		0.07	0.15	0.12		0.26	0.53	0.48
Grand-parental smoking								
None	763	Ref	Ref	Ref	591	Ref	Ref	Ref
One grandparent	840	1.32	1.27 (0.97–1.68)	1.28 (0.97–1.69)	578	1.30	1.25 (0.89–1.74)	1.26 (0.90–1.76)
Both grandparents	374	1.03	1.04 (0.72–1.48)	1.06 (0.74–1.52)	252	0.92	0.91 (0.58–1.43)	0.93 (0.59–1.46)

[1] GUTS: Growing Up Today Study

[2] Adjusted for age at 1996 baseline (Model 1)

[3] Model 1 + grand-maternal pre-pregnancy BMI [<19.9, 20–22.3, 22.3–24.9, ≥ 25.0 kg/m^2], grandmother's age during pregnancy with nurse [< 25, 25–30, 30–35, ≥ 35 years], grandmother's education at time of pregnancy with nurse [<high school, high school graduate, some college, college graduate] (Model 2)

[4] Model 2 + TV viewing [< 4, 4–13, ≥13 hours/week], vigorous activity [< 4, 4–<6.5, 6.5–10.4, ≥ 10.4 hours/week]

Table 4

Associations (odds ratios and 95% confidence intervals) between grand-parental smoking during pregnancy and overweight or obesity in grandchild among GUTS[1] **boys** at age 12(1996–2004)

	All Mothers				Non-smoking Mothers Only			
	N	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**	**N**	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**
Grand-maternal smoking								
None	1084	Ref	Ref	Ref	791	Ref	Ref	Ref
Quit during pregnancy	68	0.79	0.89 (0.47–1.70)	0.77 (0.39–1.51)	43	0.37	0.42 (0.15–1.20)	0.34 (0.12–1.00)
1–14 cig/day	197	1.14	1.22 (0.85–1.76)	1.26 (0.86–1.83)	129	1.04	1.09 (0.69–1.71)	1.08 (0.67–1.72)
15+ cig/day	105	1.08	1.11 (0.68–1.80)	1.07 (0.65–1.77)	62	1.05	1.08 (0.58–2.03)	0.93 (0.48–1.79)
P_{trend}		0.56	0.37	0.41		0.98	0.82	0.86
Grand-paternal smoking								
None	662	Ref	Ref	Ref	503	Ref	Ref	Ref
1–14 cig/day	282	1.42	1.45 (1.04–2.04)	1.42 (1.00–2.02)	199	1.48	1.49 (1.01–2.21)	1.40 (0.93–2.11)
15+ cig/day	510	1.29	1.30 (0.98–1.73)	1.31 (0.97–1.76)	323	1.09	1.11 (0.78–1.58)	1.09 (0.76–1.58)
P_{trend}		0.07	0.07	0.07		0.51	0.46	0.55
Grand-parental smoking								
None	590	Ref	Ref	Ref	457	Ref	Ref	Ref
One grandparent	566	1.25	1.23 (0.92–1.64)	1.25 (0.93–1.68)	380	1.19	1.19 (0.85–1.67)	1.22 (0.85–1.73)
Both grandparents	298	1.30	1.39 (0.99–1.96)	1.36 (0.95–1.94)	188	1.08	1.14 (0.75–1.75)	1.03 (0.66–1.60)

[1] GUTS: Growing Up Today Study

[2] Adjusted for age at 1996 baseline (Model 1)

[3] Model 1 + grand-maternal pre-pregnancy BMI [<19.9, 20–22.3, 22.3–24.9, ≥ 25.0 kg/m^2], grandmother's age during pregnancy with nurse [< 25, 25–30, 30–35, ≥ 35 years], grandmother's education at time of pregnancy with nurse [<high school, high school graduate, some college, college graduate] (Model 2)

[4] Model 2 + TV viewing < 7, 7–<13, 13–<21, ≥21 hours/week], vigorous activity [< 4, 4–<6.5, 6.5–10.4, ≥ 10.4 hours/week], Tanner stage of development [Stage 1 (reference), 2, 3, 4+]

Table 5

Associations (Odds ratios and 95% confidence intervals) between grand-parental smoking during pregnancy and overweight or obesity in grandchild among GUTS[1] **boys** at age 17(1996–2004)

	All Mothers				Non-smoking Mothers Only			
	N	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**	**N**	**Age-adjusted[2]**	**Grand-maternal covariate-adjusted[3]**	**Child covariate-adjusted[4]**
Grand-maternal smoking								
None	1098	Ref	Ref	Ref	833	Ref	Ref	Ref
Quit during pregnancy	63	0.76	0.80 (0.41–1.57)	0.84 (0.46–1.66)	40	0.29	0.29 (0.09–0.95)	0.31 (0.09–1.03)
1–14 cig/day	192	0.92	1.00 (0.68–1.47)	0.99 (0.67–1.46)	125	0.90	0.95 (0.59–1.53)	0.93 (0.58–1.51)
15+ cigs/day	103	0.77	0.76 (0.45–1.30)	0.79 (0.46–1.35)	67	0.56	0.57 (0.28–1.19)	0.63 (0.30–1.31)
P_{trend}		0.29	0.43	0.47		0.09	0.14	0.19
Grand-paternal smoking								
None	674	Ref	Ref	Ref	532	Ref	Ref	Ref
1–14 cigarettes/day	293	0.94	0.97 (0.69–1.38)	0.97 (0.68–1.38)	210	0.85	0.87 (0.58–1.32)	0.89 (0.59–1.35)
15+ cigarettes/day	489	1.09	1.09 (0.82–1.46)	1.11 (0.83–1.49)	323	0.90	0.91 (0.64–1.30)	0.93 (0.65–1.32)
P_{trend}		0.59	0.56	0.49		0.51	0.58	0.65
Grand-parental smoking								
None	598	Ref	Ref	Ref	483	Ref	Ref	Ref
One grandparent	576	0.96	0.96 (0.72–1.28)	0.97 (0.73–1.29)	399	0.89	0.90 (0.65–1.26)	0.92 (0.66–1.29)
Both grandparents	282	0.92	0.98 (0.68–1.40)	0.99 (0.69–1.42)	183	0.69	0.71 (0.45–1.12)	0.74 (0.47–1.16)

[1] GUTS: Growing Up Today Study

[2] Adjusted for age at 1996 baseline (Model 1)

[3] Model 1 + grand-maternal pre-pregnancy BMI [<19.9, 20–22.3, 22.3–24.9, ≥ 25.0 kg/m^2], grandmother's age during pregnancy with nurse [< 25, 25–30, 30–35, ≥ 35 years], grandmother's education at time of pregnancy with nurse [<high school, high school graduate, some college, college graduate] (Model 2)

[4] Model 2 + TV viewing [< 4, 4–13, ≥13 hours/week], vigorous activity [< 4, 4–<6.5, 6.5–10.4, ≥ 10.4 hours/week]

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