



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

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1 **Is grand-parental smoking associated with adolescent obesity? A three-generational**
2 **study.**
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17 **ABSTRACT**

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

22 **Subject/Methods:** Participants were grandmother-mother-child triads in the Nurses' Health
23 Study II (NHS II), the Nurses Mothers' Cohort Study, and the Growing up Today Study
24 (GUTS). Grandmothers provided information on their and their partner's smoking during
25 pregnancy with the child's mother. Information on child's weight and height at ages 12 (N =
26 3094) and 17 (N = 3433) was obtained from annual or biennial GUTS questionnaires. We used
27 logistic regression to estimate ORs of being overweight or obese, relative to normal weight.

28 **Results:** Grand-maternal smoking during pregnancy was not associated with overweight status
29 in adolescence. After adjusting for covariates, the OR of being overweight or obese relative to
30 normal weight at age 12 years in girls whose grandmothers smoked 15+ cigarettes daily during
31 pregnancy was 1.21 (95% CI 0.74-1.98; $p_{\text{trend}} = 0.31$) and 1.07 (0.65-1.77; $p_{\text{trend}} = 0.41$) in
32 boys. Grand-paternal smoking during pregnancy was associated with being overweight or obese
33 at age 12 in girls only, but not at age 17 for either sex: the OR for being overweight or obese at
34 age 12 was 1.38 (95% CI 1.01-1.89; $p_{\text{trend}} = 0.03$) in girls, and 1.31 (95% CI 0.97-1.76; $p_{\text{trend}} =$
35 0.07) in boys. Among children of non-smoking mothers, the OR for granddaughter obesity for
36 grand-paternal smoking was attenuated and no longer significant [OR 1.28 (95% CI 0.87-1.89;
37 $p_{\text{trend}} = 0.18$)].

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

42

43

44 INTRODUCTION

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

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

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

64 Grand-maternal smoking has been previously examined in relation to birth weight and childhood
65 asthma. Findings from studies on the association between grand-maternal smoking and birth

66 weight suggest that any association may be modest (22-25). For childhood asthma, a positive
67 association was reported in a study where only maternal *in utero* exposure was assessed (26),
68 whereas in another study (27), a positive association was observed among offspring of men who
69 were exposed *in utero*, but not among offspring of women. To our knowledge, the association
70 between grand-maternal smoking and body size during adolescence has not been previously
71 studied.

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

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

80

81 **METHODS**

82 **Study population**

83 Participants in this study are grandmother-mother-child triads from the Nurses' Mothers' Cohort
84 Study, the Nurses' Health Study II (NHS II), and the Growing Up Today Study (GUTS). The
85 NHS II is a prospective cohort study that began in 1989 with 116,430 female registered nurses
86 residing in the USA. Participants provided information on health and lifestyle factors in 1989,

87 and then every 2 years thereafter. In 1996, participants of the NHS II were asked if their children
88 could participate in a follow-up study, the Growing Up Today Study (GUTS). After receiving
89 consent, invitation letters were sent to 25,000 children who were aged between 9 and 14 years
90 (29). In 2001, participants of the NHS II were asked permission to contact their mothers to
91 invite them to participate in the Nurses' Mothers Cohort Study, a study designed to obtain
92 information about the nurse's early life exposures (30).

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

97 **Assessment of grand-parental smoking during pregnancy**

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

103 The reliability of self-reported smoking during pregnancy has been previously assessed.
104 Participants of the National Collaborative Perinatal Project were asked to recall pregnancy-
105 related events from 30 or more years previously (31). Recall was accurate for smoking
106 (sensitivity = 0.84, specificity = 0.94), suggesting that long-term maternal recall of smoking is a
107 reliable method of assessing smoking status.

108 **Assessment of Body Mass Index at Ages 12 and 17**

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

115 We used the age and sex-specific cut-offs from the International Obesity Task Force to classify
116 participants as normal weight, overweight, and obese at baseline, age 12, and age 17 (32). For
117 girls, the BMI cut points for overweight and obese at age 12 were 21.68 and 26.67 kg/m²,
118 respectively, and at age 17 were 24.70 and 29.69 kg/m², respectively. For boys, the BMI cut
119 points for overweight and obese at age 12 were 21.22 and 26.02 kg/m², respectively, and at age
120 17 were 24.46 and 29.41 kg/m², respectively. Self-reported height and weight have been found
121 to be reasonably accurate in children and adolescents (33), although reliability increases with age
122 (34, 35).

123 **Assessment of covariates**

124 From the Nurses' Mothers' questionnaire, we obtained grand-maternal age at time of mother's
125 birth, grand-maternal pre-pregnancy BMI, and grandmother's education. In a validation study,
126 pre-pregnancy height and weight were found to be recalled with high accuracy ($r = 0.95$), even
127 after decades (31). We obtained information on maternal smoking from the Nurses' Health
128 Study II questionnaire. From the GUTS questionnaires, we obtained Tanner stage of
129 development, weekly hours of vigorous physical activity, and weekly hours of TV viewing. If
130 available, the previous year's covariate information was substituted for information needed for

131 years in which no questionnaire was returned, or if the information was missing. Missing
132 indicators were then used for participants remaining information for any covariates. Less than
133 8% of participants had missing covariates for any variable, except Tanner stage of development
134 at age 12 in boys (11% missing).

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

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

146 Among the girls, there were 1555 single-child groups, 84 two-sibling groups, and 1 three-sibling
147 group. Among the boys, there were 1382 single-child groups, 72 two-sibling groups and no
148 three-sibling groups. After randomly selecting one child per family, 1640 girls and 1454 boys
149 remained in the Age 12 population.

150 For the analyses of BMI at age 17, we excluded those with missing information on BMI at age
151 17 (girls: n = 1466; boys: n = 1619) and those considered outliers (girls: n = 24; boys: n = 10)
152 from the base population. Among the girls, there were 1792 single-child groups, 179 two-sibling

153 groups, and 6 three-sibling groups. Among the boys, there were 1344 single-child groups, 107
154 two-sibling groups, and 5 three-sibling groups. After randomly selecting one child per family,
155 1977 girls and 1456 boys remained in the Age 17 population.

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

161 **Statistical Analysis**

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

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

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

177 We included all participants of the study population that met our inclusion criteria. Based on a
178 20% overweight/obese status in the unexposed population, and a 3:1 ratio of unexposed to
179 exposed, we require a minimum sample size of 1351 participants to detect an odds ratio of 1.50
180 with 80% power (37).

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

183 **Code Availability**

184 Specific code cannot be accessed externally.

185 **RESULTS**

186 In the Age 12 study population, 2314 (75%) of grandmothers reported not smoking during
187 pregnancy with their grandchild's mother, 138 (4%) reported quitting during pregnancy, while
188 411 (13%) smoked 1-14 cigarettes per day, and 231 (7%) smoked 15+ cigarettes per day
189 throughout the pregnancy. With the exception of heavy smokers (i.e. grandmothers who smoked
190 15 or more cigarettes/day) smokers were more highly educated than non-smokers (Table 1).
191 Grandmothers who were smokers were generally more likely to have daughters who were also
192 smokers. The average age (standard deviation) at baseline (1996) for girls was 11.0 (0.9) years
193 and 10.9 (0.9) years for boys. The average BMI (standard deviation) at baseline for girls was
194 18.2 (3.1) kg/m²; 16% were overweight, and 3% were obese. The average BMI at baseline for

195 boys was 18.4 (3.2) kg/m²; 16% were overweight and 4% were obese. The distribution of
196 participant characteristics in the Age 17 population was similar (data not shown).

197 At age 12, 18% of girls were either overweight or obese. Exposure to grand-maternal smoking
198 during pregnancy with the mother was not associated with body size at age 12 in the age- or
199 covariate-adjusted analyses (Table 2). After adjusting for grand-parental and child covariates,
200 the odds ratio of being overweight or obese, comparing girls whose grandmothers smoked 15 or
201 more cigarettes per day throughout pregnancy to non-smokers was 1.21 (95% CI 0.74-1.98; p_{trend}
202 = 0.31). Results were similar among the subset of girls whose mothers never smoked.

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

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

213 At age 17, 17% of girls were either overweight or obese. Exposure to grand-parental smoking
214 during pregnancy with the mother was unrelated to weight status at age 17 in girls, in both the
215 crude and adjusted analyses (Table 3). After adjusting for grandparent and child covariates, the
216 OR of being overweight or obese at age 17 for girls whose grandmothers smoked 15 or more

217 cigarettes/day during pregnancy compared to girls whose grandmothers did not smoke during
218 pregnancy was 0.91 (95% CI 0.56-1.48; $p_{\text{trend}} = 0.81$). Results were similar among daughters of
219 non-smoking mothers. Grand-paternal smoking and grand-parental smoking overall were also
220 unrelated to overweight or obesity at age 17.

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

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

238

239

240 **DISCUSSION**

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

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

260 We also observed that grand-paternal smoking and grand-parental smoking were associated with
261 increased odds of being overweight or obese in early adolescence, in girls but not in boys. Data

262 from studies of the epigenetic changes due to *in utero* exposure to smoking suggest that these
263 changes can persist over time (38, 39), at least from birth through late adolescence in the first
264 generation; however, studies are limited on how these changes manifest in the second or
265 subsequent generations. In a review of the dynamics of epigenetic phenomena across and within
266 generations, Burggren hypothesized that epigenetic effects could persist across one generation,
267 and gradually decline within or across subsequent generations (40), which is consistent with our
268 finding that grand-paternal smoking was associated with obesity at age 12 years but not at age 17
269 in girls. Additional epidemiological studies should be conducted to better elucidate these
270 processes across multiple generations. Nevertheless, this finding was unexpected since grand-
271 maternal smoking was unrelated to adolescent body size at any age. Moreover, after the
272 population was restricted to children of non-smoking mothers, the associations were attenuated
273 and no longer significant, suggesting that the association between grand-paternal smoking and
274 body size may be due to the correlation between grand-paternal smoking and maternal smoking.
275 In some studies (41, 42) but not all (43), parental smoking was associated with offspring
276 smoking. In our population, grand-maternal and grand-paternal smoking were associated with
277 40% and 60% increased odds of maternal smoking, respectively.

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

284 grand-parental smoking should also examine outcomes in the second filial generation from
285 paternal exposure to *in utero* smoking.

286 Our study has some limitations. At around 20%, the proportion of overweight or obese children
287 in our population is significantly less than the 35% in the United States population currently (7),
288 limiting generalizability. Differences in ethnicity and socioeconomic status, for example 97%
289 Caucasian and 63% with a family income of \geq \$75,000 compared with US population proportions
290 of 78% (45) and 35% (46) respectively, may explain this disparity in weight status (7, 47).

291 Although participants in our sample are on average slightly younger than those in the original
292 population, participant characteristics in our study sample do not differ from the original
293 population with respect to important covariates like family income, and ethnicity. Grand-
294 parental smoking during pregnancy was recalled from up to several decades earlier, introducing
295 the possibility of misclassification. However, although some misclassification is likely, another
296 study that used this measure reported significant associations (14). Finally, we may not have
297 detected an association with body size in early adolescence after restricting to non-smoking
298 mothers because of the smaller sample size and subsequently lower power. Therefore, an
299 independent association between grand-paternal smoking and offspring obesity cannot be ruled
300 out.

301 Strengths of our study include unique three generations' worth of high quality and rarely
302 available data, providing an opportunity to examine exposures and outcomes over an extended
303 time frame. Because we had detailed information on grand-maternal smoking during pregnancy,
304 we were able to evaluate the effect of different levels of smoking. Finally, to our knowledge,
305 this is the first study to examine the association between grand-parental smoking and obesity in
306 adolescence.

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

310

311

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457

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
<i>From Grandmother's (Nurses' Mother's Cohort) Questionnaire</i>				
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
<i>From Mother's (NHS II) Questionnaire</i>				
Mother ever a smoker, %	27	38	34	41
<i>From Boys' (GUTS) Questionnaire</i>				
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
<i>From Grandmother's (Nurses' Mother's Cohort) Questionnaire</i>				
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

	Grandmother's smoking during pregnancy			
	Age 12 population			
	Non-smoker	Quit during pregnancy	1-14 cigarettes/day	15+ cigarettes/day
<i>From Mother's (NHS II) Questionnaire</i>				
Mother ever a smoker, %	27	30	36	30
<i>From Girls' (GUTS) Questionnaire</i>				
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

Table 2. Associations (odds ratios and 95% CI) between grand-parental smoking during pregnancy and overweight or obesity among GUTS¹ 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
<i>Grand-maternal smoking</i>								
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)
<i>P</i> _{trend}		0.63	0.40	0.31		0.78	0.91	0.72
<i>Grand-paternal smoking</i>								
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)
<i>P</i> _{trend}		0.04	0.03	0.03		0.22	0.17	0.18
<i>Grand-parental smoking</i>								
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/m²], 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 3. Associations (odds ratios and 95% CI) between grand-parental smoking during pregnancy and overweight or obesity among GUTS¹ 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
<i>Grand-maternal smoking</i>								
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)
<i>P</i> _{trend}		0.58	0.74	0.81		0.50	0.66	0.73
<i>Grand-paternal smoking</i>								
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)
<i>P</i> _{trend}		0.07	0.15	0.12		0.26	0.53	0.48
<i>Grand-parental smoking</i>								
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/m²], 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 GUTS¹ 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
<i>Grand-maternal smoking</i>								
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)
<i>P</i> _{trend}		0.56	0.37	0.41		0.98	0.82	0.86
<i>Grand-paternal smoking</i>								
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)
<i>P</i> _{trend}		0.07	0.07	0.07		0.51	0.46	0.55
<i>Grand-parental smoking</i>								
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/m²], 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 GUTS¹ 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
<i>Grand-maternal smoking</i>								
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)
<i>P</i> _{trend}		0.29	0.43	0.47		0.09	0.14	0.19
<i>Grand-paternal smoking</i>								
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)
<i>P</i> _{trend}		0.59	0.56	0.49		0.51	0.58	0.65
<i>Grand-parental smoking</i>								
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/m²], 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]