Original article

Cigarette smoking and allergic sensitization: A 32-year population-based cohort study

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Background: Cigarette smoke has immunosuppressant effects, but its effect on allergic sensitization is unclear.
Objective: To investigate associations between parental and personal smoking and skin prick tests (SPTs) for atopy in a population-based birth cohort of 1037 participants followed to adulthood.
Methods: Parental history of atopic disease, parental smoking, and personal smoking were obtained at multiple assessments between birth and age 32 years. Atopy was assessed by SPTs for 11 common inhaled allergens at ages 13 and 32 years.
Results: Children of atopic parents were less likely to have positive SPTs at age 13 years if either parent smoked (odds ratio, 0.55; $P = .009$). This association was not significant after adjusting for breast-feeding history, number of siblings, and childhood socioeconomic status. Subjects with atopic parents were also less likely to develop positive results to SPTs between ages 13 and 32 years if they smoked themselves (odds ratio, 0.18; $P < .001$). This reduction in risk remained significant after adjusting for multiple potential confounding factors. Neither parental nor personal smoking was significantly associated with allergic sensitization among subjects whose parents did not have a history of atopic disease. Few of those with positive SPT results at age 13 years had negative tests at age 32 years, and there was no evidence that this was influenced by smoking.
Conclusion: Personal and parental smoking is associated with a reduced risk of allergic sensitization in people with a family history of atopy.
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Key words: *Atopy, allergy, cigarette smoking, cohort study, epidemiology*

Abbreviations used
OR: Odds ratio
SPT: Skin prick test

Cigarette smoke has a diverse range of effects on the immune system, including enhancement of suppressor T-cell function and decreases in T_H cells.[1] These immune-suppressant effects might be expected to influence allergic sensitization. However, currently available evidence on the effect of smoking on allergic sensitization is conflicting. Despite this uncertainty, avoiding exposure to cigarette smoke is frequently recommended to reduce the risk of allergic sensitization, particularly for children with a family history of atopic disease.[2-6]

A meta-analysis of the effects of parental smoking either before or after birth found no convincing evidence of an effect on objective indicators of allergic sensitization in children.[7] The meta-analysis identified significant heterogeneity between studies, many of which did not control for potential confounding influences. More recent studies have also been conflicting with exposure to smoking having been variably found to be associated with a reduced prevalence of allergic sensitization,[8,9] a short-lived protective effect of prenatal exposure,[10] an increased risk of sensitization,[11-13] or no association.[14-17] Furthermore, the effect of smoking may differ for those with and without a family history of atopy[9,12] and for maternal versus paternal smoking.[18] It is also likely that exposure to smoking *in utero* has different effects from postnatal exposure, but these effects are hard to separate because mothers who smoke during pregnancy are likely to continue to smoke postnatally.[8]

The effect of active smoking on allergic sensitization in adults is also unclear. Several cross-sectional surveys have found a lower prevalence of allergic sensitization among adult smokers.[19-23] However, such surveys may be affected by a healthy smoker bias: because both smoking and allergy are major risk factors for respiratory symptoms, people with allergies may avoid smoking to avoid worsening of their symptoms. More convincing evidence that smoking may reduce allergic sensitization comes from 2 longitudinal studies. These studies found that smokers had not only a lower prevalence of allergic sensitization at baseline but also a lower incidence of allergic sensitization over an 8-year follow-up.[24,25] However, in one of these studies, the highest risk of allergic sensitization was among exsmokers, leading the authors to conclude that the persistent smokers may have been a self-selected group at low risk of allergy.[24] The influence of smoking on allergic sensitization may also depend on the allergen in question. The European Community Respiratory Health

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Survey found a positive association between smoking and specific IgE levels to house dust mite, but negative associations with specific IgE for cat and grass.[22] Further, numerous reports indicate that smoking may be a risk factor for sensitization to occupational allergens, although, again, the data are not consistent.[26]

We investigated the effect of passive smoking in childhood and active smoking in adolescence and adulthood on allergic sensitization in participants in the Dunedin Multidisciplinary Health and Development Study, a prospective longitudinal population-based birth cohort study followed to age 32 years.

METHODS

The Dunedin Multidisciplinary Health and Development Study is described in detail elsewhere.[27] Briefly, this is a longitudinal study of an unselected birth cohort of 1037 individuals (52% male) born in Dunedin in 1972 or 1973. The cohort represents the full range of socioeconomic status in New Zealand's South Island, and study members are mostly of New Zealand/European ethnicity. A broad range of health, behavioral, and developmental assessments has been conducted at birth and ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, and 32 years. At the age 32 years assessment, 972 (96%) of the 1015 living study members were assessed. The Otago Ethics Committees approved the study, and written informed consent was obtained at each assessment.

Atopic status

Skin prick testing was undertaken at age 13 years in 724 of 1031 (70%) living study members using house dust mite (*Dermatophagoides pteronyssinus*; Bencard, Brentford, United Kingdom), grass, cat, dog, horse, kapok, wool, *Aspergillus fumigatus*, *Alternaria*, *Penicillium*, and *Cladosporium* (Hollister-Stier, Spokane, Wash).[28]

Skin prick tests (SPTs) were repeated at age 32 years in 946 of 1015 (93%) living study members using house dust mite (*D pteronyssinus*), rye grass, cat, dog, horse, kapok, wool, *A fumigatus*, *Alternaria*, *Penicillium*, and *Cladosporium* (ALK Allergens; Allergy Canada, Thornhill, Ontario, Canada). Cockroach allergen was also tested at age 32 years, but the results are not used in this report because it was not tested at age 13 years.

At each age, a wheal diameter at least 2 mm greater than the saline control was considered positive. Atopy was defined as a positive response to 1 or more allergens. A more stringent definition of atopy requiring a wheal at least 5 mm greater than control was also analyzed.

Cigarette smoking

Smoking history for both parents/guardians was obtained from the adult (usually mother) attending with the study member at ages 7, 9, and 11 years. Parental smoking was also asked of the study members themselves at the age 13 years assessment. Study members were regarded as having significant exposure to environmental tobacco smoke if either parent was reported to be a current cigarette smoker at any of these assessments.

Personal smoking history was obtained from the study members at each assessment from age 13 years. Cumulative smoking history to age 32 years was updated from previous assessments. At age 32 years, current smoking was defined as smoking at least 1 cigarette daily for at least 1 month in the previous year. One pack-year is defined as the equivalent of 20 cigarettes a day for 1 year. Study members were categorized as never smokers if their lifetime pack-year history was nil and exsmokers if they had a pack-year history of greater than nil but did not meet the definition for current smokers. Those who had smoked at some time between ages 13 and 32 years were also categorized as either light (up to 5 pack-years) or heavy (more than 5 pack-years) smokers at age 32 years.

Other variables

A history of asthma and hay fever in the child's natural mother and father was obtained from the guardian (usually mother) at the age 7 years assessment. This was supplemented with information obtained from the Study member themselves at the age 18 years assessment. A parental history of atopy was considered positive if either parent had a history of hay fever or asthma. Breast-feeding history was obtained from the mother at the age 3 years assessment and validated from a prospective record maintained by visiting health nurses.[29] The total number of children living in the house of the study member was recorded at the age 3 years assessment. Maternal smoking during pregnancy was recorded retrospectively at the age 9 years assessment. The socioeconomic status of study members' families was classified according the highest occupational status of either parent on a 6-point scale based on the incomes and education associated with that occupation in the New Zealand census.[30,31] The average of the families' socioeconomic status over multiple assessments between birth and age 13 years was used.

Statistical analysis

The possibility that atopic status or risk of atopy might influence subsequent smoking behavior (reverse causation) was assessed by comparing the prevalence of smoking among those with and without positive SPT results at age 13 years and among those with and without a history of parental atopy by using χ^2 tests. We also compared the prevalence of smoking among parents with and without a history of atopy.

Associations between exposure to cigarette smoke and the development of atopy were assessed by using binary logistic regression. For childhood exposure, atopy at age 13 years was the dependent variable, and parental smoking status was the main predictor. For the association between active smoking and the incidence of atopy between age 13 and 32 years, atopic status at age 32 years was the dependent variable, and personal smoking status was the main predictor. When assessing the effect of active smoking on the incidence of atopy, the analysis excluded those who had had any positive SPTs at age 13 years. When assessing the effect of smoking on the persistence of childhood atopy, the analysis was restricted to those had 1 or more positive SPT results at age 13 years.

Initial logistic regression analyses assessed whether the effects of smoke exposure differed for those with and without a parental history of atopy by testing parental atopy by smoke exposure interaction terms and analyzing these groups separately. Sex by smoke exposure interaction terms were also analyzed but were not significant. Therefore, both sexes were analyzed together, but all analyses adjusted for sex to control for male-female differences in the prevalence of atopy. Further analyses also adjusted for breast-feeding, socioeconomic status, and the number of children living in the same house at age 3 years. Supplementary analyses assessed the association between incidence of atopy between age 13 and 32 years and heavy and light pack-year histories.

All analyses were performed by using Stata version 9.1 (College Station, Tex). *P* values less than .05 were regarded as statistically significant.

RESULTS

At age 13 years, 196 of 375 (52%) male study members and 132 of 349 (38%) female study members were atopic on SPTs ($P < .001$). At age 32 years, there was no sex difference in prevalence when 292 of 479 (61%) men and 268 of 467 (57%) women were atopic ($P = .26$).

Only 7 study members (1%) were daily smokers at age 13 years, whereas 32 (4%) smoked at least weekly. Those who were atopic at age 13 years were more likely to smoke at least weekly (5.8%) compared with those who were not atopic (3.3%), although the difference was not significant ($P = .10$). There was no evidence that atopic status at age 13 years influenced later smoking behavior in either sex (Table I). Similarly, there was no evidence that parental history of atopy influenced the study members' smoking behavior (Table II). However, parents with asthma or hay fever were less likely to smoke themselves (36% of atopic vs 46% of nonatopic mothers [$P = .009$] and 43% of

TABLE I. Smoking status at age 32 years in study members with and without positive SPT results at age 13 years

	SPT at 13 y	Smoking status at 32 y: Never	Ex	Current	
Female	Negative	96 (46%)	45 (21%)	70 (33%)	
	Positive	66 (51%)	19 (15%)	44 (34%)	$\chi^2 = 2.4$; $P = .30$
Male	Negative	90 (52%)	22 (13%)	61 (35%)	
	Positive	98 (53%)	20 (11%)	68 (37%)	$\chi^2 = 0.3$; $P = .84$

TABLE II. Smoking status at age 32 years in study members with and without a parental history of atopic disease

	Parental atopy	Smoking status at 32 y: Never	Ex	Current	
Female	Negative	121 (48%)	47 (19%)	82 (33%)	
	Positive	92 (47%)	41 (21%)	64 (32%)	$\chi^2 = 0.3$; $P = .86$
Male	Negative	129 (50%)	29 (11%)	101 (39%)	
	Positive	110 (53%)	28 (13%)	71 (34%)	$\chi^2 = 1.4$; $P = .49$

atopic vs 50% of nonatopic fathers [$P = .08$]). Hence, those with a family history of atopy were less likely to be exposed to cigarette smoke in childhood ($P < .001$). Parental smoking was weakly associated with subsequent smoking in the study members. By age 32 years, 299 of 599 (53%) children of smoking parents had ever smoked themselves compared with 172 of 366 (47%) children of nonsmoking parents ($P = .053$).

Logistic regression analysis adjusting for sex and parental history of atopy showed that 13-year-olds were less likely to have positive SPT results if their parents had smoked (n = 712; odds ratio [OR] [95% CI] = 0.65 [0.47, 0.89]; $P = .007$). This association was of borderline statistical significance after additional adjustment for breast-feeding history, smoking in pregnancy, number of children in the house, and family socioeconomic status (n = 709; OR [95% CI] = 0.73 [0.52, 1.01]; $P = .055$). The parental atopy by smoke exposure interaction was not statistically significant at this age ($P = .29$), indicating that the association between parental smoking and atopy was not significantly different between those with and without a parental history of atopy. However, the effect of parental smoking on atopy appeared stronger and was only significant in children of atopic parents (Table III).

There was a significant interaction between parental atopy and adult smoking for incident allergic sensitization between ages 13 and 32 years ($P = .003$), indicating that the effect of personal smoking on atopy was different in those with and without a parental history of atopy. Analysis of those who had a parental history of atopy and who were not atopic at age 13 years showed that current smokers had lower odds of developing atopy by age 32 years (Table IV). This remained significant after adjusting for breast-feeding history, number of children in the house at age 3 years, and childhood socioeconomic status, none of which were significant independent predictors of incident atopy in the model. There was no association between smoking and incident atopy among those without a parental history of atopy. The reduction in incident atopy among exsmokers was not significant (Table IV). However, exsmokers also had lower lifetime pack-year smoking exposures than current smokers (mean [SD], 4.4 [4.3] vs 11.7 [5.9]; $P < .001$). Analyzing the data according to lifetime smoking exposure in heavy (more than 5 pack-years), light (up to 5 pack-years), and nonsmoking (0 pack-years) categories provided similar findings to the current smoker, exsmoker, and never-smoker category analyses (see this article's Table E1 in the Online Repository at www.jacionline.org).

Only 19 of 310 (6.1%) of those who had positive SPT results at age 13 years had negative tests at age 32 years. This proportion was similar in nonsmokers (10/162, 6.2%), exsmokers (3/38, 7.9%), and current smokers (6/110, 5.5%; $P = .86$). Logistic regression analysis of those who had positive SPT results for atopy at age 13 years showed no interaction between adult smoking and parental history of atopy on the persistence of atopy at age 32 years ($P = .68$).

TABLE III. Associations between parental smoking and positive skin tests at age 13 years*

Adjustments	Parents not atopic: No.	OR (95% CI)	*P* value	Atopic parents: No.	OR (95% CI)	*P* value
Sex	393	0.76 (0.49, 1.18)	.23	319	0.55 (0.35, 0.86)	.009
Multiple	392	0.79 (0.50, 1.25)	.31	317	0.72 (0.45, 1.18)	.19

*Analyses by logistic regression using any positive SPT result at age 13 years as the dependent variable and parental smoking history as the independent variable. Analyses are adjusted for sex alone or multiply adjusted for sex, breast-feeding history, number of children in house at age 3 years, and childhood socioeconomic status.

The findings were similar when we used a more stringent definition of atopy requiring a wheal of at least 5 mm greater than the negative control (see this article's Table E2 and Table E3 in the Online Repository at www.jacionline.org).

DISCUSSION

In this general population sample followed from birth to 32 years, we found that children who were exposed to parental smoking and those who took up cigarette smoking themselves had a lower incidence of atopy to a range of common inhaled allergens. These associations were found only in those with a parental history of asthma or hay fever. The findings support the hypothesis that the immune-suppressant effects of cigarette smoke may reduce the risk of allergic sensitization. By contrast, there was no evidence that smoking reversed atopic sensitization that had already developed by age 13 years.

The existing literature with regard to the effects of exposure to environmental tobacco smoke on allergic sensitization in children is inconsistent. The reasons for this inconsistency are not obvious but may be partly a result of differences in study design and lack of adjustment for confounding influences such as family history of atopy. Our findings support those of Burr et al[8] suggesting that exposure to tobacco smoke may reduce the risk of allergic sensitization in children of atopic parents. Although the reduced odds of atopy in our study was not statistically significant after adjustment for multiple confounders, a trend to a lower prevalence of atopy remained, and the data clearly do not support the apparently widespread belief that environmental tobacco smoke exposure increases allergic sensitization in children.[2-6]

The finding that personal smoking was associated with a lower incidence of allergic sensitization in adolescence and adulthood supports findings from previous longitudinal and cross-sectional

TABLE IV. Associations between personal smoking and the development of positive skin tests between ages 13 and 32 years*

Adjustments	Smoking status	Parents not atopic			Atopic parents		
		No.	OR (95% CI)	*P* value	No.	OR (95% CI)	*P* value
Sex	Never	110	Reference	—	72	Reference	—
	Ex	40	0.96 (0.43, 2.12)	.92	24	0.66 (0.26, 1.71)	.40
	Current	76	1.02 (0.54, 1.93)	.95	49	0.18 (0.07, 0.45)	<.001
Multiple	Never	110	Reference	—	71	Reference	—
	Ex	40	0.96 (0.43, 2.16)	.92	24	0.62 (0.23, 1.65)	.34
	Current	76	1.02 (0.52, 1.99)	.95	48	0.19 (0.07, 0.50)	.001

*Analyses by logistic regression using any positive SPT result at age 32 years as the dependent variable and smoking status as the independent variable. Analyses are adjusted for sex alone or multiply adjusted for sex, breast-feeding history, number of children in house at age 3 years, parental smoking, and childhood socioeconomic status. Those who had positive SPT results at age 13 years are excluded.

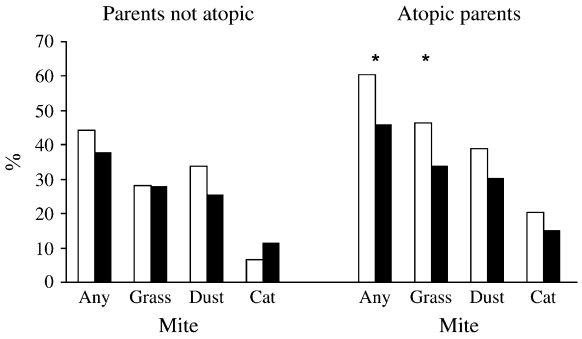

FIG 1. Prevalence of allergic sensitization at age 13 years. Percent of 13-year-olds with positive SPT results to any allergen, grass, dust mite, and cat in those with and without a parental history of atopy. *Open bars* indicate those with nonsmoking parents; *solid bars* indicate those with parents who smoked. *$P < .05$.

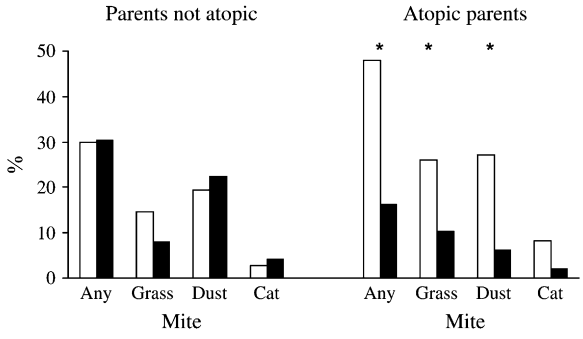

FIG 2. Development of allergic sensitization between ages 13 and 32 years. Percent of 32-year-olds with positive SPT results to any allergen, grass, dust mite, and cat in those with and without parental atopy. Individuals with any positive SPT results at age 13 years are excluded. *Open bars* indicate never or exsmokers; *solid bars* indicate current smokers. *$P < .05$.

studies and extends them in a number of important ways. To our knowledge, this is the first study to follow the effects of smoking on atopic sensitization in a large sample of people from adolescence to adulthood. Atopic responses often develop in childhood, and their development is known to be associated with a number of early life environmental factors including breast-feeding,[29] higher socioeconomic status,[31] and fewer siblings.[32] Moreover, some of these factors (such as low socioeconomic status) may also be associated with later smoking behavior, and this could give rise to spurious associations between smoking and a reduced risk of atopy. Using atopy at age 13 years as a baseline minimizes the chance of these early life factors confounding the analysis of later smoking behavior on atopic sensitization. The baseline measurement of atopy at age 13 years also has the advantage of being made before most study members took up smoking. At age 13 years, only 7 study members reported daily smoking, and most of these smoked only 1 to 3 cigarettes per day. Smoking rapidly increased in prevalence by subsequent assessments (17% at age 15 years and 33% at age 18 years).

Importantly, we found no evidence of reverse causation. The proportions of current smokers, exsmokers, and never-smokers at age 32 years were similar among those who had been atopic and not atopic at age 13 years. Further, in those who were not atopic at age 13 years, subsequent smoking behavior did not differ in those with and without a parental history of asthma or hay fever. Thus, adolescents who were atopic or at risk of atopy were not more likely to avoid smoking. However, we did find that mothers and fathers with a history of asthma or hay fever were less likely to smoke. This may be an example of parents adopting a "prudent lifestyle" because of their atopy,[33] but our data suggest it is equally plausible that smoking parents had a lower prevalence of atopy because they smoked.

How smoking may influence the development of atopy is not clear. Components of cigarette smoke, such as nicotine, are known to enhance suppressor T-cell function and suppress T_H cells.[1] However, we did not find any evidence that taking up smoking suppressed atopic responses that had already developed. Smoking could also influence allergic sensitization by an indirect mechanism. In this study, adult smokers were significantly more likely to report chronic cough and sputum production (data not shown). It is plausible that recurrent bronchitis or chronic colonization of the bronchi by pathogenic bacteria could alter immune function and reduce the risk of sensitization to inhaled allergens.

A previous study suggested that the influence of smoking on atopy differed for different allergens, such that the prevalence of cat and grass sensitization was decreased among smokers but dust mite sensitization was increased.[22] Additional analyses of our data did not confirm this but found a lower risk of developing atopy to each of these allergens, including a significant reduction in house dust mite sensitization in adult smokers (Figs 1 and 2). However, it remains possible that smoking has different effects on different allergens. Although we tested responses to the inhaled allergens thought to be most common in New Zealand, there are many other potential allergens including food allergens. It is plausible that smoking affects the response to ingested allergens differently from those that are inhaled.[13] Studies of sensitization

to occupational allergens have been inconsistent, but they include numerous reports of an increased risk among smokers.[26]

Our study has a number of limitations. Not all of the participants in this study consented to SPTs, particularly at age 13 years, when only 70% of the cohort underwent skin prick testing. However, those who did not have SPTs at age 13 years had a similar prevalence of parental atopy to those who did (42% vs 45%; $P = .41$). They also had a similar prevalence of atopy (56% vs 60%; $P = .22$) and were equally likely to be smokers at age 32 years (37% vs 35%; $P = .58$). Moreover, a sensitivity analysis that assumed all those who missed SPTs at age 13 years would have been nonatopic provided the same pattern of results (not shown). Thus it seems unlikely that missing data have led to spurious findings. The allergens used for assessments at ages 13 and 32 years were of necessity obtained from different manufacturers, and it is possible that some of the changes in atopic status reflect differences in the allergens rather than a real change in immune function. This would be expected to reduce the likelihood of finding significant associations between change in atopic status and smoking, and hence this is also unlikely explain our findings. Smoking exposure data in childhood was only obtained for the ages of 7 to 13 years. Some study members will have had significant exposure to environmental tobacco smoke at other ages or from nonparental sources during childhood, and we have not considered the effects of exposure to environmental tobacco smoke after the age of 13 years. Again, such errors would be expected to reduce the strength of our analysis rather than cause bias and are unlikely to explain our findings. Information on smoking during pregnancy was obtained only by retrospective recall by the parent at the age 9 assessment. This was not a significant predictor of atopy at either age 13 or 32 years, and including this in the analyses did not materially alter the associations between parental or personal smoking and a reduced risk of atopy (data not shown).

In summary, we have found that parental smoking during childhood and personal cigarette smoking in teenage and early adult life is associated with a lower risk of allergic sensitization in those with a family history of atopy. The underlying mechanisms for this association remain to be determined, but the findings are consistent with the hypothesis that the immune-suppressant effects of cigarette smoke protect against atopy. The harmful effects of cigarette smoke are well known, and there are many reasons to avoid it. Our findings suggest that preventing allergic sensitization is not one of them.

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Clinical implications: Avoiding exposure to cigarette smoke does not prevent allergic sensitization.

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TABLE E1. Associations between personal smoking and the development of positive skin test results between ages 13 and 32 years*

		Parents not atopic			Atopic parents		
Adjustments	**Smoking status**	**No.**	**OR (95% CI)**	***P* value**	**No.**	**OR (95% CI)**	***P* value**
Sex	Never	110	Reference	—	72	Reference	—
	Light	37	1.09 (0.49, 2.44)	.83	22	0.43 (0.15, 1.19)	.11
	Heavy	79	0.95 (0.51, 1.80)	.89	51	0.26 (0.11, 0.59)	.001
Multiple	Never	110	Reference	—	71	Reference	—
	Light	37	1.11 (0.49, 2.50)	.80	22	0.43 (0.15, 1.22)	.11
	Heavy	79	0.94 (0.48, 1.84)	.86	50	0.26 (0.11, 0.65)	.004

*Analyses by logistic regression using any SPT result at age 32 years as the dependent variable and smoking status as the independent variable. Light smokers have a lifetime smoking history of less than 5 pack-years. Heavy smokers have a lifetime smoking history of greater than 5 pack-years. Analyses are adjusted for sex alone or multiply adjusted for sex, breast-feeding history, number of children in house at age 3 years, and childhood socioeconomic status. Subjects who had positive SPT results at age 13 years are excluded.

TABLE E2. Associations between parental smoking and 5-mm positive skin test results at age 13 years*

	Parents not atopic			Atopic parents		
Adjustments	**No.**	**OR (95% CI)**	***P* value**	**No.**	**OR (95% CI)**	***P* value**
Sex	393	1.23 (0.72, 2.10)	.45	319	0.53 (0.33, 0.86)	.010
Multiple	392	1.34 (0.77, 2.34)	.31	317	0.63 (0.38, 1.05)	.074

*Analyses by logistic regression using any 5-mm positive SPT result (wheal at least 5 mm greater than negative control) at age 13 years as the dependent variable and parental smoking history as the independent variable. There was a significant interaction between parental history of atopy and parental smoking status ($P = .022$). Analyses are adjusted for sex alone or multiply adjusted for sex, breast-feeding history, number of children in house at age 3 years, and childhood socioeconomic status.

TABLE E3. Associations between personal smoking and the development of 5-mm positive skin test results between ages 13 and 32 years*

		Parents not atopic			Atopic parents		
Adjustments	**Smoking status**	**No.**	**OR (95% CI)**	***P* value**	**No.**	**OR (95% CI)**	***P* value**
Sex	Never	143	Reference	—	100	Reference	—
	Ex	48	1.03 (0.46, 2.32)	.94	33	1.19 (0.53, 2.70)	.68
	Current	103	1.33 (0.73, 2.41)	.35	67	0.45 (0.21, 0.93)	.031
Multiple	Never	143	Reference	—	99	Reference	—
	Ex	48	1.00 (0.44, 2.26)	1.00	33	1.36 (0.58, 3.18)	.48
	Current	102	1.23 (0.66, 2.27)	.52	66	0.57 (0.26, 1.26)	.165

*Analyses by logistic regression using any 5-mm positive SPT result at age 32 years (wheal at least 5 mm greater than negative control) as the dependent variable and smoking status as the independent variable. There was a significant interaction between parental history of atopy and adult smoking status ($P = .033$). Analyses are adjusted for sex alone or multiply adjusted for sex, breast-feeding history, number of children in house at age 3 years, and childhood socioeconomic status. Those who had 5-mm positive SPT results at age 13 years are excluded.