

Re: Asthma and the risk of lung cancer. Findings from the Adverse Childhood Experiences (ACE)

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Abstract Using data from 8,896 men and women aged 50–89 years from the Adverse Childhood Experiences Study who were free of a self-reported history of lung cancer or any cancer at baseline, we examined the association between self-reported asthma and incident lung cancer. The prevalence of smoking was 33% among those who developed lung cancer ($n = 52$) and 7% among those who did not. Asthma was reported by 17% of adults who developed lung cancer and by 9% of those who did not. After adjustment for age, gender, race/ethnicity, educational attainment, smoking status, number of cigarettes smoked per day, and growing up with a parent who smoked the risk of lung cancer was 2.1 (95% CI: 1.0, 4.4) times greater among adults with a history of asthma compared to those without. Among nonsmokers, a similar result was observed, although it did not attain statistical significance (RR: 2.1; 95% CI: 0.9, 5.1). Smoking-attributable lung cancer incidence and mortality are in part a function of the prevalence of smoking in the population. Thus, decreases in the prevalence of smoking in the United States that have occurred since its peak in the 1960s will inevitably result in a decline in the proportion of lung cancer in the population caused by smoking. We hope that our findings and those of others will stimulate research of the biologic mechanism(s)

underlying the occurrence of lung cancer among non-smokers so that possible treatments and prevention strategies may be developed.

Keywords: Asthma · Lung cancer

Dear Dr. Colditz,

Insights into risk factors for lung cancer among non-smokers will become increasingly important in the decades to come as the secular decline in the prevalence of smoking in the United States will necessarily result in decreases in the incidence of lung cancer attributable to smoking.

Santillan et al. [1] recently reported in *Cancer Causes & Control* a nearly twofold increased risk of lung cancer among persons with asthma independent of smoking history based on the results of five case-control studies of persons who never smoked (odds ratio [OR]: 1.8, 95% CI: 1.3–2.3) and the results of six case-control studies and four cohort studies in which data were adjusted for smoking (relative risk [RR]: 1.7; 95% CI: 1.3–2.2).

We used data from 8,896 men and women aged 50–89 years from the Adverse Childhood Experiences Study [2] who were free of a self-reported history of lung cancer or any cancer at baseline—which was completed during three periods: August–November 1995; January–March 1996; April–October 1997—and who were eligible for follow-up as of 31 December 2004, to examine the association between self-reported asthma and incident lung cancer. We identified incident cases from eligible hospital discharge records with a discharge diagnosis of lung cancer (ICD-9 codes 160–165). We used logistic regression to estimate the relative risk of lung cancer, by means of the odds ratio, comparing adults with asthma to those without after adjustment for age, gender, race/ethnicity, educational

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attainment, smoking status, number of cigarettes smoked per day, and growing up with a parent who smoked. Smoking status was characterized as current/former/never based on response to questions about lifetime history of smoking ('Have you ever smoked at least 100 cigarettes?') and current smoking status.

We identified 52 incident cases of lung cancer during a maximum of approximately 9 years of follow-up (median follow-up, 7 years). Follow-up time was available for 89% (15,472/17,337) of the baseline cohort. Persons who developed lung cancer were older (mean age, 69 versus 65 years) and more likely to be men (65% [$n = 34$] versus 48% [$n = 4256$]), white (85% [$n = 44$] versus 81% [$n = 7208$]), and have less than a college education (73% [$n = 38$] versus 63% [$n = 5579$]) than those who did not develop the disease. The prevalence of smoking was 33% ($n = 17$) among those who developed lung cancer and 7% ($n = 608$) among those who did not. Asthma was reported by 17% ($n = 9$) of adults who developed lung cancer and by 9% ($n = 816$) of those who did not. The age-adjusted risk of lung cancer associated with asthma was 2.1 (95% CI: 1.0–4.4) in the overall cohort and 2.1 (95% CI: 0.9–5.2) among nonsmokers. Similar results were observed after multivariable adjustment for sociodemographics and smoking (overall, RR: 2.1 [95% CI: 1.0–4.4]; nonsmokers, RR: 2.1; [95% CI: 0.9–5.1]).

Although we were unable to examine the relationship between asthma and lung cancer among *never* smokers due to small numbers ($n = 7$) and only one exposed case, the findings from this prospective cohort study are supportive of a relationship between asthma and lung cancer independent of smoking. Smoking-attributable lung cancer incidence and mortality are in part a function of the prevalence of smoking in the population. Thus, decreases in the prevalence of smoking in the United States that have occurred since its peak in the 1960s will inevitably result in a decline in the proportion of lung cancer in the population caused by smoking. We hope that our findings and those of others will stimulate research of the biologic mechanism(s) underlying the occurrence of lung cancer among non-smokers so that possible treatments and prevention strategies may be developed.

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