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Association between tobacco product use and asthma among US adults from the Population Assessment of Tobacco and Health (PATH) Study waves 2–4

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ABSTRACT

Background Research on cigarettes and adult asthma offers mixed findings, perhaps due to overlap with chronic obstructive pulmonary disease (COPD) and inadequate adjustment for other smoke exposures. Associations between other tobacco products, including e-cigarettes, and asthma are also understudied.

Research question Using Population Assessment of Tobacco and Health Study waves 2–4 (2014/2015–2016/2017) data, we assessed the relation between tobacco product use and asthma in persons unlikely to have COPD.

Study design and methods Prospective study of 10 267 adults aged 18–39 years without COPD diagnoses. Past-month tobacco use at wave 2 was modelled first as combustible versus non-combustible use and second as specific product categories (former, cigarettes, e-cigarettes, cigars, hookah, smokeless tobacco). Outcomes included lifetime asthma prevalence at wave 2, incidence (waves 3 and 4) and Asthma Control Test score (lower=worse). Multivariable regressions adjusted for predictors of asthma, including other smoke exposures: cigarette pack-years, secondhand smoke and marijuana use. Sensitivity analyses examined findings when persons >39 years and those with both COPD and asthma were added, and when smoke exposure adjustments were removed.

Results No product, including cigarettes and e-cigarettes, was associated with prevalence or incidence of asthma. Among people with asthma at wave 2, combustible tobacco (beta=−0.86, 95% CI (−1.32 to −0.39)) and cigarettes (beta=−1.14, 95% CI (−1.66 to −0.62)) were associated with worse asthma control. No tobacco product was associated with asthma control over time. In sensitivity analyses, tobacco use became associated with incident asthma as adults >39 years and those with asthma+COPD were added, and as adjustments for other smoke exposures were omitted.

Interpretation Although cigarette use was associated with worse asthma control, there were no longitudinal associations between combustible tobacco or e-cigarette use and new onset or worsening asthma in these preliminary analyses. Research on tobacco and asthma should exclude COPD and adjust for smoking history and other smoke exposures.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous research on the relationship between tobacco use and adult asthma is mixed. Studies with positive findings often did not account for the effects of confounders such as other smoke exposure and presence of comorbid chronic obstructive pulmonary disease (COPD) in study subjects.

WHAT THIS STUDY ADDS

⇒ This study avoids the problem of confounding seen in previous studies. After removing participants with comorbid COPD and adjusting for pack-years of smoking, secondhand smoke and use of cannabis, the cross-sectional analyses found that cigarette smoking was associated with poorer asthma control, but longitudinal analyses found that cigarettes and e-cigarettes were not associated with new-onset asthma or worsening of asthma over time.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Future research on tobacco and adult asthma should select samples to avoid confounding comorbid conditions and carefully adjust for other smoke exposures.

INTRODUCTION

Asthma is the most prevalent chronic respiratory disease worldwide.[1 2] Unlike chronic obstructive pulmonary disease (COPD), which primarily begins in middle age among people with host risk factors and long-term exposure to tobacco smoke or air pollutants,[3–5] asthma is a heterogeneous disease of reversible expiratory airflow limitation,

often beginning in childhood.[6] Asthma is thought to result from the complex interaction between genetic factors and environmental exposures at critical periods throughout life.[7 8]

The relationship between tobacco product use and adult asthma is complex. Cigarette smoking has long been thought to contribute to asthma onset and severity in adults (see reviews of prospective studies[9] and cross-sectional studies in clinical populations[10–13]). Yet, several prospective studies found no association or mixed findings.[14–18] Moreover, cigarette smokers with asthma frequently use other products, including electronic (e-) cigarettes,[19 20] about which there are very few prospective studies.[21]

Methodological problems may have contributed to previous mixed findings. Many studies of tobacco use and asthma did not assess cigarette smoking history, use of multiple tobacco products and other smoke exposures, such as secondhand smoke and marijuana use, that could be confounders,[16 18 22–25] and most prospective studies of asthma and tobacco did not account for COPD.[16 17 22–26] (Up to one-third of adults with asthma eventually develop comorbid COPD,[27 28] when patients present with features distinct from asthma.[29 30]) For example, a recent paper[22] noted that combustible tobacco and e-cigarette use were both associated with adult-onset asthma; however, that study addressed neither comorbid COPD, nor history of cigarette smoking and other smoke exposures, all important potential confounders. Careful, prospective research is needed to clarify the relation between tobacco product use and asthma outcomes.

The Population Assessment of Tobacco and Health (PATH) Study is a large, national, longitudinal survey of tobacco product use and self-reported health outcomes.[31] This report evaluated the relationships between tobacco product use and asthma diagnosis and symptoms among people aged 18–39 years old without comorbid COPD. Sensitivity analyses explored how adding participants over 40 years and those with comorbid COPD, as well as removing adjustments for cigarette smoking history and other smoke exposures, affected the association between tobacco product use and asthma.

METHODS

Study design, setting and participants

The PATH Study recruitment employed a stratified address-based, area-probability sampling design at wave 1 (W1; 2013–2014) that oversampled adult tobacco users, young adults (18–24 years) and African-American adults.

Respiratory symptoms, including asthma symptoms, were first assessed in wave 2 (W2: 2014–2015, N=28 362), which served as the baseline assessment for this study. The weighted response rate at W2 was 83.2%. Follow-up data were collected at waves 3 and 4 (W3: 2015–2016; W4: 2016–2017) including 28 148 and 27 757 adult participants, respectively, with weighted response rates of 78.4% and 73.5% of W2 participants, respectively. Respondents were assessed in person with a computer-assisted interview approximately yearly.

For this study, we selected all W2 adults aged 18–39 years, excluding adults over 39 years and those who reported COPD (including chronic bronchitis or emphysema) or other non-asthma respiratory diseases at W1–4, to increase certainty that we were studying adult asthma (N=11 675). Participants with missing data on independent or dependent variables (N=1408, 12.1%) were also excluded, for a complete case analytical sample of 10 267.[32] (Multiple imputation analyses were also conducted on the full sample, as described in the Statistical analysis section below.)

Complete PATH Study design methods have previously been published in detail;[33 34] interviewing procedures, questionnaires, sampling, weighting and response rates can be found at https://doi.org/10.3886/Series606. All adult respondents provided informed consent.

Patient and public involvement

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research.

Patient-reported asthma diagnosis and symptoms

Asthma diagnosis

Similar to the National Health and Nutritional Examination Survey (NHANES),[35] lifetime asthma diagnosis was assessed at baseline by asking: 'Has a doctor, nurse or other health professionals EVER told you that you had any of the following lung or respiratory conditions? Choose all that apply. Asthma, COPD, etc.' New diagnosis was assessed by asking: 'IN THE PAST 12 MONTHS, has a doctor ever told you that you had any of the following lung or respiratory conditions? Choose all that apply. Asthma, COPD, etc.' The asthma diagnosis questions were validated by demonstrating that self-reported asthma diagnosis in the PATH Study was associated with greater respiratory symptoms and impairments in functional status (see online supplemental appendix 1). Additionally, the prevalence of asthma diagnosis in the PATH Study was similar to the prevalence of asthma diagnosis in NHANES (see online supplemental appendix 1). Asthma at baseline (W2) and new asthma at follow-up (W3 or W4) were assessed by a combination of these two questions.

Asthma control

The Asthma Control Test (ACT), a validated questionnaire designed for patients with asthma, includes five items on self-reported asthma symptoms (online supplemental table 1), each with answer options 1–5. Summary scores range from 5 to 25 (higher=better asthma control, for example, fewer symptoms; ACT score <20 indicates poorly controlled asthma).[36] It has high internal consistency (Chronbach's alpha=0.79), test–retest reliability (r=0.77) and criterion validity (correlation with specialist rating of asthma control r=0.52).[37] An ACT score of 19

provided an optimum balance of sensitivity (71.3%) and specificity (70.8%) for detecting poorly controlled asthma in non-smokers[37] and a score of 18.6 provided the maximum area under the receiver operator characteristic curve in smokers.[38] The asthma symptom questions in the PATH Study were validated by demonstrating that self-reported asthma symptom severity was associated with functional status, and prevalence of asthma symptoms (wheeze) was similar to the prevalence of symptoms in NHANES (see online supplemental appendix 1). People with asthma were also asked whether they used asthma medications in the past 12 months ('treated asthma') and what class of medications they regularly used.

Exposures

Tobacco product use

Participants reported lifetime and past-month use of combustible products (cigarettes, traditional cigars, cigarillos, filtered cigars, pipe tobacco and hookah) and non-combustible products (snus pouches, other smokeless tobacco (loose snus, moist snuff, dip, spit or chewing tobacco) and e-cigarettes). Pictures and descriptions were displayed for each product to ensure accuracy.

Tobacco product use was modelled two ways. First, models included four mutually exclusive past-month categories—never use, former use but none in the past month, current non-combustible use only and current combustible product use (including those with non-combustible use).

Second, six product type categorical variables were developed that described past-month use: tobacco use but none in the past 30 days ('former users'), and past 30-day use of cigarettes, e-cigarettes, cigars, smokeless tobacco, pipe or hookah. These 30-day use groups were not mutually exclusive, so individuals could be counted in several groups if they had used multiple products.

Finally, a variable for intensity of product use was created for each product type (frequency of use in the past month×quantity used per day on the days used). This variable was used in a series of additional analyses to assess for any linear or non-linear dose–response relationships between each product and both asthma prevalence and asthma incidence using bivariate and multivariable analyses. Lowess curves were created to examine whether there was a threshold at which exposure impacted asthma incidence or control (online supplemental file 2). Because no threshold was observed, we did not create any 'threshold of use' variables.

Covariates

As described in table 1, covariates were derived mostly from W2 data, and included variables that could be associated both with tobacco exposure and asthma (or respiratory symptoms in people with asthma). Sociodemographic variables included age, sex, race/ethnicity, education and urbanicity. Other W2 smoke-related exposures that could be associated with respiratory symptoms included pack-years of cigarette smoking,[39] secondhand smoke exposure[40] and past-month marijuana use.[41] We included obesity categories based on self-reported height and weight (underweight: body mass index (BMI) <18.5; normal: BMI=18.5–24.9, overweight: BMI=25–29.9, class 1 obesity: BMI=30–34.9, class 2 obesity: BMI ≥35).

Statistical analysis

All main analyses were weighted using the W4 longitudinal (all waves) full-sample and replicate weights to adjust for the complex sample design and loss to follow-up. Weighted estimates from W1 to W4 of the PATH Study represent the residents of the USA at W4 who were in the civilian, non-institutionalised population at W1 (only W1 cohort was used). Variances were estimated using the Balanced Repeated Replication (BRR) method[42] with Fay's adjustment set to 0.3 to increase estimate stability.[43] Pack-years of cigarette smoking, tobacco product past 30-day frequency variables and secondhand smoke exposure were Winsorised at the 95th, 95th and 99th percentiles, respectively, to limit the influence of outliers.[44]

Missing data

Participants who had missing asthma diagnosis data, tobacco product use/intensity data, or covariate data were omitted from the analytical sample. Compared with the analytical sample, the non-analytical sample was older (online supplemental table 6), included more men and racial/ethnic minorities, and had lower education level, contained more cigarette smokers (14.9% vs 10.8%, respectively) and more with ever asthma diagnosis (16.1% vs 12.2%, respectively). We repeated all main analyses (model 1 in tables 2–5) using multiple imputation to address missing data for all predictors and covariates using BRR, as was done in the complete case analyses. The multiple imputation analyses found only very small differences for a few variables, primarily in the CIs; thus, we report the complete case analyses here.

Analytical approach

We first examined the associations between tobacco use and covariates using either X^2 or analysis of variance, as appropriate. We then examined cross-sectional associations between tobacco product use at W2 and both the presence of lifetime asthma diagnosis and asthma control (symptom severity) at W2. Finally, we evaluated the longitudinal associations between W2 tobacco product use and both new asthma diagnoses at W3 and W4 and ACT score at W3.

Multivariable weighted Poisson regression was used to obtain adjusted risk ratios (aRRs) and 95% CIs for each of the dichotomous outcomes. Multivariable linear regression was used to model asthma symptom control (ACT scores) at W3, adjusted for W2 ACT values to control for baseline asthma symptom severity.[45] Similar regressions were used in two sensitivity analyses (online supplemental

Table 1 Characteristics of adults 18–39 years at wave 2 of the PATH Study*, by lifetime asthma status (percentages and means are weighted to reflect US population)

			Doctor ever said you have asthma?			
				Yes (N=1432)		
				Asthma medication in P12M?†		
	Total (N=10 267)		No (N=8835)	No (N=1144)	Yes (N=288)	
	N‡	% or mean	%	%	%	P value§
Past 30-day tobacco use						
Combustible versus non-combustible tobacco use						0.41
Never used tobacco	2010	30.5	30.9	28.6	26.0	
Formerly used tobacco	3231	34.0	33.7	35.2	39.3	
Non-combustible use only	392	3.1	3.1	2.7	4.7	
Any combustible use	4634	32.4	32.3	33.4	29.9	
Specific tobacco products used						
Cigarette	3708	25.9	25.9	26.7	21.5	0.27
Cigar	1645	10.8	10.5	13.4	10.5	**0.03**
Hookah	984	6.2	6.1	6.7	7.5	0.44
E-cigarette	1323	9.1	9.1	9.6	9.0	0.83
Smokeless	576	4.3	4.3	4.6	3.6¶	0.77
Other smoke-related exposures						
Cigarette pack-years (mean)	10 267	2.0	2.1	1.9	1.7	0.41
Past-week hours of SHS exposure (mean)	10 267	5.4	5.4	5.8	5.8	0.32
Past-month marijuana use**	2225	15.2	14.7	19.1	17.2	**<0.01**
Relevant medical history						
Body mass index						**<0.01**
Underweight	336	2.8	2.9	2.3	3.3¶	
Normal	4292	40.3	40.9	38.7	27.0	
Overweight	2906	30.3	30.3	29.3	33.3	
Class 1 obese	1521	14.6	14.5	14.9	15.0	
Class 2+ obese	1212	12.0	11.4	14.8	21.5	
Asthma Control Test (mean score)	1420	23.1	N/A	23.7	20.6	**<0.01**
Sociodemographics						
Age						**<0.01**
18–24	5292	34.1	33.2	41.6	35.0	
25–39	4975	65.9	66.8	58.4	65.0	
Sex						**<0.01**
Female	5341	50.4	50.0	50.3	63.2	
Male	4926	49.6	50.0	49.7	36.8	
Race/ethnicity						**0.01**

Continued

Table 1 Continued

			Doctor ever said you have asthma?			
				Yes (N=1432)		
				Asthma medication in P12M?†		
	Total (N=10 267)		No (N=8835)	No (N=1144)	Yes (N=288)	
	N‡	% or mean	%	%	%	P value§
White††	5569	58.3	57.9	61.3	62.1	
Black††	1512	11.9	11.7	13.7	13.5	
Other††	884	9.8	9.9	9.5	5.8	
Hispanic	2302	19.9	20.5	15.5	18.7	
Education						0.71
No high school degree	1158	8.2	8.4	7.3	6.9	
GED	573	4.6	4.7	3.9	4.1¶	
High school grad	2484	21.6	21.7	20.6	19.9	
Some college	3950	36.2	35.8	38.9	39.6	
≥College graduate	2102	29.4	29.4	29.4	29.5	
Live in an urban area‡‡	8499	84.0	83.8	84.0	91.3	0.07

Online supplemental table 8 reports SEs for all the weighted estimates presented in this table and unweighted Ns for all the variables in the model.
*N=10 267 wave 2 adult (age 18–39) respondents without COPD or other non-asthma respiratory diseases at waves 2–4, with wave 4 PATH Study longitudinal (all waves) weights, and complete data on all analytical variables of adult tobacco users. A total of 1408 participants were excluded for missing data on one or more variables in the analysis. Young adults aged 18–24 years, and black participants (or African-Americans) were oversampled relative to population proportions. The weighting procedures adjusted for oversampling and non-response.
†Any P12M asthma meds based on an answer of 'quick-relief inhaler' or 'controller or long-acting inhaler including steroid inhaler' to the question 'In the past 12 months, which of the following medications did you regularly take for COPD or asthma?'.
‡Unweighted.
§X^2 test was used for categorical variables and ANOVA was used for continuous variables. Bold p values are statistically significant at p<0.05.
¶Estimate should be interpreted with caution because it has low statistical precision. It is based on a denominator sample size of less than 50, or the coefficient of variation of the estimate or its complement is larger than 30%.
**Marijuana use variable does not distinguish between combustible and non-combustible use.
††Non-Hispanic.
‡‡Derived at wave 1 of the PATH Study.
ANOVA, analysis of variance; COPD, chronic obstructive pulmonary disease; GED, General Education Development (high school equivalency certificate); PATH, Population Assessment of Tobacco and Health; P12M, past 12-month; SHS, secondhand smoke.

table 7) in which we first included adults over 40 years and those with both COPD and asthma diagnoses, and then also removed adjustments for cigarette pack-years, marijuana use and secondhand smoke exposure. All analyses were conducted using Stata survey data procedures, V.15.1 (StataCorp, College Station, Texas, USA), and using PATH Study W1–W4 Restricted Use Files.

RESULTS

Participants with asthma

The weighted prevalence of lifetime asthma was 12.2% (SE=0.4). Characteristics and tobacco use of people with asthma are shown in table 1. About one-fifth of people with asthma (288 of the 1432) had taken asthma medication in the past 12 months. Tobacco use characteristics were largely similar between those never having asthma, those with untreated asthma (not taking medication) and those with treated asthma (taking medication), although those with untreated asthma were more likely to be past 30-day cigar smokers and current marijuana users than the other groups (p=0.03 and p<0.01, respectively). Four tables present the association between tobacco product use and asthma prevalence (table 2), asthma incidence (table 3), cross-sectional asthma control (table 4) and prospective asthma control (table 5), as described below.

Cross-sectional relationships between tobacco exposure and asthma prevalence

Multivariable models showed significant associations between lifetime asthma (table 2, model 2) and current cigar use (lifetime prevalence 14.5% in past 30-day cigar smokers vs 11.9% non-past 30-day cigar smokers,

Table 2 Weighted cross-sectional associations between past 30-day tobacco use and lifetime asthma diagnosis at wave 2 of the PATH Study*

Risk factor at wave 2	N†	US population %	Lifetime asthma diagnosis %	Models predicting asthma			
				Model 1 Combustible versus non-combustible tobacco use		Model 2 Specific tobacco products used	
				Adjusted RR‡	95% CI	Adjusted RR‡	95% CI
Past 30-day tobacco use							
Combustible versus non-combustible tobacco use							
Never used tobacco	2010	30.5	11.2	Ref	Ref	–	–
Formerly used tobacco	3231	34.0	12.9	1.14	0.94 to 1.38	–	–
Non-combustible use only	392	3.1	12.4	1.09	0.76 to 1.55	–	–
Any combustible use	4634	32.4	12.3	1.02	0.83 to 1.24	–	–
Specific tobacco products used							
Former							
No	7036	66.0	11.8	–	–	Ref	Ref
Yes	3231	34.0	12.9	–	–	1.14	0.96 to 1.36
Cigarette							
No	6559	74.1	12.2	–	–	Ref	Ref
Yes	3708	25.9	12.1	–	–	0.98	0.83 to 1.15
Cigar							
No	8622	89.2	11.9	–	–	Ref	Ref
Yes	1645	10.8	14.5	–	–	1.17	1.00 to 1.36
Hookah							
No	9283	93.8	12.1	–	–	Ref	Ref
Yes	984	6.2	13.5	–	–	0.99	0.81 to 1.20
E-cigarette							
No	8944	90.9	12.1	–	–	Ref	Ref
Yes	1323	9.1	12.7	–	–	0.99	0.83 to 1.19
Smokeless							
No	9691	95.7	12.2	–	–	Ref	Ref
Yes	576	4.3	12.5	–	–	1.08	0.84 to 1.40
Other smoke-related exposures							
Cigarette pack-years (per each 5 pack-years)	10267	–	–	0.97	0.89 to 1.06	0.98	0.90 to 1.07
Past-week SHS exposure (per each 5 hours/week)	10267	–	–	1.01	0.99 to 1.03	1.01	0.99 to 1.03
Past-month marijuana use§							
No	8042	84.8	11.7	Ref	Ref	Ref	Ref
Yes	2225	15.2	15.1	**1.29**	**1.10 to 1.50**	**1.26**	**1.07 to 1.48**
Relevant medical history							
Body mass index							
Underweight	336	2.8	10.7	0.95	0.65 to 1.39	0.95	0.65 to 1.40
Normal	4292	40.3	11.0	Ref	Ref	Ref	Ref
Overweight	2906	30.3	12.1	**1.19**	**1.01 to 1.40**	**1.19**	**1.01 to 1.40**
Class 1 obese	1521	14.6	12.5	**1.25**	**1.00 to 1.56**	**1.25**	**1.00 to 1.56**
Class 2+ obese	1212	12.0	16.4	**1.62**	**1.30 to 2.02**	**1.62**	**1.30 to 2.01**

Online supplemental table 9 reports SEs for all the weighted estimates presented in this table and adjusted RRs for all the variables in the model.
*N=10267 wave 2 adult (age 18–39) respondents without chronic obstructive pulmonary disease or other non-asthma respiratory diseases at waves 2–4, with wave 4 PATH Study longitudinal (all waves) weights, and complete data on all analytical variables.
†Unweighted.
‡All RRs adjust for the variables in the table plus age, sex, ethnicity/race, education and lives in an urban area. Bold RRs are statistically significant at p<0.05.
§Marijuana use variable does not distinguish between combustible and non-combustible use.
PATH, Population Assessment of Tobacco and Health; RRs, risk ratios; SHS, secondhand smoke.

Table 3 Weighted prospective associations between wave 2 past 30-day tobacco use and new-onset asthma diagnosis at waves 3 or 4 of the PATH Study*

				Models predicting asthma			
				Model 1 Combustible versus non-combustible tobacco use		Model 2 Specific tobacco products used	
Risk factor at wave 2	N†	US population %	New-onset asthma diagnosis %	Adjusted RR‡	95% CI	Adjusted RR‡	95% CI
Past 30-day tobacco use							
Combustible versus non-combustible tobacco use							
Never used tobacco	1755	30.9	0.8§	Ref	Ref	–	–
Formerly used tobacco	2762	33.7	1.1	1.39	0.63 to 3.07	–	–
Non-combustible use only	345	3.1	1.2§	1.55	0.34 to 7.07	–	–
Any combustible use	3973	32.3	1.2	1.27	0.58 to 2.79	–	–
Specific tobacco products used							
Former							
No	6073	66.3	1.0	–	–	Ref	Ref
Yes	2762	33.7	1.1	–	–	1.36	0.70 to 2.63
Cigarette							
No	5652	74.1	1.0	–	–	Ref	Ref
Yes	3183	25.9	1.1	–	–	0.99	0.53 to 1.86
Cigar							
No	7464	89.5	1.0	–	–	Ref	Ref
Yes	1371	10.5	1.5	–	–	1.44	0.77 to 2.72
Hookah							
No	8000	93.9	1.0	–	–	Ref	Ref
Yes	835	6.1	1.5	–	–	1.35	0.65 to 2.80
E-cigarette							
No	7700	90.9	1.0	–	–	Ref	Ref
Yes	1135	9.1	1.3	–	–	1.12	0.50 to 2.51
Smokeless							
No	8343	95.7	1.0	–	–	Ref	Ref
Yes	492	4.3	0.9§	–	–	0.97	0.29 to 3.28
Other smoke-related exposures							
Cigarette pack-years (per each 5 pack-years)	8835	–	–	1.06	0.83 to 1.37	1.09	0.84 to 1.41
Past-week SHS exposure (per each 5 hours/week)	8835	–	–	0.98	0.91 to 1.06	0.98	0.91 to 1.06
Past-month marijuana use¶							
No	6956	85.3	1.0	Ref	Ref	Ref	Ref
Yes	1879	14.7	1.2	1.12	0.68 to 1.84	1.05	0.66 to 1.69
Relevant medical history							
Body mass index							
Underweight	294	2.9	0.8§	0.82	0.24 to 2.87	0.82	0.24 to 2.83
Normal	3749	40.9	0.8	Ref	Ref	Ref	Ref
Overweight	2510	30.3	0.8	1.11	0.59 to 2.08	1.11	0.59 to 2.09
Class 1 obese	13,03	14.5	1.0	1.30	0.67 to 2.51	1.30	0.67 to 2.52
Class 2+ obese	979	11.4	2.5	**3.12**	**1.67 to 5.86**	**3.11**	**1.66 to 5.82**

Online supplemental table 10 reports SEs for all the weighted estimates presented in this table and adjusted RRs for all the variables in the model.
*N=8835 wave 2 adult (age 18–39) respondents never diagnosed with asthma, without chronic obstructive pulmonary disease or other non-asthma respiratory diseases at waves 2–4, with wave 4 PATH Study longitudinal (all waves) weights, and complete data on all analytical variables.
†Unweighted.
‡All RRs adjust for the variables in the table plus age, sex, ethnicity/race, education and lives in an urban area. Bold RRs are statistically significant at p<0.05.
§Estimate should be interpreted with caution because it has low statistical precision. It is based on a denominator sample size of less than 50, or the coefficient of variation of the estimate or its complement is larger than 30%.
¶Marijuana use variable does not distinguish between combustible and non-combustible use.
PATH, Population Assessment of Tobacco and Health; RRs, risk ratios; SHS, secondhand smoke.

Table 4 Weighted cross-sectional associations between past 30-day tobacco use and Asthma Control Test (ACT) score among adults 18–39 years with asthma at wave 2 of the PATH Study, lower coefficients reflect worse asthma control*

				How tobacco use is modelled			
				Model 1 Combustible versus non-combustible tobacco use		Model 2 Specific tobacco products used	
Risk factor at wave 2	N†	US population %	Mean ACT score‡	Adjusted coefficient§	95% CI	Adjusted coefficient§	95% CI
Past 30-day tobacco use							
Combustible versus non-combustible tobacco use							
Never used tobacco	255	28.3	23.6	Ref	Ref	–	–
Formerly used tobacco	463	35.9	23.4	−0.13	−0.56 to 0.29	–	–
Non-combustible use only	47	3.1	22.9¶	−0.40	−1.50 to 0.69	–	–
Any combustible use	655	32.6	22.4	**−0.86**	**−1.32 to −0.39**	–	–
Specific tobacco products used							
Former							
No	957	64.1	22.9	–	–	Ref	Ref
Yes	463	35.9	23.4	–	–	−0.13	−0.53 to 0.27
Cigarette							
No	901	74.4	23.5	–	–	Ref	Ref
Yes	519	25.6	22.1	–	–	**−1.14**	**−1.66 to −0.62**
Cigar							
No	1147	87.1	23.2	–	–	Ref	Ref
Yes	273	12.9	22.5	–	–	−0.08	−0.53 to 0.37
Hookah							
No	1272	93.1	23.1	–	–	Ref	Ref
Yes	148	6.9	22.6	–	–	−0.04	−0.66 to 0.59
E-cigarette							
No	1233	90.5	23.2	–	–	Ref	Ref
Yes	187	9.5	22.3	–	–	−0.26	−0.88 to 0.36
Smokeless							
No	1337	95.6	23.1	–	–	Ref	Ref
Yes	83	4.4	22.9	–	–	0.15	−0.59 to 0.89
Other smoke-related exposures							
Cigarette pack-years (per each 5 pack-years)	1420	–	–	−0.09	−0.31 to 0.13	−0.02	−0.23 to 0.19
Past-week SHS exposure (per each 5 hours/week)	1420	–	–	−0.03	−0.09 to 0.02	−0.02	−0.08 to 0.04
Past-month marijuana use**							
No	1076	81.2	23.2	Ref	Ref	Ref	Ref
Yes	344	18.8	22.6	−0.07	−0.48 to 0.33	−0.01	−0.41 to 0.40
Relevant medical history							
Body mass index							
Underweight	41	2.5	23.2¶	0.22	−1.22 to 1.67	0.23	−1.21 to 1.68
Normal	539	36.4	23.3	Ref	Ref	Ref	Ref
Overweight	394	30.2	23.1	0.02	−0.39 to 0.43	0.01	−0.39 to 0.42
Class 1 obese	215	14.8	23.0	−0.19	−0.62 to 0.25	−0.20	−0.63 to 0.24
Class 2+ obese	231	16.1	22.7	−0.35	−0.80 to 0.09	−0.37	−0.81 to 0.07

Continued

Table 4 Continued

Risk factor at wave 2	N†	US population %	Mean ACT score‡	How tobacco use is modelled: Model 1 Combustible versus non-combustible tobacco use — Adjusted coefficient§	Model 1 — 95% CI	Model 2 Specific tobacco products used — Adjusted coefficient§	Model 2 — 95% CI
P12M asthma controller medications††							
No	1275	90.3	23.4	Ref	Ref	Ref	Ref
Yes	145	9.7	20.1	**−3.26**	**−4.05 to −2.46**	**−3.31**	**−4.09 to −2.52**
Sociodemographics							
Sex							
Female	770	53.0	22.9	Ref	Ref	Ref	Ref
Male	650	47.0	23.3	**0.47**	**0.16 to 0.78**	**0.44**	**0.11 to 0.76**
Education							
No high school degree	165	7.2	22.3	Ref	Ref	Ref	Ref
GED	73	3.9	22.5	0.31	−0.77 to 1.38	0.34	−0.74 to 1.43
High school grad	309	20.3	22.7	0.44	−0.21 to 1.09	0.40	−0.23 to 1.04
Some college	577	39.1	23.1	**0.72**	**0.13 to 1.32**	**0.70**	**0.12 to 1.29**
≥College graduate	296	29.4	23.7	**1.07**	**0.34 to 1.79**	**0.99**	**0.27 to 1.71**

Online supplemental table 11 reports SEs for all the weighted estimates presented in this table and adjusted RRs for all the variables in the model.
*N=1420 wave 2 adult (age 18–39) respondents with valid ACT scores, without chronic obstructive pulmonary disease or other non-asthma respiratory diseases at waves 2–4, with wave 4 PATH Study longitudinal (all waves) weights, and complete data on all analytical variables.
†Unweighted.
‡ACT scores can range from 5 to 25. A higher ACT score represents more controlled asthma.
§All (unstandardised) coefficients adjust for the variables in the table plus age, race/ethnicity and lives in an urban area. Bold coefficients are statistically significant at p<0.05.
¶Estimate should be interpreted with caution because it has low statistical precision. It is based on a denominator sample size of less than 50, or the coefficient of variation of the estimate or its complement is larger than 30%.
**Marijuana use variable does not distinguish between combustible and non-combustible use.
††P12M use of asthma controller medication(s).
GED, General Education Development (high school equivalency certificate); PATH, Population Assessment of Tobacco and Health; P12M, past 12-month; RRs, risk ratios; SHS, secondhand smoke.

aRR=1.17, 95% CI (1.00 to 1.36)); marijuana use (15.1% vs 11.7%, aRR=1.26, 95% CI (1.07 to 1.48)); and weight status (16.4% vs 11.0%, aRR=1.62, 95% CI (1.30 to 2.01) for class 2 obesity vs normal weight). However, the relationship between cigars and lifetime asthma was borderline statistically significant (p=0.057). Additional analyses with quantity/frequency measures of tobacco product use did not detect a dose–response relationship between intensity of tobacco product use and lifetime asthma (not shown).

Relationship between tobacco exposure and asthma incidence

New-onset asthma at W3 or W4 was diagnosed in 1.3% (SE=0.2) of young adults aged 18–24 years, and 0.9% (SE=0.1) of adults aged 25–39 years (online supplemental table 10). In the multivariable longitudinal analyses (table 3, models 1 and 2), we found no association between any type of tobacco product use and new-onset asthma; we did find significant associations between new asthma and weight status (aRR=3.12, 95% CI (1.67 to 5.86) for class 2 obesity vs normal weight). Similar to the cross-sectional findings, additional analyses using quantity/frequency measures of tobacco product use were consistent with the lack of association (not shown).

Cross-sectional relationships between tobacco exposure and asthma control among people with asthma

Figure 1 illustrates asthma control (as measured by ACT scores) by four categories of tobacco use in W2. Figure 1A shows that mean ACT score was about 1 point lower in combustible tobacco users compared with people who had never used tobacco (22.4 (SE=0.1) vs 23.6 (SE=0.2), respectively, two-sample t-test p<0.01). To illustrate the clinical significance of this finding, figure 1B shows that this difference translated into a higher percentage of combustible tobacco users with uncontrolled asthma symptoms compared with never tobacco users with uncontrolled asthma symptoms (16.1% (SE=1.6) vs 4.2% (SE=1.3), two-sample X^2 p<0.01). Although non-combustible tobacco users had numerically lower asthma control (mean ACT scores) and higher proportions of people with uncontrolled symptoms than never tobacco users, the size of the non-combustible user group was

Table 5 Weighted prospective associations between wave 2 past 30-day tobacco use and wave 3 Asthma Control Test (ACT) score among adults aged 18–39 years at wave 2 of the PATH Study, controlling for wave 2 ACT score, negative coefficients reflect worsening of asthma symptoms over time*

				How tobacco use is modelled			
				Model 1 Combustible versus non-combustible tobacco use		Model 2 Specific tobacco products used	
Risk factor at wave 2	N†	Mean wave 2 ACT score‡	Mean wave 3 ACT score‡	Adjusted coefficient§	95% CI	Adjusted coefficient§	95% CI
Past 30-day tobacco use							
Combustible versus non-combustible tobacco use							
Never used tobacco	244	23.5	23.5	Ref	Ref	–	–
Formerly used tobacco	428	23.3	23.4	0.06	−0.36 to 0.48	–	–
Non-combustible use only	44	22.9¶	22.4¶	−0.58	−1.86 to 0.70	–	–
Any combustible use	610	22.4	22.6	−0.04	−0.46 to 0.38	–	–
Specific tobacco products used							
Former							
No	898	22.9	23.0	–	–	Ref	Ref
Yes	428	23.3	23.4	–	–	0.07	−0.33 to 0.47
Cigarette							
No	844	23.4	23.4	–	–	Ref	Ref
Yes	482	22.1	22.4	–	–	0.03	−0.43 to 0.49
Cigar							
No	1075	23.2	23.2	–	–	Ref	Ref
Yes	251	22.5	22.6	–	–	−0.11	−0.55 to 0.33
Hookah							
No	1189	23.1	23.1	–	–	Ref	Ref
Yes	137	22.5	22.9	–	–	0.26	−0.17 to 0.69
E-cigarette							
No	1152	23.2	23.2	–	–	Ref	Ref
Yes	174	22.3	22.3	–	–	−0.42	−0.96 to 0.13
Smokeless							
No	1249	23.1	23.1	–	–	Ref	Ref
Yes	77	23.1	22.9	–	–	−0.06	−0.73 to 0.61
Other smoke-related exposures							
Cigarette pack-years (per each 5 pack-years)	1326	–	–	−0.10	−0.36 to 0.16	−0.09	−0.35 to 0.18
Past-week SHS exposure (per each 5 hours/week)	1326	–	–	0.00	−0.05 to 0.04	0.00	−0.05 to 0.05
Past-month marijuana use**							
No	1007	23.2	23.2	Ref	Ref	Ref	Ref
Yes	319	22.6	22.8	−0.02	−0.36 to 0.33	0.01	−0.34 to 0.37
Relevant medical history							
ACT score at wave 2	1326	–	–	**0.53**	**0.45 to 0.62**	**0.53**	**0.44 to 0.62**
Body mass index							
Underweight	39	23.3¶	22.9¶	−0.39	−1.37 to 0.59	−0.39	−1.39 to 0.61
Normal	509	23.3	23.5	Ref	Ref	Ref	Ref
Overweight	361	23.1	23.1	−0.17	−0.49 to 0.14	−0.19	−0.51 to 0.13
Class 1 obese	206	23.0	23.0	−0.17	−0.64 to 0.30	−0.17	−0.64 to 0.29
Class 2+ obese	211	22.6	22.6	−0.38	−1.03 to 0.27	−0.39	−1.03 to 0.25
P12M asthma controller medications††							
No	1186	23.4	23.5	Ref	Ref	Ref	Ref
Yes	140	20.2	20.2	**−1.47**	**−2.40 to −0.54**	**−1.49**	**−2.42 to −0.57**

Continued

Table 5 Continued

Risk factor at wave 2	N†	Mean wave 2 ACT score‡	Mean wave 3 ACT score‡	How tobacco use is modelled: Model 1 Combustible versus non-combustible tobacco use — Adjusted coefficient§	Model 1 — 95% CI	Model 2 Specific tobacco products used — Adjusted coefficient§	Model 2 — 95% CI
Sociodemographics							
Sex							
Female	727	22.8	22.8	Ref	Ref	Ref	Ref
Male	599	23.4	23.5	**0.37**	**0.09 to 0.65**	**0.37**	**0.07 to 0.67**
Education							
No high school degree	153	22.2	22.1	Ref	Ref	Ref	Ref
GED	60	22.4	21.9	−0.23	−1.13 to 0.67	−0.23	−1.14 to 0.67
High school grad	290	22.7	22.7	0.41	−0.25 to 1.08	0.4	−0.27 to 1.07
Some college	542	23.1	23.1	0.56	−0.05 to 1.17	0.57	−0.05 to 1.19
≥College graduate	281	23.6	23.8	**0.86**	**0.10 to 1.62**	**0.87**	**0.10 to 1.64**

Online supplemental table 12 reports SEs for all the weighted estimates presented in this table and adjusted coefficients for all the variables in the model.
*N=1326 wave 2 adult (age 18–39) respondents with valid wave 2 and wave 3 ACT scores, without chronic obstructive pulmonary disease or other non-asthma respiratory diseases at waves 2–4, with wave 4 PATH Study longitudinal (all waves) weights, and complete data on all analytical variables.
†Unweighted.
‡ACT scores can range from 5 to 25. A higher ACT score represents more controlled asthma.
§All (unstandardised) coefficients adjust for the variables in the table plus age, race/ethnicity and lives in an urban area. Bold coefficients are statistically significant at p<0.05.
¶Estimate should be interpreted with caution because it has low statistical precision. It is based on a denominator sample size of less than 50, or the coefficient of variation of the estimate or its complement is larger than 30%.
**Marijuana use variable does not distinguish between combustible and non-combustible use.
††P12M use of asthma controller medication(s).
GED, General Education Development (high school equivalency certificate); PATH, Population Assessment of Tobacco and Health; P12M, past-12 month; SHS, secondhand smoke.

small and these differences were not statistically significant.

In the cross-sectional, adjusted, multivariable analyses of asthma control (ACT scores; table 4), scores were lower (worse control) among current combustible tobacco users (beta=−0.86, 95% CI (−1.32 to −0.39); model 1) and cigarette users (beta=−1.14, 95% CI (−1.66 to −0.62); model 2). We also found significant associations between asthma control and sex (male sex beta=0.47 (0.16 to 0.78)) and education (eg, for some college beta=0.72 (0.13 to 1.32)). ACT scores among those with treated asthma were lower than ACT scores in untreated asthma by about 3 points (beta=−3.26, 95% CI (−4.05 to −2.46); model 1). Additional analyses with quantity/frequency measures of each tobacco product use also found a negative association between intensity of cigarette use and ACT scores (not shown).

Longitudinal relationships between tobacco exposure and asthma control among people with asthma

In the longitudinal multivariable analyses, there was little association with asthma control (mean ACT score) over time (W3 ACT score, while controlling for W2 ACT score). No tobacco use category at W2 was associated with ACT score at W3 (table 5, models 1 and 2). Of all the predictor variables, higher ACT score at W2, male sex and higher education were significantly associated with better W3 asthma control in both models, while using asthma controller medication at W2 predicted significantly worse W3 asthma control in both models. Additional analyses that modelled quantity/frequency of tobacco product use were consistent with the lack of a longitudinal association between presence or absence of specific product use and ACT scores.

Sensitivity analyses examining the relationships between tobacco exposure and asthma prevalence and incidence

To examine why these findings differed from a previous report using PATH Study data,[22] a series of sensitivity analyses were conducted to explore how including older people (≥40 years), those with COPD and asthma, and covariates indicating other smoke exposures and pack-years of smoking impacted the estimates described above. As illustrated in figure 2A, expanding the sample resulted in significant cross-sectional associations between tobacco use and asthma, suggesting that these associations are due to the relationship between tobacco and COPD rather than tobacco use and asthma. As shown in figure 2B, associations with asthma became statistically significant for former smokers, cigar users and e-cigarette users. Longitudinal associations also became larger, and the associations between new-onset asthma and any combustible use and cigarette use become statistically significant (online supplemental table 7).

DISCUSSION

In this large, nationally representative, prospective study, combustible tobacco and cigarettes were associated with poorer asthma control compared with control among

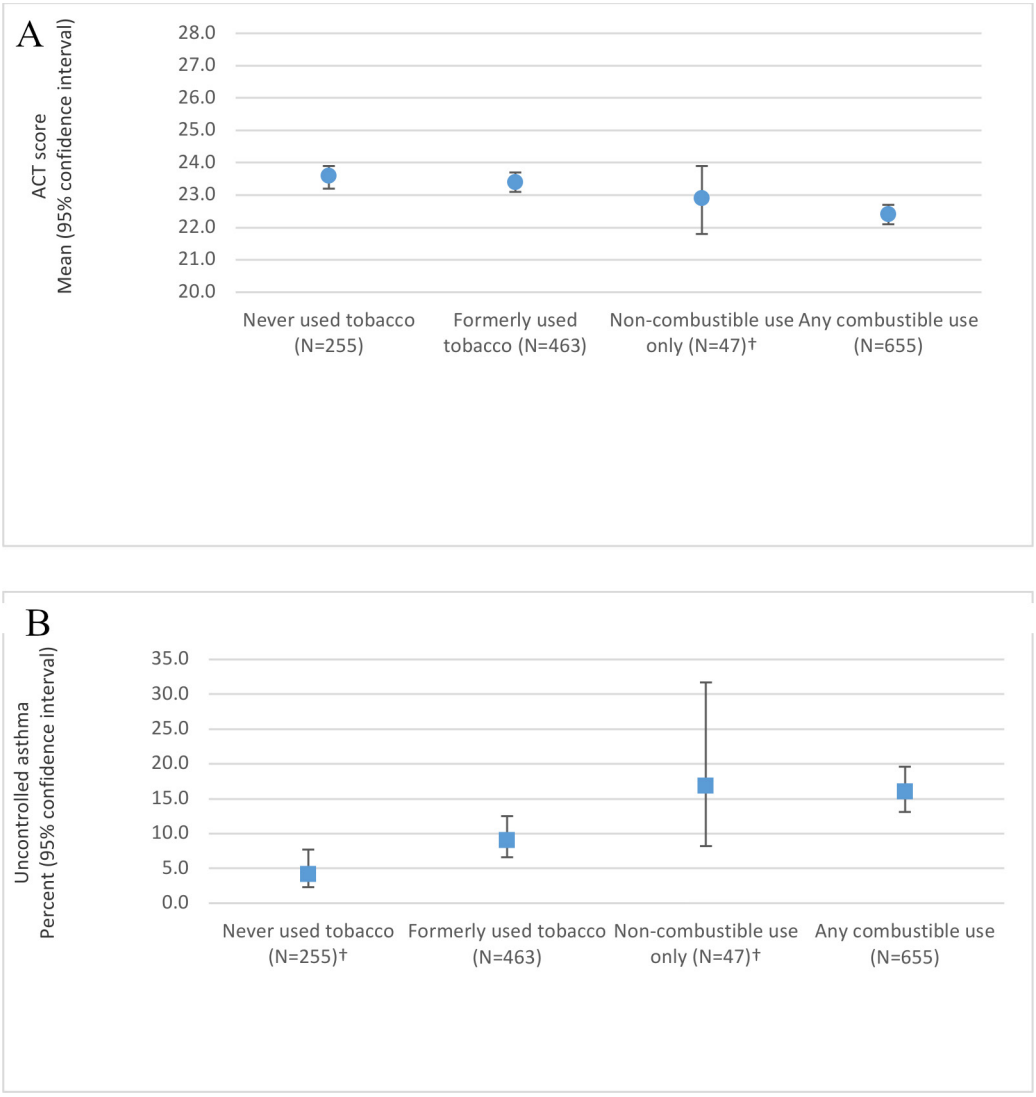

Figure 1 Asthma control by Wave 2 tobacco use[a] among adults age 18-39 of the PATH Study,[b]Panel A, Weighted mean Asthma Control Test (ACT) score, and Panel B, Percent with uncontrolled asthma[c].
[a]Never used tobacco = Never used tobacco, not even one puff; Formerly used tobacco = ever used tobacco, but not in the past 30 days; Non-combustible use only = exclusive non-combustible (e-cigarette, smokeless tobacco, or snus) use in the past 30 days; Any combustible use = combustible (cigarette, pipe, hookah, or cigar) use in the past 30 days regardless of non-combustible use.
[b]N = 1,420 Wave 2 adult (age 18-39 years) respondents with valid Wave 2 ACT scores, without chronic obstructive pulmonary disease or other non-asthma respiratory disease at Waves 2-4, and with Wave 4 Population Assessment of Tobacco and Health (PATH) Study longitudinal (all-waves) weights and complete data on all analytic variables.
[c]Uncontrolled asthma is defined as an ACT score of 19 or less. The ACT has a possible range of 5 to 25, where a higher score represents better controlled asthma.
†Estimate should be interpreted with caution because it has low statistical precision. It is based on a denominator sample size of less than 50, or the coefficient of variation of the estimate or its complement is larger than 30%.
ACT, Asthma Control Test.

non-users in the cross-sectional analysis. These findings strengthen the body of research showing adverse effects of cigarette exposure, even in a young population. No type of tobacco use was associated with a new diagnosis of asthma among adults nor with worsening asthma control over time in analyses that carefully excluded persons with COPD and adjusted for smoking history and other smoke exposures.

In contrast, unadjusted sensitivity analyses including older adults and those with COPD and asthma resulted in significant associations between tobacco use and asthma, suggesting that these associations between tobacco product use and asthma in the sensitivity analyses are spurious, or due to the relationship between tobacco and COPD rather than between tobacco and asthma. A recent meta-analysis of eight epidemiological

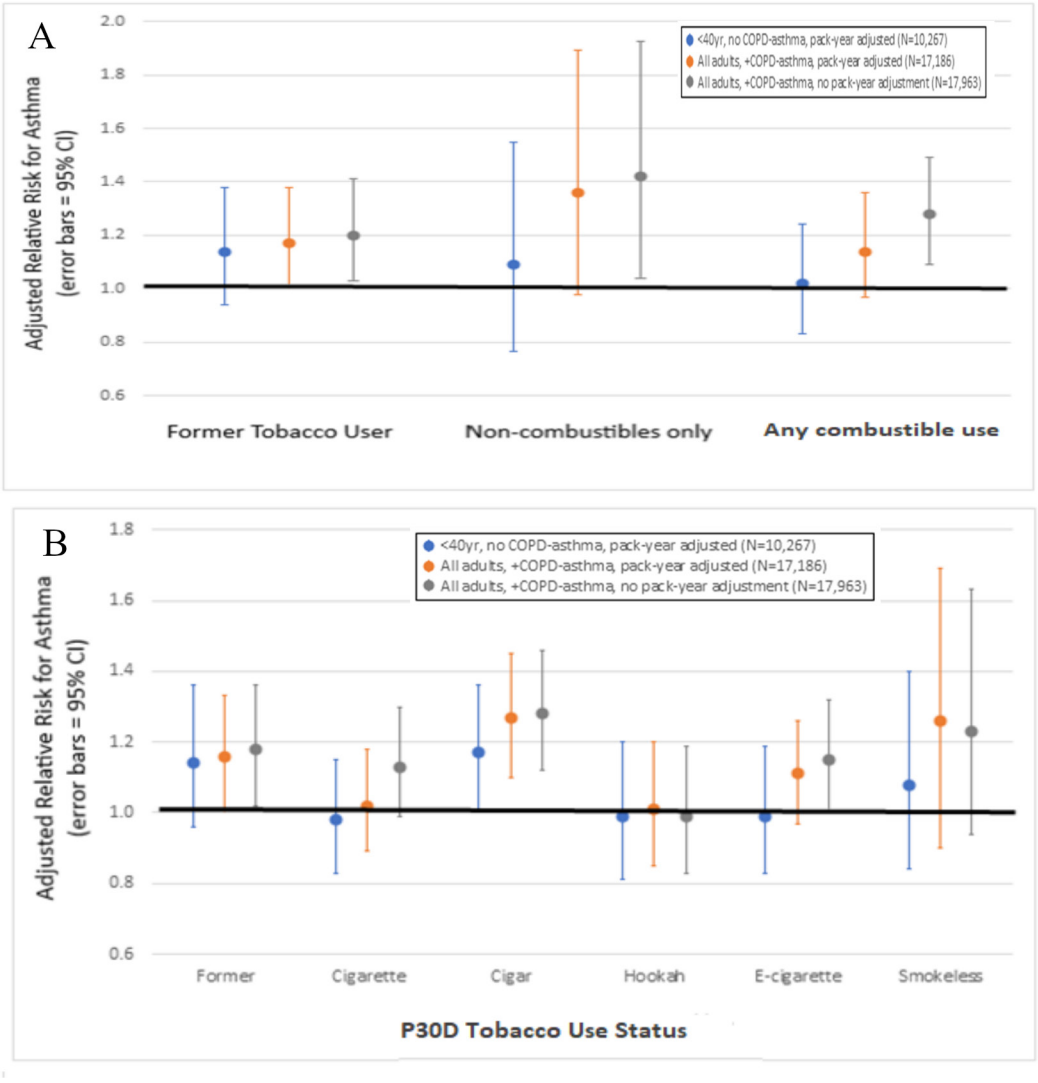

Figure 2 Weighted and adjusted[a] sensitivity analyses[b] for cross-sectional associations between past 30-day combustible v. non-combustible tobacco use[c] (Panel A) and past 30-day tobacco product use[d] (Panel B) and lifetime asthma diagnosis among adults 18+ at Wave 2 of the PATH Study.

[a]All relative risks are adjusted for body mass index, age, sex, race/ethnicity, education, and lives in urban area. Relative risks in the "<40, No COPD" and "All, COPD+Asthma" groups are also adjusted for cigarette pack-years, past-week secondhand smoke, and past-month marijuana use.

[b]<40 years, No COPD = Wave 2 adult (age 18-39 years) respondents without chronic obstructive pulmonary disease or other non-asthma respiratory disease at Waves 2-4, with Wave 4 Population Assessment of Tobacco and Health (PATH) Study longitudinal (all-waves) weights, and complete data on all analytic variables; All adults, COPD+asthma = Wave 2 adult (age 18+ years) respondents without chronic obstructive pulmonary disease at Waves 2-4, unless also having asthma at Waves 2-4, or other non-asthma respiratory disease at Waves 2-4, with Wave 4 PATH Study longitudinal (all-waves) weights, and complete data on all analytic variables; All adults, COPD+asthma, without adjustment = Wave 2 adult (age 18+ years) respondents without chronic obstructive pulmonary disease at Waves 2-4, unless also having asthma at Waves 2-4, or other non-asthma respiratory disease at Waves 2-4, with Wave 4 PATH Study longitudinal (all-waves) weights, and complete data on all analytic variables. For this group, cigarette pack-years, past-week secondhand smoke, and past-month marijuana use are not involved in defining the analytic sample and are not included in the models.

[c]Never used tobacco (reference group) = Never used tobacco, not even one puff; Formerly used tobacco = ever used tobacco, but not in the past 30 days; Non-combustible use only = exclusive non-combustible (e-cigarette, smokeless tobacco, or snus) use in the past 30 days; Any combustible use = combustible tobacco (cigarette, pipe, hookah, or cigar) use in the past 30 days regardless of non-combustible use.

[d]Each past 30-day tobacco product use category is dichotomous as any use versus no use in the past 30 days.

COPD, chronic obstructive pulmonary disease.

studies concluded that smoking was related to incident asthma (RR 1.61, 95% CI (1.07 to 2.42)),[9] but most failed to exclude people with COPD,[16 17 22–26] and many did not adjust for other smoke exposures,[16 18 22–25] which may explain the different conclusion in the present study.

Other cross-sectional research has also shown that smoking was associated with poor asthma control,[10 11 13] and unadjusted prospective studies have also indicated that smoking predicted poor asthma control and asthma exacerbation over time,[46 47] but these studies also did not remove people with COPD or adjust for cumulative past smoking and other smoke exposures. In contrast, at least one study that carefully controlled for these factors did not show an association between smoking and new asthma[48]; rather, similar to our study, use of controller medications at baseline was associated with persistence of asthma.[48]

Similar to other recent research, cigarette smoking was not associated with a higher or lower risk of lifetime asthma in W2 of the PATH Study (2014–2015),[10 14 49] indicating that asthma is not deterring smoking in the USA. Because smoking is associated with worse asthma control in this and other studies,[50 51] and causes or exacerbates multiple other diseases, people with asthma should still be encouraged to quit. Tailored interventions may be useful.[52]

Little is known about e-cigarette use and the development of asthma in adults. Our study conclusion—that there is no association between e-cigarette use and new-onset asthma—contrasts with cross-sectional epidemiological studies[53] and the only other prospective epidemiological study of e-cigarette use and asthma.[22] The prospective study used the same data as our study but included older adults as well as those with asthma and COPD and did not adjust for history of smoking and other smoke exposures. By omitting people with COPD and those over age 40 years from this study, as well as by adjusting for other smoke exposures, we carefully isolated the effect of tobacco product use on the development of asthma in adulthood. It should be noted that about 80% of e-cigarette users in this cohort also smoked cigarettes. The small numbers of e-cigarette-only users in this study limited the ability to test for modest associations.

The heterogeneity of asthma may also contribute to mixed findings in epidemiological research, with some types of asthma potentially being more sensitive to smoking. For example, in a longitudinal study that measured lung function, smoking did not worsen the decline of lung function among those with childhood-onset asthma but was associated with greater decline in lung function among patients with adult-onset asthma.[14] The PATH Study did not obtain information that would allow us to determine asthma subtypes.

Several additional study limitations warrant discussion. At the time of these analyses, PATH Study data for tobacco, asthma and asthma symptoms were available W2 through W4, or for only three waves. Analyses over longer time periods will be able to elucidate the longer-term impact of tobacco product use on asthma. Additionally, the e-cigarettes used during the years of these analyses were different from the fourth-generation e-cigarettes now on the market. E-cigarette devices are changing rapidly and are still relatively recent; thus, additional research should examine e-cigarettes over time. Finally, the PATH Study does not measure all subject characteristics and exposures associated with asthma risk, such as allergy or atopy,[54] environmental ozone specifically,[26 55] environmental air pollution in general[56] and prenatal smoke exposure.[57] Such measures could enable more specific predictive models. Despite these limitations, these carefully adjusted analyses of a US population sample provide important, current information about the impact of tobacco products on asthma.

CONCLUSION

Combustible tobacco and cigarette use were associated with worse asthma control cross-sectionally, but combustible tobacco product and e-cigarette use were not associated with asthma prevalence, incident asthma or change in symptom severity in adults with asthma when individuals with COPD were excluded and analyses were adjusted for other smoke exposures. Clinicians caring for patients with asthma should address smoking, and research on the impacts of tobacco on health should carefully measure and adjust for these potential confounders.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study involves human participants. The study was conducted by Westat and approved by the Westat Institutional Review Board (IRB) (Westat IRB # 0000695; PATH project number #8954). Participants gave informed consent to participate in the study before taking part.

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