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Cancer incidence in a general population of asthma patients[†]

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SUMMARY

Purpose Several studies have assessed the association between asthma and cancer but none of them revealed a clear pattern of association. We aimed to examine the association between asthma, chronic obstructive pulmonary disease (COPD), and cancer.

Methods We performed a cohort study with a nested case-control analysis using the General Practitioner Research Database in the UK. We defined three cohorts: patients with asthma, patients with COPD, and general population. During the follow-up, we identified a total of 5263 incident cases of cancer. We conducted a nested case-control analysis that included all cancer cases as well as 20 000 controls free of cancer frequency-matched on age, sex, and calendar year.

Results Patients with asthma did not have an overall greater risk of cancer compared with the general population (odds ratio = 0.93, 95% confidence interval (CI): 0.86–1.00). However, they presented an elevated risk of experiencing lung cancer (odds ratio = 1.84, 95%CI: 1.58–2.15). Controlling for smoking and other potential confounding factors yielded a lower estimate (odds ratio = 1.35, 95%CI: 1.15–1.59). This estimate contrasted with that observed for non-smoking related cancer (0.87, 95%CI: 0.80–0.94). Overall, respiratory drugs did not seem to be associated with cancer among asthmatic patients. Patients with COPD had an Odds ratio of cancer of 1.26 (95%CI: 1.12–1.43) compared with the general population.

Conclusions Asthma was not associated with an increased risk of cancer. In fact, the risk of non-smoking related cancer was slightly reduced. However, we observed a small-elevated risk of lung cancer among asthmatic patients. Whether this result is a due to residual confounding and/or protopathic bias remains unclear. Further investigation is warranted to confirm or discard these associations. Copyright © 2005 John Wiley & Sons, Ltd.

KEY WORDS — asthma; neoplasms; epidemiologic studies

INTRODUCTION

Asthma is a multifactorial lung disease that causes wheezing, shortness of breath, coughing, and chest tightness. Allergic mechanisms are of importance in about 80% of childhood asthma¹ and 40–50% of the adult form.²

A number of observational studies have been performed to measure the association of asthma with incidence of cancer during the last decades. Conflicting results have provided support for two different

hypotheses. Some studies suggest a protective effect of allergies due to an “enhanced immune surveillance theory,” with stimulated immune systems being able to destroy malignant cells^{3–17} whereas others report that chronic immune stimulation due to allergy causes mutations in stem cells,^{18–22} known as the “antigenic stimulation theory,” and could be associated with an increased risk of cancer.

These studies, with different designs, method of asthma ascertainment, and analysis strategies, did not reveal a consistent pattern in the association of asthma with incidence of cancer in general. Some case-control studies had methodological problems.^{12,20,23} A case-control study with more than 17 000 patients by Vena *et al.*¹⁷ reported decreased risks associated with a history of hives and other allergies for specific cancers

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in males and females. Other studies have reported decreased risks of glioma,^{24–26} pancreatic cancer,^{27,28} non-Hodgkins lymphoma,²⁹ and leukemia,^{30–32} as well as increased risks of lung cancer.³³ Among cohort studies^{11,21,31,34–36} methods for identifying asthma varied across studies, and were performed in different countries with very different sample sizes. It is worth noting the fact that two large studies produced inconsistent results. Even though they were performed in large national databases from Northern Europe and were able to identify large cohorts of asthmatic patients, they failed to control for confounding factors.³¹ Whereas Kallen *et al.*¹¹ showed a significant negative association between asthma and cancer, Vesterinen *et al.*³¹ showed a statistically significant positive association.

A recent prospective study³⁷ assessed the association between asthma and atopy (by skin prick test) with specific cancers. They found a significant association with prostate cancer, but the power of the study was limited.

In summary, the exact nature of such association remains controversial. We conducted a population-based study using the General Practice Research Database (GPRD) in order to estimate the incidence rate of cancer among asthma patients under current standards of treatment (inhaled corticoids, short acting and long acting β -agonists, aminophylines, etc.) and compare it to the risk of cancer in the general population.

We also included a cohort of COPD patients in addition to the purely asthmatic population. Patients who suffer from chronic obstructive pulmonary disease (COPD) have a certain component of bronchorreativity. Although the inflammatory mechanisms (bronchorreativity) are different from those in asthma, they both share some symptomatology and respiratory medications.

MATERIALS AND METHODS

Data source

The GPRD contains computerized medical information entered systematically by general practitioners (GPs) and sent anonymously to the Medicines and Healthcare products Regulatory Agency, that collects and organizes this information in order to be used for research projects. The information recorded includes demographic data, clinical diagnoses from outpatient visits, consultant referrals and hospital admissions, and prescriptions. Prescriptions are generated directly from the GP's computer and entered into the patient's

computerized file. More than 90% of all referrals present in the manual records in GPs' offices are entered into computer files with a code that reflects the clinical diagnosis.³⁸ Various studies have confirmed the validity of using the GPRD for respiratory epidemiological research.^{39,40}

Study population

The source population included patients 20–79 years old who were permanently registered with a GP between January 1994 and December 2001.

We defined three different cohorts drawn from the source population:

- *Asthma cohort:* Those patients from the source population who had a recorded code for asthma at any time before or during the study period (1994–2001). This cohort comprised a total of 129 860 subjects.
- *COPD cohort:* Those patients from the source population with a recorded code for COPD and no recorded code for asthma at any time before or during the study period (1994–2001). This cohort comprised a total of 9301 subjects.
- *General population:* A random sample of 200 000 patients from the source population frequency matched on age, gender, and calendar year to the asthma cohort with no recorded code for asthma or COPD.

Follow-up

Subjects became study members on the first day of the study period when they met the criteria of at least 1-year enrolment with the GP and 1 year since the first computerized prescription. In addition, follow-up for the asthma and COPD cohorts started only after the diagnosis was recorded for the first time. Subjects with a diagnosis of cancer before entering the study were excluded. All study members were followed from the first date after 1st of January 1994 when they met all the eligibility criteria until the earliest occurrence of one of the following endpoints: (a) case detection: cancer; (b) death; or (c) end of study period (December 2001).

Case ascertainment

We identified 5884 patients with a code of cancer: 2971 in the asthma cohort, 574 in the COPD cohort, and 2339 in the general population cohort. We manually

reviewed the computerized patient profiles for all of them. To maintain confidentiality all patient personal identifiers were suppressed before reviewing computerized information. Based on this review, we excluded 596 cases (10%). Most cases were excluded because the initial computer diagnosis was not subsequently confirmed (71% of them) or because the first diagnosis was made before the study period (22%). We sent questionnaires to the GPs for validation of a random sample of 454 cases of cancer. A total of 449 (99 %) questionnaires were received and 424 of them (94%) confirmed the computer diagnosis. In the end, 5263 patients were considered incident cases of cancer.

Cohort and nested case-control analysis

We calculated the crude incidence rates for cancer in the three cohorts by dividing the number of cancer cases by the corresponding number of person-years at risk. Incidence rates were also calculated within strata of age and sex. Adjusted incidence rates for cancer in the three cohorts were calculated by using direct standardization using the entire study population (the three study cohorts) as the standard.⁴¹

All 5263 cancer cases from the three study cohorts (asthma, COPD, and general population) were included in a nested case-control analysis. For cases, the index date was assigned to be the date of initial diagnosis of cancer. In selecting controls, an index date was randomly assigned during the study period to all members of the three study cohorts so that the likelihood of being selected as a control was proportional to the person-time at risk for each individual (i.e., incidence density sampling). The same eligibility criteria were applied to controls and cases. From the pool of eligible controls, 20 000 controls were frequency-matched to the cases on age (interval of 1 year), sex, and calendar year.

We classified patients according to age, sex, body mass index (less than 20, 20–24, 25–29, and 30 or more), smoking (current smokers, former smokers, and non-smokers), alcohol intake, and certain comorbidities (cardiovascular, diabetes, osteoarthritis, and rheumatoid arthritis). We also ascertained for cases and controls utilization of health care services (number of GP visits, number of hospital admissions and number of referrals to a specialist) during the 2 years before the index date.

Estimates of odds ratio (OR), assumed to be valid estimates of the rate ratio of cancer, and 95% confidence intervals (CI) were calculated for asthmatic patients and COPD patients compared to the general population using unconditional logistic regression.

Additionally, estimates of ORs and 95%CI were also calculated for the following specific cancer sites: female breast, prostate, gastro-esophageal, colorectal, lung, and other cancers.

An additional analysis including only asthmatic patients was performed in order to assess the effect of respiratory drugs on the risk of cancer. Thus, this analysis included the 2668 cases from the asthma cohort and 10 046 controls. Estimates of OR of cancer and 95%CI were calculated for users of inhaled steroids, oral steroids, inhaled antimuscarinics, theophylline, antihistamines, short acting β -agonists, and long acting β -agonists compared to non users using unconditional logistic regression.

Exposure definition

We defined three time windows of exposure for use of respiratory medications: current use, past use, and non use. Current use was defined as use that lasted to the index date or ended in the year prior to the index date based on the supply of drug therapy as prescribed by the GPs. Past use was the use that ended more than 1 year before the index date. Finally, no use was defined as no recorded prescription at any time before the index date. Current users were further subdivided into three categories by duration of treatment: less than 1 year, between 1 and 3 years, and more than 3 years of chronic use.

RESULTS

A total of 2668 incident cases of cancer were identified in the asthma cohort, 521 in the COPD cohort, and 2074 in the general population cohort. The overall crude incidence rates of cancer were 589 cases per 100 000 person-years in the asthma cohort, 2231 in the COPD cohort, and 405 in the general population cohort. Tables 1–3 show the corresponding standardized incidence rates (SIRs) in the three cohorts stratified by age (adjusted for sex and calendar year) and sex (adjusted for age and calendar year). All three cohorts were consistent in showing higher SIRs associated with male sex and older age. Overall SIR of cancer was 549 cases per 100 000 person-years (95%CI: 527–570) in asthma patients, 854 (95%CI: 738–971) in COPD patients, and 470 (95%CI: 449–493) in the general population. The markedly increased risk among COPD patients observed in the crude estimates was still present, though to a much lesser extent, in the adjusted estimates. The adjusted estimates also showed a slightly increased risk

Table 1. Incidence rate of cancer by age and gender in asthma patients

	Person-years	Cancer cases	Incidence rate per 100 000 person-years (95%CI)
Age (years)			
20–39	167 414	118	71.6 (58.3–84.8)*
40–59	158 721	607	373.2 (342.6–403.7)*
60–79	126 692	1943	1571.0 (1499.6–1642.4)*
Gender			
Male	197 497	1335	627.9 (593.3–662.5)†
Female	255 330	1333	487.7 (460.9–514.6)†
Total	452 827	2668	548.8 (527.4–570.2)‡

*Adjusted for sex, and calendar year using direct standardization.

†Adjusted for age and calendar year using direct standardization.

‡Adjusted for age, sex, and calendar year using direct standardization.

Table 2. Incidence rate of cancer by age and gender in COPD patients

	Person-years	Cancer cases	Incidence rate per 100 000 person-years (95%CI)
Age (years)			
20–39	600	0	0
40–59	5234	40	750.2 (464.0–1036.3)*
60–79	17 521	481	2375.6 (2150.8–2600.3)*
Gender			
Male	13 339	368	1024.8 (886.0–1163.7)†
Female	10 016	153	722.5 (545.1–899.9)†
Total	23 355	521	854.2 (737.7–971.2)‡

*Adjusted for sex, and calendar year using direct standardization.

†Adjusted for age and calendar year using direct standardization.

‡Adjusted for age, sex, and calendar year using direct standardization.

Table 3. Incidence rate of cancer by age and gender in the general population

	Person-years	Cancer cases	Incidence rate per 100 000 person-years (95%CI)
Age (years)			
20–39	221 217	142	64.0 (53.3–74.8)*
40–59	192 131	625	326.5 (300.1–352.8)*
60–79	98 709	1307	1333.5 (1254.8–1412.3)*
Gender			
Male	219 824	933	519.1 (482.5–555.8)†
Female	292 233	1141	433.2 (406.5–460.0)†
Total	512 057	2074	470.7 (448.7–492.6)‡

*Adjusted for sex, and calendar year using direct standardization.

†Adjusted for age and calendar year using direct standardization.

‡Adjusted for age, sex, and calendar year using direct standardization.

(17%), among asthmatic patients compared to the general population.

We further analyzed the association between cancer and prior diagnosis of asthma or COPD in the nested case-control analysis. Table 4 shows the OR estimates

and 95%CI associated with asthma and COPD compared to the general population. The first estimates are obtained including in the model only age, sex, and calendar year. The second estimates are fully adjusted for these covariates as well as body mass index, alcohol intake, smoking status, prior comorbidities, health services utilization, and NSAID use. After controlling for all these factors asthma patients presented an OR of 0.93 (95%CI: 0.86–1.00) compared to the general population, whereas the estimate for COPD was 1.26 (95%CI: 1.12–1.43). Table 4 also shows the OR estimates for individual cancers (female breast, prostate, gastro-esophagus-stomach, colon-rectum, lungs, and other cancer). Among asthmatic patients only the risk of lung cancer appeared to be greater than in the general population (OR: 1.35, 95%CI: 1.15–1.59). In an secondary analysis, we excluded asthma patients with a first ever diagnosis of asthma in the year prior to the index date. The corresponding estimate for lung cancer in this analysis was 1.22 (95%CI: 1.03–1.44).

After removing cancers aetiologically related to smoking (cancers of the mouth, oropharynx, larynx, other respiratory tract, pancreas, trachea, bladder, and lung) the risk of cancer among asthma patients was 0.87 (95%CI: 0.80–0.94).

The OR estimate for lung cancer among COPD patients was 1.86 (95%CI: 1.50–2.31), and other cancers such as gastro-esophageal or colorectal were also slightly increased. The OR of developing cancer in the COPD cohort was 1.09 (95%CI: 0.94–1.26) after removing cases of lung cancer.

To further investigate risk factors of cancer among asthmatic patients we carried out a sub-analysis that included only the 2668 cases and 10 046 controls from the asthma cohort. In this population, smoking increased the risk of cancer by 50% (OR: 1.52, 95%CI: 1.41–1.65). Similarly, a greater use of health services during the 2 years prior to the index date was associated with an increased risk of cancer. Thus having one or more hospitalizations in this period was associated with an OR of 1.89 (95%CI: 1.76–2.02), having six visits or more in this period was associated an OR of 1.31 (95%CI: 1.19–1.43), and having 2 or more referrals was associated with an OR of 1.80 (95%CI: 1.68–1.93).

Overall, respiratory drugs did not seem to be associated with cancer among asthmatic patients. As shown in Table 5, current use of inhaled steroids was not associated with cancer. A similar null result was seen for inhaled antimuscarinics. Users of oral steroids presented a small increased risk of cancer (OR: 1.18, 95%CI: 1.04–1.33). However, this increased risk was

Table 4. Risk of cancer in patients with asthma and COPD

	Controls (<i>n</i> = 20 000)	%	Cases (<i>n</i> = 5265)	%	Odds ratio* (95%CI)	Odds ratio† (95%CI)
All cancer						
General population	8746	43.7	2074	39.4	1	1
Asthma	10 046	50.2	2668	50.7	1.13 (1.06–1.21)	0.93 (0.86–1.00)
COPD	1208	6.0	521	9.9	1.85 (1.65–2.08)	1.26 (1.12–1.43)
Breast cancer						
General population	4705	46.6	419	50.7	1	1
Asthma	5006	49.6	383	46.3	0.94 (0.81–1.09)	0.91 (0.78–1.06)
COPD	381	3.8	25	3.0	1.04 (0.68–1.59)	1.03 (0.66–1.58)
Prostate cancer						
General population	4041	40.8	176	39.1	1	1
Asthma	5040	50.9	231	51.3	1.05 (0.85–1.30)	0.86 (0.69–1.07)
COPD	827	8.4	43	9.6	1.03 (0.73–1.46)	0.89 (0.62–1.28)
Gastro-esophageal cancer						
General population	8746	43.7	112	37.7	1	1
Asthma	10 046	50.2	143	48.2	1.01 (0.78–1.31)	0.86 (0.65–1.12)
COPD	1208	6.0	42	14.1	1.98 (1.37–2.88)	1.40 (0.95–2.06)
Colorectal cancer						
General population	8746	43.7	193	39.6	1	1
Asthma	10 046	50.2	243	49.8	1.02 (0.83–1.24)	0.86 (0.70–1.06)
COPD	1208	6.0	52	10.7	1.60 (1.16–2.20)	1.37 (0.98–1.91)
Lung cancer						
General population	8746	43.7	256	24.0	1	1
Asthma	10 046	50.2	610	57.2	1.84 (1.58–2.15)	1.35 (1.15–1.59)
COPD	1208	6.0	200	18.8	4.18 (3.42–5.11)	1.86 (1.50–2.31)
Other cancer						
General population	8746	43.7	918	43.0	1	1
Asthma	10 046	50.2	1058	49.6	1.07 (0.97–1.18)	0.86 (0.78–0.95)
COPD	1208	6.0	159	7.5	1.43 (1.19–1.72)	0.99 (0.82–1.20)

*Estimates are adjusted for age, sex, and calendar year.

†Estimates are adjusted for age, sex, calendar year, BMI, alcohol intake, smoking status, prior comorbidities (cardiovascular disease, diabetes, osteoarthritis, and rheumatoid arthritis), health services utilization, use of aspirin, NSAID, and paracetamol using logistic regression.

restricted to subjects using oral steroids during less than 3 years, and subjects with longer treatment duration did not present an elevated risk. Longer duration of theophylline use was associated with a small not significantly reduced risk: among long-term users of this drug (more than 3 years of use) the OR was 0.87 (95%CI: 0.69–1.09) compared to non users. The use of antihistamines for less than 3 years was associated with a reduced risk of cancer (OR: 0.83, 95%CI: 0.71–0.97). However, this risk reduction was not observed among long-term users of antihistamines. A similar result was observed for long-acting β -agonists. Use with a duration less than 3 years was associated with a decreased risk (OR: 0.83, 0.72–0.97) whereas no effect was seen among those taking these drugs during 3 years or more compared to non users.

DISCUSSION

This study has evaluated the association between cancer and asthma from 1994 to 2001 in a cohort of 129 860 patients diagnosed with asthma in a UK

general population. Whether there is a relationship between asthma and cancer due to the underlying physiopathology, and whether or not pharmacological treatments could confound such relation was the primary aim of the study.

The incidence rate estimates found in this study for the general population are well within the range of recent reports from the UK.⁴² After controlling for other potential confounders (including smoking), in addition to age and sex, asthmatic patients do not seem to carry a higher risk of cancer compared to the general population. We also studied site-specific cancer risk. Asthmatic patients presented an increased risk of lung cancer. Smoking was more common among asthmatic patients than in the general population. However, a small increased risk was still observed after controlling for smoking. This finding suggests that the underlying physiopathology in asthma patients could increase the risk of lung cancer. However, we cannot exclude residual confounding by active smoking and/or confounding by exposure to environmental tobacco smoke which has been linked to both

Table 5. Risk of cancer associated with use of respiratory drugs in asthma patients*

	Controls (<i>n</i> = 10 046)	%	Cases (<i>n</i> = 2668)	%	Odds ratio (OR) [†]	95%CI
Inhaled steroids						
Non user	1683	16.8	448	16.8		
Current (<1 year)	4644	46.2	1223	45.8	0.93	0.81–1.07
Current (1–3 years)	1340	13.3	388	14.5	1.03	0.86–1.23
Current (>3 years)	1088	10.8	305	11.4	0.94	0.77–1.15
Past users	1291	12.9	304	11.4	0.88	0.74–1.04
Oral steroids						
Non user	4386	43.7	1044	39.1		
Current (<1 year)	2382	23.7	784	29.4	1.18	1.04–1.33
Current (1–3 years)	178	1.8	71	2.7	1.22	0.90–1.66
Current (>3 years)	184	1.8	62	2.3	1.02	0.74–1.41
Past users	2916	29.0	707	26.5	0.96	0.86–1.08
Inhaled antimuscarinics						
Non user	7576	75.4	1904	71.4		
Current (<1 year)	1055	10.5	343	12.9	1.00	0.86–1.16
Current (1–3 years)	393	3.9	118	4.4	0.94	0.74–1.19
Current (>3 years)	326	3.3	120	4.5	1.15	0.90–1.48
Past users	696	6.9	183	6.9	0.96	0.80–1.16
Theophylline						
Non user	7476	74.4	1939	72.7		
Current (<1 year)	486	4.8	161	6.0	0.97	0.79–1.19
Current (1–3 years)	243	2.4	69	2.6	0.89	0.66–1.18
Current (>3 years)	437	4.4	115	4.3	0.87	0.69–1.09
Past users	1404	14.0	384	14.4	0.96	0.84–1.10
Antihistamines						
Non user	6765	67.3	1851	69.4		
Current (<1 year)	973	9.7	250	9.4	0.84	0.72–0.98
Current (1–3 years)	69	0.7	14	0.5	0.75	0.41–1.35
Current (>3 years)	54	0.5	16	0.6	1.08	0.60–1.92
Past users	2185	21.8	537	20.1	0.82	0.73–0.92
Short-acting β -agonists						
Non user	503	5.0	131	4.9		
Current (<1 year)	4679	46.6	1231	46.1	0.95	0.76–1.18
Current (1–3 years)	1155	11.5	323	12.1	0.89	0.69–1.15
Current (>3 years)	1799	17.9	536	20.1	0.97	0.76–1.24
Past users	1910	19.0	447	16.8	0.97	0.77–1.22
Long-acting β -agonist						
Non user	8402	83.6	2214	83.0		
Current (<1 year)	770	7.7	214	8.0	0.88	0.74–1.04
Current (1–3 years)	292	2.9	66	2.5	0.72	0.54–0.96
Current (>3 years)	165	1.6	52	2.0	1.15	0.82–1.62
Past users	417	4.2	122	4.6	0.99	0.80–1.24

*Among asthma cohort members only.

[†]Estimates are adjusted for age, sex, calendar year, BMI, alcohol intake, smoking status, prior comorbidities (cardiovascular disease, diabetes, osteoarthritis, and rheumatoid arthritis, health services utilization, use of aspirin, NSAID, paracetamol and all the variables in the table using logistic regression.

new-onset asthma and lung cancer.⁴³ Also since early symptoms of lung cancer could be diagnosed as asthma (i.e., protopathic bias), in an alternative analysis we discarded cases and controls with a diagnosis of asthma first made within 1 year before the index date. This resulted in a somewhat lower estimate (OR: 1.22, 1.03–1.44).

When we analyzed the risk of cancer according to the use of different respiratory drugs, there seemed to be a higher risk of cancer for those asthmatic patients

using oral corticosteroids, even after adjusting for other potential confounders. When analyzing the association with treatment duration we did not observe an increased risk among long-term users. Immunosuppressive therapy has been associated with an increased risk of both non-melanoma skin cancer and non-Hodgkin's lymphoma among patients with renal transplantation^{44–48} although there has been no strong evidence that the use of any of the new regimens adds or reduces the overall risk of developing

post-transplant malignancies. It appears that immunosuppression alone is not sufficient for tumor development, additional risk factors, such as conventional risk factors for cancer, genetic background, chronic viral infection, and prior medications can play also a role. A recent population based study of prescriptions⁴⁹ suggested that the use of systemic glucocorticoids may be a risk factor for basal cell carcinomas, squamous cell carcinomas, and lymphoma. It is well-known that asthma patients receiving oral steroids suffer from a severe form of the disease. Whether the small increased risk is an effect of the immunosuppressive therapy or the underlying physiopathological condition of the disease remains to be elucidated.

In our study, COPD patients presented an increased risk of lung cancer. Around 60% of COPD patients in our study were either current or former smokers (compared to 34% and 28% in the asthma and general population cohorts, respectively). This is a well-known risk factor for both COPD and lung cancer, and residual confounding due to imperfect control for smoking could be an explanation for part of the elevated risk of lung cancer in this population.

It should be noted that greater use of health services during the 2 years prior to the index date was associated with an increased risk of cancer in all three cohorts. This could be interpreted as a surrogate for a worse general comorbidity profile before the actual diagnosis of neoplasm. We were not able to ascertain the severity of the disease, so we could not assess whether there was a different risk of cancer depending on the severity of asthma. However, the association with oral corticosteroid use might point in such direction. Also, there are some potential confounders and predictors of cancer such as family history of cancer or exposure to certain environmental factors (exposure to environmental tobacco smoke in lung cancer or occupational exposures) that we were not able to ascertain through the database. Cancer is a low frequency disease both in general population and asthma patients and the assessment of any association requires large studies, in particular when the interest is in specific types of cancer. The use of population-based automated databases in this setting enables the study of cohorts of patients of relatively large size. Additionally, drug exposure and prior comorbidities are prospectively recorded in the database, which avoids recall bias typically present in studies based on questionnaires.

To the best of our knowledge, this is the largest study addressing the relation between cancer and asthma. The results of this study replicate previously reported lack of a direct association between asthma and cancer and even suggest a protective effect for non-smoking

KEY POINTS

- Several studies have assessed the association between asthma and cancer but results are inconsistent.
- Asthma was not associated with an increased risk of cancer in our study. However, the small-elevated risk of lung cancer observed among asthmatic patients deserves further investigation.

related cancer. Nevertheless, a small excess risk of lung cancer among asthma patients, even after adjusting for other risk factors, was still observed in our study. If this result is due to the inflammatory process in airways, an interaction between inflammation and therapeutic agents, protopathic bias, or residual confounding is unknown and warrants further investigation.

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