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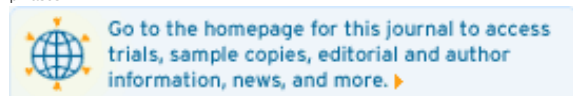


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Epidemiology

Allergies are associated with reduced pancreas cancer risk: A population-based case-control study in Ontario, Canada

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Keywords

allergy and immunology • asthma • case-control studies • hypersensitivity • pancreatic neoplasms

Abstract



Pancreatic adenocarcinoma is one of the deadliest cancers with mortality rates almost equaling incidence rates. Each year, approximately 3,500 Canadians are diagnosed with this disease. Although somewhat inconsistent, epidemiological studies have found that allergies are associated with a reduced pancreas cancer risk while there appears to be no association with asthma. These associations were evaluated in a population-based case-control study conducted in Ontario. Incident cases of pancreatic adenocarcinoma, identified through the Ontario Cancer Registry (OCR), and diagnosed April 1, 2003 to June 1, 2006, were recruited by the Ontario Pancreas Cancer Study (OPCS). Controls were recruited from the Ontario Familial Colorectal Cancer Registry (OFCCR). Data on 276 cases and 378 controls were available for the current study. Multivariable logistic regression analysis was used to obtain age-adjusted odds ratio (AOR) estimates. Ever having allergies or hayfever was associated with reduced pancreas cancer risk (OR = 0.43, 95% confidence interval (CI): 0.29-0.63). There was no association observed between a history of asthma and pancreas cancer risk. Findings are of great importance to understanding the biological mechanisms involved in pancreas cancer development. © 2007 Wiley-Liss, Inc.

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Article Text

Pancreas cancer is one of the leading causes of cancer deaths in men and women, with mortality rates closely approaching incidence rates.^[1] Approximately 3,500 Canadians are diagnosed with this disease annually^[1] and <5% survive 5 years.^[2] The high mortality is the result of the majority of patients presenting with locally advanced and/or metastatic disease, which is rapidly progressive and inevitably fatal. Less than 20% of patients are able to undergo attempted curative surgical resection, which is associated with improving 5-year survival rates of 15-20%, depending on the stage of cancer.^[3] There are no clinically recommended screening tests for the early detection of pancreas cancer. The only significant progress has been lower operative mortality rates for patients who have resections, and the slight prolongation and improved quality of life in patients with inoperable disease with the use of chemotherapeutic agents.^{[4][5]}

The etiology of pancreas cancer is poorly understood. Cigarette smoking is the only environmental exposure that has consistently been associated with an increased risk of pancreas cancer.^{[6][7][8]} Pancreas cancer risk increases with age, and is slightly more common in men, in individuals of African-American descent, and of Ashkenazi-Jewish heritage.^{[9][10]} Other factors that may increase risk include diet, such as red and processed meat consumption, and medical conditions, such as chronic pancreatitis and diabetes.^{[11][12]} Genetics also play a role, as an estimated 5-10% of cases present with a heritable form of pancreas cancer.^[9] These and other novel factors must be further explored to provide additional insight into the etiologic and biologic mechanisms involved in the development of pancreas cancer.

Allergies and cancer risk



Epidemiologic studies examining the association between prior allergic conditions and the risk of various cancers have been inconsistent.^{[13][14][15][16][17][18]} Risk differed between men and women, and depended on the type of allergy and cancer site.^{[14][15][16][19]} In a cohort study by Soderberg *et al.* (2004), there was at least a doubling of risk of certain types of leukemia among individuals with hives.^[18] A similar risk of non-Hodgkin lymphoma was noted in people with childhood eczema.^[18] Turner *et al.* (2005) reported significantly decreased risks of overall cancer mortality in people with hay fever, while a slightly increased risk was observed in people who only had asthma.^[17] More specifically, significantly decreased risks of lung cancer, pancreatic cancer and colorectal cancer mortality were associated with a reported history of hay fever. Self-reported asthma history was only associated with a significantly decreased risk of leukemia mortality and an increased risk of lung cancer mortality. In another prospective cohort study, Talbot-Smith *et al.* (2003) examined the association between allergies and several cancer sites. Individuals who were allergic to dust mites showed a tripling of prostate cancer risk, and history of asthma or any atopy was modestly associated with an increased risk.^[14] Hay fever was only associated with a doubling of melanoma risk of borderline statistical significance in men.

Abbreviations:

AOR, age-adjusted odds ratio; BMI, body mass index; CI(s), confidence interval(s); E-path, electronic pathology reporting; GTA, Greater Toronto Area; OCR, Ontario Cancer Registry; OFCCR, Ontario Familial Colon Cancer Registry; OPCS, Ontario Pancreas Cancer Study; OR, odds ratio; PHQ, Personal History Questionnaire.

Reduced risks of other cancers have also been reported in several case-control studies. For example, in a study conducted among premenopausal women, significantly decreased risks of breast cancer were observed among certain age groups with allergies.[20] Brenner *et al.* (2002) examined the association between a history of allergies and risk of brain tumors.[21] Significantly decreased risks of glioma were observed in individuals with a history of asthma, allergies to chemicals and any allergy. Similar results were found in another case-control study,[22] where significantly decreased risks of glioma, of similar magnitude, were observed in individuals with a history of asthma, hayfever and eczema. In the study by Brenner *et al.*, the risk of other brain tumors was also investigated in association with allergic status. No significant associations were observed in individuals with meningioma. Conversely, increased risks of acoustic neuromas were observed in individuals with a history of hay fever, allergies to food and allergies to other substances.[21]

Allergies and pancreas cancer risk



It has been suggested that the hyperactive immune system of allergic individuals may lead to increased immune surveillance, thus protecting against the development of pancreas cancer.[13][23] Several studies have examined the association between a history of allergies and pancreas cancer risk.[12][13][14][15][16][17][19][23][24][25][26][27][28] Among several case-control and cohort studies, a significantly reduced risk was observed with a history of any type of allergy.[12][19][23][26] More specifically, statistically significant decreased risks were observed in individuals with hay fever [12][17] and a slightly decreased risk was observed in individuals who were allergic to house dust, animals, plants, some foods, insect bites or stings and mold[19][26] although some of the confidence intervals (CI) were too wide to interpret.[15][19][24] Decreasing pancreas cancer risk was further associated with an increased number and severity of allergies, older age at onset, and increased duration of exposure to allergens.[19] Wang and Diepgen (2005) reviewed the evidence on prior atopic conditions and various cancer risks.[29] They identified 66 studies from January, 1986 to April, 2004. While results varied between the different atopic exposures (e.g., eczema, medication, animals, dust, hayfever) and various cancer sites, overall, a history of allergies was associated with a reduced risk of pancreas cancer.

Previous studies that examined the association between asthma and pancreas cancer risk were inconclusive, with the majority of studies reporting no association[12][17][24][25][28] and others reporting increased[27] and decreased risks.[26] Specifically, Stolzenberg-Solomon *et al.* (2002) observed a statistically significant doubling of risk of pancreas cancer in males with bronchial asthma. Conversely, a statistically significant reduced risk of pancreas cancer was reported in a case-control study by Mack (1986).

We have conducted a population-based case-control study to evaluate the association between a history of allergies or asthma and pancreas cancer risk in Ontario.

Materials and methods



The Ontario Pancreas Cancer Study (OPCS) began April 1, 2003, and is an ongoing prospective case-control study. 219 cases were pathology report confirmed pancreas adenocarcinoma and 57 cases were pathology confirmed adenocarcinoma metastases (site unknown) verified as pancreas cancer by treating physician. The primary objective of the OPCS is to collect data about genetic and epidemiologic factors involved in the etiology of pancreas cancer. The OPCS is also one of seven data collection sites that make up a multicenter, multidisciplinary Pancreatic Cancer Genetic Epidemiology (PACGENE) Consortium, based out of the Mayo Clinic in Rochester, Minnesota, to identify susceptibility genes in high risk familial pancreas cancer (FPC) kindreds.[30] Ethical approval was obtained for the current study proposal.

Cases

Eligible cases included men and women, of any age, diagnosed in the province of Ontario, Canada, between April 1, 2003 to June 1, 2006, with a first primary, pathologically-confirmed adenocarcinoma of the pancreas, identified using the International Classification of Diseases for Oncology Third Edition (ICD-03, C25.0-25.9) by the Ontario Cancer Registry (OCR). The Pathology Information Management System (PIMS), which relies on electronic pathology reporting (E-path) and supports rapid case ascertainment, was used to rapidly identify cases. Pathology reports were

obtained from the OCR within a week of the patient's diagnosis of pancreas cancer. E-path provides more timely pathology reporting compared with paper pathology reports.^[31] This is especially important in studies of patients with a rapidly, progressive disease such as pancreas cancer.

Confirmation of the pancreas cancer diagnosis and permission to contact the patient was requested from the physician identified on the pathology report. Cases were mailed a package including consent forms, a Family History Questionnaire (FHQ), designed to obtain information about the family history of cancer, diabetes and pancreatitis, a Personal History Questionnaire (PHQ), which included questions on environmental and epidemiologic exposures such as medical history, medication use, dietary patterns, physical activity, reproductive history, chemical exposures, and alcohol and tobacco consumption, and a Clinical Patient Questionnaire (CPQ), which addressed treatment issues and knowledge of clinical trials in pancreas cancer. Within 2 weeks of the questionnaire mailing, a follow-up postcard was sent to cases who had not returned the package. A telephone call was made 2 weeks later to individuals who had not responded, and a second questionnaire package was mailed upon request. A message was left for the individual if no one was home.

The second stage of the study occurred after receipt of the questionnaires and consent forms and involved obtaining a blood or saliva sample, medical records and a tissue or tumor sample. Patients who consented to donate a blood or saliva sample, as indicated on a blood collection form in the study package, had three options for blood collection. A blood kit was mailed to the patient to take to an MDS laboratory, doctor's office or clinic, or we arranged in-home blood collection with an MDS nurse. Saliva kits were sent to the patients' homes to do themselves or with the help of a family member. Medical records for the patient's diagnosis of pancreas cancer were collected as additional data. Because patients were enrolled in our study based on a pathologically-confirmed diagnosis of pancreatic adenocarcinoma, we did not need to confirm their diagnosis but rather, information on clinical treatment, staging of cancer and details about the type of tumor the patient had was obtained from the medical records. With the permission of the participant, relatives with cancer were asked to complete a Release of Information (ROI) form in order to confirm additional self-reported cancers in the family. Medical records of relatives were obtained for research purposes and to aid in the interpretation of the patient's family history of cancer in order to establish a genetic risk assessment.

Controls

Controls were initially recruited by the Ontario Familial Colon Cancer Registry (OFCCR) using the random digit dialing and also property assessment rolls as the sampling frame of Ontario residents.^[32] Controls were men and women (without colorectal cancer) that lived within the Greater Toronto Area (GTA), defined as Scarborough to Mississauga, Toronto to North York. During 2002-2003, controls recruited by the OFCCR were sent an initial letter outlining the study and inviting them to participate further in the OPCS. Individuals who met the pancreas control inclusion criteria, *e.g.*, lived within the GTA, were mailed a PHQ (Vol. 2). Of the 378 controls who were mailed a questionnaire, 313 (82.8%) returned them. Controls were excluded if they had been diagnosed with pancreas cancer.

Derivation of allergy/hay fever and asthma variables

Questions about prior allergies were obtained from the PHQ for cases and controls. Data on allergy exposure was obtained from the following question: "Before 1 year ago, have you ever had allergies or hay fever?" Responses included "No" and "Yes." If the participant answered "Yes," he/she was directed to answer another two questions: "How old were you when you first had this" and "how many years have you had allergies or hay fever?"

Data on asthma exposure was obtained from the following question: "Before 1 year ago, has a doctor ever told you that you have asthma?" Responses included "No" and "Yes." If the participant answered "Yes," he/she was directed to answer another two questions: "How old were you when you were first diagnosed" and "how many years have you had asthma?"

Statistical analysis

There were 276 pancreas cancer cases and 378 controls eligible for this analysis. Descriptive statistics were calculated for all study variables stratified by case-control status, and logistic regression was used to calculate age-adjusted odds ratio (AOR) estimates and 95% CIs. Multivariable unconditional logistic regression analysis was performed to obtain odds ratio (OR) estimates for the risk of pancreas cancer in individuals with a history of allergies or hay fever, and asthma. Confounders were identified when there was a greater than 15% change in estimate compared to the crude OR.^[33] Variables evaluated for confounding included: sex, medical history (diabetes, pancreatitis, body mass index (BMI), based on the patient's usual adult weight), medication/supplement use (pancreatic enzymes, Aspirin/ASA, NSAIDS, acetaminophen, NoDoze, calcium, folate and vitamin C supplements, immunosuppressants), chemical exposures (arsenic, asbestos, cadmium, chromium, nickel, pesticides and herbicides, radiation, radon), dietary patterns

(consumption of caffeine, alcohol, red meat, processed meat, fruits and vegetables), smoking (cigarettes, cigars, pipes), and education. None of these variables were identified as confounders (*i. e.*, did not change the AOR by >15%). All analyses were conducted using SAS, version 9.1.^[34]

Results



Table I shows the frequency distribution of pancreas cancer cases and controls, and the AOR estimates and 95% CIs for several pancreas cancer risk factors. The majority of the cases (68%) were 60 years of age and older. As expected, prior diagnoses of pancreatitis and diabetes, increased BMI (overweight and obese), regularly taking pancreatic enzymes, and being a current smoker were significantly more common among the cases than controls. There was a suggestion of an increased risk of pancreas cancer with increasing daily intake of caffeine; however, this was not statistically significant.

Table I. Distribution of Pancreas Cancer Cases, Controls and Age-Adjusted Odds Ratio Estimates for Several Subject Characteristics and Risk Factors, Ontario, Canada, 2003-2006

Variable	Cases (<i>n</i> = 276)	Controls (<i>n</i> = 378)		
	No. ¹ (%)	No. ¹ (%)	AOR ^{2,3}	95% CI ²
Age group (year) ³				
<50	26 (9.4)	12 (3.2)		
50-59	63 (22.8)	69 (18.3)		
60-69	94 (34.1)	153 (40.5)		
≥70	93 (33.7)	144 (38.1)		
Sex				
Male	151 (54.7)	176 (56.2)	1.00	
Female	125 (45.3)	137 (43.8)	1.08	0.78-1.51
Pancreatitis ⁴				
No	259 (94.9)	305 (98.7)	1.00	
Yes	14 (5.1)	4 (1.3)	4.12	1.33-12.79
BMI (kg/m ²) ⁵				
<25	98 (36.6)	143 (50.9)	1.00	
25-29.9 (overweight)	115 (42.9)	109 (38.8)	1.62	1.12-2.35
≥30 (obese)	55 (20.5)	29 (10.3)	2.64	1.56-4.46
Pancreatic enzyme use ⁶				
No	249 (95.4)	299 (99.7)	1.00	
Yes	12 (4.6)	1 (0.3)	15.28	1.96-19.07
Diabetes ⁷				
No	220 (80.0)	283 (91.3)	1.00	
Yes	55 (20.0)	27 (8.7)	2.83	1.72-4.67
Smoking Status				
Never	107 (40.1)	144 (46.3)	1.00	
Current	44 (16.5)	14 (4.5)	4.09	2.10-7.95
Former	116 (43.5)	153 (49.2)	1.03	0.72-1.46
Caffeine (cups daily) ⁸				
Never	9 (3.3)	19 (6.2)	1.00	
≤1	64 (23.3)	88 (28.6)	1.40	0.59-3.33
>1 and ≤2	106 (38.6)	112 (36.4)	1.91	0.82-4.45
>2	96 (34.9)	89 (28.9)	2.16	0.92-5.07

¹ Numbers may not add to total due to missing values.

² AOR, age-adjusted odds ratio; CI, confidence interval.

³ Age at pancreas cancer diagnosis date for cases and referent date (January 1, 2003) for controls.

⁴ Ever been diagnosed with pancreatitis, before one year ago.

⁵ Based on participant's usual adult weight.

⁶ Taken regularly (at least once per week for at least 1 year) prior to 1 year ago.

⁷ Diagnosed with diabetes mellitus (sugar diabetes) by a doctor (prior to 1 year ago for cases).

⁸ Average number of caffeinated drinks (12 oz. can or bottle of soft drinks, 1 medium cup of coffee/tea (hot or iced)) consumed 1 year ago, Tertile distribution based on controls.

Table II shows the frequency distribution of cases and controls and the AOR estimates and 95% CIs for several characteristics of participants with allergies or hay fever. A higher percentage of controls reported having allergies or hay fever (35%) compared with cases (20%). Ever having allergies or hay fever was associated with a statistically significant halving of pancreas cancer risk (OR = 0.43, 95% CI: 0.29-0.63). Effect modification by sex was evaluated and it appears that the reduction in risk is stronger for males (OR = 0.25, 95% CI: 0.14-0.47) than females (OR = 0.62, 95% CI: 0.36-1.06; $p = 0.5$) although CIs overlap (data not shown in Tables).

Table II. Distribution of Pancreas Cancer Cases, Controls and Age-Adjusted Odds Ratio Estimates for Subjects with a History of Allergies or Hay Fever, Ontario, Canada, 2003-2006

	Cases (<i>n</i> = 276)	Controls (<i>n</i> = 378)		
Variable	No. ¹ (%)	No. ¹ (%)	AOR ^{2,3}	95% CI ²
Allergies or hay fever ⁴				
Never	218 (79.6)	202 (65.4)	1.00	
Ever	56 (20.4)	107 (34.6)	0.43	0.29-0.63
Duration of allergies (year) ⁵				
Never	218 (83.5)	202 (69.2)	1.00	
≤20	14 (5.4)	35 (12.0)	0.31	0.16-0.60
>20 and ≤40	18 (6.9)	29 (9.9)	0.45	0.23-0.86
>40	11 (4.2)	26 (8.9)	0.42	0.20-0.88
Age of reported allergy onset (year) ⁵				
Never	218 (82.3)	202 (68.5)	1.00	
≤20	25 (9.4)	30 (10.2)	0.68	0.38-1.20
>20 and ≤37	14 (5.3)	31 (10.5)	0.38	0.19-0.73
>37	8 (3.0)	32 (10.9)	0.22	0.10-0.48

¹ Numbers may not add to total due to missing values.

² AOR, age-adjusted odds ratio; CI, confidence interval.

³ Age at pancreas cancer diagnosis date for cases and referent date (January 1, 2003) for controls.

⁴ Ever had allergies or hay fever prior to one year ago.

⁵ Tertile distribution based on controls.

In addition, the analysis was restricted to cases residing in the GTA ($n = 82$), and the association between ever having allergies or hay fever and pancreas cancer risk remained statistically significant (OR = 0.48, 95% CI: 0.26-0.87; data not shown in Tables).

Increasing duration of allergies or hayfever was not associated with a greater reduction in risk, rather individuals who reported having allergies or hayfever for 20 years or less had a slightly greater reduction in pancreas cancer risk compared with individuals who had allergies or hayfever for over 20 years. As the age of reported allergy onset increased, the pancreas cancer risk decreased. Specifically, individuals who reported an age of allergy onset over age 37 showed the greatest risk reduction (OR = 0.22, 95% CI: 0.10-0.48).

Table III shows the frequency distribution of cases and controls and the AOR and 95% CIs for several characteristics of participants with asthma. Compared with cases, a higher percentage of controls reported being diagnosed with asthma (9% vs. 5%); however this association was not statistically significant. Effect modification by sex was evaluated and there was no difference in risk reduction between males (OR = 0.71, 95% CI: 0.29-1.75) and females (OR = 0.45, 95% CI: 0.16-1.25; $p = 0.49$) (data not shown in Tables). There was no statistically significant association observed between pancreas cancer and duration of asthma or age at diagnosis.

Table III. Distribution of Pancreas Cancer Cases, Controls and Age-Adjusted Odds Ratio Estimates for Subjects with a History of Asthma, Ontario, Canada, 2003-2006

	Cases ($n = 276$)		Controls ($n = 378$)	
Variable	No. ¹ (%)	No. ¹ (%)	AOR ^{2,3}	95% CI ²
Asthma ⁴				
Never	260 (94.6)	281 (91.2)	1.00	
Ever	15 (5.4)	27 (8.8)	0.60	0.31-1.16
Duration of asthma (year) ⁵				
Never	260 (94.6)	281 (91.8)	1.00	
≤10	8 (2.9)	10 (3.3)	0.82	0.31-2.16
>10 and ≤20	2 (0.7)	7 (2.3)	0.32	0.07-1.59
>20	5 (1.8)	8 (2.6)	0.68	0.22-2.12
Age at diagnosis (year) ⁵				
Never	260 (94.9)	281 (91.8)	1.00	
≤34	6 (2.2)	9 (2.9)	0.70	0.25-2.02
>34 and ≤50	3 (1.1)	9 (2.9)	0.31	0.08-1.18
>50	5 (1.8)	7 (2.3)	0.87	0.27-2.79

¹ Numbers may not add to total due to missing values.

² AOR, age-adjusted odds ratio; CI, confidence interval.

³ Age at pancreas cancer diagnosis date for cases and referent date (January 1, 2003) for controls.

⁴ Ever been diagnosed with asthma by a doctor prior to one year ago.

⁵ Tertile distribution based on controls.

Discussion



It has been proposed that individuals with allergic conditions have increased immune surveillance.^{[16][23]} Natural killer (NK) cells, which are active during allergic responses, may contribute to pancreas cancer immune surveillance.^[23] In addition, subjects with atopic diseases, which include conditions such as allergies and asthma, display a Th2-type response to antigens.^[17] Th2 cytokines have been found to demonstrate antitumor properties, which may account for the associations between reduced cancer risks in people with allergies.^[17] Epidemiologic studies have investigated the association between prior allergic conditions and various cancers; however results have been inconsistent.^{[13][14][15][16][17][18]} A prior history of allergic conditions has been found to increase the risk of some cancers but decrease the risk of others. These observations emphasize the complexity of immune mechanisms involved in cancer development.

In the current study, we found a statistically significant reduction in pancreas cancer risk in individuals with reported allergies or hay fever. These findings are consistent with previous studies suggesting a protective effect of allergies.^{[12][17][19][26]} Silverman *et al.* (1999) observed reduced risks of pancreas cancer in individuals with a history of any allergy (OR = 0.7, 95% CI: 0.5-0.9) and hay fever (OR = 0.6, 95% CI: 0.5-0.9). Similar results were observed in other case-control^{[19][26]} and cohort studies.^[17] A recent meta-analysis by Gandini *et al.* (2005) also provides additional support to our findings. We did not observe an association between asthma and pancreas cancer risk. This is consistent with the majority of previous studies that found a null association between a history of asthma and pancreas cancer risk.^{[12][17][24][25][28]}

The current study explored a number of confounders but none of these factors confounded the association between allergies or hay fever, or asthma and pancreas cancer risk. However, individuals with allergies or hay fever, and/or asthma may have avoided other carcinogens or allergic triggers that were not measured in this study, and which accounted for the protective observations.^[17] Effect modification was investigated for sex and our data suggests that reduction in risk may be stronger for males, though this difference was not statistically significant. Future studies should be designed with enough power to evaluate this possible interaction.

As pancreas cancer is rapidly fatal, survival bias may have affected our results. Although we used rapid case ascertainment to recruit patients, approximately a third of the cases had died prior to enrollment. In addition, our response rate has never exceeded 30%. It is possible that the disease and exposure may have differed between responders and non-responders (*e.g.*, refusals, deceased).

It can be hypothesized that patients who underwent surgery may have been more eager to participate than patients who had inoperable disease. This would have resulted in a response bias if the exposure differed between these 2 groups. In fact, over 40% of responders underwent a surgical resection, which is double that seen in the general population of pancreas cancer cases.^{[2][30]} Selection bias is also possible because we only recruited individuals with a pathologically-confirmed diagnosis of pancreas cancer. Over 50% (59% in 2002, OCR, personal communication, 2006) of pancreas cancer cases in Ontario never have tissue confirmation while they are alive, and are only reported to the OCR from hospital records or death certificates. Furthermore, we only recruited controls from the GTA and not from all over Ontario (70% of cases were from outside of the GTA).

Misclassification of exposure status is always a concern in case-control studies. For example, cases may have been more likely than controls to report a sensitivity as an allergic reaction. However, in the current study, controls reported a higher prevalence of allergies and asthma compared with cases, and recall bias is associated with an increased risk estimate in cases due to over reporting of exposures. To minimize misclassification errors in future studies, self-reported allergy and asthma

prevalence could be validated against biological measures such as allergy skin tests.

Our study has many strengths and contributes to the existing literature examining the association between allergies and/or asthma and pancreas cancer and suggests a possible role for the allergic response in preventing the development of pancreas cancer. Our findings suggest that laboratory studies are needed to investigate immune function and the prevention of pancreas cancer. In addition, further studies, in particular prospective studies, are needed to collect information on several specific types of allergies, age at onset and diagnosis, and duration and severity of exposures, with validation of self-reported data (e.g., skin-prick testing of IgE antibodies, radioallergosorbent testing (RAST)[35]), in order to understand the specific biological mechanisms involved in pancreas cancer development. Future epidemiological studies should also examine possible confounding due to allergy medications, as a recent study demonstrated the association between cromolyn, an antiallergy drug, and reduced pancreas tumor growth in mice.[36]

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