

The association between allergic diseases and cancer: a systematic review of the literature

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ABSTRACT

Introduction: Atopic syndrome (allergic rhinitis, asthma and eczema) and food allergies are frequently reported, especially in developed countries. Studies have previously suggested an inverse association between allergic diseases and cancer. The aim of this study was to investigate the association between allergic diseases and different types of cancers by performing a systematic review of the literature. **Methods:** A systematic literature search of Ovid Medline, Embase, Web of Science, Cochrane Library and Google Scholar was performed for studies on the association between allergic diseases and cancers.

Results: We identified a total of 5868 articles through our search, with 145 articles describing an association between allergic diseases and cancers. Allergies were associated with reduced risk of brain cancer, pancreatic cancer and melanoma and with possibly reduced risk of lymphatic and hematopoietic cancer, colorectal cancer, urogenital cancers of women and cancers in general. Asthma, but not atopy without asthma, was however associated with increased risk of lung cancer. There is possibly no association between allergic diseases and the risk of breast cancer and prostate cancer.

Conclusion: Overall, allergic diseases are inversely associated with the risk of cancers.

KEY WORDS

Allergic diseases, allergic diseases and cancer, atopy, cancer, malignancy

INTRODUCTION

Immunoglobulin E (IgE)-mediated allergic diseases (hereon called allergies) are frequently reported, especially in developed countries, and result in high morbidity and high costs for healthcare systems.¹ The most commonly reported allergies are atopic diseases (allergic rhinitis, asthma and eczema) and food allergies. The diagnostics and treatment options for patients with allergies have improved significantly in the past decades. Although still controversial, the hygiene hypothesis proposes a decrease in infectious disease in early childhood as the cause of high incidence of allergies and asthma in developed countries.² The lack of early infections leads to the stimulation of a T-helper 2 (Th-2) cell-mediated immune response favoring allergic diseases. The genetic susceptibility of the host however, may also play a key role in developing atopic symptoms.³

Previous studies have highlighted the potential inverse association between allergies and cancer.⁴⁻⁶ Currently, the association between allergy and oncology is of high interest and the European Academy of Allergy and Clinical Immunology (EAACI) has established a Task Force to better understand basic immune responses in both fields.⁷ Patients with allergic diseases may develop a state of enhanced immune surveillance leading to fewer occurrences of malignancies such as glioma and pancreatic cancer.^{8,9} The purpose of this study was to give an overview of the association between allergic diseases and different types of cancers by performing a systematic review of the literature.

METHODS

A systematic literature search was performed to include all articles that addressed an association between allergy and cancer. This systematic review was performed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.

Outcomes were structured by cancer category. The number of studies reporting a positive, negative or no association was noted. For each category the lowest and highest values of the most frequent risk estimates, such as the relative risk (RR) odds ratio (OR), hazard ratio (HR) and the standardized incidence ratio (SIR) were reported.

Data source

Studies on the association between allergy and cancer were conducted from the following online databases: Embase, Ovid Medline, Web of Science, Cochrane Library and Google Scholar.

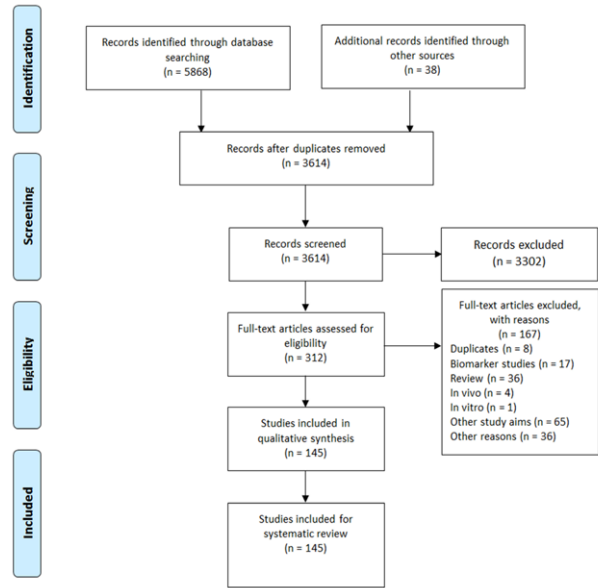
The last search was run on June 2nd, 2017. No filters for date or language were used in the search strategy (see the additional *Appendix* for the full search strategies).

Study selection

The titles and abstracts of all studies were reviewed after extracting duplicates. The studies were evaluated using the following criteria for inclusion: articles in English or English translation, original studies focusing on the relationship between allergy and cancer. Studies focusing on serological parameters such as serum IgE and malignancy, *in vivo* and *in vitro* animal studies, review articles and meta-analysis were excluded. Three reviewers (AFK, LW, RO) independently performed a review of the full text and could reach consensus on the relevance for inclusion of each article.

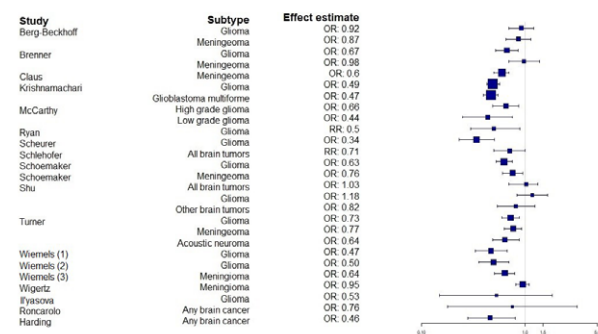
Data visualization

In order to visualize the various risk estimates, we used the R Statistical Software to plot forest plots for all included studies and plotted separate forest plots for the different cancer subgroups. We made forest plots for all study outcomes reported in relative risk (RR), OR, HR and SIR. Studies that reported other outcomes, such as the standardized mortality ratio, are not plotted in the forest plots; neither are studies that did not report 95% confidence intervals. No overall estimates were calculated, as the use of different methods to express risk estimates did not allow us to pool the studies. For the same reason, the degree of heterogeneity of studies could not be calculated.



RESULTS

Of a total of 5868 articles identified by the search, 312 articles publishing an association between allergy and cancer were eligible (*Supplementary figure 1*). After screening, we further narrowed down our selection to 145 articles that reported an association between allergies and malignancies. The main outcomes of this study are shown in *table 1*, *table 2* (at the end of this article) and *figure 1*, *Forest plots of the association between allergic diseases and cancer types*.



Brain cancer

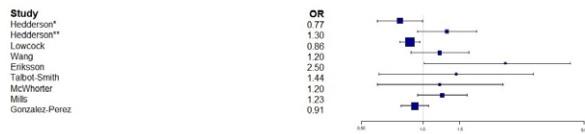
In total, we identified 19 studies describing an association between allergic diseases and brain cancer.

Positive association with brain cancer: no study demonstrated a positive association between allergic diseases and a brain tumor.

Negative association with brain cancer: We included 19 studies reporting the association between allergic disease and brain cancer. Of these, six studies showed no association between allergic diseases and brain cancer,¹⁰⁻¹⁶ 12 studies demonstrated a consistent reduced risk of brain tumors in patients with allergic diseases (OR between 0.34 and 0.76),^{11,17-28} and one study identified no association between allergic disease and meningioma, but did show a negative association between allergic disease and glioma. No studies reported a positive association.

Of the 19 studies, 16 examined the association between allergic diseases and brain cancer in adults, while three studies examined this association in children and adolescents.

Conclusion: Allergic diseases are mostly associated with a reduced risk of brain tumors.



* women aged > 35 years

** women aged 35 or less

Breast cancer

In total, eight studies on the association between allergic diseases and breast cancer were included.

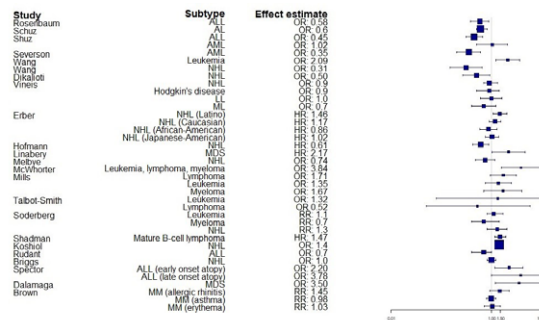
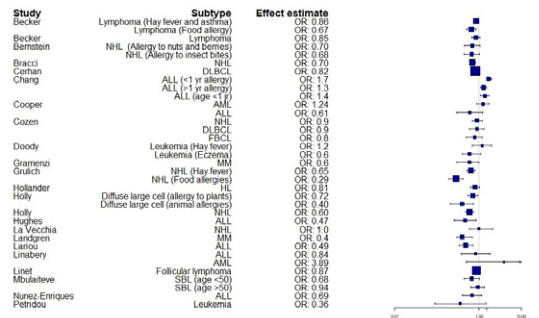
Positive association with breast cancer: only one out of eight studies identified a positive association between allergic diseases and breast cancer (OR 2.5).²⁹

Negative association with breast cancer: a negative association between allergic diseases and breast cancer was found in two studies (OR 0.77 and 0.86).^{30,31} Hedderson et al. found a decreased risk (OR 0.77) of breast cancer in women aged 35 years or older having a history of allergic diseases.³⁰ However, in the same study, no association was observed between breast cancer and allergic diseases in women younger than 35 years. The other five studies did not identify a positive or negative association between allergic diseases and breast cancer.³²⁻³⁶

Conclusion: In general, allergic diseases do not appear to influence the breast cancer risk in women.

Lymphatic and hematopoietic cancer

We included a total of 47 studies on the association between allergic diseases and lymphatic and hematopoietic cancers. Negative as well as positive associations between allergic diseases and lymphatic and hematopoietic cancers have been published. Of the 47 studies, 20 showed no association, 15 reported a negative association (range OR: 0.29 to 0.87) and eight demonstrated a positive association



(range OR: 1.3 to 3.84); four studies presented different associations for different subgroups.

Positive association with lymphoma: A positive association between allergic diseases and lymphoma was demonstrated in four studies (range OR:1.4-3.84).³⁴⁻³⁷⁻³⁹ A positive association between airborne allergies and development of hematological malignancies, in particular, mature B-cell lymphoma (HR: 1.47) was found in one study.³⁸ In this study however, the risk of malignancy was increased in women with a history of allergies to airborne allergens of plants, grass or trees, but not in men. Another study showed overall increased risk for non-Hodgkin lymphoma (NHL) in patients with allergic diseases (OR: 1.4).³⁷ The high risk was mostly associated with erythema and allergic alveolitis, rather than with airborne allergies, and black patients with allergies seemed to be at a higher risk of developing NHL than white patients.

Negative association with lymphoma: A total of 10 studies showed a protective, negative association between allergic diseases and lymphoma (range OR: 0.29-0.87).⁴⁰⁻⁴⁹ In the study of Becker et al., hay fever and asthma did not influence the risk of lymphoma, and the association between food allergies and lymphoma was negative (OR: 0.67).⁴⁷ The only study investigating the association between allergic diseases and NHL in children demonstrated a negative association (OR: 0.50).⁴⁸

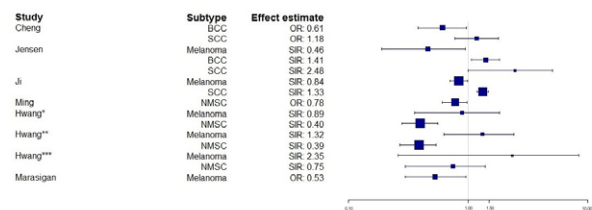
In total, 14 studies however could not find any association between allergic diseases and lymphoma.³³⁻³⁵⁻³⁹⁻⁴⁷⁻⁵⁰⁻⁵⁹

Positive association with other hematological malignancies: Seven studies of other hematological malignancies including lymphatic or myeloid leukemia, multiple myeloma and myelodysplastic syndrome, demonstrated positive associations between allergic diseases and these malignancies (range OR: 1.3-3.5).^{34,60-65} In Linabery et al., no association was found between allergic diseases and hematological malignancies, but a clear association was noted between asthma and myelodysplastic syndrome (HR: 2.17).⁶³ This study was however limited to post-menopausal women.

Negative association with other hematological malignancies: A total of seven studies demonstrated a negative association between other hematological malignancies and history of allergic diseases (range OR: 0.4-0.6).⁶⁶⁻⁷²

A total of 10 studies (out of 47) examined the association between hematological malignancies and allergic diseases in children. As mentioned earlier, one study studied the association between allergic diseases and NHL and found a protective, negative association (OR:0.5).⁴⁸ Another study found a positive association between allergic diseases and acute lymphocytic leukemia (ALL) in children (OR 2.2).⁶⁴ The other 10 studies investigated the association between allergic diseases and leukemia in children. Only two studies showed a positive association between allergic diseases and leukemia (OR 1.4-1.7 and OR 2.2 respectively).^{60,64} In Spector et al., the early onset atopy was associated with increased risk of ALL, while there was no association between late onset atopy and ALL in children.⁶⁴ In five studies, no associations between leukemia and allergic diseases were found.^{64,72-75}

Conclusion: Most of the studies demonstrated no association between allergic diseases and lymphatic and hematopoietic cancers. However, there are more studies showing a protective role of allergies than studies with a positive association between allergic diseases and lymphatic and hematopoietic cancers.



* Allergic rhinitis
 ** Asthma
 *** Atopic dermatitis

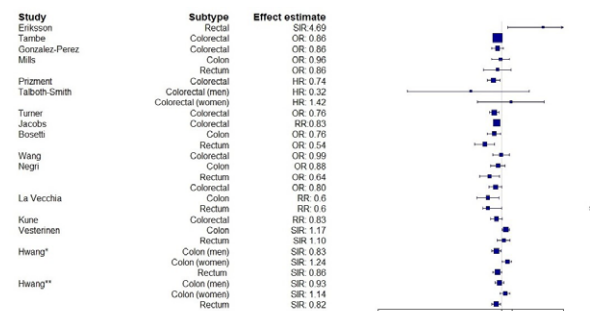
Skin cancer

There is a limited number of studies on the association between skin cancers and allergic diseases available. We included seven studies.

Positive association with skins cancers: In two studies, a positive association between allergic diseases and skin cancer was described; SIR: 1.41 for basal cell carcinoma (BCC), SIR: 1.33 for squamous cell carcinoma (SCC).^{76,77}

Negative association with skin cancers: A total of six studies described negative associations between allergic diseases and skin cancers (range SIR 0.39 to 0.84; range OR 0.53 to 0.78).⁷⁶⁻⁸² In Cheng et al., the risk for developing BCC was decreased (OR: 0.61), while there was no association between allergic diseases and SCC.⁷⁸ Two studies found a negative association between atopic dermatitis and non-melanoma skin cancers (NMSC) (OR 0.78 and SIR 0.40).^{79,80} Four out of five studies investigating the relationship between allergies and malignant melanoma observed a decreased risk for melanoma (range SIR: 0.46-0.84).^{76,77,81,82} In Hwang et al., the risk for developing malignant melanoma was unchanged in patients with allergic rhinitis, asthma and atopic dermatitis.⁸⁰

Conclusion: Allergic diseases appear to reduce the risk for developing malignant melanoma and NMSC.



* Asthma
 ** Allergic rhinitis

Colorectal cancers

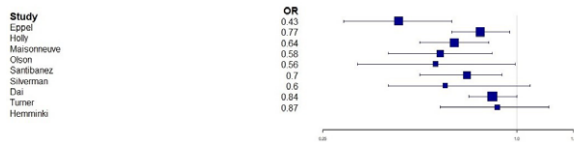
We included 17 studies that evaluated the association between allergic diseases and colorectal cancers.

Positive association with colorectal cancers: Three studies described positive associations between allergic diseases and colorectal cancers (range SIR: 1.17-4.69).^{80,83,84} Vesterinen et al. found a positive association between asthma and colon carcinoma (SIR:1.17), but could not identify any association between asthma and rectal carcinoma.⁸⁴ In Hwang et al., only a positive association

was seen between asthma and colon carcinoma in women (SIR: 1.24).⁸⁰

Negative association with colorectal cancer: A negative association between allergies and colon cancer was found in nine studies (range OR: 0.54-0.86).^{80,85-92} Prizment et al. studied the risk of colorectal cancer only in women and found a negative association (HR:0.74).⁸⁶ Negri et al. described only a negative association between allergic diseases and rectum carcinoma, but no association between allergic diseases and colon carcinoma (OR: 0.64).⁹⁰ In contrast La Vecchia et al. identified a negative association between allergic diseases and colon carcinoma, yet no association with rectal carcinoma (RR: 0.6).⁹¹ No associations were observed between allergic diseases and colorectal cancers in 11 studies.^{32,34,36,80,84,88,90,91,93,94}

Conclusion: Overall, the risk of colorectal cancer is possibly reduced in patients with allergic diseases.



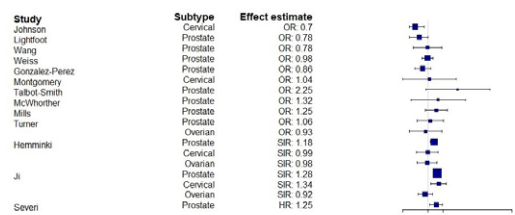
Pancreatic cancer

We identified 10 studies on the association between allergic diseases and pancreatic cancer.

Positive association with pancreatic cancer: No studies were published describing a positive association between allergic diseases and pancreatic cancer.

Negative association with pancreatic cancer: In total, seven studies reported a negative association between allergic diseases and pancreatic cancer (range OR: 0.43-0.77).^{9,95-100} In Olson et al., hay fever and allergies to animals were related to a reduced risk of pancreatic cancer, while asthma and other allergies did not appear to influence the risk of pancreatic cancer (OR 0.58).⁹⁸ Three other studies did not observe an association between allergic diseases and pancreatic cancer.^{87,101,102}

Conclusion: Overall, allergic diseases are associated with a reduced risk of pancreatic cancer.



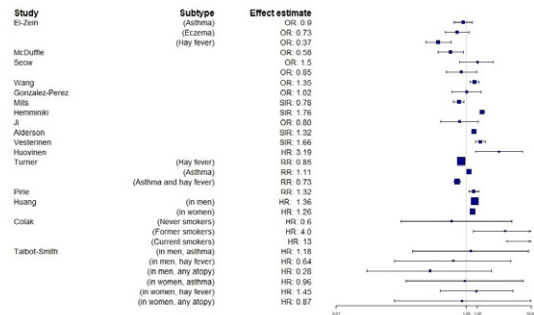
Urogenital cancers

Among urogenital cancers, a total of 12 studies were identified reporting the association between allergic diseases and prostate cancer^{32-36,76,81,87,102-105} and seven studies described the association with female urogenital cancers.^{76,81,87,102,106-108}

Positive association with urogenital cancers: In total, three studies demonstrated an increased risk of prostate cancer in patients with allergic diseases (range SIR: 1.18-1.64).^{76,102,105} Only one study showed a positive association between allergic diseases and cervix cancer (SIR 1.34),⁷⁶ however, only the association between asthma and cancer was studied.

Negative association with urogenital cancers: Only one study showed a negative association between allergic diseases and prostate cancer (SMR 72).⁸¹ In eight studies, no significant association was described between allergic diseases and prostate cancer.^{32-36,87,103,104} Three studies on uterine leiomyomas, squamous cell cervical cancer, cervix and ovarian cancer showed reduced risks of these cancers in women with allergic diseases.^{81,106,107} In Kallen et al. however, only the association between asthma and cervix and ovarian cancer was studied.⁸¹ Four other studies looking at the association between allergic diseases and cervical cancer and ovarian cancer observed no changes in the risk of developing these cancers in women.^{76,87,102,108} Ji et al. however, despite observing no general association between allergic diseases and ovarian cancer, did see a positive association between asthma and cervix cancer (SIR 1.34).⁷⁶

Conclusion: In general, there is possibly no association between allergic diseases and prostate cancer in men. Studies on the association between allergic diseases and female urogenital cancers are limited, but favor a protective role of allergies.



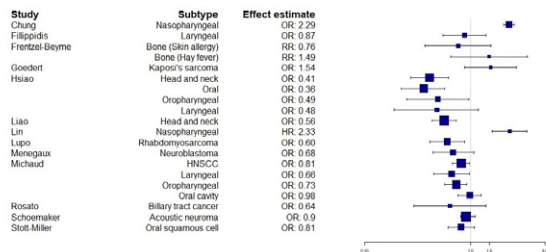
Lung cancer

We included a total of 19 studies, which studied the relationship between allergic diseases and lung cancer.

Positive association with lung cancer: In 10 studies, increased risks of lung cancer in allergic diseases were observed (range HR: 1.26- 13).^{36,76,81,84,87,109-113} In Reynolds et al., the lung cancer risk was increased only in men with asthma.¹⁰⁹ In all except for two studies,^{114,115} focusing only on examining the associations between asthma (and not other allergic disorders) and lung cancer, showed an increased risk of lung cancer.^{33,35,36,76,81,84,87,109-113} In Turner et al., lung cancer mortality was increased in patients with asthma, but reduced in patients with hay fever only or patients with both asthma and hay fever (RR 1.11, 0.85 and 0.73, respectively).⁸⁷ In another study, lung cancer incidence was increased in current smokers and former smokers with a history of asthma, but in patients with asthma who never smoked, the cancer risk was unchanged (HR 13, 4.0 and 0.6, respectively).¹¹³

Negative association with lung cancer: In five studies, negative associations between allergic diseases and lung cancer were found (OR 0.37-0.85).^{87,102,115-117} These studies usually examined the association between allergies (not only asthma) and lung cancer, and showed a reduced risk of developing lung cancer. The same applied to studies where, in general, no association was found between allergic diseases and lung cancer.^{32,33,35,113-115,118}

Conclusion: Asthma is related with an increased risk of lung cancer, while atopic patients without asthma may be protected.



Other cancers

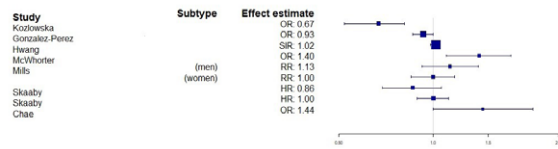
In total, we included 13 studies that studied the association between other cancers and allergic diseases.

Positive association with other cancers: In two studies, a positive association between allergic diseases and nasopharyngeal cancers was observed (OR 2.29 and HR: 2.33).^{119,120}

Negative association with other cancers: Four studies found a negative association between allergic diseases and cancers, including head and neck cancers and rhabdomyosarcoma.¹²¹⁻¹²⁴ However, no associations were noticed for most of other cancers including laryngeal

cancer,¹²⁵ neuroblastoma,¹¹⁹⁻¹²⁶ biliary tract cancer,¹²⁷ acoustic neuroma,¹²⁸ oral squamous cell carcinoma¹²⁹ and Kaposi's sarcoma.¹³⁰

Conclusion: Most of the studies published do not show a change of risk for developing cancers in patients with allergic diseases.



Cancer in general

We investigated the risks of developing cancer in 12 studies.

Positive association with cancer: The risk of developing cancer was increased (OR 1.40) in only one study by McWorther.³⁴ In this study, hives were associated with the strongest cancer risk and the strongest allergy association was with lymphatic-hematopoietic cancers.

Negative association with cancer: In total, five studies described a negative association between allergic diseases and cancer in general.¹³¹⁻¹³⁵ Six other studies did not find an association between allergic diseases and cancer.^{35,36,80,136-138}

Conclusion: Mixed results were noticed, but in general, allergic diseases may reduce the cancer risk.

DISCUSSION

In this systematic review, we described the association between allergic diseases and different types of malignancies. This review delivers a comprehensive overview of the risk of malignancies in patients with allergies.

In this study we demonstrate an inverse association between allergic diseases and most of the cancers. Allergic diseases appear to reduce the risk of brain cancer, pancreatic cancer, melanoma and possibly the risk of lymphatic and hematopoietic cancers, colorectal cancers, female urogenital cancers and cancer in general. The current available studies do not provide sufficient evidence for a protective role of allergic diseases in developing breast cancer and prostate cancer. Asthma appears to increase the risk of lung cancer, however, patients with atopic diseases without asthma possibly do not have an increased risk of lung cancer.

The question of interest is how allergies may cause immunosurveillance. Allergic immunity depends on Th2-cells, basophils, eosinophils, macrophages and the antibodies type IgG1 and IgE.¹³⁹ Allergy is a consequence of improved and hyper-responsive immune system, which may possibly recognize dysregulated or damaged cells, including cancer cells, and may efficiently eradicate these cells (immunosurveillance hypothesis). Patients with allergic diseases have thus an adapted immune system, which may protect against cancers.¹⁴⁰ The production of tumor-specific IgE alone, which has antitumor effects of dendritic cells, eosinophils, basophils and mast cells offer better tumor surveillance and reduced risk of cancers.⁷ Furthermore, it is suggested that allergic reactions in specific tissues may be able to remove mutagenic triggers before transformation to malignant cells occur (prophylaxis hypothesis).

Despite an inverse association between allergic diseases and cancer, asthma appears to be independently associated with increased risk of lung cancer, after adjustment for smoking habits. The patients with atopic constitution without asthma however, have a possibly reduced risk of lung cancers. Patients with asthma have mostly other subtypes of lung cancer than adenocarcinoma.¹⁴¹ Despite the protective role of allergies in cancers, patients with asthma are regularly characterized by airway inflammation, which possibly plays a crucial role in the pathogenesis of lung cancer. Chronic inflammatory conditions may promote development of cancer because of oxidative damage resulting in tumor suppressor gene mutations. Different studies have indeed demonstrated a relationship between chronic airway inflammation and lung cancer.^{142,143} Furthermore, recurrent treatment with local or systemic glucocorticoids may also lead to better tumor outcomes and increased cancer risk.⁶

A next interesting question addresses the role of allergen immunotherapy in the development of cancer. Studies have suggested that tumor microenvironment may favor switching to a tumor-specific IgG4, a less potent immunoglobulin, instead of IgG1 and IgE.¹⁴⁴ IgG4 antibodies do not have sufficient immunostimulatory capacities, may block the cytotoxic activities of other antibodies and are correlated with shorter survival and disease progression.^{144,145} On the other hand, current data also suggest positive correlation between IgG4-related disease and enhanced cancer risk.¹⁴⁶ In allergic patients undergoing allergen-specific immunotherapy, increased IgG4-specific antibodies have been observed and correlate with allergen tolerance.¹⁴⁷ However, to date, no data are available on cancer incidence and mortality in patients being successfully desensitized.

The results of this study may be limited by studies relying on self-reported ascertainment of allergies, different methods of establishing the diagnosis of allergies, retrospective studies and not always adjusting for cofounders. The variety in methodology of the different studies did not permit us to calculate pooled estimates. Furthermore, by classifying all tumors in broad categories such as lung cancer, lymphatic and hematopoietic cancer, we do not consider possible differences between associations in subtypes of tumors. However, a substantial amount of evidence for the inverse association between allergic diseases and malignancies is reported. Exceptions are patients with asthma who have increased risk of lung cancer. Large prospective studies with validated measurement of allergies and data on potentially confounding factors are required for better understanding the association between allergy and oncology.

ACKNOWLEDGMENTS

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DISCLOSURES

All authors declare no conflicts of interest. No funding or financial support was received.

APPENDIX

Search terms used in the medical database for the literature search in this systematic review on the association between allergy and cancer.

Embase.com (2694)

('allergy'/de OR 'atopy'/de OR 'rhinoconjunctivitis'/de OR 'allergic asthma'/de OR 'allergic rhinitis'/exp OR 'atopic dermatitis'/de OR 'food allergy'/exp OR (allerg* OR atopy OR atopic OR rhinoconjunctivit* OR (rhino NEXT/1 conjunctivit*) OR 'hay fever'):ab,ti) AND (oncology/de OR 'neoplasm'/de OR 'malignant neoplastic disease'/exp OR 'precancer and cancer-in-situ'/exp OR 'skin cancer'/de OR 'cancer risk'/de OR 'cancer incidence'/de OR 'digestive system cancer'/exp OR 'breast cancer'/exp OR 'prostate cancer'/de OR 'bladder cancer'/de OR 'thyroid cancer'/de OR 'brain tumor'/exp OR 'lung cancer'/exp OR 'carcinogenicity'/de OR (oncolog* OR allergooncolog* OR neoplas* OR cancer* OR (tumo* NOT ('tumor necrosis factor')) OR malign* OR leukemia* OR leukaemia* OR glioma* OR glioblastoma* OR astrocytom* OR carcino* OR

lymphoma* OR hodgkin OR myeloma OR meningioma* OR melonoma*):ab,ti) AND ('disease association'/de OR 'health hazard'/de OR 'hazard assessment'/de OR 'incidence'/de OR 'population risk'/de OR 'cancer risk'/de OR 'cancer incidence'/de OR 'odds ratio'/de OR risk'/de OR 'neoplasm'/exp/dm_et OR 'risk factor'/de OR (((associat*s NEAR/6 (cancer* OR risk* OR disease* OR factor*)) OR ((risk*) NEAR/6 (cancer* OR disease* OR factor*)) OR hazard* OR incidence OR 'odds ratio' OR relationship* OR allergooncolog* OR (allergo NEXT/I oncolog*)):ab,ti) AND ('observational study'/exp OR 'cohort analysis'/exp OR 'longitudinal study'/exp OR 'retrospective study'/exp OR 'prospective study'/exp OR 'health survey'/de OR 'health care survey'/de OR 'epidemiological data'/de OR 'case control study'/de OR 'cross-sectional study'/de OR 'correlational study'/de OR 'population research'/de OR 'family study'/de OR 'major clinical study'/de OR 'multicenter study'/de OR 'comparative study'/de OR 'follow up'/de OR 'clinical study'/de OR 'clinical article'/de OR 'clinical trial'/exp OR 'randomization'/exp OR 'intervention study'/de OR 'open study'/de OR 'community trial'/de OR (((observation* OR epidemiolog* OR famil* OR comparativ* OR communit*) NEAR/6 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* NEAR/3 (stud* OR survey)) OR (health* NEAR/3 survey*) OR ((case OR cases OR match*) NEAR/3 control*) OR (cross NEXT/I section*) OR correlation* OR multicenter* OR (multi* NEXT/I center*) OR 'follow up' OR followup* OR clinical* OR trial OR random*):ab,ti) NOT ([Conference Abstract]/lim) AND [english]/lim NOT ([animals]/lim NOT [humans]/lim)

Medline ovid (1585)

("Hypersensitivity"/ OR exp "Rhinitis, Allergic"/ OR "Dermatitis, Atopic"/ OR exp "Food Hypersensitivity"/ OR (allerg* OR atopy OR atopic OR rhinoconjunctivit* OR (rhino ADJ conjunctivit*) OR "hay fever").ab,ti.) AND ("Medical Oncology"/ OR "Neoplasms"/ OR exp "Skin Neoplasms"/ OR exp "Digestive System Neoplasms"/ OR exp "Breast Neoplasms"/ OR exp "Prostatic Neoplasms"/ OR exp "Urinary Bladder Neoplasms"/ OR exp "Thyroid Neoplasms"/ OR exp "Brain Neoplasms"/ OR exp "Lung Neoplasms"/ OR (oncolog* OR allergooncolog* OR neoplas* OR cancer* OR (tumo* NOT ("tumor necrosis factor")) OR malign* OR leukemia* OR leukaemi* OR glioma* OR glioblastoma* OR astrocytom* OR carcino* OR lymphoma* OR hodgkin OR myeloma OR meningioma* OR melonoma*):ab,ti.) AND ("Association"/ OR "Incidence"/ OR "Odds Ratio"/ OR exp risk/ OR exp "Neoplasms"/et OR (((associat*) ADJ6 (cancer* OR risk* OR disease* OR factor*)) OR ((risk*) ADJ6 (cancer* OR disease* OR factor*)) OR hazard* OR incidence OR "odds ratio" OR relationship* OR allergooncolog* OR (allergo

ADJ oncolog*)):ab,ti.) AND (exp "observational study"/ OR exp "Cohort Studies"/ OR exp "health surveys"/ OR "Health Care Surveys"/ OR "Epidemiological Monitoring"/ OR "Case-Control Studies"/ OR exp "Epidemiologic Studies"/ OR "multicenter study"/ OR "comparative study"/ OR exp "clinical study"/ OR "Random Allocation"/ OR (((observation* OR epidemiolog* OR famil* OR comparativ* OR communit*) ADJ6 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* ADJ3 (stud* OR survey)) OR (health* ADJ3 survey*) OR ((case OR cases OR match*) ADJ3 control*) OR (cross ADJ section*) OR correlation* OR multicenter* OR (multi* ADJ center*) OR "follow up" OR followup* OR clinical* OR trial OR random*):ab,ti.) AND english.la. NOT (exp animals/ NOT humans/)

Cochrane (150)

((allerg* OR atopy OR atopic OR rhinoconjunctivit* OR (rhino NEXT/I conjunctivit*) OR 'hay fever'):ab,ti) AND ((oncolog* OR allergooncolog* OR neoplas* OR cancer* OR (tumo* NOT ("tumor necrosis factor")) OR malign* OR leukemia* OR leukaemi* OR glioma* OR glioblastoma* OR astrocytom* OR carcino* OR lymphoma* OR hodgkin OR myeloma OR meningioma* OR melonoma*):ab,ti) AND (((associat*) NEAR/6 (cancer* OR risk* OR disease* OR factor*)) OR ((risk*) NEAR/6 (cancer* OR disease* OR factor*)) OR hazard* OR incidence OR 'odds ratio' OR relationship* OR allergooncolog* OR (allergo NEXT/I oncolog*)):ab,ti)

Web of science (1239)

TS=((allerg* OR atopy OR atopic OR rhinoconjunctivit* OR (rhino NEAR/I conjunctivit*) OR "hay fever")) AND ((oncolog* OR allergooncolog* OR neoplas* OR cancer* OR (tumo* NOT ("tumor necrosis factor")) OR malign* OR leukemia* OR leukaemi* OR glioma* OR glioblastoma* OR astrocytom* OR carcino* OR lymphoma* OR hodgkin OR myeloma OR meningioma* OR melonoma*)) AND (((associat*) NEAR/5 (cancer* OR risk* OR disease* OR factor*)) OR ((risk*) NEAR/5 (cancer* OR disease* OR factor*)) OR hazard* OR incidence OR "odds ratio" OR relationship* OR allergooncolog* OR (allergo NEAR/I oncolog*)) AND (((observation* OR epidemiolog* OR famil* OR comparativ* OR communit*) NEAR/5 (stud* OR data OR research)) OR cohort* OR longitudinal* OR retrospectiv* OR prospectiv* OR population* OR (national* NEAR/2 (stud* OR survey)) OR (health* NEAR/2 survey*) OR ((case OR cases OR match*) NEAR/2 control*) OR (cross NEAR/I section*) OR correlation* OR multicenter* OR (multi* NEAR/I center*) OR "follow up" OR followup* OR clinical* OR trial OR random*)) AND DT=(article) AND LA=(english)

Google scholar (200)

Allergy/allergies/allergic/atopy/atopic/rhinoconjunctivitis/“hay fever” oncology/neoplasms/cancer/malignant/malignancies association/risk/hazard/incidence/“odds ratio”/relationship

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Table 1. *The association between allergies and cancers*

Brain cancer, case control studies				
Reference	Allergy	Type of cancer: statistical value (95% CI)	Association	Comments
(10) Berg-Beckhoff	Any allergy (hay fever, eczema, asthma)	Glioma: OR 0.92 (0.70-1.22) Meningioma: OR 0.87 (0.66-1.14)	No association	
(11) Brenner	Any allergy (hay fever, eczema, asthma)	Glioma: OR 0.67 (0.52-0.86), Meningioma: OR 0.98 (0.70-1.38)	Negative No association	
(17) Claus	Any allergy (not specified)	Meningioma OR 0.6 (0.-50.7)	Negative	
(18) Krishnamachari	Any allergy (allergies, asthma, eczema)	Glioma: OR 0.49 (0.43-0.57) Glioblastoma multiforme: OR 0.47 (0.40-0.55)	Negative	
(19) McCarthy	Any allergy (seasonal, medication, pet, food, not specified)	High grade glioma: OR 0.66 (0.49-0.87) Low grade glioma: OR 0.44 (0.25-0.76)	Negative	
(20) Ryan	Any allergy (not specified)	Glioma: RR 0.5 (0.3-0.9)	Negative	
(21) Scheurer	Any allergy (asthma, allergy not specified)	Glioma: OR 0.34 (0.23-0.51)	Negative	Adjusted odds ratio for the use of antihistamines and anti-inflammatory agents among glioma cases and controls
(12) Schlehofer	Any allergy (asthma, eczema, allergy not specified)	All brain tumors: RR 0.71 (0.5-1.0)	No association	
(23) Schoemaker	Any allergy (asthma, hay fever, eczema)	Glioma: OR 0.63 (0.53-0.76)	Negative	
(23) Schoemaker	Any allergy (asthma, hay fever, eczema)	Meningioma: OR 0.76 (0.61-0.96)	Negative	
(13) Shu	Any allergy (asthma, eczema, allergic rhinitis, wheezing)	All brain tumors: OR 1.03 (0.70-1.34), Glioma: OR 1.18 (0.84-1.67), Other brain tumors (PNET, other specified brain tumors, unspecified brain tumors: OR 0.82 (0.54-1.25)	No association	Study with adults and children.
(24) Turner	Any allergy (asthma, hay fever, eczema)	Glioma: OR 0.73 (0.60-0.88), Meningioma: OR 0.77 (0.63-0.93), Acoustic neuroma: OR 0.64 (0.49-0.83)	Negative	
(25) Wiemels	Any allergy (hay fever and food allergy)	Glioma: OR 0.47 (0.33-0.67)	Negative	
(26) Wiemels	Any allergy (hay fever and food allergy)	Glioma: OR 0.50 (0.36-0.70)	Negative	
(27) Wiemels	Any allergy (not specified)	Meningioma: OR 0.64 (0.51-0.80)	Negative	
(14) Wigertz	Any allergy (asthma, eczema, hay fever, food allergy, not specified)	Meningioma: OR 0.95 (0.82-1.10)	No association	

(15) Il'yasova	Any allergy (hay fever, medication and food allergy)	Glioma: OR 0.53 (0.15-1.84)	No association	
(16) Roncarolo	Allergic asthma and eczema	Any brain cancer: OR 0.76 (0.18-3.2)	No association	Study in children
(28) Harding	Allergic asthma and eczema	Any brain cancer: OR 0.46 (0.28-0.81)	Negative	Study in children. Reduced risk of malignancy in asthma and combination of asthma and eczema, no reduction of risk in eczema alone.
Breast cancer, case control studies				
Reference	Allergy	Statistical value (95% CI)	Association	Comments
(30) Hedderson	Any allergy (hay fever, drug reaction, insect venom, food)	Breast cancer in women aged 35 years or older: OR 0.77 (0.60-0.99), Breast cancer in women younger than 35: OR 1.30 (0.94-1.81)	Negative No association	
(31) Lowcock	Any allergy (hay fever, not specified)	Breast cancer: OR 0.86 (0.77-0.96)	Negative	
(32) Wang	Any allergy (asthma, hay fever, atopic dermatitis)	Breast cancer: OR 1.20 (0.87-1.66)	No association	
(29) Eriksson	Atopy (confirmed with skin prick test)	Breast cancer: OR 2.50 (1.01-5.16)	Positive	
(33) Talbot-Smith	Any atopy	Breast cancer: OR 1.44 (0.61-3.41)	No association	
(34) McWhorter	Any allergy	Breast cancer: OR 1.20 (0.60-2.43)	No association	
(35) Mills	Any allergy	Breast cancer: OR 1.23 (0.94-1.63)	No association	
(36) Gonzalez-Perez	Asthma	Breast cancer: OR 0.91 (0.78-1.06)	No association	Adjusted for age/sex/calendar year/BMI/ alcohol/smoking/prior comorbidities/health services utilization/aspirin/NSAID/ paracetamol
Lymphatic and hematopoietic cancer, case control studies				
Reference	Allergy	Cancer type: statistical value (95% CI)	Association	Comments
(47) Becker	Hay fever and asthma; Food allergy	Lymphoma: OR 0.86 (0.73-1.01); Lymphoma: OR 0.67 (0.52-0.85)	No association; Negative	
(59) Becker	Any allergy (not specified)	Lymphoma: OR 0.85 (0.68-1.07)	No association	
(58) Bernstein	Allergy to nuts and berries; Insect bites allergy	NHL: OR 0.70 (0.46-1.05), NHL: OR 0.68 (0.44-1.04)	No association	
(49) Bracci	Allergic rhinitis	NHL: OR 0.70 (0.60-0.83)	Negative	
(46) Cerhan	Any allergy (excluding drug allergies)	DLBCL: OR 0.82 (0.76-0.89)	Negative	Pooled analysis from 19 InterLymph studies

(60) Chang	Any allergy (hay fever, asthma, atopic dermatitis, anaphylaxis and unspecified allergy)	ALL: OR 1.7 (1.5-2.0): in cases of having an allergy less than one year before ALL diagnosis, ALL: OR 1.3 (1.1-1.5): having an allergy more than one year before ALL diagnosis, ALL: OR 1.4 (1.1- 1.7): having allergy before the age of one year.	Positive	Childhood ALL
(148) Cooper	Any allergy	AML: OR 1.24 (0.88-1.73), ALL: OR 0.61 (0.30-1.25)	No association	
(57) Cozen	Any allergy (hay fever, food, animal, insect, dust, medication allergies)	NHL: OR 0.9 (0.7-1.2), DLBCL: OR 0.9 (0.6-1.3), FBCL: OR 0.8 (0.5-1.2)	No association	
(149) Doody	Hay fever; Eczema	Leukemia: OR 1.2 (0.7-2.0); Leukemia: OR 0.6 (0.4-1.1)	No association	Leukemia: AML, CML, AUL, CLL Statistical value for MM, NHL, and the above separately
(61) Gallagher	Any allergy (not specified)	MM: RR 3.1, $p < 0.001$	Positive	Myeloma patients described the symptoms mainly as skin rashes, swellings and hives.
(150) Gramenzi	Any allergy (drug and food allergies, asthma, eczema)	MM: RR 0.6 (0.3-1.0)	No association	
(45) Grulich	Hay fever; Food allergies	NHL: OR 0.65 (0.52-0.82); NHL: OR 0.29 (0.20-0.42)	Negative	
(56) Hollander	Allergic rhinitis	HL: OR 0.81 (0.64-1.03)	No association	
(44) Holly	Allergy to plants; Animal allergies	Diffuse large cell: OR 0.72 (0.55-0.94); Diffuse large cell: OR 0.40 (0.21-0.73)	Negative; Negative	
(43) Holly	Plant allergies	NHL: OR 0.60 (0.48-0.75)	Negative	
(66) Hughes	Hay fever	ALL: 0.47 (0.26-0.85)	Negative	
(55) La Vecchia	Any allergy (drug, food, asthma eczema)	NHL: RR 1.0 (0.6-2.1)	No association	
(67) Landgren	Any allergy (not specified)	MM: OR 0.4 (0.3-0.7)	Negative	
(70) Lariou	Any allergy (respiratory, food, not specified)	ALL: OR 0.49 (0.34-0.72)	Negative	Patient population: children
(73) Linabery	Any allergy (inhaled, food, medication and contact allergies)	ALL: OR 0.84 (0.38-1.85), AML: OR 3.89 (0.50-29.95)	No association	Patient population: children with Down syndrome
(42) Linet	Any allergy (asthma, eczema, hay fever, not specified, excluding drug allergies)	Follicular lymphoma: OR 0.87 (0.80-0.94)	Negative	
(54) Mbulaiteye	Any atopic condition	SBL: Age < 50 years: OR 0.68 (0.45-1.02), Age > 50 years: OR 0.94 (0.64-1.37)	No association	

(74) Nunez-Enriquez	Any allergy (skin allergy, bronchial asthma, rhinitis, not specified)	ALL: 0.69 (0.40-1.17)	No association	Patient population: children with Down syndrome
(71) Petridou	Allergic disease (not specified)	Leukemia: OR 0.36 (0.09-1.43)	No association	Childhood leukemia
(151) Rosenbaum	Any allergy (hay fever, asthma, animal, food-drug-bee, eczema)	ALL: OR 0.58 (0.38-0.88)	Negative	Childhood ALL
(68) Schuz	Any allergy (not specified)	AL: OR 0.6 (0.5-0.8)	Negative	
(72) Schuz	Hay fever	ALL: OR 0.45 (0.31-0.66), AML: OR 1.02 (0.50-2.08)	Negative, No association	Childhood leukemia
(69) Severson	Any allergy (not specified)	AML: OR 0.35 (0.20-0.60)	Negative	
(62) Wang	Any allergy (asthma, hay fever, food or drug allergies, and eczema)	Leukemia: OR 2.09 (1.22-3.58)	Positive	
(41) Wang	Any allergy (hay fever, animal or egg allergy, plant allergy, asthma, eczema)	NHL: OR 0.31 (0.15-0.64)	Negative	
(48) Dikaloti	Any allergy	NHL: OR 0.50 (0.27-0.29)	Negative	Childhood NHL
(53) Vineis	Any allergy	NHL: 0.9 (0.7-1.3) Hodgkin's disease: 0.9 (0.5-1.4), LL: OR 1.0 (0.6-1.6), ML: OR 0.7 (0.4-1.2)	No association for all listed	
Lymphatic and hematopoietic cancer, cohort studies				
(39) Erber	Any allergy (asthma, hay fever, skin, food or not specified)	NHL: HR 1.46 (1.07-2.00): Latinos NHL: HR 1.17 (0.90-1.52): Caucasian NHL: HR 0.86 (0.58-1.27): African American NHL: HR 1.02 (0.75-1.38): Japanese American	Positive, No association, No association, No association	
(40) Hofmann	Any allergy (hay fever, eczema)	NHL: HR 0.61 (0.42-0.87)	Negative	
(63) Linabery	Any allergy (not specified)	Asthma: MDS HR 2.17 (1.01-4.64) No significant association between allergy and lymphoid and myeloid malignancies	Positive	Large study among post-menopausal Caucasian women
(52) Melbye	Any allergy (not specified)	NHL: OR 0.74 (0.48-1.15)	No association	
(34) McWhorter	Any allergy	Leukemia, lymphoma, or myeloma OR 3.84 (1.55-9.51)	Positive	
(35) Mills	Any allergy (hay fever, asthma, plant allergy, bee allergy)	Lymphoma: OR 1.71 (0.95-3.09), Leukemia: OR 1.35 (0.75-2.46), Myeloma: OR 1.67 (0.70-4.00)	No association	
(33) Talbot-Smith	Any allergy (asthma, hay fever)	Leukemia: OR 1.32(0.08-21.54), Lymphoma: OR 0.52 (0.05-5.77)	No association	

(51) Soderberg	Any allergy (asthma, hay fever, eczema during childhood or allergic eczema)	Leukemia: RR 1.1 (0.8-1.7), Myeloma: RR 0.7 (0.4-1.4), NHL: RR 1.3 (0.8-2.0)	No association	
(38) Shadman	Allergies to airborne antigens	Mature B-cell lymphoma: HR 1.47 (1.14-1.91)	Positive	Patients who developed malignancies were older ($p < 0.001$) and a moderate risk for lymphoma was seen in women, but not in men.
(37) Koshiol	Any allergy (rhinitis, asthma, dermatitis, erythema, allergic alveolitis)	NHL: OR 1.4 (1.3-1.5)	Positive	Increased risk especially in patients with allergic alveolitis and dermatitis. Furthermore, the risk was slightly higher in black than white patients.
(75) Rudant	Allergic asthma	ALL: OR 0.7 (0.4-1.0)	No association	Childhood ALL
(50) Briggs	Any allergy	NHL: OR 1.0 (0.8-1.2)	No association	
(64) Spector	Atopy	Early onset atopy and ALL: OR 2.20 (1.16-4.16), Late onset atopy and ALL: OR 3.78 (1.00-14.29)	Positive, No association	Association between allergic diseases and ALL in children
(65) Dalamaga	Any allergy	MDS: OR 3.50 (1.19-10.26)	Positive	
Lymphatic and hematopoietic cancer, retrospective studies				
(152) Brown	Allergic rhinitis; Asthma; Erythema	MM: RR 1.45 (0.93-2.25); MM: RR 0.98 (0.79-1.22); MM: RR 1.03 (0.72-1.48)	No association	
Skin cancer, case control studies				
Reference	Allergy	Statistical value (95% CI)	Association	Comments
(78) Cheng	Any allergy (animal, insect sting, food, plant, mold, and dust)	Early onset: BCC: OR: 0.61 (0.38-0.97), Early onset: SCC: OR: 1.18 (0.78-1.79)	Negative, No association	
(77) Jensen	Atopic dermatitis	Melanoma: SIR 0.46 (0.19-0.95), BCC: SIR 1.41 (1.07-1.83), SCC: SIR 2.48 (1.00, 5.11)	Negative, Positive, No association	
(76) Ji	Asthma	Melanoma: SIR 0.84 (0.71-0.99), SCC: SIR 1.33 (1.19, 1.48)	Negative, Positive	
(79) Ming	Atopic dermatitis	NMSC OR 0.78 (0.61-0.98)	Negative	
(80) Hwang	Allergic rhinitis; Asthma; Atopic dermatitis	Melanoma: SIR 0.89 (0.36-1.84), NMSC SIR 0.40 (0.28-0.56); Melanoma: SIR 1.32 (0.63-2.43), NMSC: SIR 0.39 (0.27-0.54); Melanoma: SIR 2.35 (0.26-8.47), NMSC: SIR 0.75 (0.30-1.54)	No association, Negative; No association, Negative; No association, No association	
(81) Kallen	Allergic asthma	Melanoma: SMR 34 (26.3-44.4), Other skin cancers: SMR 76 (65.2-87.7)	Negative, Negative	
(82) Marasigan	Any allergy (atopic dermatitis, asthma, hay fever)	Melanoma: OR: 0.53 (0.30-0.96)	Negative	

Colorectal cancer, cohort studies				
Reference	Allergy	Cancer type: statistical value (95% CI)	Association	Comments
(83) Eriksson	Positive skin prick test	Rectal cancer: SIR 4.69 (1.25-12.0)	Positive	
(85) Tambe	Any allergy (asthma, hay fever)	Colorectal cancer: RR 0.86 (0.80-0.92)	Negative	
(36) Gonzalez-Perez	Asthma	Colorectal cancer: OR 0.86 (0.70-1.06)	No association	Adjusted for age/sex/calendar year/BMI/ alcohol/smoking/prior comorbidities/health services utilization/aspirin/NSAID/ paracetamol
(35) Mills	Any allergy (asthma, hay fever, drug allergy, bee allergy)	Colon cancer: RR 0.96 (0.69-1.33), Rectal cancer: RR 0.86 (0.51-1.44)	No association, No association	
(86) Prizment	Any allergy (asthma, hay fever, eczema, skin allergy)	Colorectal cancer: HR: 0.74 (0.59-0.94)	Negative	Patient population: women only
(93) Talbot-Smith	Any allergy (not specified)	Colorectal cancer Men: HR 0.32 (0.03-2.84), Women: HR 1.42 (0.41-4.95)	No association	
(87) Turner	Asthma and hay fever both	Colorectal cancer: OR 0.76 (0.64-0.91)	Negative	
(88) Jacobs	Asthma and hay fever both	RR CPS-I: 0.90 (95% CI, 0.74-1.09), RR CPS-II 0.79 (95% CI, 0.69-0.91), When results combined with meta-analyses: RR 0.83 (0.74-0.92)	No association, Negative, Negative	CPS = cancer prevention study
(34) McWhorter	Any allergy	ROR 1.69 (0.92-3.11)	No association	
Colorectal cancer, case control studies				
(89) Bosetti	Any allergy (not specified)	Colon cancer: OR 0.76 (0.59-0.97), Rectal cancer: OR 0.54 (0.37-0.77)	Negative	History of allergy first diagnosed within five years before cancer diagnosis. Also, negative association when both sexes studied separately.
(32) Wang	Any allergy (hay fever, asthma, atopic dermatitis)	Colorectal cancer: OR: 0.99 (0.73-1.35)	No association	
(90) Negri	Any allergy (allergic rhinitis, asthma, atopic dermatitis)	Colon cancer: OR 0.88 (0.67-1.14), Rectal cancer: OR 0.64 (0.44-0.92), Colorectal cancer: OR 0.80 (0.63-1.00)	No association, Negative, No association	
(91) La Vecchia	Drug allergy	Colon cancer: RR: 0.6 (0.4-0.9), Rectal cancer: RR: 0.6 (0.5-1.0)	Negative, No association	
(94) Kune	Allergies or hay fever	RR 0.83 (0.67-1.03)	No association	
Colorectal cancer, retrospective studies				
(84) Vesterinen	Asthma	Colon cancer: SIR 1.17 (1.02-1.33), Rectal cancer: SIR 1.10 (0.86-1.38)	Positive, No association	

(80) Hwang	Asthma;	Colon cancer: SIR 1.00 (0.88-1.13), SIR Men: 0.83 (0.69-0.99), SIR Women: 1.24 (1.03-1.47), Rectal cancer: SIR 0.86 (0.73-1.01);	No association, Negative, Positive, No association (both sexes); No association, No association, No association, Negative (both sexes)	
	Allergic rhinitis	Colon cancer: SIR 1.02 (0.90-1.15), SIR Men: 0.93 (0.78-1.10), SIR Women: 1.14 (0.94-1.37), Rectal cancer: SIR 0.82 (0.69-0.97)		
(92) Vena	Asthma; Hay fever; Asthma; Hay fever	Colon: Men OR 1.33, women OR 0.61; Colon cancer: Men OR 1.27, women OR 1.00; Rectal cancer: Men OR 0.60, women OR 0.82; Rectal cancer: Men OR 1.22, women OR 0.61	Negative	95% CI not included.
Pancreatic cancer, case control studies				
Reference	Allergy	Statistical value (95% CI)	Association	Comments
(95) Cotterchio	Atopy	MVOR 0.66 (0.51-0.85)	Negative	
(9) Eppel	Any allergy (hay fever, not specified)	AOR 0.43 (0.29-0.63)	Negative	
(96) Holly	Any allergy (not specified)	OR 0.77 (0.63-0.95)	Negative	
(97) Maisonneuve	Any allergy (asthma, eczema, hay fever, not specified)	OR 0.64 (0.50-0.82)	Negative	
(98) Olson	Any allergy	OR 0.58 (0.40-0.84)	Negative	Hay fever and animal allergies were related to lower risk. No association between other allergies and asthma
(99) Santibanez	Nasal allergies (including hay fever)	OR 0.56 (0.32-0.99)	Negative	
(100) Silverman	Any allergy (hay fever, asthma, eczema, animal allergy, insect bite/sting allergy, dust or mold allergy, drug allergy, household products)	OR 0.7 (0.5-0.9)	Negative	
(101) Dai	Any allergy	OR 0.6 (0.4-1.1).	No association	
Pancreatic cancer, cohort studies				
(87) Turner	Hay fever	OR 0.84 (0.71-1.00)	No association	No association between asthma and pancreas cancer or asthma/hay fever and pancreas cancer
(102) Hemminki	Hay fever/allergic rhinitis	OR 0.87 (0.58-1.26)	No association	
Urogenital cancers, case control studies				
Reference	Allergy	Cancer types: statistical value (95% CI)	Association	Comments
(106) Gloria-Bottini	Any allergy (asthma, rhinitis and AEDS (Atopic Eczema/Dermatitis Syndrome)	Uterine leiomyomas	Negative	Uterine leiomyomas is lower in allergic than non-allergic women (p < 0.004)

(107) Johnson	Any allergy (not specified)	Squamous cell cervical cancer: OR 0.7 (0.6-0.9)	Negative	
(103) Lightfoot	Any allergy (not specified)	Prostate cancer: OR 0.78 (0.60-1.00)	No association	
(32) Wang	Any allergy (asthma, hay fever, atopic dermatitis)	Prostate cancer: OR 0.98 (0.66-1.45)	No association	
(104) Weiss	Any allergy (hay fever, medication, food, dust, animals)	Prostate cancer: OR 0.98 (0.84-1.14)	No association	
(36) Gonzalez-Perez	Asthma	Prostate cancer: OR 0.86 (0.69-1.07)	No association	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.
Urogenital cancers, cohort studies				
(108) Montgomery	Hay fever	Cervical cancer: OR 1.04 (0.50-2.17)	No association	
(33) Talbot-Smith	Atopy	Prostate cancer: OR 2.25 (0.94-5.47)	No association	Adjusted for age, smoking status, and body mass index.
(34) McWhorther	Any allergy	Prostate cancer: OR 1.32 (0.62-2.80)	No association	Adjusted for smoking, age and race.
(35) Mills	Any allergy (hay fever, asthma, bee sting, medication)	Prostate cancer: OR 1.25 (0.93-1.69)	No association	Adjusted for smoking and age
(87) Turner	Asthma and hay fever	Prostate cancer: OR 1.06 (0.74-1.53); Ovarian cancer: OR 0.93 (0.60-1.45)	No association; No association	
(102) Hemminki	Hay fever/allergic rhinitis	Prostate cancer: SIR 1.18 (1.06-1.30), Cervix cancer: SIR 0.99 (0.73-1.32), Ovarian cancer: SIR 0.98 (0.74-1.27)	Positive, No association, No association	
(81) Kallen	Asthma	Prostate cancer: SMR 72 (66.7-77.6), Cervix cancer: SMR 52 (38.9-69.1), Ovarian cancer: SMR 52 (42.1-63.1)	Negative, Negative, Negative	
(76) Ji	Asthma	Prostate cancer: SIR 1.28 (1.20-1.36), Cervix cancer SIR 1.34 (1.07-1.66), Ovarian cancer SIR 0.92 (0.76-1.12)	Positive, Positive, No association	
(105) Severi	Asthma	Prostate cancer: HR 1.25 (1.05-1.49)	Positive	Adjusted for age, country of birth, education, body mass index, fat and fat-free mass, smoking, alcohol consumption, and total energy intake.

Lung cancer, case control studies				
Reference	Allergy	Statistical value (95% CI)	Association	Comments
(115) El-Zein	Asthma Eczema Hay fever	OR 0.90 (0.65-1.24); OR 0.73 (0.48-1.12); OR 0.37 (0.24-0.59)	No association; No association; Negative	Adjusted for age, sex, education, respondent status, ethnocultural origin, fruit and vegetable consumption and smoking.
(116) McDuffie	Any allergy (house dust mite, animals, mixed molds, mixed weed pollen, mixed tree pollen, mixed grass pollen)	OR 0.58 (0.37-0.91)	Negative	
(117) McDuffie	Any allergy (house dust mite, mixed grain dust, mixed animal dander, mixed molds, mixed weed pollen, mixed tree pollen, mixed grass pollen)	-	Negative	The study used seven common allergens for allergy skin prick test. Historic evidence of allergy was greater in both control groups compared to the cancer groups.
(118) Seow	Any allergy (asthma, allergic rhinitis, atopic dermatitis)	All histological types: OR 1.5 (0.8-2.6), Adenocarcinoma: OR 1.6 (0.9-3.1)	No association	Study population: non-smoking Chinese women
(32) Wang	Any allergy (asthma, hay fever, atopic dermatitis)	OR 0.85 (0.50-1.47)	No association	
(36) Gonzalez-Perez	Asthma	OR 1.35 (1.15-1.59)	Positive	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.
Lung cancer, cohort studies				
(35) Mills	Any allergy (hay fever, asthma, bee sting, medication)	OR 1.02 (0.60-1.72)	No association	In cases of asthma alone, the association with lung cancer was also positive. Adjusted for age, sex, smoking history, and time since last physician contact.
(102) Hemminki	Hay fever/allergic rhinitis	SIR 0.78 (0.64-0.93)	Negative	
(81) Kallen	Asthma	All respiratory tract cancers: SMR 105 (97.0-113.4)	Positive	
(76) Ji	Asthma	SIR 1.76 (1.63-1.90)	Positive	
(114) Alderson	Asthma	OR 0.80 (0.41-1.56)	No association	Covariants are not mentioned.
(109) Reynolds	Asthma	Men: relative risk incidence lung cancer is RR 6.3 and mortality is RR 5.3; Women: relative risk incidence lung cancer is RR 1.2.	Positive in men	Adjusted for gender and smoking.
(84) Vesterinen	Asthma	Men: SIR 1.32 (1.22-1.43), Women: SIR 1.66 (1.39-1.98)	Positive	Covariants are not mentioned.
(110) Huovinen	Asthma	Men: HR 3.19 (1.39-7.31)	Positive	Risk of mortality due to lung cancer. Adjusted for age and smoking

(87) Turner	Asthma and hay fever	Only hay fever: RR 0.85 (0.80-0.90); Only asthma: RR 1.11 (1.02-1.20); Asthma and hay fever: RR 0.73 (0.65-0.83)	Negative; Positive; Negative	Lung cancer mortality. Adjusted for gender, race, smoking, education, marital status, body mass index, diabetes, exercise, alcohol drinking, aspirin use, vegetable intake, and fat intake.
(111) Pirie	Asthma	Women: RR 1.32 (1.10-1.58)	Positive	Non-smoker women. Adjusted for age, region, deprivation quintile, height.
(112) Huang	Asthma	Men: HR 1.36 (1.30-1.41), Women: 1.26 (1.18-1.34)	Positive	Adjusted for lung diseases, low income, age, comorbidities, urbanization and geographic area
(113) Colak	Asthma	Never smokers with asthma: HR 0.6 (0.1-5.1), Former smokers with asthma HR 4.0 (1.3-12), Current smokers with asthma HR 13 (4.3-41)	No association, Positive, Positive	Adjusted for age, sex, BMI, allergy, familial predisposition for asthma, childhood asthma, hay fever, or eczema.
(33) Talbot-Smith	Asthma, hay fever or any atopy	Risk of lung cancer Men: Asthma: HR 1.18 (0.15-9.06), Hay fever: HR 0.64 (0.08-4.87), Any atopy: HR 0.28 (0.03-2.49), Women: Asthma: HR 0.96 (0.12-7.48), Hay fever: HR 1.45 (0.40-5.30), Any atopy: HR 0.87 (0.08-9.89)	No association	
Other cancers, case control studies				
Reference	Allergy	Cancer type: statistical value (95% CI)	Association	Comments
(119) Chung	Allergic rhinitis	Nasopharyngeal carcinoma: OR 2.29 (2.05-2.56)	Positive	
(125) Fillippidis	Any allergy (not specified)	Laryngeal cancer: OR 0.87 (0.55-1.4)	No association	
(153) Frentzel-Beyme	Skin allergy (not specified) Hay fever	Bone tumors: RR 0.76 (0.37-1.55), RR 1.49 (0.65-3.43)	No association	
(130) Goedert	Any allergy (not specified)	Kaposi's sarcoma OR 1.54 (0.88-2.70)	No association	
(121) Hsiao	Any allergy (not specified)	Head and neck cancer: OR 0.41 (0.27-0.62), Oral cancer: OR 0.36 (0.22-0.57), Oropharyngeal cancer: OR 0.49 (0.25-0.96), Laryngeal cancer: OR 0.48 (0.19-1.18)	Negative, Negative, Negative, No association	Original study plus meta-analysis
(122) Liao	Any allergy (allergic rhinitis, skin allergy, food allergy, drug allergy and asthma)	Head and neck cancer: OR 0.56 (0.43-0.73)	Negative	Diagnosis of squamous cell carcinoma of the head and neck, including oral cavity, oropharynx, hypopharynx, larynx.
(120) Lin	Allergic rhinitis Men Women	Nasopharyngeal carcinoma HR 2.33 (1.59-3.40) HR 2.06 (1.31-3.25) HR 3.02 (1.47-6.22)	Positive	

(124) Lupo	Any allergy (Asthma, eczema, hives, not specified)	Rhabdomyosarcoma OR 0.60 (0.41-0.87)	Negative	Patient population: Children
(126) Menegaux	Any allergy (asthma, hay fever, other ear, nose, and throat allergy such as rhinitis and sinusitis, eczema, and other dermatologic allergy as urticaria, contact dermatitis, food dermatitis, or hypersensitivity to drugs)	Neuroblastoma: OR 0.68 (0.44-1.07)	No association	Patient population: among children over 1 year of age
(123) Michaud	Any allergy (not specified)	HNSCC: OR 0.81 (0.67-0.98), Laryngeal: OR 0.66 (0.45-0.97), Oropharyngeal cancers: OR 0.73 (0.57-0.92), Oral cavity cancers: OR 0.98 (0.76-1.26)	Negative, Negative, Negative, No association	
(127) Rosato	Any allergy	Biliary tract cancer: OR 0.64 (0.29-1.40)	No association	Using data from two cc
(128) Schoemaker	Any allergy (history of seasonal or non-seasonal allergic nasal catarrh and conjunctivitis, food allergy, contact allergy or other types of allergy specified by the participant)	Acoustic neuroma: OR 0.9 (0.8-1.1)	No association	
(129) Stott-Miller	Any allergy (not specified)	Oral squamous cell carcinoma: OR 0.81 (0.61-1.08)	No association	
Cancer in general, case control studies				
Reference	Allergy	Cancer type: statistical value	Association	Comments
(131) Allegra	Any allergy (hives, eczema, frequent colds, frequent unexplained rashes, hay fever, asthma)	15-fold decrease in prevalence of cancer ($p < 0.01$)	Negative	
(132) Fisherman	Any allergy prevalence	Malignant tumors: 3.2% Control group: 12.9%	Negative	Prevalence of allergy in patients with malignant tumors and control group.
(133) Kozłowska	Allergic rhinitis	OR 0.67 (0.52-0.81)	Negative	
(134) McKee	Seasonal allergy No history of allergy	23.7% at operation for cancer, 25.4% at operation for cancer	Negative	
(135) Pompei	Any allergy prevalence	Tumor-bearing patients 8%, Non-tumor-bearing subjects 16-37%	Negative	Prevalence of allergy in tumor-bearing patients and non-tumor-bearing patients.
(36) Gonzalez-Perez	Asthma	OR 0.93 (0.86-1.00)	No association	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.

Cancer in general, cohort studies				
(80) Hwang	Allergic rhinitis	SIR 1.02 (0.98-1.05)	No association	Table 2 in this article shows the SIR's for many types of cancer and allergic rhinitis.
(34) McWhorter	Any allergy (not specified)	OR 1.40 (1.10-1.77)	Positive	The specific allergy type with the strongest cancer risk was hives. The cancer group with the strongest allergy association was lymphatic-hematopoietic (leukemia, lymphoma, myeloma). Also, further determination of colorectal cancer.
(35) Mills	Any allergy (not specified)	Men: RR 1.13 (0.92-1.39), Women: RR: 1.00 (0.85-1.17)	No association	Cancer sites among males include: colon, rectum, prostate, lung, bladder, melanoma, stomach, kidney, lymphoma, leukemia, multiple myeloma, and sarcoma. Cancer sites among females include: colon, rectum, breast, endometrium, cervix, ovary, lung, bladder, melanoma, stomach, kidney, lymphoma, leukemia, multiple myeloma, and sarcoma.
(138) Skaaby	Any allergy (not specified)	HR 0.86 (0.69-1.06)	No association	
(137) Skaaby	Any allergy (not specified)	HR 1.00 (0.89-1.12)	No association	
Cancer in general, retrospective data analysis				
(136) Chae	Rhinoconjunctivitis	OR 1.44 (1.00-2.08)	No association	

CI = confidence interval; OR = odds ratio; RR = relative risk; PNET = primitive neuroectodermal tumour; HR = hazard ratio; SIR = standardized incidence ratios; SMR = standardized morbidity rate; ROR = risk odds ratio; MVOR = multi variable odds ratio; AOR = age-adjusted odds ratio; NSAID = non-steroidal anti-inflammatory drugs; HL = Hodgkin's lymphoma; NHL = non-Hodgkin's lymphoma; DLBCL = diffuse large B-cell lymphoma; ALL = acute lymphatic leukemia; AML = acute myeloid leukemia; CML = chronic myeloid leukemia; AUL = acute undifferentiated leukemia; CLL = chronic lymphocytic leukemia; FBCL = follicular B-cell lymphoma; MM = multiple myeloma; SBL = sporadic Burkitt lymphoma; LL = lymphocytic leukemia; ML = myloid leukemia; MDS = myelodysplastic syndrome; SCC = squamous cell carcinoma; BCC = basal cell carcinoma; NMSC = non-melanoma skin cancer; AEEDS = atopic eczema / dermatitis syndrome; HNSCC = head and neck squamous cell carcinoma.

Table 2. Overview of the studies on the association between allergic diseases and cancer

Types of cancers	Positive association (reference number)	Negative association (reference number)	No association (reference number)	Conclusion
Brain cancer	-	(11, 17-28)	(10-16)	Allergic diseases are associated with reduced risk of brain cancer
Breast cancer	(29)	(30, 31)	(32-36)	No association between allergic diseases and breast cancer
Lymphatic and hematopoietic cancer	Lymphoma: (34, 37-39) Other hematological malignancies: (34, 60-65)	Lymphoma: (40-49) Other hematological malignancies: (66-72).	Lymphoma: (33, 35, 39, 47, 50-59) Other hematological malignancies: (33, 35, 39, 47, 50-59)	In general, allergic diseases are possibly associated with decreased risk of lymphatic and hematopoietic cancer
Skin cancers	(77)	(76-82)	(77, 78, 80)	Negative association between allergic diseases and melanoma
Colorectal cancers	(80, 83, 84)	(80, 85-92)	(32, 34-36, 80, 84, 88, 90, 91, 93, 94)	The risk of colorectal cancers is possibly reduced in patients with allergic diseases
Pancreatic cancer	-	(9, 95-100)	(87, 101, 102)	Allergic diseases are associated with reduced risk of pancreatic cancer
Urogenital cancers	Prostate cancer in men: (76, 102, 105) Urogenital cancers in women: (76)	Prostate cancer in men: (81) Urogenital cancers in women: (81, 106, 107)	Prostate cancer in men: (32-36, 87, 103, 104) Urogenital cancers in women: (76, 87, 102, 108)	Possibly no association between allergies and prostate cancer. Possibly a reduced risk of urogenital cancers in Women with allergic diseases
Lung cancer	(36, 76, 81, 84, 87, 109-113)	(87, 102, 115-117)	(32, 33, 35, 113-115, 118)	Asthma is related with an increased risk of lung cancer in contrast to atopy without asthma
Other cancers	(119, 120)	(121-124)	(125-130, 133)	No evident association between allergic diseases and other cancers
Cancer in general	(34)	(131-135)	(35, 36, 80, 136-138).	Allergic diseases are possibly associated with decreased risk of cancers