Impact of climate change-related environmental factors on the allergens production and the epidemiology and severity of allergic pathologies

Brief running title: Environmental and allergens in allergic diseases

Montoro J[1,2], Antolín-Amérigo D[3,4], Artés M[5], Izquierdo-Domínguez A[6], Zapata JJ[7], Mur P[8], Carrillo T[9], Antépara I[10], Feo F[11], Moral A[12], Valero A[13,14,15]

[1]Sección de Alergia, Unidad Especializada de Asma Grave, Hospital de Arnau de Vilanova - Líria, Valencia, Spain
[2]Facultad de Medicina, Universidad Católica de Valencia "San Vicente Mártir", Valencia, Spain
[3]Servicio de Alergia, Hospital Universitario Ramón y Cajal, Madrid, Spain
[4]Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain
[5]Adelphi Targis, Barcelona, Spain
[6]Servicio de Alergología, Consorcio Sanitario de Terrassa, Terrassa-Barcelona, Spain
[7]Clínica de Alergia Dr. Zapata, Almería, Spain
[8]Servicio de Alergia, Hospital de Puertollano, Puertollano-Ciudad Real, Spain
[9]Servicio de Alergia, Hospital Universitario de Gran Canaria Dr. Negrín, Las Palmas de Gran Canaria-Las Palmas, Spain
[10]Servicio de Alergia, Hospital Universitario de Basurto, Bilbao, Spain
[11]Servicio de Alergia, Hospital General de Ciudad Real, Ciudad Real, Spain
[12]Hospital Virgen del Valle, Toledo, Spain
[13]Servicio de Alergología, Hospital Clínic de Barcelona, Barcelona, Spain
[14]Instituto de Investigaciones Biomédicas August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[15]CIBER de Enfermedades Respiratorias (CIBERES), Spain

Corresponding author:

Javier Montoro Lacomba M.D., Ph.D.
Allergy Section. Severe Asthma Specialized Unit. Hospital Arnau de Vilanova-Líria. Valencia
Department of Medicine. Catholic University of Valencia "San Vicente Mártir"
E-mail: montoro_fra@gva.es

doi: 10.18176/jiaci.0988

Abstract

Background: Allergic disease affects up to 40% of the global adult population, a proportion that is increasing with environmental changes related to global warming.

Methods: We undertook a systematic review of the literature to identify and evaluate the current evidence of the impact of climate change-related environmental factors on the allergen production and the epidemiology and severity of allergic pathologies. PECO criteria were established and guided the literature searches of the PubMed and Cochrane databases (Jan 1, 2016 to Dec 31, 2021). Study outcomes were categorized and grouped to facilitate data synthesis. Outcomes were classified as significant (statistical significance <0.05), non-significant (p>0.05) or undetermined (p value not reported). Study quality was assessed using MMAT analysis.

Results: Of 195 studies, 40 were considered relevant and 9 of them provided data to be included in the data quantitative synthesis. Environmental factors, including the presence of pollutants, temperature, and drought, influenced the type, volume, and timing of exposure to local aeroallergens. The most relevant environmental factor was the presence of environmental pollutants, of which tropospheric ozone was the most frequently associated to changes in allergen production, prevalence, and severity of allergic disease. Also, several publications demonstrated the impact of environmental factors on the healthcare burden.

Conclusions: Climate-change related environmental factors increased allergic disease in terms of prevalence, severity, and healthcare burden due to alterations in allergen exposure (volume and type) with the presence of pollutants such as ozone being the most commonly reported driver of such increase.

Key words: Allergen. Environment. Allergy. Pollutant. Epidemiology. Climate change.

doi: 10.18176/jiaci.0988

Resumen

Antecedentes: Las enfermedades alérgicas afectan hasta el 40% de la población adulta mundial, una proporción que se incrementa con los cambios ambientales relacionados con el calentamiento global.

Métodos: Realizamos una revisión sistemática de la literatura para identificar y evaluar la evidencia actual del impacto de los factores ambientales relacionados con el cambio climático en la producción de alérgenos y en la epidemiología y gravedad de las patologías alérgicas. Se establecieron criterios PECO que guiaron las búsquedas bibliográficas en las bases de datos de PubMed y Cochrane (del 1 de enero de 2016 al 31 de diciembre de 2021). Los resultados de los estudios fueron categorizados y agrupados para facilitar la síntesis de datos. Los resultados se clasificaron como significativos (significación estadística $p<0.05$), no significativos ($p>0.05$) o indeterminados (valor de p no proporcionado). La calidad del estudio se evaluó utilizando el análisis MMAT.

Resultados: De 195 registros, se consideraron relevantes 40 y 9 publicaciones proporcionaron datos que fueron incluidos en la síntesis cuantitativa de datos. Factores ambientales, como la presencia de contaminantes, la temperatura y la sequía, influyeron en el tipo, volumen y momento de exposición a los aeroalérgenos locales. El factor ambiental más relevante fue la presencia de contaminantes ambientales, entre los cuales el ozono troposférico fue el más frecuentemente asociado a cambios en la producción de alérgenos, prevalencia y gravedad de las enfermedades alérgicas. Adicionalmente varias publicaciones demostraron el impacto de factores medioambientales sobre la presión asistencial.

Conclusiones: Los factores ambientales relacionados con el cambio climático incrementan la prevalencia, gravedad y presión asistencial de las enfermedades alérgicas debido a alteraciones en la exposición a alérgenos (volumen y tipo). El ozono es el contaminante más implicado en este incremento.

Palabras clave: Alérgeno, medio ambiente, alergia, contaminante, epidemiología, cambio climático.

doi: 10.18176/jiaci.0988

Introduction

Allergic disease has been estimated to affect up to 40% of the global population imposing a substantial burden on individuals, communities, and healthcare systems [1–3]. The prevalence of allergic disease has increased sharply in recent decades, most notably in developed countries [2, 4]. Industrialization, urbanization and changing lifestyles may have contributed to this increase through changes in exposure to environmental allergens both in terms of volume and type [3–6].

The precise effect of environmental factors on allergic disease remains controversial due, in part, to the complex aetiological mechanisms driving the emergence and severity of these diseases [2, 4, 7] . Epidemiological research on air pollution as a potential risk factor for allergic disease has gained increased attention in recent years. For example, in Spain numerous studies have indicated associations between pollen count and various allergic diseases including respiratory diseases such as asthma and allergic rhinitis as well as conditions such as allergic sensitization [8–14]. More accurate results have been reported for other environmental factors such as traffic-related air pollution in association with respiratory diseases (allergic or not) [15]. For example, while one cohort study found an increase in the prevalence of eczema in adults related to exposure to traffic-related air pollution [16], another study found no such effect [2]. Similarly, conflicting results have been reported for the impact of air pollution and childhood eczema and on exposure to particulate matter less than 2.5 micrometres in diameter (PM2.5) and allergic rhinitis [17].These disparate results further reinforce the suggestion of a complex inter-relationship between environmental factors and the range of allergic diseases.

The impact of climate change-related environmental factors, such as drought, flooding and temperature (e.g. heat waves), on allergic disease have also begun to receive more attention in recent years [18, 19]. Such factors may have both direct effects on allergic pathology and indirect effects by changing local and regional ecosystems including pollen volume and type, mould exposure due to damp housing, local air pollution and heat stress [18–22]. Of critical importance in mitigating the future burden on individuals and healthcare systems is an understanding of the modifiable factors associated with climate change that influence the prevalence and severity of allergic disease. Indeed, the United Nations, through the 2015 Paris Agreement and subsequent iterations, continue to emphasise the issue of climate change on human health and allergic disease and call global understanding and cooperation to mitigate these impacts [23]

doi: 10.18176/jiaci.0988

The objectives of this systematic literature review were to identify and evaluate the current evidence regarding the impact of climate change-related environmental factors on the expression, prevalence, and nature of allergens, and on the incidence, prevalence, and severity of allergic diseases, particularly on rhinitis/conjunctivitis, asthma, food allergy and atopic dermatitis.

Methods

We undertook a systematic review of the literature following The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, published in 2009 [24].

Search strategy

PECO (Population, Exposure, Comparison, Outcome) criteria were developed to guide the literature search and review. *Population*: adults with allergic disease; *Exposure*: climate change-related environmental factors (e.g. climate factors, air quality); *Comparison*: not applicable; *Outcomes*: expression, prevalence and nature of allergens and incidence, prevalence and severity of allergic diseases.

The research questions to be addressed were "*Do climate change and air quality modify the expression, prevalence, or nature of different allergens, turning them into more aggressive allergens?* "*Do climate change and air quality have a direct and significant impact on the incidence, prevalence or severity of allergic diseases?*"," and "*What is the impact of climate change and air quality specifically on rhinitis, conjunctivitis, asthma, food allergy and atopic dermatitis?*".

The literature searches were conducted in the PubMed and the Cochrane database of systematic reviews for the period January 1, 2016 to December 31, 2021 and was restricted to publications in English or Spanish for which an abstract was available. Search terms were defined as: (climate change[Title/Abstract]) OR (greenhouse gas*[Title/Abstract])) AND ((airway diseases [Title/Abstract] OR airway pathology [Title/Abstract] OR Respiratory diseases[Title/Abstract] OR Respiratory pathology[Title/Abstract] OR allergic diseases [Title/Abstract] OR asthma[Title/Abstract] OR conjunctivitis[Title/Abstract] OR rhinitis[Title/Abstract] OR "food allergy"[Title/Abstract] OR "Atopic dermatitis"[Title/Abstract] OR eczema)[Title/Abstract])) AND ((inciden* OR prevalen* OR sever* OR epidemiol* OR allergenicity) OR ("house dust mites" OR pollen OR alternaria)) ("2016/01/01"[Date - Publication] : "3000"[Date - Publication]).

Inclusion criteria and screening process

doi: 10.18176/jiaci.0988

All types of original studies (randomized clinical trials (RCTs), non-randomized trials, post hoc analyses of RCTs, and observational studies) and systematic reviews (with or without meta-analyses) were searched for. Studies were considered for inclusion in the systematic review if they presented quantitative data related to the impact of climate change-related environmental factors on either the expression, prevalence, or nature of allergens, or the incidence, prevalence, or severity of allergic diseases. Studies dealing with diseases other than the following were excluded: rhinitis/conjunctivitis, asthma, food allergy, and atopic dermatitis. (Supplementary material 1).

Publications in languages other than English or Spanish were identified but appear as excluded in the PRISMA flowchart (Figure 1). Publications without an abstract and unpublished studies were also excluded. The full texts of all the studies fulfilling the selection criteria (Supplementary material 2) were retrieved. The titles and abstracts of all identified studies were independently screened for relevance by two reviewers (Gloria González and Sara García), educated to degree level in biology and chemistry, and duplicates were removed. The full text of potential studies for inclusion were then interrogated for relevance to the PECO questions. Disagreements in study selection between the two lead reviewers were resolved by a third reviewer. An additional reviewer (Maite Artés) double-checked selection criteria of a random sample of 15% of the records.

The publications that were excluded and the reasons why are provided in Supplementary material 3.

Data synthesis

Reported study outcomes were categorized and grouped to facilitate data synthesis. Given the heterogeneity of the type of outcomes found, data were classified as significant ($p<0.05$) and non-significant ($p>0.05$). In publications with no direct comparison, when a p-value was not provided, or when data were descriptive, results were counted as undetermined.

Quality assessment

Study quality was assessed using MMAT (Mixed Methods Appraisal Tool) analysis [25].This tool allows evaluation of the quality of qualitative, quantitative, and mixed methods studies focusing on methodological criteria.

doi: 10.18176/jiaci.0988

Results

A total of 195 studies were identified and reviewed, 40 studies were considered initially eligible, and 9 reports provided relevant quantitative data related to the PECO and were finally included in the data synthesis (**Figure 1**). Of these 9 reports, 8 had an MMAT score >60%.

Impact of climate change-related environmental factors on allergens

Across the 9 studies included in the data synthesis, a total of 8 outcomes were identified that could be categorised as providing information of impact of climate change-related environmental factors on allergenicity (from 2 different studies) [26, 27], changes in allergen production (alteration of time/quantity of allergen production; 25 outcomes from 7 different studies) [26, 28–33] and epitope modification (2 outcomes from 1 study) [34]).

Climate change-related environmental factors reported as causing adverse changes in the volume or type of allergens included the presence of pollutants (up to 11 study outcomes were provided by 5 different studies indicating a relationship between pollutants and increased allergenicity and changes in the production of allergens. Temperature increase due to climate change was related to allergenicity and epitope modification as reported by Choi et al [26]). Droughts were related to increases in the ambient dust levels (PM2.5 / PM 2.5-10) due to changes in aridity as reported by Achakulwisut et al [28](for 3 outcomes) and other weather conditions were related to changes in the production of allergens (pollen and house dust mites) [30] (for 2 outcomes) (**Table 1**). Three studies [29, 31, 34] reported a statistically significant association between the presence of environmental pollutants and a change in the production or type of allergens (for 7 outcomes).

More concretely, the environmental pollutants contributing to changes in the volume or type of allergens included black carbon, carbon dioxide, PM2.5, tropospheric ozone, and various (including a combination of traffic-related pollutants and the previous described) (**Table 2**). The association between the presence of black carbon and changes in local allergen production reached statistical significance in one study [31] (for 1 outcome). The association between PM2.5 and the change in allergen production reached statistical significance in 1 study [29] (for 2 outcomes). The association between tropospheric ozone and the change in allergen production reached statistical significance in two studies [29, 34] (for 4 outcomes).

doi: 10.18176/jiaci.0988

Impact of allergen alterations on allergic pathologies

Studies reporting associations between allergen alterations and allergic disease were explored (**Table 3**). Associations were reported for asthma, respiratory diseases, sensitization, and various other allergic pathologies. One study reported a statistically significant association between the change in the production of allergens regarding asthma[29]. For respiratory diseases, in general, statistically significant associations were reported for 4 outcomes related to a change in allergen production [31, 34].

The environmental pollutants more frequently associated to allergic pathologies were tropospheric ozone (associated to respiratory disease in general in one study [34] (for 3 outcomes) and PM2.5 associated to asthma in one study [29](for 2 outcomes) (**Table 4**).

Associations were noted between allergen alterations and the epidemiology and healthcare burden of allergic diseases. A statistically significant association were reported for the association between change in production and the epidemiology of allergic disease (for 3outcomes) and severity of allergic pathologies (for 3 outcomes) in one study [34] (**Table 5**).

Several studies highlighted the impact of environmental factors on the epidemiology and healthcare burden of allergic disease (**Table 6**). One study [34] reported a statistically significant association between the presence of environmental pollutants and the epidemiology of allergic pathologies (for 3 outcomes) (**Table 7**).

Discussion

We undertook a systematic review of the literature to evaluate the current scientific evidence base on the impact of climate change-related environmental factors on allergen production and in the epidemiology and severity of the allergic pathologies. Our analysis of the current literature base supports an adverse impact of environmental factors, including those driven by global climate changes, on the volume and type of allergens to which local populations are exposed. These changes impact the type, prevalence, and burden of allergic disease at a global level in both developed and developing countries.

Environmental factors, including the presence of pollutants, temperature, and drought, influence the type (allergenicity, epitope modifications), volume (production and pollen count) and timing of exposure to local aeroallergens [26–34]. The most relevant environmental factor was the presence of

doi: 10.18176/jiaci.0988

environmental pollutants, of which tropospheric ozone was the most frequently reported [26, 27, 29–31, 34]. Other environmental pollutants including black carbon [31], carbon dioxide [30] and PM2.5 [27, 29] were also identified as factors driving adverse exposure to aeroallergens.

The changes in production (in terms of time or quantity) of allergens had an impact on both allergic sensitization and allergic diseases, including respiratory diseases such as asthma [26–34]. Increases in the prevalence or severity of allergic diseases [26, 30, 33, 34],and associated increases in the healthcare burden [26, 28, 32], were the principal effects reported. These effects were influenced by changes in allergen production, with changes in tropospheric ozone the most frequently reported environmental factor [26, 29–34] . A more recent study, published since our literature search was performed, indicates that exposure to particulate levels lower than current recommendations can have adverse effects for individuals with allergic respiratory diseases such as asthma, increasing the risk for potentially fatal exacerbations [35]. In relation to the impact of pMDIs, prescribed for any indication, on total value of CO2 eq/year, we previously reported that the use of pMDIs accounts for 0.0909% of total emissions in Spain [36]. Furthermore, we showed that a switch of all pMDIs to DPIs, other than for the delivery of rescue medications, would cut the associated CO_2 emissions from pMDI to 0.0579% of the total emissions in Spain. However, the potential impact on asthma control and patient outcomes was not well defined and pending further research inhaler selection should be based on patients' clinical criteria rather than environmental considerations [36].

The strengths of the current systematic literature review including well-defined PECO questions to guide the literature search and subsequent data extraction and analysis and the evaluation of the quality of included studies using MMAT criteria. In addition, our analysis has global generalizability as there were no exclusion criteria according to geographical area and all environmental pollutants and pathologies were considered. Diverse limitations should be considered when evaluating the results of the current systematic literature review. Only publications in English and Spanish have been included and the search was conducted solely in Cochrane and PubMed databases for the last 5 years before 2021. However, although only one publication was discarded for language reasons, and it is not thought that this limit on eligible literature compromised the validity or generalizability of the analysis presented herein. A potential limitation for no mitigation could be applied was that studies without statistically significant results might not have been published. Finally, there was some considerable heterogeneity of study design and outcome definitions as the studies included in the current analysis were performed in many different countries and using different methodological approaches. While

doi: 10.18176/jiaci.0988

the heterogeneity in study design precluded formal statistical analyses or pooling of the reported results, it doesn´t compromise the external validity of the review.

Climate change and increased levels and type of environmental pollution are among the greatest threats to human health in both developed and developing regions of the world [37, 38]. Weather-related changes such as heat waves, thunderstorms and changes in precipitations patterns will continue to alter and increase allergen exposure [39, 40] as will increasing levels of environmental pollution [41]. Geopolitical factors such as population health and health-inequalities, poverty, famine, education, political instability, and conflict will continue to amplify the adverse effects of climate change on allergen exposure and the evolution and consequences of allergic disease [37]. Climate change and the consequences for human health mandate urgent action to mitigate these impacts for future generations and novel approaches to understanding the complex inter-relationships and opportunities for their reduction [42, 43].

Conclusions

Climate change-related environmental factors increased allergic diseases in terms of prevalence, severity, and healthcare burden. This effect occurs due to alterations in the allergen (mainly change in production) caused by various environmental factors, including the presence of pollutants such as ozone. The effect of environmental pollution was observed for multiple allergic pathologies, including allergic respiratory diseases such asthma. Exposure to particulate levels lower than current recommendations can have adverse effects for individuals with allergic respiratory diseases such as asthma. Further research in this field avoiding heterogeneity is of paramount importance.

Acknowledgements

Editorial support for the preparation of this manuscript was provided by Adelphi Targis and was funded with an unconditional grant from Chiesi España.

Funding

The research was made possible through the support of an unrestricted grant provided by Chiesi España. In this context, while Chiesi España was apprised of the research's progress, it refrained from active involvement in the formulation and design of the protocol, the execution of the systematic review, the data extraction and analysis, or the writing of this publication.

doi: 10.18176/jiaci.0988

Conflicts of interest

Montoro J. Grants: SEAIC, consulting fees: Chiesi, Astra Zeneca, and Sanofi, as speaker: Astra Zeneca, GSK, Faes, Sanofi, and Novartis.
Antolín-Amérigo D. Grants: SEAIC, consulting fees: ALK-Abelló, Astra Zeneca, Chiesi and Gebro, as speaker: Astra Zeneca, Chiesi, Gebro, GSK, Leti Pharma, Mundipharma, Novartis, Roxall, Sanofi.
Izquierdo A. Grants: SEAIC, as speaker: GSK, Sanofi, Novartis, Menarini, Lofarma, Viatris and Uriach.
Zapata JJ. Grants: SEAIC, consulting fees: Allergy T and Stallergenes, as speaker: Astra Zeneca, GSK, Stallergenes, Diater, Leti Pharma, Inmuntek, ALK, Allergy Therapeutics, Thermo Fisher, Asac Pharmaceutical Immunology, Hal Allergy, Chiesi.
Valero A.L. Grants: SEAIC, consulting fees: ALK-Abelló, Astra Zeneca, Chiesi and Gebro, as speaker: Astra Zeneca, Chiesi, Gebro, GSK, Leti Pharma, Mundipharma, Novartis, and Sanofi.
Carrillo T. Speaker: GSK, AstraZeneca and Sanofi, as member of adboard: GSK and Sanofi.

None of the authors received fees for their participation in this research and its subsequent publication.

References

1. Hu J, Chen J, Ye L, Cai Z, Sun J, Ji K (2018) Anti-IgE therapy for IgE-mediated allergic diseases: from neutralizing IgE antibodies to eliminating IgE+ B cells. Clin Transl Allergy 8:27

2. Wang H, Li X-B, Chu X-J, Cao N-W, Wu H, Huang R-G, Li B-Z, Ye D-Q (2022) Ambient air pollutants increase the risk of immunoglobulin E–mediated allergic diseases: a systematic review and meta-analysis. Environmental Science and Pollution Research 29:49534–49552

3. González-Díaz SN, De Lira-Quezada CE, Villarreal-González RV, Canseco-Villarreal JI (2022) Contaminación ambiental y alergia. Rev Alerg Mex 69:s24–s30

4. Luschkova D, Traidl-Hoffmann C, Ludwig A (2022) Climate change and allergies. Allergo J Int 31:114–120

5. Oh J-W (2022) Pollen Allergy in a Changing Planetary Environment. Allergy Asthma Immunol Res 14:168

6. Melén E, Koppelman GH, Vicedo-Cabrera AM, Andersen ZJ, Bunyavanich S (2022) Allergies to food and airborne allergens in children and adolescents: role of epigenetics in a changing environment. Lancet Child Adolesc Health 6:810–819

7. Murrison LB, Brandt EB, Myers JB, Hershey GKK (2019) Environmental exposures and mechanisms in allergy and asthma development. Journal of Clinical Investigation 129:1504–1515

8. Armentia A, Lombardero M, Callejo A, Barber D, Martín Gil FJ, Martín-Santos JM, Vega JM, Arranz ML (2002) Is Lolium pollen from an urban environment more allergenic than rural pollen? Allergol Immunopathol (Madr) 30:218–224

9. Blanca-Lopez N, Campo P, Salas M, García Rodríguez C, Palomares F, Blanca M, Canto G, Feo Brito F, Rondon C (2016) Seasonal Local Allergic Rhinitis in Areas With High Concentrations of Grass Pollen. J Investig Allergol Clin Immunol 26:83–91

doi: 10.18176/jiaci.0988

10. Mazdiyasni O, AghaKouchak A (2020) Natural Disasters Are Prejudiced Against Disadvantaged and Vulnerable Populations: The Lack of Publicly Available Health-Related Data Hinders Research at the Cusp of the Global Climate Crisis. Geohealth. https://doi.org/10.1029/2019GH000219

11. Feo Brito F, Mur Gimeno P, Martínez C, Tobías A, Suárez L, Guerra F, Borja JM, Alonso AM (2007) Air pollution and seasonal asthma during the pollen season. A cohort study in Puertollano and Ciudad Real (Spain). Allergy 62:1152–1157

12. Alfaya Arias T, Feo Brito F, Somoza Álvarez M, Amo-Salas M, Lucas J, Gutiérrez Mañero J, Urra Ardanaz J (2022) Allergenicity of Grass Pollen From Polluted and Nonpolluted Areas Measured Using the Skin Prick Test and Basophil Activation Test. J Investig Allergol Clin Immunol 32:393–395

13. Feo-Brito F, Alfaya Arias T, Amo-Salas M, Somoza Álvarez ML, Haroun Díaz E, Mayorga Mayorga C, Fernández Santamaría R, Urra Ardanaz JM (2022) Clinical impact and immunological alterations in asthmatic patients allergic to grass pollen subjected to high urban pollution in Madrid. Clinical & Experimental Allergy 52:530–539

14. Mur Gimeno P, Feo Brito F, Martínez C, Tobías A, Suárez L, Guerra F, Galindo PA, Gómez E (2007) Decompensation of pollen-induced asthma in two towns with different pollution levels in La Mancha, Spain. Clinical & Experimental Allergy 37:558–563

15. Altzibar JM, Tamayo-Uria I, De Castro V, et al (2015) Epidemiology of asthma exacerbations and their relation with environmental factors in the <scp>B</scp> asque <scp>C</scp> ountry. Clinical & Experimental Allergy 45:1099–1108

16. Schnass W, Hüls A, Vierkötter A, Krämer U, Krutmann J, Schikowski T (2018) Traffic-related air pollution and eczema in the elderly: Findings from the SALIA cohort. Int J Hyg Environ Health 221:861–867

17. Lopez DJ, Lodge CJ, Bui DS, et al (2021) Association between ambient air pollution and development and persistence of atopic and non-atopic eczema in a cohort of adults. Allergy 76:2524–2534

18. Demain JG (2018) Climate Change and the Impact on Respiratory and Allergic Disease: 2018. Curr Allergy Asthma Rep 18:22

19. Ray C, Ming X (2020) Climate Change and Human Health: A Review of Allergies, Autoimmunity and the Microbiome. Int J Environ Res Public Health 17:4814

20. Singh AB, Kumar P (2022) Climate change and allergic diseases: An overview. Frontiers in Allergy. https://doi.org/10.3389/falgy.2022.964987

21. Rorie A (2022) Climate Change Factors and the Aerobiology Effect. Immunol Allergy Clin North Am 42:771–786

22. D'Amato G, Chong-Neto HJ, Monge Ortega OP, et al (2020) The effects of climate change on respiratory allergy and asthma induced by pollen and mold allergens. Allergy 75:2219–2228

doi: 10.18176/jiaci.0988

23. United Nations (2015) Adoption of Paris Agreement. https://unfccc.int/files/essential_background/convention/application/pdf/english_paris_agreement.pdf. Accessed 5 Dec 2023

24. Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6:e1000097

25. Hong QN, Fàbregues S, Bartlett G, et al (2018) The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers. Education for Information 34:285–291

26. Choi Y-J, Lee KS, Oh J-W (2021) The Impact of Climate Change on Pollen Season and Allergic Sensitization to Pollens. Immunol Allergy Clin North Am 41:97–109

27. Shiraiwa M, Ueda K, Pozzer A, et al (2017) Aerosol Health Effects from Molecular to Global Scales. Environ Sci Technol 51:13545–13567

28. Achakulwisut P, Anenberg SC, Neumann JE, Penn SL, Weiss N, Crimmins A, Fann N, Martinich J, Roman H, Mickley LJ (2019) Effects of Increasing Aridity on Ambient Dust and Public Health in the U.S. Southwest Under Climate Change. Geohealth 3:127–144

29. Huang W, Schinasi LH, Kenyon CC, et al (2021) Effects of ambient air pollution on childhood asthma exacerbation in the Philadelphia metropolitan Region, 2011–2014. Environ Res 197:110955

30. Tham EH, Lee AJ, van Bever H (2016) Aeroallergen sensitization and allergic disease phenotypes in Asia. Asian Pac J Allergy Immunol 34:181–189

31. Jung KH, Goodwin KE, Perzanowski MS, Chillrud SN, Perera FP, Miller RL, Lovinsky-Desir S (2021) Personal Exposure to Black Carbon at School and Levels of Fractional Exhaled Nitric Oxide in New York City. Environ Health Perspect. https://doi.org/10.1289/EHP8985

32. Neumann JE, Anenberg SC, Weinberger KR, Amend M, Gulati S, Crimmins A, Roman H, Fann N, Kinney PL (2019) Estimates of Present and Future Asthma Emergency Department Visits Associated With Exposure to Oak, Birch, and Grass Pollen in the United States. Geohealth 3:11–27

33. Van Cleemput J, Poelaert KCK, Laval K, Impens F, Van den Broeck W, Gevaert K, Nauwynck HJ (2019) Pollens destroy respiratory epithelial cell anchors and drive alphaherpesvirus infection. Scientific Reports 2019 9:1 9:1–15

34. Stas M, Aerts R, Hendrickx M, et al (2021) Exposure to green space and pollen allergy symptom severity: A case-crossover study in Belgium. Sci Total Environ. https://doi.org/10.1016/J.SCITOTENV.2021.146682

35. Betancourt A, Zapatero A, Pola-Bibian B, Dominguez-Ortega J (2021) Impact of short-term exposure to below recommended PM10 pollution levels on Asthma exacerbations. J Investig Allergol Clin Immunol 31:439–440

doi: 10.18176/jiaci.0988

36. Montoro, J; Antolin-Amerigo, D; Izquierdo-Dominguez, A; Zapata, JJ; Gonzalez, G; Valero A (2023) The impact of inhalers for asthma on the global climate: a systematic review of carbon footprint and clinical outcomes in Spain. J Investig Allergol Clin Immunol. https://doi.org/10.18176/jiaci.0887

37. Agache, I; Sampath, V; Aguilera, J; Akdis, CA; Akdis, M; Barry, M; Bouagnon, A; Chinthrajah, S; Collins, W, Dulitzki, C; Erny, B; Gomez, J; Goshua, A; Jutel, M; Kizer, KW; Kline, O; LaBeaud, AD; Pali-Schöll, I; Perrett, KP; Peters, RL; Plaza, MP; Prunicki K (2022) Climate change and global health: A call to more research and more action. Allergy 77:1389–1407

38. Urrutia-Pereira, M; Guidos-Fogelbach, G; Solé D (2022) Climate changes, air pollution and allergic diseases in childhood and adolescence. J Pediatr (Rio J) 98(Suppl 1:S47–S54

39. Hughes KM, Price D, Suphioglu C (2022) Importance of allergen–environment interactions in epidemic thunderstorm asthma. Ther Adv Respir Dis. https://doi.org/10.1177/17534666221099733

40. Liu S-H, Kazemi S, Karrer G, Bellaire A, Weckwerth W, Damkjaer J, Hoffmann O, Epstein MM (2022) Influence of the environment on ragweed pollen and their sensitizing capacity in a mouse model of allergic lung inflammation. Frontiers in Allergy. https://doi.org/10.3389/falgy.2022.854038

41. Nassikas NJ, Chan EAW, Nolte CG, Roman HA, Micklewhite N, Kinney PL, Carter EJ, Fann NL (2022) Modeling future asthma attributable to fine particulate matter (PM2.5) in a changing climate: a health impact assessment. Air Qual Atmos Health 15:311–319

42. Urrutia-Pereira M, Badellino H, Ansotegui IJ, Guidos G, Solé D (2022) Climate change and allergic diseases in children and adolescents. Allergol Immunopathol (Madr) 50:7–16

43. Shamji MH, Ollert M, Adcock IM, et al (2023) EAACI guidelines on environmental science in allergic diseases and asthma – Leveraging artificial intelligence and machine learning to develop a causality model in exposomics. Allergy: European Journal of Allergy and Clinical Immunology. https://doi.org/10.1111/all.15667

doi: 10.18176/jiaci.0988

Table 1. Environmental factors causing alterations in allergen parameters.

Environmental factor (exposition factor)	**Impact on allergen (outcome)**			
	Allergenicity	**Change in production (time/quantity)**	**Epitope modification**	**Total**
Drought	–	**3** [28]	–	**3**
Other weather conditions (pollen and house dust mites)	–	**2** [30]	–	**2**
Pollutant[a]	**3** [26, 27]	**7*** [29, 31, 34] **1** [30]	–	**11**
Temperature	**3** [26]	–	**1** [26]	**4**
Various[b]	**2** [26]	**12** [26, 30, 32, 33]	**1** [26]	**15**
Total	**8**	**25**	**2**	**35**

Study design; location; period of study

[26] Review; N/A; N/A

[27] Review; North America, Europe and Asia countries; N/A

[28] Epidemiological study; United States; projections for up to 2090

[29] Time-stratified case-crossover study: Philadelphia (United States); 2011-2014

[30] Review; Asia; last 20 year

[31] Observational study; New York (United States); 24h during a 6-day sampling period)

[32] Epidemiological study; United States; projections for up to 2090

[33] Ex vivo and in vitro assay; N/A

[34]Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

*Indicates statistically significant association.

[a]Black carbon, carbon dioxide, PM2.5, tropospheric ozone; [b] The category various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Table 2. Environmental pollutants causing alterations in allergen parameters.

Environmental pollutant (exposition factor)	**Impact on allergen (outcome)**			
	Allergenicity	**Change in production (time/quantity)**	**Epitope modification**	**Total**
Black carbon	–	**1*** [31]	–	**1**
Carbon dioxide	–	**1** [31]	–	**1**
PM2.5	**1** [27]	**2*** [29]	–	**3**
Tropospheric ozone	–	**4*** [29, 34]	–	**4**
Various[a]	**2** [26]	–	–	**2**
Total	**3**	**8**		**11**

Study design; location; period of study

[26] Review; N/A; N/A

[27] Review; North America, Europe and Asia countries; N/A

[29] Time-stratified case-crossover study: Philadelphia (United States); 2011-2014

[31]Observational study; New York (United States); 24h during a 6-day sampling period)

[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

*Indicates statistically significant association.

[a] The category various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Table 3. Impact of allergen alteration on allergic pathologies.

Allergen alteration (exposition factor)	Impact on allergic pathology (outcome)				
	Asthma	**Respiratory disease**	**Sensitization**	**Various**[a]	**Total**
Allergenicity	**–**	**1** [26]	**–**	**3** [26]	**4**
Change in production (time/quantity)	**3*** [29] **2** [32]	**4*** [31, 34] **2** [33]	**4** [30]	**4** [26]	**19**
Epitope modification	**–**	**–**	**–**	**1** [26]	**1**
Total	**5**	**7**	**4**	**8**	**24**

Study design; location; period of study

[26] Review; N/A; N/A

[29] Time-stratified case-crossover study: Philadelphia (United States); 2011-2014

[30] Review; Asia; last 20 year

[31] Observational study; New York (United States); 24h during a 6-day sampling period)

[32] Epidemiological study; United States; projections for up to 2090

[33] Ex vivo and in vitro assay; N/A

[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

*Indicates statistically significant association.

[a] The category various refers to a combination of the previous allergy disease without specification

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Table 4. Impact of pollutants on allergic pathologies.

Environmental pollutant (exposition factor)	**Impact on allergic pathology (outcome)**				
	Asthma	**Respiratory disease**	**Sensitization**	**Other**	**Total**
Black carbon	–	**1*** [31]	–	–	**1**
Carbon dioxide	–	–	**1** [30]	–	**1**
PM2.5	**2*** [29]	–	–	–	**2**
Tropospheric ozone	**1** [29]	**3*** [34]	–	–	**4**
Various[a]	–	**1** [26]	–	**1** [26]	**2**
Total	**3**	**5**	**1**	**1**	**10**

Study design; location; period of study

[26] Review; N/A; N/A

[29] Time-stratified case-crossover study: Philadelphia (United States); 2011-2014

[30] Review; Asia; last 20 year

[31] Observational study; New York (United States); 24h during a 6-day sampling period)

[34]Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

*Indicates statistically significant association.

[a] The category various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Table 5. Impact of allergen alterations on epidemiology, severity, and healthcare burden of allergic disease.

Allergen alterations (exposition factor)	**Impact (outcome)**					
	Epidemiology	**Prevalence**	**Severity**	**Healthcare burden**	**Other**[a]	**Total**
Allergenicity	**3** [26]	–	**3** [26]	–	**1** [27]	**7**
Change in production (time/quantity)	**3*** [34] **6** [26, 28, 33]	**4** [26, 30, 33]	**3*** [34] **1** [34]	**5** [26, 28, 32]	**1*** [31] **1** [26]	**24**
Epitope modification	–	–	–	–	–	–
Total	**12**	**4**	**7**	**5**	**3**	**31**

Study design; location; period of study

[26] Review; N/A; N/A

[27] Review; North America, Europe and Asia countries; N/A

[28] Epidemiological study; United States; projections for up to 2090

[30] Review; Asia; last 20 year

[31] Observational study; New York (United States); 24h during a 6-day sampling period)

[32] Epidemiological study; United States; projections for up to 2090

[33] Ex vivo and in vitro assay; N/A

[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

*Indicates statistically significant association.

[a]Other (general adverse health effects).

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Table 6. Impact of environmental factors on epidemiology, and burden of allergic pathologies.

Environmental factor (exposition factor)	**Impact (outcome)**			
	Epidemiology	**Healthcare burden**	**Other[c]**	**Total**
Drought	–	**1** [28]	–	**1**
Unspecified weather conditions	**1** [28]	–	–	**1**
Pollutant[a]	**3*** [34] **3** [26]	–	**1*** [31] **1** [27]	**8**
Various[b]	**5** [26]	**4** [26, 32]	–	**9**
Total	**12**	**5**	**2**	**19**

Study design; location; period of study

[26] Review; N/A; N/A

[27] Review; North America, Europe and Asia countries; N/A

[28] Epidemiological study; United States; projections for up to 2090

[31] Observational study; New York (United States); 24h during a 6-day sampling period)

[32] Epidemiological study; United States; projections for up to 2090

[34]Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

*Indicates statistically significant association.

[a]Black carbon, carbon dioxide, PM2.5, tropospheric ozone, various other; [b]Pollen and house dust mite; [c] The category "other" refers to general adverse health effects.

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Table 7. Impact of environmental pollutants on allergic disease epidemiology

Environmental pollutant (exposition factor)	**Impact (outcome)**		
	Epidemiology	**Other[a]**	**Total**
Black carbon	–	**1*** [31]	**1**
Carbon dioxide	**1** [30]	–	**1**
PM2.5	–	**1** [27]	**1**
Tropospheric ozone	**3*** [34]	–	**3**
Various[b]	**2** [26]	–	**2**
Total	**6**	**2**	**8**

Study design; location; period of study

[26] Review; N/A; N/A

[27] Review; North America, Europe and Asia countries; N/A

[30] Review; Asia; last 20 year

[31] Observational study; New York (United States); 24h during a 6-day sampling period)

[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan.-May (pollen season)

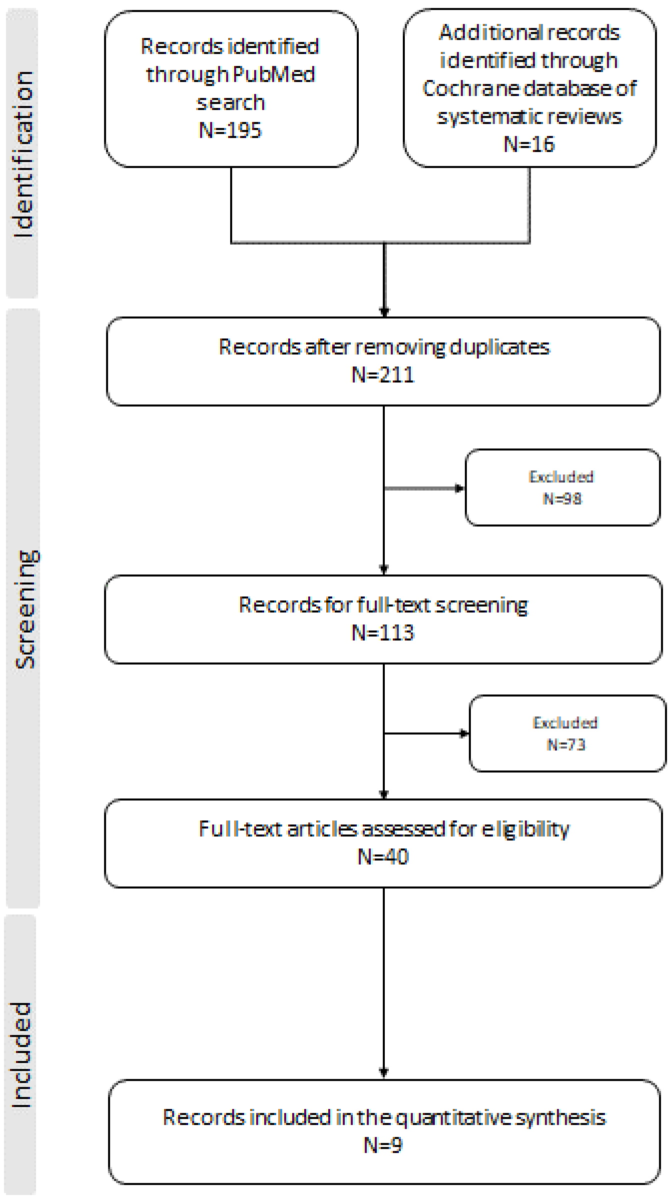
*Indicates statistically significant association.

[a]Pollen and house dust mite; [b] The category "various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

N/A: Not available; Not applicable

doi: 10.18176/jiaci.0988

Figure 1. PRISMA flowcharts for the systematic literature review



doi: 10.18176/jiaci.0988