# Climate Change–Associated Environmental Factors and Pollutants: Impact on Allergic Diseases, Epidemiology, Severity, and Health Care Burden

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## Abstract

*Background:* Allergic diseases affect up to 40% of adults worldwide, a percentage that is increasing with environmental changes related to global warming.

*Methods:* A systematic review of the literature was performed to identify and evaluate current evidence of the effect of climate change– related environmental factors on the prevalence, incidence, and severity of allergic diseases in terms of the impact on patients with allergy. PECO criteria for 2 research questions were established and guided the literature searches of the PubMed and Cochrane databases (January 1, 2016 to December 31, 2021). Study outcomes were categorized and grouped to facilitate data synthesis. Outcomes were classified as significant (*P*<.05), nonsignificant (*P*>.05), or undetermined (*P* value not reported).

*Results:* Assessment of the 2 questions enabled us to identify 609 publications. Of these, 96 were assessed for eligibility and 42 provided data. Environmental factors, including the presence of pollutants, influenced patients' conditions in terms of effects on allergy, exposure to allergen(s), and the immune system. The pollutants most frequently reported to have an impact were nitrogen dioxide (NO<sub>2</sub>) and particles <2.5  $\mu$ m in diameter. The allergic diseases most frequently reported to be affected by environmental factors were respiratory disease (asthma and rhinitis) and atopic dermatitis, with an impact on epidemiology and health care burden.

Conclusion: Environmental pollution increased the frequency and health care burden of allergic diseases. The effect of environmental pollution was predominantly caused by pollutants such as NO<sub>2</sub> and particles <2.5 µm in diameter and was observed across allergic diseases, including respiratory disease (asthma and rhinitis) and atopic dermatitis.

Key words: Environment. Allergy. Patient. Severity. Epidemiology. Climate change.

## Resumen

Antecedentes: Las enfermedades alérgicas afectan hasta al 40% de la población adulta mundial, proporción que está aumentando debido a los cambios ambientales relacionados con el calentamiento global.

*Métodos:* Se realizó una revisión sistemática de la literatura para identificar y evaluar la evidencia actual sobre el impacto de los factores ambientales relacionados con el cambio climático en la prevalencia, incidencia y gravedad de las patologías alérgicas, en cuanto al impacto en los pacientes con alergia. Se establecieron dos preguntas PECO de investigación que guiaron las búsquedas en las bases de datos de

PubMed y Cochrane (1 de enero de 2016 a 31 de diciembre de 2021). Los resultados se categorizaron y agruparon según su significancia (p<0,05), no significancia (p>0,05) o indeterminación (p no reportado).

*Resultados:* En las dos preguntas, se identificaron 609 publicaciones, de las cuales 96 fueron evaluadas para determinar su elegibilidad y 42 proporcionaron datos. Los factores ambientales, incluidos los contaminantes, influyeron en las condiciones de los pacientes en cuanto a los efectos sobre las alergias, la exposición a alérgenos y el sistema inmunológico. Los contaminantes más frecuentemente reportados fueron el dióxido de nitrógeno (NO<sub>2</sub>) y las partículas <2,5 µm de diámetro. Las enfermedades alérgicas más frecuentemente afectadas por factores ambientales fueron las enfermedades respiratorias (asma y rinitis) y la dermatitis atópica, con impacto en la epidemiología y la carga asistencial.

*Conclusión:* La contaminación ambiental aumentó las enfermedades alérgicas en términos de epidemiología y carga asistencial. El efecto de la contaminación ambiental fue causado principalmente por contaminantes, como el NO<sub>2</sub> y las partículas <2,5 µm de diámetro, y se observó en enfermedades alérgicas como enfermedades respiratorias (asma y rinitis) y dermatitis atópica.

Palabras clave: Medio ambiente. Alergia. Paciente. Gravedad. Epidemiología. Cambio climático.

## Introduction

Recent decades have seen a marked increase in the prevalence of allergic diseases, particularly in developed countries [1,2], and these are now estimated to affect up to 40% of the world's population, imposing a substantial health care burden [1,3,4]. It is thought that environmental factors such as industrialization, urbanization, and changing lifestyles have contributed to this increase [2,4-6].

Attempting to determine the effects of environmental factors on allergic diseases is challenging because of the range of diseases and the complex etiological mechanisms driving their prevalence [1,2,7]. While several studies have reported associations between pollen count and allergic diseases (asthma and rhinitis), as well as allergic sensitization [8-14], more conflicting findings have been reported for other environmental factors such as traffic-related air pollution. For example, Schnass et al [15] found an increase in the prevalence of eczema in adults associated with exposure to traffic-related air pollution, although Wang et al [1] reported no such effect. Similarly, conflicting results have been reported for the impact of air pollution (exposure to particles <2.5 µm in diameter) and childhood eczema and allergic rhinitis [16]. Findings such as these provide further support for the idea of a complex interrelationship between environmental factors and the range of allergic diseases.

In recent years, the impact of a variety of climate changerelated environmental factors, such as drought, flooding, and increased temperature, on allergic diseases has received more attention [17,18]. Environmental factors may directly affect allergic disease and indirectly affect local and regional ecosystems that can influence the amount and type of pollen, mold exposure, local air pollution, and heat stress [17-21]. Of critical importance in mitigating the future burden, both in individuals and in health care systems, is an improved understanding of the factors associated with climate change that can influence the prevalence and severity of allergic diseases.

Epidemiological research on air pollution as a potential risk factor for allergic diseases has increased in recent years despite methodological hurdles, including study design, pollutants (types, measurements, and interactions), diagnosis of allergic and nonallergic conditions in the short and long terms, impact on different populations, potential confounding factors, and climatic, geographical, and socioeconomic variables, as well as statistical models. The aim of this systematic review was to identify and evaluate the current evidence regarding the impact of environmental pollution and climate change on the prevalence, incidence, and severity of allergic diseases in terms of the impact on patients with allergy.

# Methods

#### Design

A systematic review of the published literature was performed by 2 independent experts following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, published in 2009 [22]. The entire process, including the initial concept and structure, was supervised and reviewed by the authors of this publication.

#### Search Strategy

Population, Exposure, Comparison, Outcome (PECO) criteria were developed to guide the literature search and review. The research questions to be addressed fell into 2 PECO searches. For PECO 1 the questions were "Do climate change and air quality have a direct and significant impact on the incidence, prevalence, and/or severity of global allergic diseases?", "Do climate change and pollutants modify the expression of the proteins of different allergens, turning them into more aggressive allergens?", and "What is the impact of climate change and air quality specifically on conjunctivitis, asthma, rhinitis, food allergy, and/or atopic dermatitis?" For PECO 2 the questions were "Do pollutants have a direct impact on the inflammatory immune response?", "Does this response depend on factors inherent to the patient (genetic and/or epigenetic factors)?", and "Is this response dependent on external factors (eg, exposure time)?"

The literature searches were conducted in the PubMed and Cochrane databases of systematic reviews for the period January 1, 2016 to December 31, 2021 and were restricted to publications in English or Spanish for which abstracts were available. Data were collected from publications over a 5-year period because of the extensive quantity of literature published on the subject in recent years. Search terms for PECO 1 and PECO 2 are defined in Supplementary Table 1.

#### Inclusion Criteria and Screening Process

All types of original studies (randomized clinical trials [RCTs], nonrandomized trials, post hoc analyses of RCTs, and observational studies) and systematic reviews (with or without meta-analyses) were included. 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 the incidence, prevalence, or severity of allergic diseases or on the expression of proteins in the genes of allergens that intensifies their action (PECO 1) (Supplementary Table 1). Similarly, studies were included if they presented quantitative data related to changes in the immune response/inflammatory mediators (PECO 2) (Supplementary Table 1).

Publications in languages other than English or Spanish were excluded. Publications without an abstract and unpublished studies were also excluded. The full texts of all the studies fulfilling the selection criteria were retrieved. The titles and abstracts of all identified studies were independently screened for relevance by 2 reviewers qualified in biology and chemistry (Gloria González and Sara García from Adelphi Targis), and duplicates were removed. The full text of potential studies for inclusion was then evaluated for relevance to the PECO questions. Disagreements in study selection between the 2 lead reviewers were resolved by a third reviewer. An additional reviewer (Maite Artés from Adelphi Targis) doublechecked the selection criteria of a random sample of 15% of the records.

#### Data Synthesis

No search software was used, and studies were extracted directly from databases to Mendeley and to an .XML file. The characteristics of the studies were collected in order to identify information sources and possible confounding factors. Reporting of the data obtained from the publications was heterogeneous. Coding was applied in order to homogenize the items and outcomes for PECO 1. Given the marked heterogeneity in the type of outcomes found for PECO 1 and PECO 2, results could only be combined by counting the statistically significant results (P<.05) and the nonsignificant results (P<.05). In publications with no direct comparison, when a P value was not provided or when data were descriptive, results were counted as undetermined.

Table 1. Environmental Factors Causing Alterations in Patients Conditions.				
	Impact on the patient's condition (outcome)			
Environmental factor (exposure factor)	Effect on allergy	Exposure to allergen	Effect on immune system	Total
Droughts	7 [25]	_	-	7
Earlier onset of flowering	12ª [26] 3 [26]	-	-	15
Floods/humidity	6ª [27]	_	-	6
Heat waves	3ª [26,28] 2 [28]	-	-	5
Humidex (temperature and humidity)	21ª [29]	_	-	21
Pollutant (CO <sub>2</sub> , etc.)	151ª [30-54] 31 [36,48-50,54-56]	6ª [43,57] 1 [57]	5ª [32,33] 3 [49]	197
Precipitation	4ª [46,52]	_	-	4
Seasonal changes	2ª [45]	-	-	2
Storms	1 [27]	-	-	1
Temperature	8ª [43,45,46,52]	-	-	8
Wildfire	25ª [36] 2 [58]	-	-	27
Various	17ª [36,52] 5 [59,60]	-	-	22
Other <sup>b</sup>	6 [61]	_	4ª [62] 2 [62]	12
Total	306	7	14	327

alndicates a statistically significant association.

<sup>b</sup>"Other" includes agents such as bioaerosols, the PAR2 agonist SLIGKV-NH2, trypsins, lipopolysaccharides, and agents used in the seafood industry.



Figure. PRISMA flowchart for PECO 1 and PECO 2.

#### Quality Assessment

Study quality was assessed using the Mixed Methods Appraisal Tool (MMAT) [23]. This tool enables evaluation of the quality of qualitative, quantitative, and mixed methods studies, focusing on methodological criteria.

# Results

For the research questions in PECO 1, a total of 211 studies were identified and reviewed; of these, 40 were considered initially eligible, and, following full-text assessment, 35 articles provided relevant quantitative data and were included in the quantitative synthesis (Figure). Of the 35 reports, 30 had an MMAT score  $\geq 60\%$ . For the PECO 2 research questions, 398 articles were identified and reviewed; of these, 56 were considered initially eligible and 7 provided quantitative data and were included in the quantitative synthesis following fulltext assessment (Figure). Of these 7 reports, 5 had an MMAT score  $\geq 60\%$ .

Of all the publications addressing PECO 1 and PECO 2, 9 reported data on the influence of environmental factors on allergens and allergic diseases, and a total of 37 examined the impact of various environmental factors on patients' conditions. The former results were recently published [24], while the latter are analyzed in the present article. For both PECO 1 and PECO 2, the lists of publications that were included or excluded, together with the justification for this, are provided in Supplementary Tables 2 and 3, respectively.

### Impact of Environmental Factors on Patients' Conditions

A total of 37 publications included in this systematic review examined the impact of different environmental factors on patients' conditions, with 35 addressing one research question and 7 addressing another. The total number of publications was 37 because some studies contributed to both research questions (Figure) (Table 1). Among these 37 publications, a total of 327 study outcomes referred to environmental factors having an impact on patients' conditions in terms of an effect on allergy, exposure to allergens, or effect on the immune system (Table 1). Of these, a total of 197 outcomes, of which 162 were considered statistically significant, were from 27 publications that reported the impact of pollutants on patients' conditions (Table 1). The second most frequently reported environmental factor to impact patients' conditions was wildfire, which was mentioned in 27 study outcomes, 25 of which were statistically significant, from 1 publication (Table 1). In 306 of the 327 reported outcomes of environmental factors impacting patients' conditions, the impact was via an effect on allergy (Table 1).

## Pollutant-Induced Changes in Allergy and Immune Response

Evaluation of the publications that examined the impact of pollutants on patients' conditions found that out of the 197 outcomes that reported pollutants having an impact on patients' conditions, 54 referred to environmental allergen pollutants (including grass and tree pollen data, pollen count, and air quality [pollutants] index), 29 to nitrogen dioxide (of which 22 were reported with statistical significance from 10 publications), and 29 to particles <2.5  $\mu$ m in diameter (PM2.5; 18 were statistically significant from 10 publications) (Table 2). Out of the 197 outcomes, an effect on allergy was reported in 182 outcomes, 7 were related to exposure to the allergen and 8 were an effect on the immune system (Table 2).

Table 2. Pollutant-Induced Changes in A	llergy and Immune Response.			
	Impact on the patient's condition (outcome)			
Environmental pollutant (exposure factor)	Effect on allergy	Exposure to allergen	Effect on immune system	Total
5VOCs	1ª [39]	-	-	1
Air emissions from animals	1ª [42]	-	-	1
Benzene	1ª [39]	-	-	1
Black carbon	3ª [38]	-	-	3
Carbon dioxide	1ª [31] 1 [56]	-	_	2
Carbon monoxide	5ª [41,44,50] 1 [54]	-	-	6
Diesel exhaust particles/traffic-related	2ª [48] 1 [48]	-	-	3
Ethylbenzene	1 [39]	-	-	1
Formaldehyde	1 [39]	_	_	1
Methane	1 [47]	-	-	1
Nitrogen dioxide	22ª [30,31,41,44,46,51-54] 7 [54,55]	-	-	29
Nonmethane hydrocarbon	2ª [47]	-	-	2
PM10	17ª [32,40,41,43,44,46,50,51,54] 7 [54,55]	1ª [57] 1 [57]	2a [32]	28
PM2.5	15ª [31,34,35,37,40,41,48,52] 8 [49,54,55]	3ª [43,57]	3 [49]	29
Polycyclic aromatic hydrocarbons	2ª [50]	-	-	2
Smoke	9ª [34,36] 2 [36]	-	-	9
Sulphur dioxide	1ª [44] 1 [54]	-	-	2
Toluene	1ª [39]	-	-	1
Total hydrocarbon	2ª [47]	-	-	2
Tropospheric ozone	17ª [31,35,41,44,46,51,54]	-	-	17
TVOCs	1ª [39]	-	-	1
Xylene	1ª [39]	-	-	1
Environmental allergens <sup>b</sup>	46ª [29,33,34,43,46,50,51] 3 [48,49]	1ª [43] 1 [50]	3ª [33]	54
Total	182	7	8	197

Abbreviations: PM, particulate matter; 5VOC, 5 volatile organic compounds; TVOC, total volatile organic compounds.

<sup>a</sup>Indicates a statistically significant association.

<sup>b</sup>" Environmental allergens" includes data on grass and tree pollen (oak and birch), pollen count (general), and air quality index (pollutants).

Table 3. Environmental Impact on Different Types of Allergic Diseases.				
	Impact on allergic diseases			
Disease	Epidemiology	Exacerbation	Healthcare burden	Total
Allergy	3ª [48,61] 2 [48]	_	_	5
Asthma	7ª [35,42,48] 19 [48,55,58]	3ª [35]	69ª [26,29,31,36,37,47] 12 [26,28,36,60]	110
Atopic dermatitis	17ª [27,34,39,44,46]	5ª [44]	6ª [27,34] 1 [27]	29
Conjunctivitis	-	-	3ª [30]	3
Coughing	3ª [50]	_	-	3
Itching	-	-	3ª [34]	3
Respiratory diseases (various) <sup>b</sup>	45ª [33,38,43,49,51,61] 5 [25,56,59]	1ª [53]	66ª [36,40,41,47,54] 8 [36,54,59]	125
Rhinitis	8ª [39,43,50] 1 [50]	-	19ª [52]	28
Sensitization	1 [56]	_		1
Wheezing	1 [48]	-	-	1
Total	112	9	187	308

alndicates a statistically significant association.

<sup>b</sup>These data refer to respiratory diseases (general), allergic conditions (general), or the combination of allergic rhinitis, asthma, and atopic dermatitis.

Table 4. Environmental Factors Affecting Allergic Diseases.					
	Impact on allergic diseases				
Environmental factors (exposure factor)	Epidemiology	Exacerbation	Healthcare burden	Various	Total
Droughts	2 [25]	_	1 [25]	4 [25]	7
Earlier onset of flowering	-	-	12ª [26] 3 [26]	-	15
Floods/humidity	4ª [27]	_	2ª [27]	-	6
Heat waves	2ª [28]	-	1ª [26] 2 [28]	-	5
Humidex (temperature and humidity)	_	_		-	21
Other	10ª [61,62] 1 [56]	2 [62]	-	-	13
Pollutant (CO <sub>2</sub> , etc.)	71ª [32,33,37-39,42, 43,46,48,50,56,57] 28 [48-50,55-57]	9ª [34,35,44]	82ª [30,31,34,36,37, 40,41,45,47,52,54] 7 [36,54]	_	197
Precipitation	1ª [46]	-	3ª [52]	-	4
Seasonal changes	-	_	2ª [45]	_	2
Storms	-	-	1 [27]	_	1
Temperature	2ª [43,46]	_	6ª [29,52]	-	8
Environmental allergens <sup>b</sup>	2 [59]	-	17ª [36,52] 8 [59,60]	-	27
Wildfire	2 [58]	_	25ª [36]	_	27
Total	125	11	193	4	333

<sup>a</sup>Indicates a statistically significant association.

b" Environmental allergens" includes data on grass and tree pollen (oak and birch), pollen count (general), and air quality index (pollutants).

For outcomes involving the immune system, the effects included secretion of interleukin (IL) 8, activation of nuclear factor  $\kappa$ B (NF- $\kappa$ B), increase in transforming growth factor  $\beta$ 1 (TGF- $\beta$ 1) and hydroxyproline in sputum, decrease in neutrophils, and increase in monocytes and C-reactive protein (CRP).

### Environmental Impact on Allergic Diseases

A total of 35 publications reported a total of 308 study outcomes regarding the impact of environmental factors on allergic diseases (Table 3). Of these, most reported the environmental effect on various respiratory diseases (125 outcomes), followed by asthma (110 outcomes), atopic dermatitis (29 outcomes), and rhinitis (28 outcomes) (Table 3). The environmental impact on allergic diseases was related to health care burden (187 outcomes), followed by epidemiology (including severity, incidence, and prevalence) (112 outcomes) and exacerbation (9 outcomes) (Table 3). Among the 333 outcomes that were reported on the environmental factors affecting allergic diseases, most (197 outcomes) were related to the effect of environmental allergens (pollutants) (Table 4).

## Discussion

Our systematic review of the literature was conducted to assess the current scientific evidence on how climate changerelated environmental factors influence allergic disease and affect patients' health conditions. This analysis supports a negative impact of environmental factors, including those driven by global climate change, on patients' health in terms of effects on allergic conditions such as respiratory disease (asthma and rhinitis) and atopic dermatitis.

Overall, 35 publications provided relevant quantitative data and indicated that environmental factors had a negative impact on patients' conditions in terms of allergy, exposure to allergen(s), and the immune system, including secretion of IL-8 and activation of NF-kB, higher TGF-B1 and hydroxyproline in sputum, decreased neutrophils, and increased monocytes and CRP. Across the range of environmental factors, including droughts, floods, heat waves, temperature, humidity, earlier onset of flowering, wildfires, and pollutants, which were reported to impact on the patients' allergic conditions, pollutants were the most frequent topic of the publication. Further analysis of the publications that examined the impact of different pollutants on patients' conditions found that nitrogen dioxide, PM2.5, particles <10 µm in diameter (PM10), and tropospheric ozone were the most frequently reported. Moreover, nonanthropogenic pollutants such as desert sand dust have been shown to exacerbate respiratory and allergic conditions, particularly during dust storms. These particles may trigger inflammatory responses and activate immune pathways involving cytokines and immune cells [63].

Across all the publications that evaluated the impact of environmental factors on allergic diseases/conditions, most of the outcomes measured involved respiratory diseases (asthma and rhinitis) and atopic dermatitis. And within this dataset, pollutants were the main environmental factor that impacted the epidemiology (severity, incidence, and prevalence) of allergic diseases and health care burden.

These findings align with those of other publications reporting that climate change-related environmental factors increased the incidence of allergic diseases owing to increases in allergen exposure (volume and type), with the presence of pollutants such as ozone being the most commonly reported driver of such increases [24,64]. Furthermore, the changes in allergen exposure (in terms of quantity and/or type) have been reported to have an impact both on the allergic sensitization process itself and on allergic diseases, which include respiratory diseases (eg, asthma), increasing the prevalence and/or severity of allergic diseases and the associated health care burden [24]. In addition, the elevated allergen burden can alter the human exposome (ie, the cumulative environmental exposures encountered by an individual in a lifetime) and result in immune dysregulation [64]. These circumstances are potentially worsened by the combined exposure of an individual to an allergen and to an air pollutant, which can make sensitization to the allergen and onset of an allergic condition more likely [65]. This increased likelihood of sensitization to an allergen in the presence of an air pollutant indicates that the pollutant is acting as an adjuvant in the sensitization process [65]. The role of air pollutants as adjuvants is supported by a recent study indicating that exposure to PM levels below the current recommendations can have serious adverse effects for individuals with allergic respiratory diseases such as asthma and thus heighten the risk for potentially fatal exacerbations [66]. While the pathophysiological pathways through which air pollution affects rhinitis may diverge from those that affect asthma, Rosario et al [67] reported on the interplay between climate change and air pollution in patients with rhinitis and the way in which air pollution acts as an adjuvant, augmenting responses to inhaled allergens, inducing mucosal inflammation, and aggravating symptoms of rhinitis.

The environmental impact of pressurized metered-dose inhalers (pMDIs), commonly prescribed in respiratory diseases, is often discussed owing to the potential offset of their health benefits by their indirect global effects associated with propellant use. However, our prior research highlighted that pMDI usage contributes to approximately 0.0909% of Spain's total emissions. Moreover, transitioning from pMDIs to dry powder inhalers, excluding emergency use, could reduce  $CO_2$  emissions to 0.0579% of Spain's overall emissions [68]. Nonetheless, clinical considerations should remain the priority when selecting inhalers, and further research is needed to assess the impact on asthma control and patient outcomes [24].

A key strength of this systematic review was the inclusion of well-defined PECO questions to help guide the literature search, the subsequent data extraction, and the analysis, together with the evaluation of the quality of the articles included using MMAT criteria (85% of the articles included in the quantitative data analysis had an MMAT value above 60%). In addition, the results of the analysis can be generalized, as there were no exclusion criteria according to geographical area or the methodological approaches used, and all environmental pollutants and diseases were considered. While the heterogeneous study design precluded formal statistical analyses or pooling of the reported results,

<b>Table 5.</b> Strategies to Minimize the Impact of Climate Change and Its Associated Factors on Allergic Diseases from Different Perspectives [64,68,74-78]				
Roles	Strategies			
Government authorities	<ul> <li>Implement policies to reduce emissions from fossil fuels and greenhouse gases.</li> <li>Provide the general population with accurate, up-to-date, and free information on air quality (pollutants, allergens), weather forecasts (storms, heatwaves, floods, sandstorms), and wind direction during wildfires or natural disasters (volcanic eruptions).</li> <li>Promote the use of public transportation powered by renewable energy sources.</li> </ul>			
Patients	<ul> <li>Stay informed daily about air quality.</li> <li>Avoid outdoor exposure and/or physical exercise on days with high pollen concentrations (especially for pollen-allergic individuals and if heavy rainstorms are forecasted) and/or pollution. In the case of pollution, use clean alternative routes.</li> <li>Avoid outdoor exposure during heatwaves and sandstorms.</li> <li>Ventilate home spaces for at least 10 min daily if outdoor air quality is favorable.</li> <li>Minimize/avoid indoor pollutants, such as tobacco, coal, fuel, or wood-based cooking/heating, as well as candles, incense, essential oils, or cleaning products with high concentrations of volatile organic compounds.</li> <li>Adhere to prescribed treatments for respiratory allergies to maintain asthma control, minimizing or eliminating the need for rescue medications with pressurized inhalers.</li> <li>Use allergy symptom diaries to adjust treatments and plan outdoor activities in conjunction with air quality information.</li> </ul>			
Health care professionals	<ul> <li>As trusted sources of scientific knowledge, educate patients about the impact of climate change on health.</li> <li>Ensure proper management of patients' allergic conditions (particularly bronchial asthma) to minimize the use of rescue pressurized metered-dose inhalers.</li> <li>Whenever clinically feasible, prescribe dry powder inhalers because of their lower carbon footprint.</li> <li>Raise awareness of the importance of recycling inhalers (all types) once they are empty and ensuring their proper disposal at collection points (eg, SIGRE points in Spanish pharmacies).</li> <li>Use telemedicine whenever possible to avoid unnecessary patient trips to health care facilities.</li> </ul>			

it did not compromise the external validity of the review. Our findings are potentially limited in terms of language bias, as only publications in English and Spanish were included and the search was conducted solely in the PubMed and Cochrane databases for the 5 years up to and including 2021. This approach could limit representation of non-Western studies in our review, where pollutant effects in large and industrialized countries are likely different and potentially more pronounced. That said, only 1 publication was ruled out for language reasons, although this limit on eligible literature was not thought to compromise the validity or generalizability of the analysis presented. Selection bias was possible, as results that were not statistically significant might not have been published. Unpublished studies have not been included, nor have studies where an abstract was unavailable. Additionally, the heterogeneity in outcome measures across the studies included posed a limitation, as it prevented consistent quantification of effect sizes and prevalence rates. As a result, our analysis focused on identifying whether an impact was observed, rather than its precise magnitude, which may limit the ability to draw detailed quantitative conclusions.

From a practical perspective, the most effective strategies for minimizing the impact of climate change on allergic diseases are outlined in Table 5.

# Conclusion

Climate change-related environmental factors, including droughts, floods, heat waves, temperature fluctuations, humidity, earlier onset of flowering, wildfires, and pollutants, significantly impact patients' health, particularly in relation to allergic diseases such as respiratory conditions (asthma and rhinitis) and atopic dermatitis. Among these factors, pollutants were the most frequently discussed in the literature.

Further analysis of studies that examined the impact of different pollutants on patients' conditions identified nitrogen dioxide, PM2.5, PM10, and tropospheric ozone as the most frequently reported pollutants. These environmental air pollutants can act as adjuvants in the presence of allergens, increasing the likelihood of sensitization and exacerbating disease burden.

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Izquierdo-Domínguez A. Speaker: GlaxoSmithKline, AstraZeneca, Viatris, Sanofi, Loafarma, Novartis, Menarini, Organon, Uriach, Inmunotek, Leti Pharma, and Diater.

Zapata JJ. Grants: SEAIC, Diater, GSK, Leti Pharma, Chiesi, and Allergy Therapeutics.

García-Gallardo MV. Consulting fees: AstraZeneca, GSK, and Sanofi. Speaker: AstraZeneca, GSK, Sanofi, Chiesi, and Gebro. Expert testimony: AstraZeneca, GSK, and Sanofi. Support for attending meetings: AstraZeneca, GSK, and Sanofi. Advisory boards: AstraZeneca, GSK, and Sanofi.

González R. Consulting fees: GSK, Sanofi, and AstraZeneca. Speaker: GSK, Inmunotek, Leo Pharma, and Roxall Medicine. Expert testimony: GSK and AstraZeneca. Attendance at meetings: GSK, Leti Pharma.

Fernández MM. Speaker: GSK, AstraZeneca, Sanofi, and ALK-Abelló.

#### Conflicts of Interest

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