

Review

Exposome and Respiratory Allergic Diseases: A Structured Narrative Review

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Abstract

Background: Allergic respiratory diseases, primarily asthma and allergic rhinitis, affect hundreds of millions worldwide. Their rising prevalence reflects complex gene–environment interactions that the exposome framework organizes into external, internal, and social domains shaping the development and progression of respiratory allergic diseases. **Methods:** Narrative review based on structured searches in PubMed/MEDLINE and Scopus (2015–2025), supplemented with 11 key references; 42 publications were selected from 1015 records. **Results:** Air pollution showed consistent but modest associations with asthma (HR 1.04–1.12); household dampness and mold showed larger effect sizes on symptom severity (OR 1.48–1.52); and occupational exposures showed the largest effect sizes across studies (RR 3.2–4.3). Systemic inflammation, oxidative stress, and nasal microbiome alterations were identified as internal mediators linking exposures to allergic phenotypes, though mechanistic pathways remain incompletely defined. Social exposome studies suggested context-dependent patterns: socioeconomic advantage correlated with greater sensitization in some settings, while deprivation could amplify disease progression and mortality risk (HR 1.18–1.32). **Conclusions:** The exposome offers a valuable integrative framework, but clinical translation is limited by scarce longitudinal multi-exposure studies and underrepresentation of low- and middle-income regions. Priorities include life-course cohorts integrating all three domains and targeted interventions in housing and occupational settings.

Keywords: exposome; allergic asthma; allergic rhinitis; air pollution; environmental determinants; public health

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1. Introduction

The global burden of respiratory allergies, particularly allergic rhinitis and asthma, has grown substantially in recent decades, with prevalence estimates exceeding 30% in several regions and projections suggesting that up to 50% of the global population could be affected within the next 20–25 years [1]. This translates into an estimated 400 million people worldwide suffering from allergic rhinitis and 300 million from allergic asthma.

These numbers are projected to continue rising in coming years, negatively impacting economies and quality of life [2].

This rise cannot be explained by a single factor. Rather, it reflects complex interactions between genetic predisposition and environmental changes, potentially shaped by increasing urbanization and population growth, which drive shifts in lifestyle (diet, indoor time, physical activity) and in key exposures such as air pollution, tobacco smoke, mold, and infections, all of which affect allergic mechanisms and contribute to rising prevalence and exacerbations [3].

The exposome concept, proposed by Wild in 2005, provides a comprehensive framework for understanding respiratory allergies by encompassing all exposures an individual encounters across the life course, from conception to death [4]. This framework integrates three interconnected domains: the external exposome (air pollution, occupational exposures, diet, infections), the internal exposome (metabolism, inflammatory responses, oxidative stress, microbiome), and the social exposome (socioeconomic position, housing characteristics, psychosocial stressors) [5]. However, despite its conceptual promise, comprehensive measurement and longitudinal integration of these exposures remains methodologically challenging, with current studies capturing only selected components [6]. Whether environmental exposures act independently or synergistically remains debated, and evidence on the relative weight of each domain is still inconsistent across populations. This review examines how these domains influence allergic respiratory diseases, finding that high-intensity exposures such as occupational allergens and damp indoor environments carry the greatest risk, and that social and biological factors shape both disease onset and progression in ways that current research has only begun to capture.

2. Materials and Methods

This structured narrative review used rigorous search and selection methods to minimize bias, following recommended practices as outlined by the SANRA criteria [7]. Formal methodological quality assessment is not a standard requirement for narrative reviews; however, we addressed the strength and limitations of the available evidence by explicitly discussing study designs, potential sources of bias, and methodological constraints within each exposome domain throughout the text. Although this review employed structured search and screening procedures to enhance reproducibility, it does not constitute a systematic review; conclusions are based on narrative synthesis, and formal quantitative pooling of results was not performed.

A structured search of PubMed/MEDLINE and Scopus identified 1015 articles published between January 2015 and December 2025. PubMed/MEDLINE was chosen as the primary database because of its extensive coverage of biomedical and clinical literature and its recognized standing as a key resource in health sciences research. Scopus was included to complement this search, given its broader multidisciplinary scope and wider journal coverage. The complete search strings, including MeSH terms and Boolean operators used in each database, are presented in Figure 1.

We supplemented the structured search with 11 key references published between 2001 and 2019, identified through manual searching of reference lists and expert knowledge of foundational exposome literature. These were included on the basis of their conceptual and methodological contribution to the exposome framework, a standard practice in narrative reviews addressing theoretical constructs that predate the search window. Figure 1 presents the complete study selection process. Given the heterogeneity of included study designs, outcomes, and populations, comparisons of effect sizes across exposome domains are intended as descriptive observations to inform research priorities, not as formal quantitative rankings.

Artificial intelligence tools were not used at any stage of the literature search, study selection, data extraction, or evidence synthesis. Claude Sonnet 4.6 (Anthropic) was used solely to support language style editing and English translation of content drafted by the authors. ChatGPT (GPT-5.5; OpenAI) was used to assist in the creation of Figure 2. All AI-assisted content was reviewed and approved by the author team

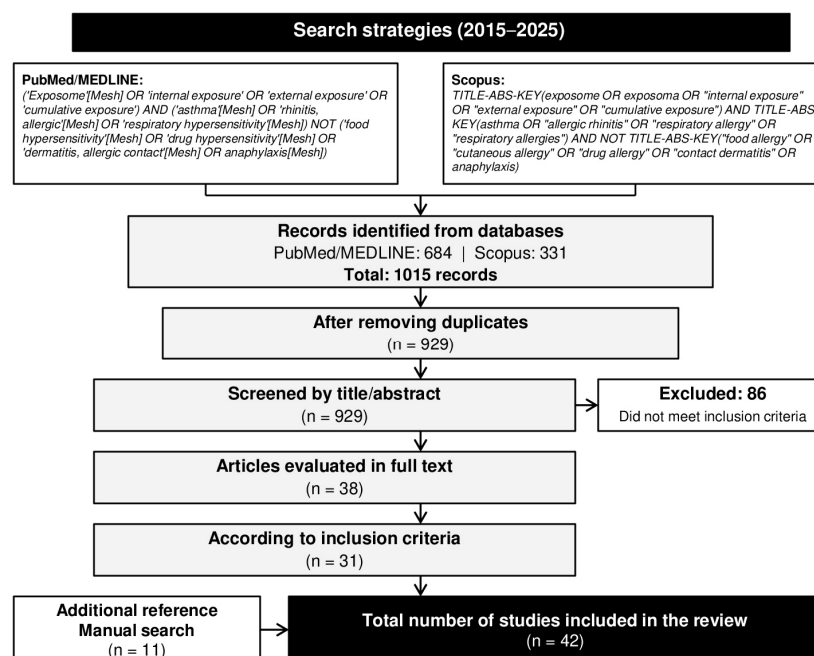


Figure 1. Flow chart of study selection for narrative review on exposome and respiratory allergic diseases.

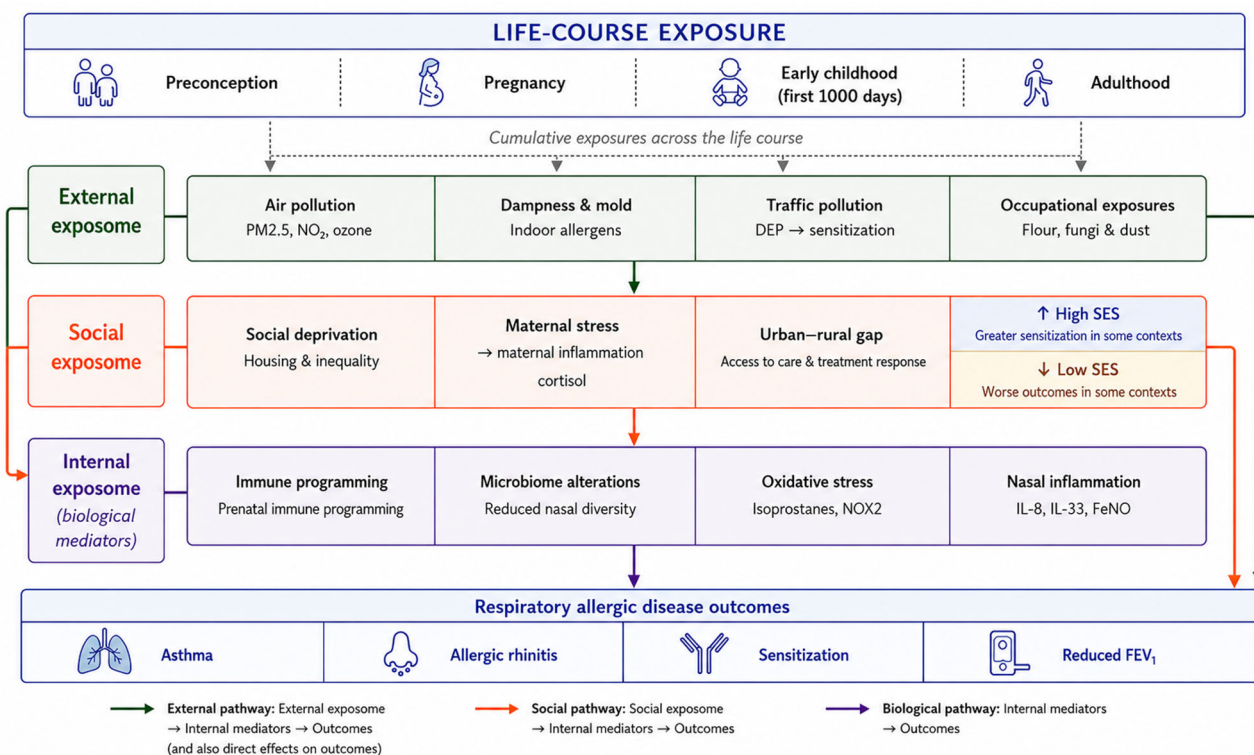


Figure 2. Integrative exposome framework for respiratory allergic diseases across the life course.

Eligibility Criteria and Study Selection

To address the review objective of analyzing how the external, internal, and social exposome domains influence the development and progression of respiratory allergic diseases, the following eligibility criteria were applied. We included studies with human populations of all ages, using observational or experimental designs, with outcomes related to allergic respiratory diseases, including asthma incidence or exacerbation, allergic rhinitis, aeroallergen sensitization, and lung function. The search encompassed publications in English, Spanish, and Portuguese to minimize language bias; however, all studies meeting eligibility criteria were ultimately in English. We excluded case reports, editorials, comments, letters to the editor, literature reviews, exclusively in vitro or animal studies, purely genetic research without environmental factors, and studies on cutaneous or food allergies without respiratory data. Two reviewers independently evaluated 929 records using Rayyan, followed by full-text review and consensus resolution of discrepancies. We included 31 studies from the structured search conducted as part of this narrative review, plus 11 key references, totaling 42 publications. Data extraction was performed by one reviewer and verified by a second, covering study design, country, population characteristics, exposure type, outcomes, and main effect estimates.

3. External Exposome and Allergic Respiratory Diseases

3.1. Air Pollution

Literature consistently shows that air pollution associates with incidence and exacerbation of allergic respiratory diseases, though with generally modest effect sizes (HR 1.04–1.12) [8]. This consistency has been observed across European and Asian cohorts; however, available evidence concentrates in contexts with relatively controlled pollution levels, limiting extrapolation to regions with more intense exposures.

The Cincinnati Childhood Allergy and Air Pollution Study showed that early-life diesel exhaust particle exposure significantly associated with increased risk of aeroallergen sensitization (OR: 1.40; 95% CI: 1.10–1.78 at age 2) [9]. When considering the life course, studies suggest relevant differences by exposure age, with early childhood exhibiting clearer effects on sensitization, while adults predominantly show low-magnitude cumulative associations. This variation in effect magnitude by age suggests the existence of specific windows of immunological susceptibility that remain incompletely characterized.

Acute effects of air pollution on allergic respiratory diseases have been documented in time-series studies. A study in Nanjing showed that daily increases in PM₁₀ and PM_{2.5} associated with 5.86% and 5.39% increases in allergic rhinitis medical visits, respectively [10]. Beyond particulates, tropospheric ozone showed distinctive effects on quality of life in established asthma patients (OR: 1.85, 95% CI: 1.32–2.59), probably through direct epithelial damage [11]. The French EGEA study, employing Bayesian regression with 53 simultaneous environmental factors, identified vehicular proximity as one component associated with reduced lung function (FEV₁ 79% predicted) [12].

Experimental evidence on indoor air pollution interventions remains limited but promising. A randomized controlled trial in South Korea demonstrated that HEPA purifiers reduced indoor PM_{2.5} by 51.8% and significantly improved patient symptoms (mean difference: −2.8 points, 95% CI: −4.1 to −1.5). However, with only 44 participants and a 6-week follow-up, critical questions remain unanswered: whether benefits persist with prolonged use, economic viability in low-income populations, and generalizability across different contexts [13]. Until larger studies evaluate real-world sustainability, public health recommendations cannot be firmly established. Conversely, outdoor air pollution modulates allergic responses through multiple mechanisms. A Belgian case-crossover study documented that tropospheric ozone markedly amplified severe pollen allergy symptoms, surpassing birch pollen effects alone, with both PM₁₀ and O₃ acting as effect modifiers during pollen season [14]. Collectively, these findings confirm a consistent but modest

role of air pollution in allergic respiratory diseases, with evidence concentrated in settings of regulated exposure. This limits extrapolation to high-pollution regions where the burden is likely greatest, and where intervention studies, including scalable alternatives to HEPA purifiers, remain urgently needed.

3.2. Environmental Allergens

Indoor allergens exhibit notably stronger associations than atmospheric pollutants. Dampness and mold showed robust effects (OR 1.48–1.52), substantially exceeding those of air pollutants, with associations remaining consistent across repeated surveys in 2010 and 2019 [15,16]. A natural experiment during COVID-19 lockdown in Turkey illustrated this indoor allergen burden: 75 days of home confinement significantly worsened nasal symptoms in asthmatic children sensitized to mites (score from 3.2 ± 1.8 to 5.7 ± 2.1 , $p < 0.001$) [17].

Molecular allergen profiling has identified specific mite components like Der p 21, Der p 5, and Der p 7 in subtropical climates [18], with predictive models developed based on aeroallergen sensitization patterns; however, their limited discriminative capacity and lack of independent validation currently preclude clinical application [19]. Fungal allergen sensitization (*Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus fumigatus*) associated with higher specific IgE levels and exhaled nitric oxide fraction, indicating greater eosinophilic inflammation [20].

Outdoor allergens exhibit predictable seasonal patterns. The Spanish LANDSCAPE study showed pollen exposure associated with FEV₁ decrease (difference: −4.2%, 95% CI: −6.1 to −2.3) and elevated exhaled nitric oxide during versus outside season [21]. A multi-center European study validated these findings, documenting significant correlations between pollen concentration and symptoms ($r = 0.55$ – 0.78 for birch; $r = 0.48$ – 0.79 for grasses). However, symptoms persisted outside pollen season in one-third of asthmatics (33%) and nearly half of rhinitis patients (41.8%), suggesting that pollen exposure triggers sustained airway inflammation beyond the exposure period [22]. Regional variability was substantial: pediatric studies in Croatia and Korea revealed dust mites representing 20.2% of sensitization in Croatia, while *Dermatophagoides* and Japanese cedar pollen predominated in Jeju, Korea [23,24]. Together, these findings highlight that indoor allergens, particularly dampness, mold, and mites, carry greater and more consistent risk than outdoor pollutants, though regional allergen profiles vary substantially, limiting the generalizability of sensitization data across geographic contexts.

3.3. Occupational Environment and Housing Characteristics

A prospective cohort of baker apprentices in Alberta found flour allergen sensitization reached 21% at 3 years, with high exposures tripling risk (RR: 3.2, 95% CI: 1.8–5.7) [25]. Among Egyptian agricultural workers, exposure to insecticide aerosols, pollens, and fungal allergens quadrupled work-related asthma odds (OR: 4.3, 95% CI: 2.1–8.8) [26]. A Finnish study of 16,000 adults found occupational exposures to vapors, gases, dusts, and fumes more frequent in patients with respiratory disease worsened by non-steroidal anti-inflammatory drugs than controls (45.7% vs. 38.8%, $p = 0.007$) [27]. Occupational studies consistently reported larger effect sizes than those observed for ambient pollution or domestic allergens, which may reflect higher exposure intensity, more susceptible populations, or differences in study design and outcome definition. These figures come from heterogeneous designs and should be read as descriptive observations rather than a formal quantitative ranking. Critically, occupational evidence comes almost exclusively from countries with surveillance systems. In informal work settings common in Latin America, Africa, and Asia, where agricultural and construction workers lack basic respiratory pro-

tection, the true problem magnitude remains unknown. This knowledge gap reflects a justice gap: the most exposed populations are the least studied and protected.

Beyond occupational settings, built environment characteristics act as structural determinants that concentrate multiple simultaneous exposures. Chinese multicenter studies identified poor ventilation, construction materials, and heating systems as modifiable risk factors with stronger associations in children spending significant time indoors [15,16]. The EXPANSE project integrated variables like population density, vegetation coverage, green space access, and air pollution, demonstrating how urban design generates distinct exposure patterns between neighborhoods [8].

These findings collectively suggest that risk appears to increase with exposure intensity and proximity, with occupational settings and damp indoor environments showing greater and more consistent effect sizes than ambient pollution in the available studies. Interventions targeting specific workplaces and housing conditions may therefore be more effective than broad environmental policies alone, though evidence remains concentrated in Europe and Asia, limiting conclusions for settings where informal labor and sub-standard housing are most prevalent. A summary of the main studies on external exposure components is provided in Table A1 (Appendix A).

4. Internal Exposome and Susceptibility to Allergic Respiratory Disease

4.1. Systemic Inflammation and Oxidative Stress

Internal exposome components act as biological bridges connecting external exposures with allergic responses. A Taiwanese national cohort with 84,551 mother–child pairs followed for 9 years demonstrated that maternal periodontal disease during pregnancy increased offspring risk of allergic rhinitis (HR: 1.17, 95% CI: 1.10–1.24), allergic conjunctivitis (HR: 1.27, 95% CI: 1.18–1.37), and eczema (HR: 1.14, 95% CI: 1.08–1.20). Periodontitis-induced inflammation crosses the placental barrier, potentially affecting how the fetus develops immunity [28].

This inflammatory pathway extends to psychological stress. A cohort of 3160 mother–child pairs showed that maternal anxiety during pregnancy was associated with higher childhood allergy risk, with severe anxiety yielding higher odds (OR: 1.82, 95% CI: 1.34–2.47), likely through elevated cortisol and inflammatory responses [29]. Machine learning analyses in 1151 dyads identified maternal inflammatory markers and infant markers as potential links between early exposures and allergic disease [30]. However, differences between studies limit firm conclusions. The Taiwanese study used a large national cohort followed for 9 years [28], while the anxiety study used a smaller regional sample with self-reported data [29]. No study measured the same markers at the same pregnancy stages, making it unclear whether differences reflect true biological variation or study design differences.

Cellular-level evidence reveals broader immune changes, though from studies with important limitations. Allergic asthmatics showed altered immune cell receptors indicating systemic immune imbalance (IL-17RB, ST2, TSLPR) [31], and a Polish study found no significant differences in regulatory immune cells between asthmatic children from agricultural versus rural areas [32]. However, the small sample sizes in both studies preclude firm conclusions, and these findings should be interpreted as hypothesis-generating rather than confirmatory.

Oxidative stress is a key mechanism linking external exposures to tissue damage. An Italian study with 130 children showed that allergic rhinitis was associated with elevated oxidative stress markers (isoprostanes: 352 ± 98 pg/mL versus 198 ± 54 pg/mL in controls, $p < 0.001$) [33]. Importantly, children with allergies who were also exposed to tobacco smoke showed even higher oxidative stress levels, illustrating how underlying vulnerability amplifies the effects of external exposures. The same environmental exposure produces different effects depending on whether someone's immune system is already inflamed. Taken together, evidence from this section suggests that maternal inflammation, regardless of its source, and oxidative stress in early life represent promising mechanistic links between environmental exposures and allergic disease, though the predominance of observational designs and heterogeneous biomarker measurement limit causal interpretation.

4.2. Microbiome and Exposure Biomarkers

The nasal microbiome has emerged as a link between environmental exposures and immune responses. Three recent studies ($n = 50, 110$, and 347) found that allergic rhinitis and asthma patients have reduced bacterial diversity ($p < 0.01$ – 0.04) and altered bacterial communities compared to healthy individuals [34–36]. Lower diversity appeared specifically in patients with uncontrolled asthma and rhinitis ($p = 0.040$), but not in isolated asthma. However, these studies were conducted at single time points, making it impossible to determine whether microbial changes precede disease or result from it. Of 12 microbiome studies reviewed, 11 were cross-sectional. The only longitudinal study confirmed a link between pregnancy conditions and subsequent allergy but did not explain the underlying mechanism. Additionally, when PM exposure and active allergic rhinitis were measured simultaneously during pollen season, it remained unclear whether reduced bacterial diversity reflected pollutant effects alone, consequences of allergic inflammation, or both. This design limitation is not exclusive to microbiome research: studies on oxidative stress face the same problem, and in both cases we are left unable to determine whether these biological changes are a cause or a consequence of disease.

Understanding these microbial changes requires examining internal inflammatory responses through biomarkers. A German longitudinal study identified nasal biomarkers (IL-8, IL-33) that correlated with symptom severity during natural pollen exposure, while allergen-specific protective antibodies (IgA and IgG) provided protection [37]. A Polish study ($n = 84$) of adults previously diagnosed with non-allergic rhinitis revealed a striking finding: 25% (21 patients) actually had local allergic rhinitis, where immune reactions occur only in the nasal lining without systemic sensitization [38]. This challenges current diagnostic approaches and suggests allergic rhinitis may be more common than we think when using only blood and skin tests.

Despite consistent findings across studies, microbiome research faces important methodological constraints. Different sampling methods and sequencing techniques complicate comparisons between studies, and the cross-sectional nature of most evidence prevents causal inference [34–36]. The clinically relevant finding on local allergic rhinitis [38] further illustrates a broader diagnostic gap: if a substantial proportion of patients classified as non-allergic actually have localized immune responses undetectable by standard testing, prevalence estimates and treatment outcomes in the literature may be systematically underestimated. Longitudinal studies with standardized microbiome protocols and objective diagnostic criteria are therefore needed before these findings can inform clinical practice. These findings are summarized in Table A2 (Appendix A).

5. Social Exposome and Disparities in Allergic Respiratory Diseases

Socioeconomic Determinants and Health Inequities

The social exposome remains the least studied of the three domains examined in this review, with evidence drawn from a small number of studies that differ substantially in design and geographic scope. Findings should therefore be read as preliminary observations rather than established conclusions. Socioeconomic status does not uniformly increase allergic risk but rather creates different exposure patterns with opposing health effects. A UK Biobank analysis ($n = 109,018$ adults, 11.2-year follow-up) found that lower socioeconomic status and higher deprivation were associated with a higher risk of developing allergic disease (HR: 1.32, 95% CI: 1.21–1.44) and dying from it (HR: 1.18, 95% CI: 1.11–1.26), alongside exposure to violence, smoking, and air pollution [39].

The Tenerife–Lima study revealed an unexpected pattern: Spanish populations showed higher allergic sensitization than Peruvian populations (45.2% vs. 28.7%, $p < 0.001$) despite similar climates. Both cities share a desert climate (Köppen BWh), but differ in socioeconomic equity and pollution patterns. Lima exhibits stark income disparities (13:1 ratio) and persistent air pollution from aging vehicles and geographical trapping, while Tenerife has minimal income gaps (1.1:1) and benefits from trade winds that disperse pollutants. This translated into opposing exposure profiles: wealthier groups had greater exposure to pollutants that trigger sensitization but lower home allergen levels, while poorer groups showed the opposite pattern, with higher domestic allergen exposure but potentially greater protection from microbial diversity [40]. These findings show that socioeconomic status does not simply increase or decrease allergy risk but creates different combinations of exposures with divergent immunological effects. Importantly, these social conditions have real biological consequences: chronic stress dysregulates immune responses, while poor housing promotes mold and dampness that directly inflame the airways, reinforcing that the social and biological dimensions of the exposome are deeply interconnected.

Beyond environmental factors, access to specialized care independently affects disease outcomes. A Polish study ($n = 87$) found that urban children responded better to allergy treatment than rural–agricultural children (67% vs. 48%, $p = 0.03$) [41], illustrating that socioeconomic disadvantage shapes not only disease susceptibility but also treatment effectiveness. Taken together, these findings suggest that social position influences the entire trajectory of allergic disease, from initial sensitization to long-term prognosis, making the social exposome arguably the most actionable dimension for public health intervention, despite remaining the least studied. The evidence reviewed points to several modifiable targets, including housing conditions such as dampness and poor ventilation, occupational hazard regulation in informal sectors lacking surveillance systems, and equitable access to specialized allergy care, all of which could simultaneously reduce disease burden and address health inequities.

Key findings on social factors and disparities in allergic respiratory diseases are summarized in Table A3 (Appendix A).

6. Discussion

6.1. Integrated Exposome Approaches

Figure 2 synthesizes the integrative framework proposed in this review, illustrating how external, internal, and social exposome domains operate concurrently across the life course. Although this review examined each domain separately for clarity of presentation, this separation does not reflect how exposures operate in real populations. Individuals experience simultaneous exposure to air pollution, psychosocial stress, and metabolic

changes, and their combined effects do not simply aggregate but interact in ways that remain invisible when exposures are analyzed in isolation.

Studies integrating multiple exposome domains simultaneously reveal patterns hidden in single-exposure investigations. The EGEA study evaluated 53 factors and identified that the worst exposure profile combined traffic proximity, heavy smoking, poor diet, and high outdoor humidity, with these factors appearing to work together rather than independently, and associated with reduced lung function in asthmatic adults [12]. The EXPANSE urban framework similarly found that when air pollutants and neighborhood characteristics were analyzed together across 14 European cohorts, their effects amplified, suggesting that addressing only one factor may underestimate the benefits of integrated strategies [8]. Machine learning applied to early-pregnancy exposure data identified complex interaction patterns linked to childhood allergic disease that traditional statistical methods missed [30], though these models require external validation before clinical implementation.

These interaction patterns are further shaped by critical susceptibility windows across the life course. The preconception period is particularly relevant, as maternal exposures have been associated with embryonic development and epigenetic programming [30]. During pregnancy, maternal inflammation appears to influence fetal immune development [28,29], and the first 1000 days represent the period of greatest immune plasticity [9,23,24]. Adulthood introduces new risks through occupational exposures [25–27]. Characterizing how exposures during these windows interact synergistically represents the central methodological frontier of exposome research in respiratory allergic diseases, and will require prospective cohort designs integrating environmental, biological, and social data from preconception onward.

6.2. Public Health Implications and Future Research

Evidence across the three exposome domains suggests a possible hierarchy of intervention targets, though the heterogeneity of study designs and populations warrants caution when translating these observations into definitive recommendations. In terms of what is currently actionable, ambient air pollution, despite modest individual effect sizes, justifies population-level action given the universality of exposure. Domestic environments, where dampness and mold carry stronger and more consistent associations, represent higher-yield targets particularly in vulnerable populations, where ventilation improvements and mold remediation are both feasible and cost-effective relative to large-scale pollution control [15,16]. HEPA purifiers show symptom benefit under trial conditions, but sustainability and affordability in low-resource settings remain undemonstrated [13].

Occupational settings, where the strongest dose–response relationships were observed, represent priority areas for prevention. Systematic monitoring, protective equipment, and process redesign represent plausible strategies to reduce sensitization and symptom progression [25,26]. However, implementation depends on regulatory frameworks often absent in low- and middle-income countries.

Several aspects of the exposome framework, by contrast, remain primarily research priorities at this stage. Molecular diagnostics and predictive models offer potential clinical applications. Component-resolved diagnostics refine individual sensitization profiles to guide environmental control measures [18], and predictive models explore anticipating allergenic risk according to exposure patterns [19]. However, both require prospective validation in diverse populations and demonstration of real clinical benefit before widespread use.

From a preventive perspective, screening for pregnancy risk factors like maternal periodontal disease or psychosocial stress could identify vulnerable offspring [28–30]. However, the modest effect sizes (HR 1.14–1.82) raise important questions about universal screening cost-effectiveness versus broad public health approaches. Since maternal inflammation, regardless of source, appears to affect fetal immune development similarly, population-level interventions addressing multiple inflammatory pathways may be more efficient than targeted screening programs.

Clinical trials evaluating integrated exposome interventions are essential to confirm causality and measure effectiveness [13]. Without these, public health recommendations will continue relying on consistent but potentially confounded observations, and the gap between what the exposome framework promises conceptually and what it can deliver clinically will remain unresolved.

6.3. Limitations

This narrative review has several limitations. Methodological quality of individual studies was not formally assessed using standardized scales, and included studies show substantial heterogeneity in designs, sample sizes (50 to 349,037 participants), and geographic contexts, complicating direct comparisons. Most evidence originates from high-income countries, limiting applicability to settings where exposome profiles differ substantially [40]. The search was also restricted to PubMed/MEDLINE and Scopus, without systematic consultation of LILACS, CINAHL, or grey literature, which may have contributed to underrepresentation of evidence from Latin America, sub-Saharan Africa, and other low- and middle-income regions.

Measuring the exposome accurately remains a fundamental challenge. Most studies rely on single assessments that cannot capture exposure variation across seasons, environments, and life stages, and the frequent use of area-level estimates and self-reported data introduces measurement error. Climate change adds further complexity by altering pollen seasons and increasing pollen potency in ways that current models do not yet adequately capture [21,22].

The predominance of observational designs limits causal inference, and evidence on social determinants remains restricted to cross-sectional studies using income-based proxies, which cannot capture how structural inequities shape exposure trajectories over time [39]. Although machine learning has begun identifying complex multi-exposure patterns [30], prospective studies with external validation remain lacking. Finally, multi-omics integration offers promising tools for linking environment to disease [42], but reproducibility across laboratories and distinguishing predictive biomarkers from disease consequences remain methodologically unresolved.

7. Conclusions

Respiratory allergic diseases result from the accumulation of multiple exposures over time, which is precisely why the exposome framework is so relevant for understanding how they develop and progress. High-intensity and proximal exposures, particularly damp indoor environments and occupational allergens, carry greater risk than ambient pollution and should therefore be priority targets for prevention. Internal components, including inflammation, oxidative stress, and microbiome alterations, appear to act as biological links between environmental exposures and disease, with critical windows during pregnancy and early childhood, though whether these changes contribute to disease onset or simply reflect it remains unresolved.

The social exposome is the least studied dimension, yet arguably the most relevant for public health action. Socioeconomic disadvantage consistently concentrates the burden of severe disease, poor outcomes, and limited access to care in the most vulnerable populations, and addressing this requires coordinated action across environmental, housing, occupational, and healthcare policies. Future research should prioritize longitudinal studies integrating environmental, biological, and social data simultaneously, with active inclusion of populations from Latin America, Africa, and Asia. Without this broader approach, the exposome framework risks remaining a conceptually rich but clinically limited tool, and the populations bearing the greatest exposure burden will continue to be the least represented in the evidence informing their care.

Beyond its conceptual contributions, this review offers some practical implications that could be beneficial for clinicians, researchers, and public health practitioners. The accumulated evidence suggests that incorporating occupational and housing history into clinical evaluations is a reasonable step, while targeted policies addressing housing conditions, occupational hazards, and healthcare access would likely strengthen existing intervention strategies. At the same time, the review highlights important evidence gaps, particularly the limited availability of prospective cohort designs with active inclusion of underrepresented populations and the underrepresentation of low- and middle-income populations, suggesting that such designs integrating environmental, biological, and social data could be a productive direction for future work.

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Conflicts of Interest: Fernando Pineda De La Losa is employed by Inmunotek S.L. Laboratories, Madrid, Spain. César A. Galván has delivered informative presentations on the ALEX-2 platform (Inmunotek S.L.) without receiving honoraria. Inmunotek S.L. had no role in the design of this study, in the collection, analyses, or interpretation of data, in the writing of the manuscript, or in the decision to publish the results. The remaining authors declare no conflicts of interest.

Abbreviations

Der p	<i>Dermatophagoides pteronyssinus</i> allergen component
EGEA	Epidemiological study on the Genetics and Environment of Asthma
EXPANSE	EXPosure Assessment in current and future climates for urban and non-urban populations in and across Europe
FEV ₁	Forced expiratory volume in 1 s
HEPA	High-efficiency particulate air
HR	Hazard ratio
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IL	Interleukin
MeSH	Medical Subject Headings
OR	Odds ratio
PM _{2.5}	Particulate matter ≤ 2.5 μm in aerodynamic diameter
PM ₁₀	Particulate matter ≤ 10 μm in aerodynamic diameter
RR	Relative risk
SANRA	Scale for the Assessment of Narrative Review Articles
ST2	Suppression of tumorigenicity 2 receptor
TSLPR	Thymic stromal lymphopoietin receptor

Appendix A

Table A1. Key studies on external exposome and respiratory allergic diseases.

Author (Year)	Country	Design	Population (n)	Exposure	Outcome	Main Result	Key Limitations
Yu et al. (2025) [8]	Europe (EXPANSE project, 8 countries)	Prospective cohort	Birth to >70 years (n = 349,037)	Air pollution (PM _{2.5} , NO ₂ , temperature)	Asthma	PM _{2.5} +5 µg/m ³ : HR 1.04 (95% CI: 1.01–1.07); NO ₂ +10 µg/m ³ : HR 1.10 (95% CI: 1.05–1.15); 11.6% of cases attributable to environmental factors	Restricted to European cohorts with regulated pollution levels
Codispoti et al. (2015) [9]	USA	Prospective cohort	Children 0–4 years (n = 634)	Diesel exhaust particles (DEP)	Aeroallergen sensitization	High DEP exposure: OR 1.40 (95% CI: 1.10–1.78) at 2 years; OR 1.35 (95% CI: 1.08–1.69) at 3 years; sensitization increased from 6.9% to 21.9%	Single urban area; limited generalizability
Chu et al. (2019) [10]	China	Ecological time-series	Allergic rhinitis patients (n = 33,063)	Air pollution (PM ₁₀ , PM _{2.5})	Allergic rhinitis	PM ₁₀ : +5.86% cases (95% CI: 3.0–8.81); PM _{2.5} : +5.39% (95% CI: 2.73–8.12); OR 1.12 (95% CI: 1.08–1.16) for PM _{2.5} >75 µg/m ³	Ecological design; individual-level causality cannot be established
Guillien et al. (2021) [12]	France	Cross-sectional	Adults with asthma (n = 599)	Multiple exposures (tobacco, diet, dampness, traffic)	Lung function (FEV1)	Multiple exposures: FEV1 79% ± 21 vs. 90% ± 19 and 93% ± 16 in lower exposure groups	Cross-sectional; reverse causality cannot be excluded
Hillerich et al. (2024) [11]	Germany	Cross-sectional	Adults (n = 2505)	Tropospheric ozone (O ₃)	Quality of life in asthma	OR 1.85 (95% CI: 1.32–2.59) for quality of life deterioration	Cross-sectional; single pollutant assessment
Park et al. (2020) [13]	South Korea	Randomized controlled trial	Adults with allergic rhinitis (n = 44)	Indoor air pollution (PM _{2.5} , PM ₁₀)	Allergic rhinitis symptoms	PM _{2.5} reduction: 51.8% (<i>p</i> = 0.045); symptoms: −2.8 points (95% CI: −4.1 to −1.5); medication use: −26.3% (<i>p</i> = 0.033)	Small sample (n = 44); short follow-up (6 weeks)
Stas et al. (2021) [14]	Belgium	Case-crossover	Adults (n = 144)	Birch pollen, air pollution (PM ₁₀ , O ₃)	Allergic symptoms	Ozone amplified severe pollen allergy symptoms, surpassing direct birch pollen effect; PM ₁₀ and O ₃ acted as effect modifiers during pollen season	Small sample; single geographic area
Yucel et al. (2021) [17]	Turkey	Retrospective cohort	Children with asthma/allergic rhinitis (n = 165)	House dust mites	Asthma, allergic rhinitis	Nasal symptom score: 3.2 ± 1.8 to 5.7 ± 2.1 (<i>p</i> < 0.001) in mite-sensitized patients; fewer asthma attacks (<i>p</i> < 0.001)	Retrospective design; single center

Cai et al. (2019) [15]	China	Cross-sectional	Preschoolers 3–6 years (n = 40,010)	Household dampness (mold, leaks)	Asthma, allergic rhinitis	Asthma: OR 1.52 (95% CI: 1.32–1.75); rhinitis: OR 1.48 (95% CI: 1.28–1.71); dose-response AOR 1.16–2.64	Cross-sectional; self-reported exposures
Cai et al. (2020) [16]	China	Cross-sectional	Preschoolers 3–6 years (n = 5625)	Household dampness	Asthma, allergic rhinitis	Adjusted OR 1.3–2.5 for asthma and respiratory symptoms	Cross-sectional; single city; self-reported exposures
Kołodziejczyk et al. (2016) [20]	Poland	Cross-sectional	Allergic rhinitis patients (n = 229)	Mold sensitization	Allergic rhinitis, asthma	Elevated IgE and FeNO in mold allergy ($p < 0.05$)	Cross-sectional; selected clinical population
Dominguez-Ortega et al. (2020) [21]	Spain	Longitudinal	Adults with grass allergy (n = 101)	Seasonal pollen (grasses)	Asthma, rhinoconjunctivitis	FEV1: −4.2% (95% CI: −6.1 to −2.3); symptoms persisted outside pollen season in 33% asthmatics and 41.8% rhinitis patients	Small sample; single allergen type
Pfaar et al. (2020) [22]	Europe (Austria, Finland, France)	Ecological observational study	Variable number of voluntary PHD app users across 3 regions; 23 pollen monitoring stations	Pollen (grasses, birch)	Allergic rhinitis	Pollen-symptom correlation: birch $r = 0.55$ – 0.78 ; grasses $r = 0.48$ – 0.79 ($p < 0.001$)	Ecological correlations; voluntary app-based symptom reporting; no individual-level data
Aberle et al. (2018) [23]	Croatia	Cross-sectional	Schoolchildren 10–11 years (n = 1687)	Environmental allergens	Allergic rhinitis	Rhinitis 22.5%; SPT+ 20.2%; dust mites most common allergen	Cross-sectional; single region
Oh et al. (2025) [24]	Korea (Jeju)	Cross-sectional	Schoolchildren 9–16 years (n = 1067)	Environmental aeroallergens	Allergic rhinitis	Prevalence 29.0%; sensitization 51.5%; polysensitization OR 1.58 (95% CI: 1.017–2.455, $p = 0.042$)	Cross-sectional; single island population
Beach et al. (2022)[25]	Canada (Alberta)	Prospective cohort	Baker apprentices (n = 220)	Occupational allergens (flour, additives)	Occupational asthma, allergic rhinitis	Sensitization incidence 2.49/100 person-years; high dust exposure: RR 3.2 (95% CI: 1.8–5.7); sensitization reached 21% at 3 years	Single occupation and region
Ahmed et al. (2022) [26]	Egypt	Cross-sectional	Agricultural workers (n = 150)	Occupational allergens (pollens, fungi, insecticides)	Occupational asthma	Occupational asthma prevalence 7.3%; OR 4.3 (95% CI: 2.1–8.8); symptom onset 13.45 ± 6.93 months post-job start	Small sample; cross-sectional design

Table A2. Key studies on internal exposome and susceptibility to respiratory allergic diseases.

Author (Year)	Country	Design	Population (n)	Exposure	Outcome	Main Result	Key Limitations
Hsieh et al. (2016) [28]	Taiwan	Prospective cohort	Newborns (n = 84,551; 9-year follow-up)	Maternal periodontal disease	Allergic rhinitis, allergic conjunctivitis, eczema	Rhinitis HR 1.17 (95% CI: 1.10–1.24); conjunctivitis HR 1.27 (95% CI: 1.18–1.37); eczema HR 1.14 (95% CI: 1.08–1.20)	Administrative data; residual confounding possible
Zhou et al. (2024) [29]	China	Birth cohort	3160 mother–child pairs	Maternal anxiety	Eczema, allergic rhinitis	Severe anxiety: OR 1.82 (95% CI: 1.34–2.47) for any allergy; rhinitis aOR 1.67 (95% CI: 1.17–2.37)	Self-reported anxiety; regional sample
Dong et al. (2024) [30]	Singapore	Birth cohort with machine learning analysis	1151 mother–child pairs	Preconception and pregnancy exposure (alcohol, depressive symptoms, micronutrients)	Atopic eczema, rhinitis, wheeze	Preconception alcohol and maternal depression increased eczema and rhinitis risk; maternal neopterin and child dimethylglycine protective against wheeze; early postnatal infection key driver of eczema and rhinitis	Single-country Asian cohort; questionnaire-based exposures; external validation pending
Tworek et al. (2017) [31]	Canada	Case–control	Adults: 10 healthy, 11 allergic asthmatic (n = 21)	TLR ligand stimulation of haemopoietic progenitor cells	Immune receptor expression in asthma	Asthmatics showed lower TLR-2 and TLR-9 expressing HPC; TLR-4 stimulation yielded higher TSLPR+ cells in asthmatics; allergen challenge further augmented TLR-induced ST2 expression	Very small sample (n = 21); single-center; not validated in larger populations
Fuss et al. (2019) [32]	Poland	Cross-sectional	Children 8–16 years, asthmatic and HDM-sensitized (n = 35: farm = 19, rural = 16)	Residential environment (farm vs. rural area)	CD4+CD25+Foxp3+ regulatory T cell expression	No significant differences in CD4+/CD25+ or CD4+/CD25+Foxp3+ expression between farm and rural area children	Very small sample (n = 35); single region; HDM-sensitized children only
Loffredo et al. (2018) [33]	Italy	Cross-sectional	130 children (65 cases, 65 controls)	Oxidative stress (NOX2, isoprostanes)	Persistent allergic rhinitis	Isoprostanes: 352 ± 98 pg/mL vs. 198 ± 54 pg/mL in controls ($p < 0.001$); tobacco smoke exacerbated oxidative stress in allergic patients	Small sample; cross-sectional design
Mariani et al. (2021) [34]	Italy	Case–control	Adults (n = 50: 26 AR, 24 controls)	Nasal microbiome	Allergic rhinitis	Alpha diversity reduced 11.5% in AR (Shannon: 4.32 vs. 4.88; $p = 0.04$);	Very small sample; single time point

Pérez-Losada et al. (2023) [35]	Portugal	Cross-sectional	347 (99 controls, 53 AR, 183 AR + AS, 12 AS)	Nasal microbiome dysbiosis	Allergic rhinitis, asthma	lower microbial species number (145.8 vs. 188.5 ASVs; $p = 0.03$) All alpha-diversity indices reduced in disease ($p < 0.01$); 72 differential metabolic pathways identified ($p < 0.05$)	Cross-sectional; single time point
Chen et al. (2022) [36]	China	Cross-sectional	110 (20 controls, 30 AR, 30 AS, 30 AR + AS)	Nasal microbiome dysbiosis	Allergic rhinitis, asthma	Lower diversity (Shannon, $p = 0.040$) only in uncontrolled AR + AS; Pseudoflavonifractor predominated in controlled or partially controlled disease in both isolated asthma and combined asthma + AR	Small sample; cross-sectional; single center
Gökkaya et al. (2020) [37]	Germany	Prospective panel study	Adults: 7 with seasonal allergic rhinitis, 7 non-allergic ($n = 14$)	Natural pollen exposure (birch)	Nasal biomarkers for symptom severity	Nasal IL-8, IL-33, birch-specific IgG4 and IgE identified as predictive biomarkers for symptom severity; nasal IgA and IgG potentially protective	Very small sample ($n = 14$); single pollen type and season; single geographic area
Krajewska-Wojtys et al. (2017) [38]	Poland	Cross-sectional	Adults ($n = 84$)	Local nasal hyperre-activity	Local allergic rhinitis	LAR confirmed in 25% (21/84); D. pteronyssinus most frequent trigger (22.6%)	Small sample; single center

Table A3. Major studies on social exposome and disparities in respiratory allergic diseases.

Author (Year)	Country	Design	Population (n)	Exposure	Outcome	Main Result	Key Limitations
Wu et al. (2025) [39]	United Kingdom	Prospective cohort	Adults ($n = 109,018$; 11.2-year follow-up)	Low socioeconomic status, social deprivation	Allergic disease, mortality	Low SES: HR 1.32 (95% CI: 1.21–1.44) for allergic disease transition; HR 1.18 (95% CI: 1.11–1.26) for mortality	UK-specific; income-based SES proxy
González-Pérez et al. (2025) [40]	Spain-Peru	Cross-sectional	Adults with rhinitis/asthma ($n = 181$: Tenerife = 91, Lima = 90)	Urbanization, socioeconomic status	Allergic sensitization	Higher sensitization in Spain vs. Peru (45.2% vs. 28.7%, $p < 0.001$) despite similar climate; socioeconomic determinants surpass climatic factors	Small sample; two cities only
Pawlowski et al. (2017) [41]	Poland	Non-randomized intervention study	Children ($n = 87$)	Residence area (urban vs. rural)	Response to immunotherapy	Better clinical response in urban vs. rural-agricultural children (67% vs. 48%, $p = 0.03$)	Very small sample; pilot study; single country

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