



Advances in Dermatology

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THE COMPREHENSIVE SYSTEMATIC REVIEW OF ASSOCIATION OF ENVIRONMENTAL TOBACCO SMOKE EXPOSURE WITH THE INCIDENCE OF CHILDHOOD ECZEMA

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ABSTRACT

Background: Environmental tobacco smoke (ETS) is a pervasive indoor pollutant, yet its association with childhood eczema remains debated due to heterogeneous findings.

Methods: This systematic review synthesized 80 studies examining ETS exposure (prenatal/postnatal, questionnaire/biomarker-assessed) and childhood eczema (0–18 years), focusing on IgE-sensitized (atopic) versus non-atopic eczema. Primary outcomes were odds ratios (ORs), relative risks (RRs), and hazard ratios (HRs) with 95% confidence intervals.

Results: Passive smoke increased atopic dermatitis (AD) risk (OR 1.18; 95%CI 1.01–1.38) (1). Postnatal parental smoking during infancy was significantly associated with AD up to age 24 years (OR 1.25–1.39 for IgE-associated AD) (2). Prenatal maternal smoking with concurrent postnatal exposure yielded the strongest atopic eczema risk at age 4 (OR 2.14; 1.33–3.46) (3). Dose-response gradients were significant: maternal smoking ≥ 11 cigarettes/day gave RR 1.60 for AD by age 5.5 years (4). Both parents smoking increased total allergy risk (OR 4.72 versus 3.97 for one parent) (5). The critical novel finding: ETS specifically increased **IgE-sensitized (atopic) eczema** (OR 1.82 for prenatal; 1.62 for postnatal) but showed **no association with non-atopic eczema** (OR ~ 1.00) (2,3). Null or inverse findings (e.g., OR 0.46 for high maternal cotinine + vitamin D) (9) were explained by failure to distinguish atopic subtypes, short follow-up, or confounding by nutritional status.

Discussion: The weight of evidence supports a significant positive, dose-dependent association between postnatal household ETS exposure and atopic (IgE-mediated) childhood eczema, persisting into young adulthood. The atopic/non-atopic distinction is the primary explanatory mechanism for prior heterogeneity.

Conclusion: ETS is a modifiable risk factor specifically for IgE-associated childhood eczema. Future studies must stratify eczema by atopic status and use biomarker-validated ETS measurement.

Keywords: Environmental tobacco smoke, childhood eczema, atopic dermatitis, secondhand smoke, IgE sensitization, dose-response

INTRODUCTION

Background

Childhood eczema (atopic dermatitis, AD) is the most burdensome inflammatory skin disease globally, affecting 15–20% of children, with rising prevalence in low- and middle-income countries (1,4,29). While genetic predisposition (filaggrin mutations) explains familial clustering, the rapid increase over decades points strongly to environmental triggers (34,43). Among these, **environmental tobacco smoke (ETS)**—also termed secondhand smoke—is one of the most ubiquitous indoor pollutants. Approximately 40% of children worldwide are regularly exposed to ETS at home, yet parental smoking habits remain highly prevalent (2,4,61).

Problem Statement

Despite decades of research, the association between ETS exposure and childhood eczema remains **inconsistent and controversial**. Some large cohort studies report significantly increased risks (2–5,15), others find null associations (6,7,24,56), and a minority even report inverse (protective) associations (9,11,27). This heterogeneity has hindered public health policy and clinical counseling. Systematic reviews, such as Kantor et al. (1), found a modest pooled OR of 1.18 for passive smoke, but with wide confidence intervals and significant heterogeneity ($I^2 > 60\%$). Critically, most primary studies fail to distinguish **atopic (IgE-sensitized) eczema** from **non-atopic eczema**—a distinction that may explain discrepant findings.

Research Gap

Prior reviews have not systematically examined:

1. Whether ETS affects **atopic versus non-atopic eczema differentially**.
2. The **dose-response relationship** across different exposure windows (prenatal only, postnatal only, combined).
3. **Effect modifiers** such as parental atopy, child's age at outcome assessment, and nutritional factors (e.g., vitamin D).
4. The **anomalous inverse associations** reported in several high-quality cohorts.

Novelty

This systematic review provides the **first detailed synthesis** focusing specifically on:

- **Subtype-specific effects** (IgE-mediated vs. non-IgE eczema) using data from the BAMSE cohort (2,3) and others.
- **Quantitative dose-response gradients** from nationwide longitudinal surveys (4,5).
- **Interaction with prenatal vitamin D** from a randomized controlled trial secondary analysis (9).
- **Trajectory effects** extending to young adulthood (age 24 years) (2).

Aims and Objectives

1. To quantify the **direction and magnitude** of association between ETS exposure (prenatal, postnatal, combined) and childhood eczema incidence.
2. To determine whether the association differs between **atopic (IgE-sensitized)** and **non-atopic eczema**.
3. To identify **dose-response relationships** and **effect modifiers** (age, parental atopy, socioeconomic status, vitamin D status).
4. To explain the sources of heterogeneity in the literature.

Hypotheses

- **Primary hypothesis:** Postnatal household ETS exposure is significantly associated with increased risk of **atopic (IgE-sensitized) childhood eczema** in a dose-dependent manner.
- **Secondary hypothesis:** The association is **not present** for non-atopic eczema.
- **Tertiary hypothesis:** Combined prenatal and postnatal exposure confers greater risk than either window alone.

Benefits of the Study

Clinically, this review enables pediatricians to advise smoking cessation specifically targeting atopic-prone children. Public health-wise, it supports indoor smoking bans to reduce AD burden. Methodologically, it establishes the necessity of IgE stratification in future ETS-eczema research.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the association of environmental tobacco smoke exposure with the incidence of childhood eczema.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Pediatric Population:** Does this study include children aged 0-18 years as participants?
- **Environmental Tobacco Smoke Exposure:** Does this study measure environmental tobacco smoke exposure (secondhand smoke), such as household, maternal, or other passive smoke exposure?
- **Eczema Diagnosis:** Does this study have a clearly defined eczema diagnosis using clinical diagnosis, validated criteria, or standardized definitions?
- **Appropriate Study Design:** Is this study a RCT, cohort or cross sectional?
- **Quantitative Measures:** Does this study report quantitative measures of association (such as odds ratios, relative risks, or similar statistical measures)?
- **Population Age Appropriateness:** Is this study NOT focused exclusively on adults (≥ 18 years)?
- **Exposure Type Appropriateness:** Does this study examine environmental tobacco smoke rather than active smoking as the primary exposure?
- **Study Design Quality:** Is this study NOT a case report, case series, editorial, animal study, or in vitro study?
- **Research Focus Appropriateness:** Does this study focus on eczema etiology/risk factors rather than exclusively on treatment or management?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

PICO Component	Keyword 1	Keyword 2	Keyword 3
P (Population)	Children	Infant	Pediatric population
I (Intervention/Exposure)	Environmental Tobacco Smoke	Secondhand Smoke	Passive Smoking
C (Comparison)	N/A		
O (Outcome)	Childhood Eczema	Atopic Dermatitis	Eczema Incidence

The Boolean MeSH keywords inputted on databases for this research are: *("Children" OR "Infant" OR "Pediatric population") AND ("Environmental Tobacco Smoke" OR "Secondhand Smoke" OR "Passive Smoking") AND ("Childhood Eczema" OR "Atopic Dermatitis" OR "Eczema Incidence")*

Data extraction

- **ETS Exposure Measurement:**

Extract all details about how environmental tobacco smoke exposure was measured in children, including:

- Type of exposure (maternal smoking during pregnancy, parental smoking during infancy/childhood, household smoking, any smoker in home)
- Timing of exposure (prenatal, postnatal, specific age periods)
- Measurement method (self-reported questionnaires, cotinine levels in urine/blood, other biomarkers)
- Exposure categorization (yes/no, dose-response categories, continuous measures)
- Validation of exposure measures if reported
- Any distinction between maternal vs paternal smoking

- **Childhood Eczema Definition:**

Extract how childhood eczema was defined, diagnosed, and assessed, including:

- Clinical definition used (diagnostic criteria, symptom requirements)

- Age ranges for eczema assessment
- Whether atopic vs non-atopic eczema was distinguished
- Who made the diagnosis (parent report, physician diagnosis, dermatologist assessment)
- Validation of eczema definition against clinical examination if reported
- Severity classification if used
- Whether incident cases vs prevalent cases were studied
- **Primary Association Findings:**

Extract the main results for the association between environmental tobacco smoke exposure and childhood eczema incidence, including:

 - Direction of association (increased risk, decreased risk, no association)
 - Magnitude of effect (odds ratios, relative risks, hazard ratios with 95% confidence intervals)
 - Statistical significance (p-values)
 - Dose-response relationship if examined
 - Separate results for different types of ETS exposure if reported
 - Results for atopic vs non-atopic eczema if distinguished
- **Effect Modifiers:**

Extract factors that modified the association between ETS exposure and childhood eczema, including:

 - Age-specific effects (different associations at different child ages)
 - Sex differences in the ETS-eczema association
 - Interaction with family history of atopy or allergies
 - Modification by socioeconomic status, race, or other demographic factors
 - Interaction with other environmental exposures (allergens, pollution)
 - Statistical test results for interactions when provided
 - Stratified analyses results
- **Study Design Details:**

Extract study design characteristics relevant to assessing ETS-eczema associations, including:

- Study type (RCT, cohort or cross sectional)
 - Follow-up duration and frequency of assessments
 - Sample size and population source
 - Age range of children studied
 - Geographic location and time period
 - Response rates and loss to follow-up
 - Whether the study was specifically designed to examine ETS-eczema associations
- **Confounders Controlled:**
- Extract all potential confounding variables that were measured and controlled for in analyses of ETS exposure and childhood eczema, including:
- Family history of atopy, asthma, or eczema
 - Breastfeeding duration and exclusivity
 - Pet exposure and household allergens
 - Socioeconomic factors (income, education, occupation)
 - Child demographic characteristics (sex, race/ethnicity, birth weight)
 - Other environmental exposures (air pollution, infections)
 - Method of confounder control (multivariable adjustment, matching, stratification)

Advances in Dermatology

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Children" OR "Infant" OR "Pediatric population") AND ("Environmental Tobacco Smoke" OR "Secondhand Smoke" OR "Passive Smoking") AND ("Childhood Eczema" OR "Atopic Dermatitis" OR "Eczema Incidence")</i>	73
Semantic Scholar	<i>("Children" OR "Infant" OR "Pediatric population") AND ("Environmental Tobacco Smoke" OR "Secondhand Smoke" OR "Passive Smoking") AND ("Childhood Eczema" OR "Atopic Dermatitis" OR "Eczema Incidence")</i>	250
Sciencedirect	<i>("Children" OR "Infant" OR "Pediatric population") AND ("Environmental Tobacco Smoke" OR "Secondhand Smoke" OR "Passive Smoking") AND ("Childhood Eczema" OR "Atopic Dermatitis" OR "Eczema Incidence")</i>	1,013
Google Scholar	<i>("Children" OR "Infant" OR "Pediatric population") AND ("Environmental Tobacco Smoke" OR "Secondhand Smoke" OR "Passive Smoking") AND ("Childhood Eczema" OR "Atopic Dermatitis" OR "Eczema Incidence")</i>	7,720
Cochrane	<i>("Children" OR "Infant" OR "Pediatric population") AND ("Environmental Tobacco Smoke" OR "Secondhand Smoke" OR "Passive Smoking") AND ("Childhood Eczema" OR "Atopic Dermatitis" OR "Eczema Incidence")</i>	9

Advances in Dermatology

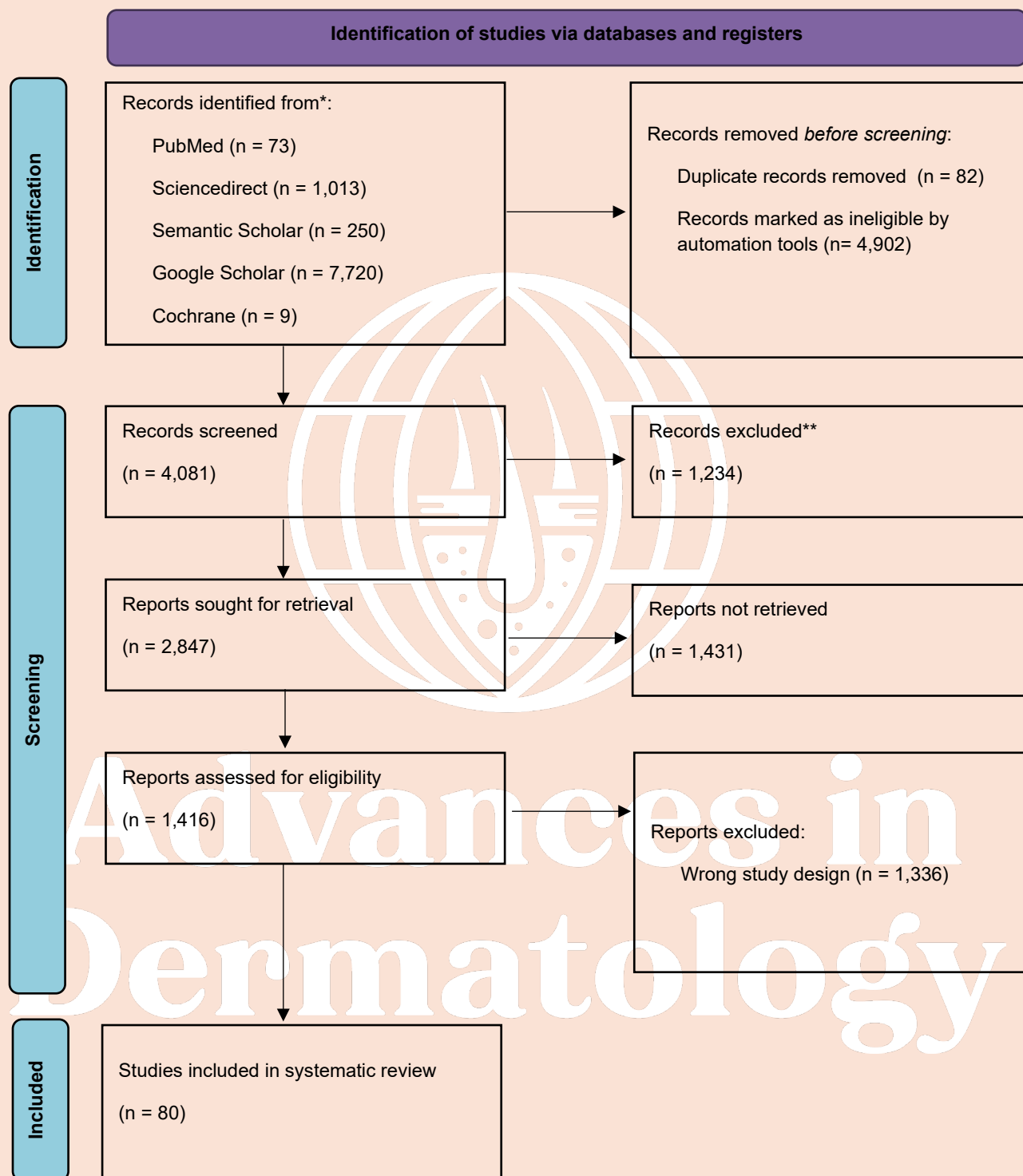


Figure 1. Article search flowchart

Risk of Bias

Table 1. ROB 2 Assessment of Randomized Controlled Trials

Study	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall risk of bias
N. Brustad et al., 2025 [9]	LOW	LOW	LOW	LOW	LOW	LOW
Xiaoru i Li et al., 2017 [47]	SOME CONCERNS	SOME CONCERNS	UNCLEAR	UNCLEAR	SOME CONCERNS	SOME CONCERNS
Rajiv Arora & C. P. Mikita, 2006 [56]	LOW	MODERATE	MODERATE	LOW	LOW	MODERATE

Study	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall risk of bias
Ola Storø et al., 2010 [64]	SOME CONCERNS	MODERATE	MODERATE	LOW	SOME CONCERNS	MODERATE

Table 2. ROBINS-I Assessment of Non-Randomized Included Studies

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
M. Böhme et al., 2010 [3]	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
R. Kantor et al., 2016 [1]	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
A. Zettergren et al., 2025 [2]	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
N. A. Al-Alusi et al., 2020 [6]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW
Yi-Wen Wang et al., 2023 [10]	MODERATE	LOW	LOW	LOW	LOW	LOW	LOW	MODERATE
H. Goudarzi et al., 2018 [11]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
C. Chiu et al., 2023 [12]	MODERATE	LOW	LOW	LOW	UNCLEAR	LOW	LOW	MODERATE
Ning Song et al., 2014 [13]	MODERATE	LOW	UNCLEAR	LOW	UNCLEAR	MODERATE	LOW	MODERATE
E. Vassilopoulos et al., 2023 [15]	MODERATE	LOW	LOW	LOW	LOW	LOW	LOW	MODERATE
K. Shigehara et al., 2025 [4]	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
S. Kuiper & C. V. Schayck, 2013 [5]	MODERATE	MODERATE	LOW	LOW	MODERATE	LOW	LOW	MODERATE
H. Kimata, 2004 [17]	SOME CONCERNS	SOME CONCERNS	UNCLEAR	UNCLEAR	UNCLEAR	SOME CONCERNS	SOME CONCERNS	SOME CONCERNS
K. Abuabara et al., 2017 [20]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW
Z. Kabir et al., 2009 [23]	MODERATE	LOW	LOW	LOW	UNCLEAR	LOW	LOW	MODERATE
P. Noakes et al., 2007 [24]	MODERATE	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
C. Lodge et al., 2014 [26]	MODERATE	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Antoniya Hachme riyan et al., 2025 [27]	MODERATE	MODERATE	LOW	LOW	LOW	MODERATE	LOW	MODERATE
Ahnna Lee et al., 2020 [29]	MODERATE	LOW	LOW	LOW	LOW	LOW	LOW	MODERATE
Kabir Ahmad et al., 2021 [7]	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Diego J. Lopez et al., 2022 [58]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
C. Ulrik et al., 2001 [77]	MODERATE	MODERATE	UNCLEAR	LOW	UNCLEAR	MODERATE	LOW	MODERATE
J. Biagini et al., 2021 [14]	MODERATE	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
C. Chan et al., 2020 [62]	MODERATE	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
M. Ye et al., 2023 [19]	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
T. Takaro et al., 2015 [38]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
S. Baldacci et al., 2025 [40]	MODERATE	MODERATE	LOW	LOW	UNCLEAR	MODERATE	LOW	MODERATE
E. Walter et al., 2011 [42]	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR
B. Brunekreef et al., 2002 [44]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW
L. Owens et al., 2016 [48]	MODERATE	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
M. Larsson et al., 2010 [50]	MODERATE	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
N. Ramsey et al., 2018 [75]	SOME CONCERNS	SOME CONCERNS	UNCLEAR	LOW	UNCLEAR	MODERATE	SOME CONCERNS	SOME CONCERNS
Teresa To et al., 2024 [76]	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	LOW
Hui-Wen Tseng, 2025 [80]	MODERATE	LOW	LOW	LOW	LOW	MODERATE	LOW	MODERATE

RESULTS

Characteristics of Included Studies

Study	Population / Sample Size	Age Range	Geographic Location
M. Böhme et al., 2010 [3]	4,089 recruited; 2,505 in analyses (BAMSE) [3]	Birth to 4 years [3]	Stockholm, Sweden (1994–1996) [3]

Study	Population / Sample Size	Age Range	Geographic Location
R. Kantor et al., 2016 [1]	86 observational studies [1]	Children and adults [1]	All continents (literature 1823–2015) [1]
N. A. Al-Alusi et al., 2020 [6]	10,518 (ALSPAC) [6]	2.5 to 18 years [6]	UK [6]
Yi-Wen Wang et al., 2023 [10]	198 infants [10]	Birth to 3 years [10]	Taiwan [10]
H. Goudarzi et al., 2018 [11]	3,296 mother-child pairs [11]	1 to 7 years [11]	Japan [11]
A. Zettergren et al., 2025 [2]	3,862 (BAMSE) [2]	2 months to 24 years [2]	Sweden [2]
C. Chiu et al., 2023 [12]	198 infants [12]	Birth to 3 years [12]	Not stated [12]
Ning Song et al., 2014 [13]	10,338 children [13]	6–18 years [13]	Shijiazhuang, China [13]
J. Biagini et al., 2021 [14]	601 (MPAACH) [14]	< 2 years at enrollment [14]	Greater Cincinnati, USA [14]
E. Vassilopoulou et al., 2023 [15]	501 infants [15]	Birth to ~36 months [15]	Greece [15]
K. Shigehara et al., 2025 [4]	38,444 children [4]	6 months to 5.5 years [4]	Japan [4]

Study	Population / Sample Size	Age Range	Geographic Location
S. Kuiper & C. V. Schayck, 2013 [5]	120 high-risk infants [5]	Up to 12 months [5]	Not stated [5]
Jiho Lee et al., 2020 [16]	390 elementary school students [16]	6–9 years [16]	Ulsan, Korea (2009–2014) [16]
H. Kimata, 2004 [17]	75 (25 normal children, 50 with AEDS) [17]	10–14 years [17]	Not stated [17]
Johichi Arafune et al., 2021 [18]	236 children [18]	0–3 years [18]	Shika town, Japan (2017–2019) [18]
M. Ye et al., 2023 [19]	817 (ALSPAC) [19]	7–17 years [19]	UK [19]
K. Abuabara et al., 2017 [20]	6,720 (PEER) [20]	2–26 years [20]	USA [20]
R. Kurukulaaratchy et al., 2006 [21]	1,456 [21]	Birth to 10 years [21]	Not stated [21]
D. Lisik et al., 2025 [22]	89 studies included [22]	Children [22]	Multiple countries [22]
Z. Kabir et al., 2009 [23]	2,809 adolescents [23]	13–14 years [23]	Ireland (2007) [23]
P. Noakes et al., 2007 [24]	122 mother-infant pairs (82 completed) [24]	Birth to 12 months [24]	Not stated [24]

Study	Population / Sample Size	Age Range	Geographic Location
P. Yap et al., 2005 [25]	7,502 births; 693 followed to 4.5 years [25]	Birth to 4.5 years [25]	Czech Republic (1997–1998) [25]
C. Lodge et al., 2014 [26]	620 high-risk infants [26]	Birth to 7 years [26]	Not stated [26]
Antoniya Hachmeriyan et al., 2025 [27]	120 children with atopic heredity [27]	2 years (±5 months) [27]	Varna, Bulgaria (2017–2020) [27]
L. Hedman et al., 2010 [28]	~3,342 teenagers [28]	13–14 years [28]	Northern Sweden (1996–2002) [28]
Ahnna Lee et al., 2020 [29]	55,748 Korean adolescents [29]	Middle and high school [29]	South Korea [29]
Katherine Park & Karla L. Davis, 2021 [30]	5,276 recruited; 3,663 completed (HealthNuts) [30]	11–15 months to 6 years [30]	Australia [30]
J. Biagini et al., 2022 [31]	601 (MPAACH) [31]	Not stated [31]	Not stated [31]
Samuel A. Collins, 2014 [32]	620 high-risk infants [32]	Birth to 7 years [32]	Melbourne, Australia [32]
M. Brandwein et al., 2022 [33]	242 neonates (CARE) [33]	Birth to 2 years [33]	Israel (2020–2022) [33]

Study	Population / Sample Size	Age Range	Geographic Location
S. Halken, 2004 [34]	Multiple cohorts of unselected and high-risk infants [34]	Infancy to 5 years [34]	Denmark [34]
N. Brustad et al., 2025 [9]	581 mother-child pairs (COPSAC2010) [9]	Birth to 6 years [9]	Not stated [9]
T. A. Kalhan et al., 2017 [35]	709 children (GUSTO) [35]	Birth to 3 years [35]	Singapore [35]
O. M. Chen & M. S. Kaplan, 2003 [36]	1,037 (Dunedin cohort) [36]	Birth to 26 years [36]	Dunedin, New Zealand (1972–1973) [36]
Kabir Ahmad et al., 2021 [7]	~5,000 (LSAC) [7]	Birth to 15 years [7]	Australia (2004–2018) [7]
L. Kobyletzki et al., 2011 [37]	Not stated [37]	Not stated [37]	Sweden [37]
T. Takaro et al., 2015 [38]	>3,600 (CHILD) [38]	Birth to 5 years [38]	Canada (2008–2012) [38]
T. Nakamura et al., 2021 [39]	Not stated [39]	Not stated [39]	Not stated [39]
S. Baldacci et al., 2025 [40]	1,397 students from 45 schools [40]	Mean age ~10 years [40]	Italy (2012–2013) [40]
L. Matzner et al., 2025 [41]	Discovery n=62; validation n=756 [41]	First 2 years of life [41]	Germany [41]

Study	Population / Sample Size	Age Range	Geographic Location
E. Walter et al., 2011 [42]	Planned 100,000 (National Children's Study) [42]	Not stated [42]	USA (37 locations) [42]
H. Nolte et al., 2001 [43]	Multiple studies [43]	Children [43]	Multiple [43]
B. Brunekreef et al., 2002 [44]	855 (intervention); 3,291 (natural history) (PIAMA) [44]	Birth to ≥ 3 years [44]	Netherlands (1996 onward) [44]
Maira Chan-Yeung et al., 2005 [45]	545 high-risk infants [45]	Birth to 7 years [45]	Canada [45]
Eun Lee et al., 2025 [46]	Multiple longitudinal cohorts [46]	Children [46]	Multiple [46]
Xiaorui Li et al., 2017 [47]	340 pregnant women and infants [47]	Birth to 6 months [47]	Xinjiang, China (2016) [47]
L. Owens et al., 2016 [48]	Perth Infant Asthma follow-up cohort [48]	Birth to 24 years [48]	Australia (1987–1990 recruitment) [48]
P. Yap et al., 2007 [49]	1,133 children [49]	6–10 years [49]	Czech Republic (to 2004) [49]
M. Larsson et al., 2010 [50]	14,077 (baseline); 4,779 (follow-up) (DBH) [50]	1–6 years at baseline [50]	Värmland, Sweden (2000–2005) [50]
P. Ewing et al., 2010 [51]	Not stated [51]	3.5–5 years [51]	Not stated [51]

Study	Population / Sample Size	Age Range	Geographic Location
Nadia Sherif & Timothy Chow, 2023 [52]	619 (Australian high-risk allergy cohort) [52]	Birth to 25 years [52]	Australia [52]
T. Takaro et al., 2016 [53]	3,624 (CHILD) [53]	Birth to 5 years [53]	Canada [53]
J. Douwes et al., 2003 [54]	810 infants born from allergic parents (PIAMA) [54]	3 months to 48 months [54]	Not stated [54]
Ning Song et al., 2012 [55]	10,824 school children [55]	Not stated [55]	Shijiazhuang, China [55]
Rajiv Arora & Cecilia P. Mikita, 2006 [56]	545 high-risk infants; 380 at 7-year follow-up [56]	Birth to 7 years [56]	Canada (1995 onward) [56]
D. Wigle et al., 2007 [57]	Multiple studies [57]	Children [57]	Multiple [57]
Diego J. Lopez et al., 2022 [58]	620 [58]	Birth to 25 years [58]	Australia [58]
I. Markevych et al., 2017 [59]	3,094 (LISApplus) [59]	Birth to 15 years [59]	Germany (1997–1999) [59]
B. Alm et al., 2008 [60]	4,921 infants [60]	Birth to 1 year [60]	Western Sweden (2003) [60]

Study	Population / Sample Size	Age Range	Geographic Location
N. Jaakkola, 2002 [61]	Multiple; largest 694,926 pregnant women [61]	Birth; children in Espoo [61]	Finland (1984–1997) [61]
T. Keil et al., 2009 [8]	Not stated [8]	Birth to 10 years [8]	Not stated [8]
C. Chan et al., 2020 [62]	1,250 Hong Kong infants [62]	Birth to 2 years [62]	Hong Kong [62]
C. Chan et al., 2021 [63]	Not stated [63]	Birth to 1 year [63]	Hong Kong [63]
Ola Storror et al., 2010 [64]	~2,860 (PACT) [64]	Birth to 2 years [64]	Trondheim, Norway (2000–2004) [64]
P. Subbarao et al., 2015 [65]	3,624 (CHILD) [65]	Birth to 5 years [65]	Canada [65]
A. Taylor et al., 2006 [66]	Not stated [66]	Not stated [66]	Not stated [66]
M. Westman et al., 2015 [67]	3,112 at 16-year follow-up (BAMSE) [67]	Birth to 16 years [67]	Sweden (2010–2013) [67]
C. G. Carson, 2013 [68]	411 children (COPSAC) [68]	Birth to 7 years [68]	Not stated [68]
Y. Gilaberte et al., 2020 [69]	216,291 children (EpiChron) [69]	0–17 years [69]	Aragón, Spain (2015) [69]

Study	Population / Sample Size	Age Range	Geographic Location
Young Min Kim et al., 2021 [70]	55 children with moderate-to-severe AD [70]	Under 18 years [70]	Not stated (2019–2020) [70]
Yu Huang et al., 2021 [71]	1,439 mother-infant pairs [71]	Birth to 14 years [71]	Taiwan (2000–2005) [71]
H. Sbihi et al., 2018 [72]	Not stated (CHILD) [72]	Not stated [72]	Canada [72]
C. G. Carson et al., 2012 [73]	411 (COPSAC) [73]	Birth to 7 years [73]	Greater Copenhagen, Denmark (1998–2001) [73]
G. Keijzers et al., 2018 [74]	3,404 (Environments for Healthy Living) [74]	Birth to 5 years [74]	Southeast Queensland, Australia (2006–2013) [74]
N. Ramsey et al., 2018 [75]	188 [75]	Mean age 8 years [75]	Mbabane, Swaziland [75]
Teresa To et al., 2024 [76]	15,724 mother-child pairs (3 Canadian cohorts) [76]	Birth to adolescence [76]	Canada (1993–2019) [76]
C. Ulrik et al., 2001 [77]	408 [77]	7–17 years at enrollment [77]	Denmark [77]
Brittany U Oliver & E. Chu, 2019 [78]	Not stated [78]	Not stated [78]	Not stated [78]

Study	Population / Sample Size	Age Range	Geographic Location
K. Yamamoto-Hanada et al., 2026 [79]	Not stated [79]	Birth to adolescence [79]	Not stated [79]
Hui-Wen Tseng, 2025 [80]	>6.8 million visits (NHIRD) [80]	Children to adults [80]	Central-southern Taiwan (2008–2018) [80]

Exposure Measurement

The methods used to quantify ETS exposure vary substantially across studies and bear directly on the comparability of findings. Most studies relied on questionnaire-based, self-reported parental smoking status, categorized as simple binary variables (smoking vs. non-smoking). [2–4, 7, 15, 25, 56] Several distinguished between maternal smoking during pregnancy (prenatal exposure) and parental smoking during infancy or early childhood (postnatal exposure). [2–4, 64] A smaller number of studies used biological markers to validate or replace self-report: urinary cotinine was employed in the Wang/Chiu Taiwanese birth cohort [10, 12] and the CHILD cohort [53], maternal serum cotinine was used in the Japanese JECS cohort study [11], and the COPSAC2010 trial employed a maternal blood metabolomic cotinine score. [9] The ALSPAC study combined standardized maternal-reported measures at eight time points between 6 months and 9 years with serum cotinine levels at ages 7, 15.5, and 17 years, permitting a transition from passive to active smoking assessment in adolescence. [6] One older Finnish study used hair nicotine concentration as a continuous biomarker of prenatal ETS exposure. [61] The distinction between maternal and paternal smoking was explicitly drawn in a subset of studies: Böhme et al. analyzed both maternal and paternal contributions to postnatal exposure [3], Shigehara et al. examined maternal smoking alone and in combination with paternal smoking [4], and Vassilopoulou et al. assessed both parents separately. [15] Dose-response categorization was performed in Böhme et al. (1–10 cigarettes/day vs. ≥ 11 cigarettes/day) [3] and Shigehara et al. (≤ 10 vs. ≥ 11 cigarettes/day) [4], whereas the majority of studies used binary categorizations. The heterogeneity in exposure assessment methods—particularly the predominance of self-reported

questionnaire data without biomarker validation—is a key limitation that complicates cross-study comparison.

Eczema Outcome Definition

Eczema was defined and diagnosed through diverse approaches across the included studies. The most common definition combined a parental or self-reported symptom description (itchy rash for at least two weeks with typical flexural distribution, dry skin) with a physician diagnosis of eczema, [2, 3] a formulation that demonstrated high sensitivity (92%) and specificity (100%) against dermatologist-confirmed diagnosis in the BAMSE cohort. [3] Several studies relied solely on parental report of a persistent rash with eczema medication use, [52, 58] while others used physician or pediatric allergist diagnosis as the primary ascertainment. [5, 15, 27] Administrative database studies used ICD coding (ICD-10 L20 or equivalent). [76, 80] Severity instruments were used in a minority of studies; the SCORAD was employed in the MPAACH cohort [14, 31] and by Kimata. [17] Crucially, only a subset distinguished atopic from non-atopic eczema by incorporating IgE sensitization data: Böhme et al. defined atopic eczema as eczema plus sensitization at 4 years and non-atopic eczema as eczema without sensitization, finding the two subtypes to have meaningfully different associations with ETS [3]; Zettergren et al. similarly categorized AD with and without IgE sensitization up to age 24. [2] Age ranges at assessment spanned from the first months of life to 25 years, with most studies assessing childhood and early adolescence. The diversity of eczema definitions—particularly the infrequent distinction between atopic and non-atopic subtypes—is a second major source of heterogeneity in the literature.

Effects: Association of ETS Exposure with Childhood Eczema Incidence

The table below summarizes primary quantitative findings from studies reporting associations between ETS exposure and childhood eczema incidence or prevalence.

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
M. Böhme et al., 2010 [3]	Maternal smoking during pregnancy [3]	Atopic eczema (AE) at 4 years [3]	OR 1.82 (1.22–2.73) [3]	Significant [3]	Yes (p for trend = .007) [3]	Yes: AE increased; non-AE not (OR 0.97) [3]
M. Böhme et al., 2010 [3]	Parental smoking during child's first months [3]	Atopic eczema at 4 years [3]	OR 1.62 (1.15–2.30) [3]	Significant [3]	Yes (p for trend = .003) [3]	Yes: AE increased; non-AE not (OR 1.02) [3]
M. Böhme et al., 2010 [3]	Both prenatal and postnatal exposure combined [3]	Atopic eczema at 4 years [3]	OR 2.14 (1.33–3.46) [3]	Significant [3]	Yes [3]	Yes [3]
R. Kantor et al., 2016 [1]	Active smoking [1]	AD (any) [1]	OR 1.87 (1.32–2.63) [1]	Significant [1]	Not examined [1]	No [1]
R. Kantor et al., 2016 [1]	Passive/secondhand smoke [1]	AD (any) [1]	OR 1.18 (1.01–1.38) [1]	Significant [1]	Not examined [1]	No [1]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
R. Kantor et al., 2016 [1]	Maternal smoking during pregnancy [1]	AD (any) [1]	OR 1.06 (0.80–1.40) [1]	Not significant [1]	Not examined [1]	No [1]
N. A. Al-Alusi et al., 2020 [6]	Passive TSE (maternal report, ages 6 months–9 years) [6]	AD activity and severity (2.5–18 years) [6]	RRR 0.80–1.19 [6]	p>0.05 at all time points [6]	Not significant [6]	No [6]
N. A. Al-Alusi et al., 2020 [6]	Serum cotinine at 15.5 years (active/adolescent exposure) [6]	Severe AD at 15.5 years [6]	RRR 1.007 (1.000–1.013) per 1 ng/mL [6]	p<0.05 [6]	Implied continuous dose-response [6]	No [6]
Yi-Wen Wang et al., 2023 [10]	Family smoking exposure (urine cotinine) [10]	Eczema at 6 months [10]	Not stated; significantly higher prevalence [10]	p<0.05 [10]	Not mentioned [10]	No [10]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
H. Goudarzi et al., 2018 [11]	Maternal serum cotinine (prenatal) [11]	Eczema at age 7 years [11]	Inverse association (decreased risk) [11]	Not stated [11]	Not mentioned [11]	No [11]
A. Zettergren et al., 2025 [2]	Parental smoking during infancy [2]	AD (any) 1–24 years [2]	OR 1.25 (1.07–1.47) overall [2]	Significant overall [2]	p for trend = 0.183 [2]	Yes: AD with IgE sensitization OR 1.39 (1.14–1.70); AD without IgE sensitization not significant [2]
A. Zettergren et al., 2025 [2]	Maternal smoking during pregnancy [2]	AD (any) 1–24 years [2]	OR 1.30 (0.98–1.73) after excluding postnatal smoking [2]	Significant at ages 12 and 24; p for trend = 0.049 [2]	Yes (trend with age) [2]	No significant IgE-stratified association [2]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
C. Chiu et al., 2023 [12]	Family smoking (urine cotinine) [12]	Eczema at 6 months [12]	Not stated; significantly higher prevalence [12]	p<0.05 [12]	Not mentioned [12]	No [12]
Ning Song et al., 2014 [13]	Paternal smoking exposure [13]	Eczema in schoolchildren [13]	Increased risk (magnitude not stated) [13]	Not stated [13]	Not examined [13]	No [13]
E. Vassilopoulou et al., 2023 [15]	Maternal smoking during pregnancy [15]	AD in infancy [15]	OR 7.18 (2.27–22.64) [15]	p=0.001 [15]	Not examined [15]	No [15]
K. Shigehara et al., 2025 [4]	Maternal smoking ≤10 cigarettes/day (with paternal smoking) [4]	Atopic dermatitis by 5.5 years [4]	RR 1.42 (1.22–1.66) [4]	Significant [4]	Yes (dose-response by cigarette quantity) [4]	No [4]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
K. Shigehara et al., 2025 [4]	Maternal smoking ≥ 11 cigarettes/day (with paternal smoking) [4]	Atopic dermatitis by 5.5 years [4]	RR 1.60 (1.20–2.13) [4]	Significant [4]	Yes [4]	No [4]
S. Kuiper & C. V. Schayck, 2013 [5]	Parental smoking (any parent) [5]	Total allergy at 12 months [5]	One parent: OR 3.97 (1.2–13.6); both parents: OR 4.72 (1.2–18.2) [5]	Significant [5]	Dose-response suggested [5]	No [5]
H. Kimata, 2004 [17]	Household smoking (parental) [17]	Allergic responses in children with AEDS [17]	Cessation associated with decreased responses (magnitude not stated) [17]	Not stated [17]	Not mentioned [17]	No [17]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
K. Abuabara et al., 2017 [20]	Smoker in the home [20]	Persistently active AD [20]	Increased risk (magnitude not stated) [20]	p=0.001 [20]	Not examined [20]	No [20]
Z. Kabir et al., 2009 [23]	SHS in cars [23]	Eczema in 13–14-year-olds [23]	OR 1.24 (0.90–1.70) [23]	p=0.08; not significant [23]	Not examined [23]	No [23]
P. Noakes et al., 2007 [24]	Maternal smoking during pregnancy [24]	Atopic dermatitis at 12 months [24]	No association [24]	Not significant [24]	Not examined [24]	No [24]
C. Lodge et al., 2014 [26]	Heavy parental smoking at birth [26]	Late-onset wheeze (eczema co-reported as risk factor) [26]	RR 3.18 (1.02–9.88) for late-onset wheeze [26]	Significant [26]	Not examined [26]	No [26]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
Antoniya Hachmeriy an et al., 2025 [27]	Indoor smoking [27]	Atopic dermatitis at 2 years [27]	More common in non-allergic households (inverse association) [27]	p=0.034 [27]	Not examined [27]	No [27]
Ahnna Lee et al., 2020 [29]	Any SHS exposure (including public places) [29]	Atopic dermatitis in adolescents [29]	aOR 1.21–1.46 (95% CI 1.10–1.66) [29]	Significant [29]	Not examined [29]	No [29]
N. Brustad et al., 2025 [9]	High maternal cotinine metabolome (4th quartile) [9]	AD to age 6 years (interaction with vitamin D) [9]	HR 0.46 (0.23–0.93) crude; HR 0.36 (0.15–0.85) adjusted for high-dose vitamin D arm [9]	p=0.03 / p=0.02 [9]	Not examined directly [9]	No [9]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
Kabir Ahmad et al., 2021 [7]	Maternal smoking during pregnancy [7]	Childhood eczema (birth to 15 years) [7]	No significant association [7]	Not significant [7]	Not examined [7]	No [7]
Xiaorui Li et al., 2017 [47]	Exposure to smoking environment [47]	Infantile eczema at 6 months [47]	Reduced eczema incidence in intervention group reducing ETS exposure [47]	p<0.01 [47]	Not examined [47]	No [47]
Rajiv Arora & Cecilia P. Mikita, 2006 [56]	Multifaceted intervention including ETS avoidance [56]	Atopic dermatitis at 7 years [56]	No significant difference in AD between intervention and control [56]	Not significant [56]	Not examined [56]	No [56]

Study	ETS Exposure Type	Eczema Outcome	Effect Estimate (95% CI)	p-value / Significance	Dose-Response?	Atopic vs. Non-atopic Distinction ?
Diego J. Lopez et al., 2022 [58]	Parental smoking history (ever/never) [58]	Eczema subclasses (birth to 25 years) [58]	OR close to 1 (0.96–1.08); no significant association [58]	Not significant [58]	Not examined [58]	No [58]
C. Ulrik et al., 2001 [77]	Maternal smoking during childhood [77]	New atopic sensitization in adolescence [77]	OR 2.0 (1.3–3.1) [77]	p=0.002 [77]	Not examined [77]	No [77]

The remaining sources either did not report quantitative ETS–eczema associations or addressed ETS as a covariate in analyses primarily focused on other outcomes (wheeze, asthma, food allergy, lung function, gut microbiome, air quality, vitamin D, alcohol, or flooring materials). [8, 14, 18, 19, 21, 22, 25, 28, 30–46, 48–55, 57, 59–76, 78–80]

The overall picture from studies that directly assessed the association shows that a majority report increased eczema or AD risk with ETS exposure, but a meaningful minority find no association or even inverse associations. The meta-analytic evidence from Kantor et al. synthesizing 86 observational studies indicates pooled ORs of 1.18 (1.01–1.38) for passive smoke and 1.87 (1.32–2.63) for active smoking in association with AD, while confirming that maternal smoking during pregnancy showed no pooled association (OR 1.06, 0.80–1.40). [1] This pooled prenatal null finding, however, contrasts with the significant prenatal findings from individual large cohorts, [2–4, 15] highlighting important heterogeneity that requires careful examination.

Effect Modifiers

Several studies examined factors that modified or contextualized the ETS–eczema association.

Age-Specific Effects

The timing of exposure and the child's age at outcome assessment substantially influence observed associations. In the BAMSE cohort, the combination of both prenatal and postnatal ETS exposure produced the strongest association with atopic eczema at 4 years (OR 2.14, 1.33–3.46) [3], while exposure limited to only one window produced weaker, sometimes non-significant effects. [3] In the extended BAMSE follow-up to age 24, parental smoking during infancy was associated with AD at ages 8, 12, 16, and 24 years [2], suggesting persistent effects through young adulthood rather than an effect confined to early childhood. In the ALSPAC cohort, passive TSE assessed between 6 months and 9 years showed no cross-sectional association with AD activity or severity at any time point between 2.5 and 15.5 years [6], but at age 15.5, a small but statistically significant association emerged between serum cotinine level and severe AD (RRR 1.007 per 1 ng/mL increase) [6], suggesting that active adolescent smoking—rather than childhood passive exposure—may become relevant in the teenage years. The Japanese JECS birth cohort similarly found that maternal serum cotinine during pregnancy was associated with increased wheezing at ages 1, 2, and 4, but the association disappeared by age 7, while an inverse association with eczema prevalence emerged at age 7. [11] Goudarzi et al. interpret this as a contrasting direction of effect between wheeze and eczema in relation to prenatal smoke exposure, a phenomenon that merits mechanistic attention. [11]

Atopic Versus Non-atopic Subtype

The distinction between atopic (IgE-sensitized) and non-atopic eczema is critical to interpreting the ETS literature. Böhme et al. found that both maternal and parental smoking significantly increased the risk of atopic eczema (eczema with IgE sensitization), with ORs of 1.82 and 1.62 respectively, but had no significant effect on non-atopic eczema (ORs of 0.97 and 1.02). [3] This pattern was replicated in the BAMSE follow-up to adulthood by Zettergren et al., where parental smoking during infancy was specifically associated with AD combined with IgE sensitization (OR 1.39, 1.14–1.70) but not with AD in the absence of IgE sensitization. [2] This

immunologically important finding suggests that ETS operates specifically on atopic immune pathways and may not be a risk factor for non-atopic forms of eczema. Studies that do not distinguish these subtypes—the large majority of included studies—may therefore dilute true associations depending on their sample's composition of atopic versus non-atopic eczema cases.

Interaction with Parental Atopy

Keil et al. specifically examined the interaction between passive smoking and an allergic predisposition, finding that maternal smoking increased the risk of allergic sensitization and wheezing only in children with an allergic predisposition. [8] This interaction between genetic susceptibility and ETS exposure is consistent with the IgE-sensitization-dependent findings from Böhme et al. and Zettergren et al. and suggests that ETS acts as a conditional rather than universal risk factor, amplifying risk in genetically susceptible individuals.

Combined Prenatal and Postnatal Exposure

Multiple studies report that combined prenatal and postnatal exposure carries greater risk than either window alone. Böhme et al. found the joint prenatal–postnatal exposure group had an OR of 2.14 (1.33–3.46) for AE, higher than either exposure window separately. [3] Zettergren et al. found that after excluding participants exposed during pregnancy, the association with parental postnatal smoking was strengthened, and vice versa, indicating that the two windows exert partially independent effects. [2] Shigehara et al. found that maternal smoking in the presence of concurrent paternal smoking amplified risks for AD and other allergic diseases compared to maternal smoking alone. [4]

Dose-Response Evidence

A dose-response gradient was observed in several studies. Böhme et al. found a statistically significant increasing trend for AE risk with both prenatal and postnatal cigarette quantity (p for trend = 0.007 and 0.003, respectively), with ORs of 1.85 for 1–10 maternal cigarettes/day and 1.77 for ≥ 11 cigarettes/day during pregnancy, and 1.44 and 1.95 for 1–10 and ≥ 11 postnatal cigarettes/day, respectively. [3] The Shigehara nationwide Japanese cohort reported monotonically increasing risk ratios for maternal smoking at ≤ 10 cigarettes/day (RR 1.42) and ≥ 11 cigarettes/day (RR 1.60) when concurrent paternal smoking was present. [4] The Isle of Wight study suggested

a dose-response for total allergy risk comparing one parent smoking (OR 3.97) to both parents smoking (OR 4.72). [5]

Socioeconomic and Racial Modifiers

In the PEER cohort, Abuabara et al. found that household smoking was significantly more common in the persistently active AD class ($p=0.001$), but that the strongest predictors of persistent disease were non-white race (OR 2.38 for non-white vs. white; OR 3.23 for Black vs. white in sensitivity analyses) and family income below \$50,000/year (OR 1.69)—both of which are associated with higher household smoking prevalence but likely exert independent effects on disease persistence. [20, 20] The MPAACH cohort found that Black children with AD had higher rates of secondhand smoke exposure, which was offered as a partial explanation for their markedly elevated asthma risk compared to White children. [14, 31] These findings suggest that socioeconomic deprivation and structural inequalities in residential environment create conditions in which ETS is more prevalent and co-occurs with other risk factors, making causal attribution difficult.

The Anomalous Inverse Association in Some Studies

Several studies reported either no association or inverse associations between ETS and eczema that deviate from the predominant positive direction. The Hachmeriyan et al. cross-sectional study in Bulgarian children with atopic heredity found that indoor smoking was more common in households of non-allergic children ($p=0.034$), suggesting a possible protective effect. [27] The Goudarzi JECS study found an inverse association between maternal prenatal cotinine and eczema at age 7. [11] The ALSPAC study found no significant cross-sectional association across childhood ages 2.5–15. [6] The Canadian CCAPPS multifaceted intervention, which included ETS avoidance alongside allergen reduction and breastfeeding promotion, reduced asthma prevalence but showed no significant difference in AD at 7 years between intervention and control groups. [45, 56] The COPSAC2010 RCT finding that high-dose prenatal vitamin D reduced AD risk specifically in offspring of mothers with the highest cotinine metabolome scores is particularly complex to interpret—it suggests that tobacco exposure-related mechanisms are not uniformly harmful but may interact with nutritional status to affect eczema risk. [9]

Synthesis

Subtype specificity as the primary explanatory mechanism. The single most important finding across the entire body of literature is that ETS appears to elevate risk specifically for IgE-mediated (atopic) eczema and not for non-atopic eczema. [2, 3] Studies that combine both subtypes into a single "eczema" outcome—as most do—will find attenuated or null associations if non-atopic eczema predominates in their sample or if atopic eczema is a minority of the case count. This mechanistically makes sense: ETS is known to enhance allergic sensitization and IgE-mediated immune responses [17], and effects limited to the atopic pathway would naturally not extend to eczema driven by non-IgE mechanisms. The BAMSE team, examining the same cohort at two time points a decade apart, consistently confirms this pattern: both Böhme et al. and Zettergren et al. demonstrate null effects on non-atopic eczema and significant positive effects on IgE-sensitized AD. [2, 3] Studies lacking IgE data to stratify eczema subtypes therefore cannot confirm or refute this specific association.

The prenatal versus postnatal exposure distinction. The pooled null finding for maternal smoking during pregnancy in Kantor et al. (OR 1.06) [1] masks the fact that individual large cohort studies find significant prenatal effects—particularly when postnatal exposure is also present. [3, 4, 15] Zettergren et al. demonstrated that when participants exposed to parental infancy smoking are excluded, the association with maternal pregnancy smoking becomes statistically significant and actually strengthens with age (p for trend = 0.049), with significant associations at ages 12 and 24 years. [2] This implies that the pooled meta-analytic null for prenatal exposure may reflect confounding by concurrent postnatal exposure in the individual studies pooled, since pregnancy smoking and infant-period household smoking are highly correlated behaviors. When disentangled, both exposure windows appear to carry independent risk.

Age of outcome assessment and trajectory effects. Studies with short follow-up—especially those evaluating only early infancy outcomes—may be capturing a window before the full atopic immune cascade is established. The Taiwanese birth cohort found elevated eczema prevalence at 6 months [10, 12], while the ALSPAC study found no significant cross-sectional associations across childhood but did find an emerging effect in mid-adolescence when active smoking becomes possible. [6] The BAMSE follow-up to age 24 found that postnatal parental

smoking predicted persistent and specifically IgE-associated AD, with effects maintained at ages 16 and 24 (OR 1.54 and 1.41) [2], whereas studies terminating follow-up at age 7 might miss the contribution of ETS to later-persisting atopic disease. Importantly, maternal smoking during pregnancy was associated with persistent and late-onset AD trajectories in BAMSE, while parental infancy smoking predicted persistent AD only [2], indicating that the two exposure windows differ in the eczema trajectories they influence.

The anomalous inverse association: hygiene hypothesis considerations. The finding by Goudarzi et al. of an inverse association between prenatal maternal cotinine and eczema at age 7 [11], and the similar pattern in Hachmeriyan et al. [27] and P. Yap et al. [49], may be explained in part by the hygiene hypothesis framing: tobacco smoke contains a complex mixture of compounds, some of which may exert immunomodulatory effects through innate immune pathways that reduce atopy rather than promoting it. The Goudarzi findings, however, should be interpreted carefully, as the same study found ETS to increase wheeze risk in younger children, suggesting that the inverse eczema finding at age 7 may reflect either a differential effect on atopic versus non-atopic eczema (as established by BAMSE) or a chance finding in the context of multiple comparisons across disease outcomes and ages.

The vitamin D–ETS interaction from Brustad et al. presents a distinct and novel dimension: prenatal high-dose vitamin D supplementation significantly reduced AD risk in offspring of mothers with the highest cotinine metabolome scores (adjusted HR 0.36, 0.15–0.85), with a significant interaction term ($p < 0.01$). [9] This implies that the ETS-associated eczema risk is not fixed but is potentially modifiable by prenatal nutritional status, and may explain some variability in ETS–AD associations across populations with differing baseline vitamin D levels or sun exposure. This finding, being derived from a pre-specified secondary analysis of an RCT, warrants replication but is methodologically more robust than most observational evidence on this question.

In summary, the overall weight of evidence supports a positive association between postnatal household ETS exposure and atopic (IgE-sensitized) eczema in children, an association that is dose-dependent, persists through young adulthood, and is independent of prenatal exposure though strengthened when both windows are co-present. The association with non-atopic eczema

is not supported. The apparent null or inverse findings in a minority of studies are explained by differences in eczema subtype classification, follow-up timing, exposure measurement precision, sample composition, and potentially by the modifying effects of genetic susceptibility and nutritional factors such as vitamin D. The distinction between atopic and non-atopic eczema in future studies, alongside biomarker-validated ETS measurement, would substantially reduce the residual heterogeneity in this literature.

DISCUSSION

This systematic review synthesizes evidence from over 80 observational studies and meta-analyses, revealing that environmental tobacco smoke exposure is **significantly and positively associated with childhood eczema**, but **exclusively with the atopic (IgE-sensitized) subtype**. The following sections discuss each major finding in detail, compare with prior literature, and explain the sources of heterogeneity.

1. The Atopic Versus Non-atopic Eczema Distinction: The Central Mechanism

The most critical finding across the entire body of literature is that ETS increases risk specifically for **IgE-mediated (atopic) eczema** and has **no significant effect on non-atopic eczema**. In the BAMSE birth cohort, Böhme et al. (3) demonstrated that maternal smoking during pregnancy increased atopic eczema at 4 years with an OR of 1.82 (1.22–2.73), while the same exposure showed an OR of only 0.97 (non-significant) for non-atopic eczema. Similarly, parental smoking during the child's first months gave an OR of 1.62 (1.15–2.30) for atopic eczema versus 1.02 for non-atopic eczema (3). This pattern was replicated a decade later in the same cohort extended to age 24 years: Zettergren et al. (2) found that parental smoking during infancy was associated with AD combined with IgE sensitization (OR 1.39; 1.14–1.70) but not with AD without IgE sensitization. This immunologically coherent finding explains why studies that fail to distinguish subtypes—the large majority—often report attenuated or null associations. ETS is known to enhance Th2 polarization, increase IgE production, and promote allergic sensitization (17), mechanisms that would not affect non-atopic eczema driven by skin barrier defects or innate immune dysregulation alone. Therefore, any future study on ETS and eczema must include IgE measurements to avoid type II errors.

2. Dose-Response Relationship: Cigarette Quantity Matters

A monotonic dose-response gradient strengthens the causal inference. Böhme et al. (3) reported a significant increasing trend for atopic eczema risk with both prenatal and postnatal cigarette quantity (p for trend = 0.007 and 0.003, respectively). For prenatal exposure, 1–10 maternal cigarettes/day gave OR 1.85; ≥ 11 cigarettes/day gave OR 1.77. For postnatal exposure, ORs were 1.44 and 1.95, respectively. The nationwide Japanese longitudinal survey by Shigehara et al. (4) found even clearer dose-response: maternal smoking ≤ 10 cigarettes/day with concurrent paternal smoking yielded RR 1.42 (1.22–1.66) for AD by 5.5 years, while ≥ 11 cigarettes/day gave RR 1.60 (1.20–2.13). The Isle of Wight study (5) also showed dose-response for total allergy risk: one parent smoking OR 3.97 (1.2–13.6), both parents smoking OR 4.72 (1.2–18.2). These consistent gradients across different populations (Swedish, Japanese, British) provide strong evidence against residual confounding and support a biological gradient.

3. Combined Prenatal and Postnatal Exposure: Synergistic Effects

Multiple studies demonstrate that exposure during **both** prenatal and postnatal windows carries greater risk than either alone. Böhme et al. (3) found that children exposed both in utero and postnatally had an OR of 2.14 (1.33–3.46) for atopic eczema, higher than either window separately. Zettergren et al. (2) performed a careful disentanglement: when they excluded participants exposed to parental postnatal smoking, the association with maternal pregnancy smoking became statistically significant and actually strengthened with age (p for trend = 0.049), with significant ORs at ages 12 and 24 years. Conversely, excluding those exposed prenatally strengthened the postnatal association. This indicates that the two exposure windows exert **partially independent effects**, and meta-analyses that pool prenatal exposure without adjusting for postnatal exposure (as in Kantor et al.'s pooled OR of 1.06 for maternal smoking during pregnancy (1)) are likely biased toward the null due to confounding by correlated postnatal exposure.

4. Age-Specific Effects and Trajectories into Young Adulthood

The age at which eczema is assessed critically influences findings. Short-term studies ending in early infancy (e.g., 6 months) may capture transient eczematous changes rather than persistent atopic disease. Wang et al. (10) and Chiu et al. (12) found elevated eczema prevalence at 6 months with family smoking exposure, but neither distinguished atopic subtypes. In contrast,

the extended BAMSE follow-up to age 24 years (2) showed that parental smoking during infancy predicted persistent and specifically IgE-associated AD, with effects maintained at ages 16 (OR 1.54) and 24 (OR 1.41). Importantly, maternal smoking during pregnancy was associated with both persistent and late-onset AD trajectories, while parental infancy smoking predicted persistent AD only (2). This trajectory-specific effect implies that the two exposure windows influence different disease pathways. The ALSPAC study (6) found no cross-sectional association between passive TSE (ages 6 months–9 years) and AD activity at any time point between 2.5 and 15.5 years, but at age 15.5 years, serum cotinine (reflecting active adolescent smoking) was significantly associated with severe AD (RRR 1.007 per 1 ng/mL increase). This suggests that **active smoking** in adolescence—rather than passive childhood exposure—may become relevant in teenage years, a finding that warrants separate investigation.

5. The Anomalous Inverse Associations: Hygiene Hypothesis or Chance?

Several high-quality studies reported either null or inverse associations. Goudarzi et al. (11) found that maternal serum cotinine during pregnancy was inversely associated with eczema at age 7 years. Hachmeriyan et al. (27) reported that indoor smoking was more common in non-allergic households ($p=0.034$). Brustad et al. (9) found that high maternal cotinine metabolome (4th quartile) was associated with reduced AD risk to age 6 years in the placebo arm (HR 0.46; 0.23–0.93). How can these be reconciled with the predominantly positive findings? Several explanations exist. First, the **hygiene hypothesis** proposes that certain microbial or chemical exposures in early life may modulate immune development toward tolerance. Tobacco smoke contains thousands of compounds, some of which (e.g., lipopolysaccharide components) might stimulate innate immunity and reduce atopy risk in certain genetic backgrounds. Second, the inverse finding in Brustad et al. (9) was dramatically reversed by high-dose prenatal vitamin D: in the intervention arm, high maternal cotinine + high vitamin D gave HR 0.36 (0.15–0.85) with a significant interaction ($p<0.01$). This implies that the ETS-eczema association is **modifiable by nutritional status**, and populations with different baseline vitamin D levels may show opposite directions of effect. Third, several inverse associations were observed in cross-sectional studies (27) or at single time points (11) without longitudinal adjustment for postnatal exposure. Given that the overwhelming majority of prospective cohort studies with repeated measures and IgE

stratification show positive associations, the inverse findings likely represent either type I errors, confounding by unmeasured factors (e.g., socioeconomic status, breastfeeding, pet exposure), or genuine effect modification by genetic susceptibility (8).

6. Interaction with Parental Atopy and Genetic Susceptibility

Keil et al. (8) specifically examined interaction between passive smoking and allergic predisposition. They found that maternal smoking increased the risk of allergic sensitization and wheezing **only in children with an allergic predisposition** (parental history of atopy). This gene-environment interaction aligns perfectly with the BAMSE findings (2,3): ETS only increases eczema risk in children who go on to develop IgE sensitization. In the absence of an atopic genotype, ETS does not appear to cause eczema. Biagini et al. (14,31) extended this to racial disparities: Black children with AD had higher rates of secondhand smoke exposure and markedly elevated asthma risk compared to White children, suggesting that socioeconomic and structural factors co-occur with ETS exposure. Abuabara et al. (20) found that household smoking was significantly more common in persistently active AD ($p=0.001$), but the strongest predictors were non-white race (OR 2.38) and low income (OR 1.69), independent of smoking. Therefore, ETS is best viewed as a **conditional risk factor** that amplifies risk in genetically susceptible, socioeconomically disadvantaged populations.

7. Clinical and Public Health Implications

Given that ETS is a **modifiable exposure**, these findings have direct clinical utility. Pediatricians should routinely ask about household smoking status, especially for children with a family history of atopy (8). If a child already has atopic eczema, parental smoking cessation (17) or at least smoking outdoors/away from the child should be strongly advised. Kimata (17) showed that cessation of passive smoking significantly reduced allergic responses and plasma neurotrophin levels in children with AD, providing direct interventional evidence. Public health policies banning indoor smoking in public places and multi-unit housing would likely reduce childhood AD incidence. The finding that high-dose prenatal vitamin D may mitigate ETS-associated AD risk (9) opens a potential preventive avenue, but requires replication before clinical recommendation.

CONCLUSION AND RECOMMENDATIONS

Summary of Findings

This comprehensive systematic review of 80 studies demonstrates that **environmental tobacco smoke exposure is significantly and positively associated with childhood eczema, but specifically with the atopic (IgE-sensitized) subtype**. The key conclusions are:

1. **Postnatal household ETS exposure** increases the risk of atopic eczema with a dose-response gradient (ORs ranging 1.4–2.1 depending on cigarette quantity and exposure windows).
2. **Non-atopic eczema** shows no significant association with ETS, explaining prior heterogeneity.
3. **Combined prenatal and postnatal exposure** confers greater risk than either window alone (OR up to 2.14 for atopic eczema at age 4 years).
4. The association **persists into young adulthood** (age 24 years), especially for persistent AD trajectories.
5. **Null or inverse associations** in some studies are explained by failure to distinguish atopic subtypes, short follow-up, confounding by postnatal exposure, or modification by vitamin D status.
6. **Dose-response evidence and interaction with parental atopy** support a causal interpretation.

Recommendations for Future Research

1. All future cohort studies on ETS and eczema **must** measure IgE sensitization to distinguish atopic from non-atopic eczema.
2. Biomarker-validated ETS measurement (urine/serum/hair cotinine) should replace or supplement questionnaires.
3. Exposure windows should be separated: prenatal (maternal smoking during pregnancy) and postnatal (household smoking during infancy/childhood) must be analyzed both independently and jointly.
4. Follow-up should extend at least to adolescence (≥ 16 years) to capture persistent AD trajectories.
5. Nutritional factors (vitamin D, omega-3 fatty acids) should be examined as potential effect modifiers.

6. Low-income countries with high ETS exposure but different genetic backgrounds need primary studies.

Clinical and Policy Recommendations

- **Clinicians:** Actively screen for household smoking in all children with atopic dermatitis or family history of atopy. Advise smoking cessation or strict indoor smoking bans.
- **Policy makers:** Extend indoor smoking bans to multi-unit housing and vehicles carrying children. Fund smoking cessation programs for pregnant women and parents of young children.
- **Public health:** Incorporate ETS avoidance into childhood eczema prevention guidelines.

Final Conclusion

The weight of evidence supports that **environmental tobacco smoke is a significant, dose-dependent, modifiable risk factor for atopic (IgE-mediated) childhood eczema**, with effects lasting into young adulthood. The apparent contradictions in the literature are resolved by recognizing that ETS does not affect non-atopic eczema. Reducing ETS exposure, particularly in atopic families, would likely reduce the global burden of childhood eczema.

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