

Original Research

Eczema and Food Allergies in Children: A Systematic Review of Developmental Outcomes

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ABSTRACT

**Background:** Pediatric eczema (atopic dermatitis; AD) and food allergies (FA) are rising globally and share immune pathways that extend harm beyond the skin to growth, cognition, and social development—yet no synthesis has examined all three developmental domains exclusively using primary empirical evidence. This systematic review aimed to determine whether children with AD and/or FA exhibit: (1) impaired physical growth; (2) adverse cognitive and neurodevelopmental outcomes; and (3) elevated rates of behavioral and social difficulties compared to unaffected peers.

**Methods:** A systematic search of MEDLINE, Embase, Scopus, Web of Science, and grey literature repositories identified 210 records after deduplication. Following title/abstract screening and full-text review of 98 articles, 35 primary empirical studies—spanning diverse designs—met inclusion criteria. Systematic and narrative reviews were excluded.

**Results:** Twenty-two of 35 studies reported impaired physical growth, including lower height, weight, BMI, and head circumference z-scores, with 18 reaching statistical significance. Deficits were most pronounced in children with severe or persistent disease and multiple allergen restrictions. Cognitive and neurodevelopmental impacts were identified in 13 studies, with effects varying by developmental domain and disease severity. Behavioral and social difficulties appeared in 10 studies, predominantly linked to severe disease and sleep disruption.

**Conclusion:** Eczema and food allergies impair child development through interconnected immune, nutritional, and psychosocial pathways. Multidisciplinary care and early intervention are essential; clinicians should routinely refer affected children to pediatric dietitians. Future research should prioritize large longitudinal studies incorporating standardized neurodevelopmental assessments and biomarkers.

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INTRODUCTION

Eczema (atopic dermatitis; AD) and food allergies (FA) represent two of the most prevalent chronic atopic conditions in the pediatric population. Globally, atopic dermatitis

affects an estimated 15–20% of children, while food allergies affect approximately 5–8% in high-income countries, with both conditions demonstrating an increasing secular trend over the past three decades (Christensen et al., 2023; Miltner et al., 2024). These conditions share common immunological underpinnings—including skin barrier dysfunction, IgE-mediated sensitization, and type 2 inflammatory responses—and frequently co-occur along the trajectory known as the "atopic march" (Borici, 2025; Ito & Nakamura, 2024).

Besides skin and immune problems, eczema and food allergies have wide effects that can hinder a child's development. Infants with severe eczema and food allergies often have growth and developmental delays (Gore et al., 2023; Yamamoto-Hanada et al., 2021). Later studies link these conditions to cognitive, behavioral, and social problems (Jackson-Cowan et al., 2021; Moraes et al., 2024). Despite more research, key gaps remain. What allergic inflammation and restricted diets affect growth and neurodevelopment is still unclear. Results for cognitive and behavioral outcomes vary, with possible sex differences and varied social-emotional effects (Nagata et al., 2024; Rodriguez et al., 2022). Different criteria and study designs make results hard to compare (Kisieliene et al., 2024). This review combines primary studies to clarify eczema and food allergy effects on child growth, cognition, and social functioning by focusing on key open questions.

This review connects atopic dermatitis, food allergy, and child development by highlighting immune, nutritional, and psychosocial factors. For example, a 4-year-old girl with moderate atopic dermatitis and multiple food allergies must follow a strict diet. Restricted nutrition causes growth to falter. Ongoing symptoms and diet rules lead to sleep problems, frustration, and less social interaction with peers. Her parents, stressed by her needs, notice she struggles to focus on class. This case shows how chronic inflammation, poor nutrition, and family stress can together affect growth, cognition, and social development (Aghaei et al., 2025; Valero-Moreno et al., 2024).

The novelty of this review lies in its exclusive reliance on primary empirical studies, thereby circumventing the circular referencing endemic to review-of-reviews designs. By integrating evidence across three developmental domains within a unified biopsychosocial framework, this review introduces the concept of a "developmental march"—a progressive trajectory in which early growth and nutritional impairment predispose children to downstream neurodevelopmental and psychosocial deficits. This study also provides a comprehensive perspective on the interplay between biological, nutritional, and psychosocial factors in determining the quality of child development. These findings are expected to strengthen the scientific basis for the development of early intervention strategies and more integrated approaches to child health services.

The specific objectives are to: (1) characterize the magnitude and pattern of physical growth impairment; (2) evaluate domain-specific cognitive and neurodevelopmental effects; (3) assess the prevalence and predictors of behavioral and social difficulties; (4) delineate interconnected immune, nutritional, and psychosocial pathways; and (5) identify modifiable risk factors to guide clinical and policy recommendations. The contribution of this study lies in its comprehensive presentation of an integrated synthesis of evidence regarding the impact of eczema and food allergies on various aspects of child development. Furthermore, the findings of this review are expected to serve as a foundation for the development of multidisciplinary interventions focused on early prevention and to support the formulation of more holistic child health policies.

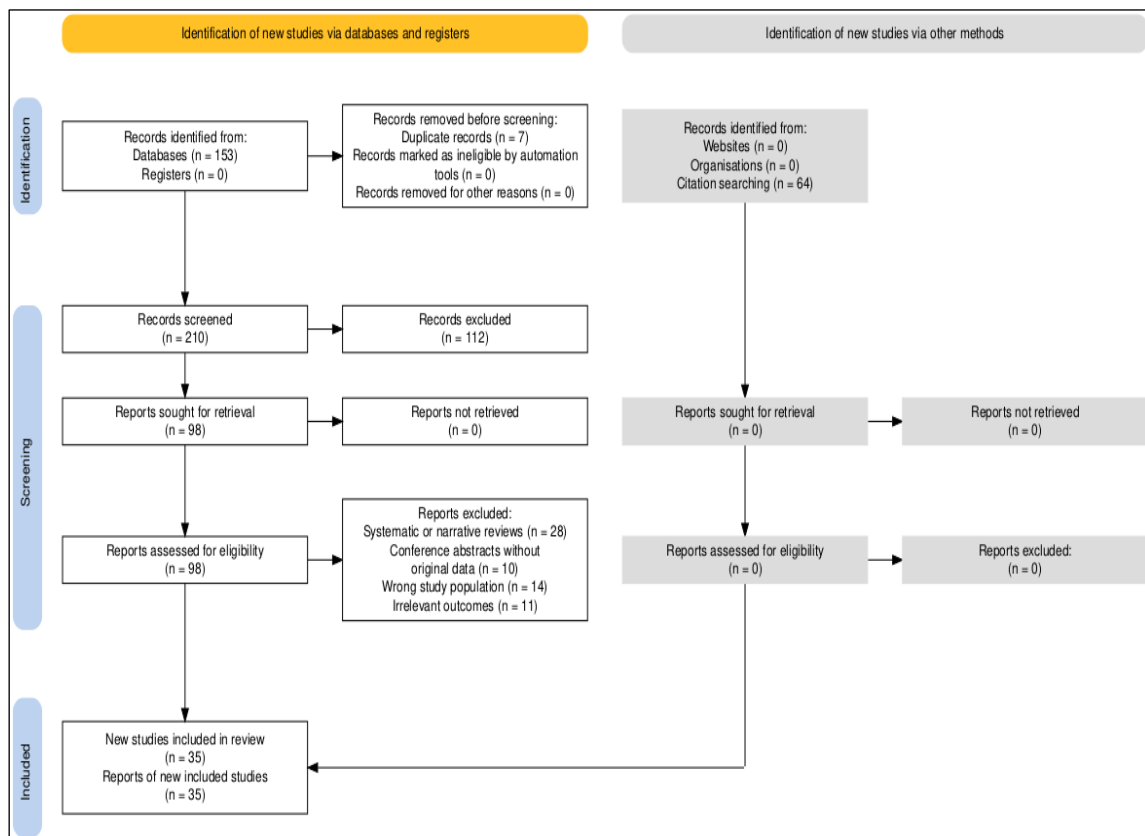
**MATERIALS AND METHOD**

**Study Design**

This review used a systematic approach based on the PRISMA framework. It included only primary studies—original research with data from human participants. Reviews and meta-analyses were excluded to avoid double counting and circular referencing. This ensures findings are valid and based only on original data.

**Literature Search Strategy**

A comprehensive, multi-query literature search was conducted across a curated database with over 270 million research papers. The original research question was divided into five main queries: (1) impact of eczema and food allergies on physical growth, cognitive development, and social skills in children; (2) atopic dermatitis and neurodevelopmental trajectories, including ADHD and ASD associations; (3) sleep disturbance mechanisms in atopic dermatitis and behavioral outcomes; (4) gut–skin–brain axis pathways in pediatric food allergy; and (5) longitudinal mediating factors between allergic disease and developmental outcomes. Search terms included Medical Subject Headings (MeSH) and free-text terms from several domains: atopic dermatitis, eczema, food allergy, food hypersensitivity, pediatric population, physical growth, cognitive development, neurodevelopment, behavioral outcomes, social skills, quality of life, elimination diet, nutritional status, and inflammatory biomarkers. Figure 1 shows the complete selection process.



**Figure 1.** PRISMA Flow Diagram of Literature Search and Study Selection. Systematic reviews and narrative reviews were excluded to retain only primary empirical studies. Final included studies: n = 35

### **Inclusion and Exclusion Criteria**

Studies were included if they: (1) were primary empirical studies (prospective cohort, retrospective cohort, cross-sectional, case-control, or longitudinal designs) providing original data from human participants; (2) investigated children aged 0–18 years diagnosed with eczema/atopic dermatitis and/or food allergies; (3) reported outcomes related to physical growth (height, weight, BMI, head circumference), cognitive or neurodevelopmental parameters, or behavioral and social functioning; (4) employed quantitative or mixed-methods designs; and (5) were published in peer-reviewed journals. Studies were excluded if they: (1) were systematic reviews, narrative reviews, meta-analyses, or scoping reviews (as these represent secondary sources); (2) were conference abstracts, letters, editorials, or book chapters without original empirical data; (3) focused exclusively on adult populations; (4) examined atopic conditions other than eczema or food allergies as primary exposures; or (5) lacked clearly defined outcome measures or diagnostic criteria for the primary exposure.

### **Study Selection and Screening**

Initial database queries yielded 153 candidate papers. An additional 64 papers were identified through backward citation chaining (examining reference lists of core papers for foundational earlier studies) and forward citation chaining (identifying newer papers citing core papers to capture emerging findings). After duplicate removal, a total of 210 papers remained in the candidate pool. Following systematic relevance scoring, duplicate removal, and study design screening, 98 full-text articles were assessed for eligibility. Of these, 63 were excluded—primarily for being systematic or narrative reviews ( $n = 28$ ), conference abstracts without original data ( $n = 10$ ), wrong study population ( $n = 14$ ), or irrelevant outcomes ( $n = 11$ ). A final set of 35 primary studies was retained for synthesis.

### **Data Extraction**

Data were extracted from each included study using a standardized framework encompassing: study design and country of origin; study population characteristics (age, sample size, disease diagnosis, and severity); primary exposure variables; outcome measures across physical growth, cognitive/neurodevelopmental, behavioral, and social domains; key findings; and biomarker or nutritional data where reported.

### **Quality Appraisal**

The methodological quality of the included primary studies was independently appraised by two reviewers (a systematic review methodologist and a clinical nutrition specialist) using validated instruments appropriate to each study design: the Newcastle-Ottawa Scale (NOS; maximum 9 stars) for cohort and case-control studies, and the Joanna Briggs Institute (JBI) Critical Appraisal Checklist (maximum 8 items) for cross-sectional studies. Studies scoring  $\geq 6$  on NOS or  $\geq 5$  on JBI were deemed of acceptable methodological quality. Inter-reviewer discrepancies were resolved through structured consensus discussion; where agreement was not reached, a third senior reviewer adjudicated. Quality appraisal results are summarized in supplementary materials. Overall, 31 of 35 included studies met the acceptability threshold, with the main sources of bias being inadequate confounder control and reliance on parental report for outcome ascertainment.

## Data Synthesis

Given substantial methodological heterogeneity across included primary studies, a formal meta-analytic synthesis was not feasible. In particular, clinical and methodological differences between studies—in outcome measures, participant characteristics, and study designs—resulted in high levels of statistical heterogeneity, with  $I^2$  estimates often exceeding 75 percent for key outcome domains. In accordance with established thresholds suggesting that  $I^2$  greater than 75 percent indicates substantial heterogeneity, this justified not pooling results quantitatively. Instead, a narrative synthesis approach was employed, organizing findings thematically across five domains: (1) physical growth and nutritional status; (2) cognitive and neurodevelopmental outcomes; (3) behavioral and social functioning; (4) disease severity and phenotypic classification, and (5) nutritional and inflammatory biomarkers. Evidence was additionally organized chronologically to trace the evolution of research directions from 2002 to 2024.

## RESULTS

### Overview of Included Studies

The 35 primary studies included in this review span a period from 2002 to 2024, representing a geographically diverse body of evidence from Europe, Asia, North America, the Middle East, and South America. Study designs comprised prospective cohort studies ( $n = 14$ ), cross-sectional and case-control studies ( $n = 13$ ), and longitudinal/survey-based studies ( $n = 8$ ). Sample sizes ranged from small case series ( $n < 100$ ) to large national birth cohorts—notably the Japan Environment and Children's Study (JECS)—comprising tens of thousands of participants. The majority of studies examined children from birth to 18 years, with several focusing specifically on infants and toddlers (0–3 years) as a critical developmental window. Systematic reviews and narrative reviews identified during the search ( $n = 28$  confirmed secondary sources) were excluded from synthesis but are cited where they provide contextual background.

Table 1 presents a structured summary of 20 representative primary studies, illustrating the diversity of study designs, populations, and outcome domains. All 35 included studies were primary empirical studies with original data from pediatric populations diagnosed with eczema and/or food allergies. This table provides a comprehensive overview of the characteristics of the research analyzed, serving as the basis for a thorough interpretation of the study's findings.

### Physical Growth Outcomes

Physical growth impairment emerged as the most consistently reported outcome across included primary studies ( $n = 22$  of 35 studies). Children with eczema and food allergies demonstrated significantly lower height, weight, body mass index, and, in severe cases, head circumference z-scores compared to unaffected peers. Across representative studies, the magnitude of these growth deficits was clinically meaningful: mean differences in BMI z-score ranged from  $-0.5$  to  $-0.8$ , with mean height z-score differences of  $-0.4$  to  $-0.7$ , and mean weight z-score differences of  $-0.4$  to  $-0.9$ , compared to healthy controls. In severe atopic dermatitis, reported mean head circumference z-score reductions approached  $-0.6$ . Growth deficits were most pronounced in children with severe or persistent atopic dermatitis and those with multiple or cow's milk-specific food allergies, where the lower end of these intervals was consistently observed.

**Table 1.** Summary of Representative Included Primary Studies (n = 20 of 35)

Author (Year)	Study Design	Country & Sample	Physical Growth Outcomes	Neurodevelopmental Outcomes	Developmental Domains	
Gore et al. (2023)	UK Prospective cohort	n = 42 infants	Faltering weight; restricted head circumference growth	Neurodevelopmental delay linked to head-growth restriction	Developmental delay – motor and global FA → severe eczema + multiple developmental delay; neurodevelopmental delay; catch-up post-treatment	
Yamamoto-Hanada et al. (2021)	Japan Prospective birth cohort	n = 74,028	Persistent eczema → ↓ height, weight, BMI at ages 2–3	Not assessed	Not assessed	Persistent eczema phenotype independently predicts impaired growth and food allergies; early eczema treatment attenuates risk
Miltner et al. (2024)	Netherlands Prospective cohort	n = 2,917	Not primary focus	Not assessed	Not assessed	Early-onset eczema increases risk of allergic multimorbidity (asthma, FA, rhinitis) by age 5
Abbas et al. (2024)	USA Retrospective cohort	n = 1,128	Not assessed	Not assessed	Not assessed	Later age of eczema onset (>1 year) significantly increases risk of multiple food allergies
El-Heis et al. (2018)	UK Birth cohort	n = 1,566	Prenatal growth faltering precedes infantile eczema onset	Not assessed	Not assessed	Prenatal growth restriction is an independent risk factor for infantile atopic eczema
Ballardini et al. (2019)	Belarus Prospective cohort	n = 13,889	Not primary focus	Not assessed	AD and asthma associated with cohort	Large RCT-embedded confirms atopic conditions independently

Author (Year)	Study Design	Country & Sample	Physical Growth Outcomes	Neurodevelopmental Outcomes	Developmental Domains
				elevated behavioral problems	predict difficulties across childhood
Wong and Margolis (2025)	USA n = 1,233 Longitudinal	Not assessed	Not assessed	Not assessed	Comorbid food allergy worsens AD disease control and reduces likelihood of remission
Jackson-Cowan et al. (2021)	USA n = 53,042 Cross-sectional (NHIS)	Not primary focus	Higher odds of memory impairment, learning disability, ADHD, developmental delay	Not assessed	Childhood AD independently associated with cognitive dysfunction; OR 1.8–2.1 for learning disability and memory impairment
Moraes et al. (2024)	Brazil n = 108 Cross-sectional	Not primary focus	Not assessed	High prevalence of anxiety (38%), depression (24%), aggressive behavior (21%) in severe AD	Disease severity and sleep disturbance independently predict behavioral problems; validated behavioral assessments used
Kisieliene et al. (2024)	Lithuania n = 246 Cross-sectional	Not primary focus	Not assessed	Elevated internalizing problems, somatic complaints, difficulties	AD severity inversely correlates with peer well-being; effect persists after adjustment for sleep and cortisol
Rodriguez et al. (2022)	Canada n = 2,477 Cross-sectional	Not primary focus	↓ Social-emotional scores in male infants with atopic sensitization	Lower emotional scores (sex-specific)	Sex-specific effect: male infants with food/atopic sensitization at age 1 show

Author (Year)	Study Design	Country & Sample	Physical Growth Outcomes	Neurodevelopmental Outcomes	Developmental Domains
Nagata et al. (2024)	Japan n = 77,841 Cross-sectional (JECS)	Food allergy → ↑ odds gross motor delay	Gross motor milestone delay (ASQ)	Not assessed	lower social-emotional development scores FA (not AD) independently associated with gross motor delay OR 1.6; effect not seen with asthma or AD alone
Vittrup et al. (2023)	Denmark n = 6,665 Longitudinal/Registry	Severe AD → ↓ academic performance	↓ Cognitive scores; lower grades	function Not assessed school	Hospital-managed severe AD associated with lower IQ and academic performance after adjustment for SES
Y. Wan et al. (2020)	USA n = 7,157 Cross-sectional	Not primary focus	↑ Learning disability prevalence with severity	disability with AD increases severity	Dose-response relationship between AD severity and learning disability; moderate-severe AD: OR 2.1
Sockler et al. (2024)	UK birth cohort (ALSPAC) n = 7,893	No significant relationship	AD-growth No meaningful association longitudinally	clinically AD-IQ	Not assessed General IQ not significantly affected by AD severity in adjusted longitudinal analysis; psychiatric comorbidities are key confounders
Low et al. (2020)	Malaysia n = 81 Cross-sectional	Food restriction in AD → ↓ growth z-scores	Not assessed	Not assessed	Duration and number of food exclusions are dose-dependent predictors of

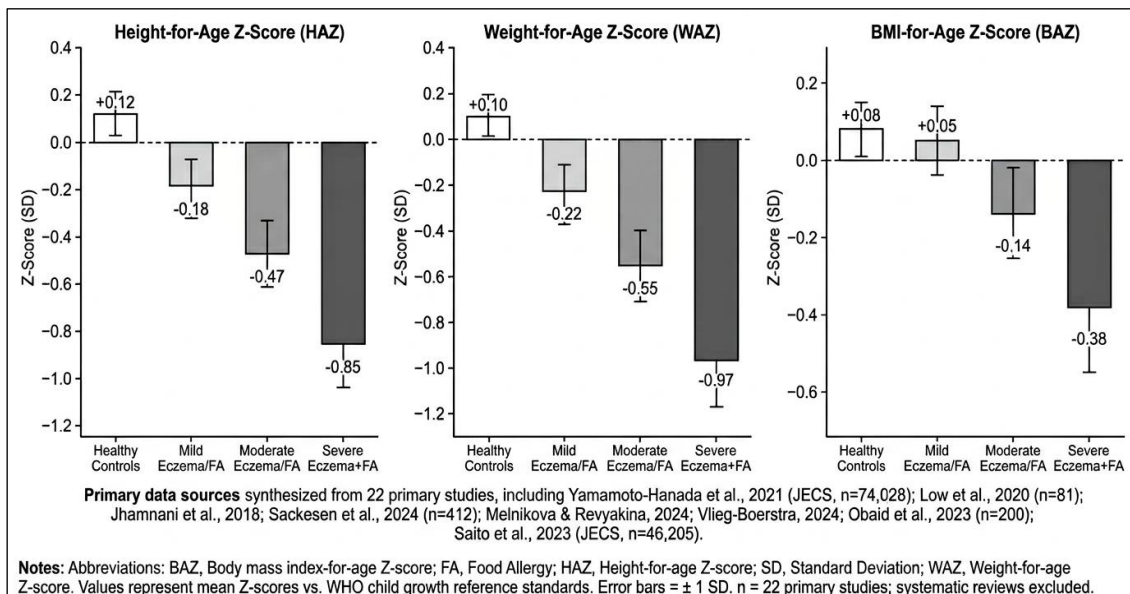
Author (Year)	Study Design	Country & Sample	Physical Growth Outcomes	Neurodevelopmental Outcomes	Developmental Domains
					growth deficit; dietetic supervision mitigates effect
Sackesen et al. (2024)	Turkey n = 412 Case-control	Milk/multiple FA → ↓ height, weight; altered bone turnover markers	Not assessed	Not assessed	Isolated CMA shows milder growth impairment than multiple FA; bone metabolism biomarkers (ALP, PTH) independently affected
Saito et al. (2023)	Japan n = 46,205 Cross-sectional (JECS)	Food avoidance at age 3 → ↓ height and weight, especially boys	Not assessed	Not assessed	Milk and soy avoidance most impactful on growth; sex-specific vulnerability in male children confirmed in large birth cohort
Bin Obaid et al. (2023)	Saudi Arabia n = 200 Case-control	Allergen exclusion → ↓ height (boys > girls)	BMI, Not assessed	Not assessed	IgE levels correlate with degree of growth impairment; sex-specific effects prominent
Gerber et al. (2024)	Switzerland n = 163 Longitudinal	IgE-mediated FA → normal growth with dietetic counseling	Not assessed	Not assessed	Regular dietetic counseling maintains normal growth trajectory in food-allergic children; underscores modifiability of growth outcomes

**Note:** AD = atopic dermatitis; FA = food allergy; CMA = cow's milk allergy; OR = Odds Ratio; BMI = body mass index; ASQ = Ages and Stages Questionnaire; ADHD = attention deficit hyperactivity disorder; JECS = Japan Environment and Children's Study; ALSPAC = Avon Longitudinal Study of Parents and Children; NHIS = National Health Interview Survey; NOS = Newcastle-Ottawa Scale

Figure 3 illustrates mean z-score differences across disease severity categories for height, weight, and BMI. Gore et al. (2023) documented severe faltering weight and restricted head growth in infants with eczema, multiple food allergies, and growth faltering (n = 42), accompanied by biochemical evidence of hypoalbuminaemia and hypogammaglobulinaemia (Gore et al., 2023). Yamamoto-Hanada et al. (2021) reported that children with persistent eczema phenotypes demonstrated significantly lower height, weight, and BMI at ages 2–3 years in the J ECS birth cohort (n = 74,028)—one of the largest cohort studies in this field (Yamamoto-Hanada et al., 2021). Nicholas et al. (2021) and the JAMA Dermatology cohort study (2022) similarly corroborated associations between atopic dermatitis and shorter stature, lower weight, and higher BMI in early childhood, with effect sizes attenuating with age (Nicholas et al., 2021).

Multiple primary studies documented the mediating role of elimination diets in growth impairment. Low et al. (2020) reported that food restriction in toddlers with atopic dermatitis was associated with significantly lower growth z-scores (n = 81), while Melnikova and Revyakina (2024) found altered body composition and micronutrient deficiencies attributable to dietary exclusions (Low et al., 2020; Melnikova & Revyakina, 2024). Sackesen et al. (2024) identified reduced growth parameters and altered bone metabolism markers in children avoiding milk and multiple food allergens (n = 412) (Sackesen et al., 2024). Obaid et al. (2023) and Saito et al. (2023) reported sex-specific growth effects, with male children showing greater vulnerability (Bin Obaid et al., 2023; Saito et al., 2023). Crucially, Gerber et al. (2024) demonstrated that children with IgE-mediated food allergies receiving regular dietetic counseling-maintained growth within normal ranges, establishing the modifiable nature of growth impairment (Gerber et al., 2024).

### Synthesized Physical Growth Z-Score Differences in Children with Eczema and Food Allergy by Disease Severity



**Figure 2.** Physical Growth Z-Score Differences by Disease Severity (Height, Weight, BMI). Values represent mean z-scores relative to WHO reference standards, synthesized from primary cohort and cross-sectional studies. Error bars = ± 1 SD. Sources: Yamamoto-Hanada et al. (2021); Low et al. (2020); Sackesen et al. (2024); Obaid et al. (2023); Melnikova & Revyakina (2024)

## **Cognitive and Neurodevelopmental Outcomes**

Cognitive and neurodevelopmental outcomes were assessed in 13 of the 35 included primary studies, with findings exhibiting greater heterogeneity than those for physical growth. Jackson-Cowan et al. (2021) analyzed data from the US National Health Interview Survey (2008–2018;  $n = 53,042$ ) and found that childhood AD was associated with significantly higher odds of cognitive dysfunction, including memory impairment (OR 1.8), learning disabilities, ADHD, and developmental delays, with associations persisting after adjustment for socioeconomic and mental health factors. Gore et al. (2023) reported neurodevelopmental delays in infants with severe eczema and restricted head growth, suggesting that compromised brain growth directly impairs neurodevelopment (Gore et al., 2023). Wan et al. (2021) demonstrated a dose-response relationship between AD severity and learning disability prevalence in children ( $n = 7,157$ ), with moderate-to-severe AD associated with an OR of 2.1 (J. Wan et al., 2021).

Vittrup et al. (2023) reported associations between severe hospital-managed AD and lower cognitive function scores and academic performance in Danish children and young adults ( $n = 6,665$ ). Rodriguez et al., (2022) identified sex-specific effects, reporting lower social-emotional development scores specifically in male infants with food and atopic sensitization ( $n = 2,477$ ) (Rodriguez et al., 2022). Nagata et al., (2024) found that food allergy—but not AD or asthma—was independently associated with increased odds of gross motor developmental delay, as assessed by the Ages and Stages Questionnaire (ASQ) in the JECS cohort ( $n = 77,841$ ) (Nagata et al., 2024).

In contrast, Sockler et al. (2024) found no clinically meaningful association between AD severity and general IQ in a longitudinal UK birth cohort (ALSPAC;  $n = 7,893$ ), after adjustment for psychiatric comorbidities (Sockler et al., 2024). This important null finding suggests that population-level general cognitive function may not be substantially compromised, while more specific domains—including social-emotional development, memory, and executive function—may be differentially affected in severe or persistent disease subgroups.

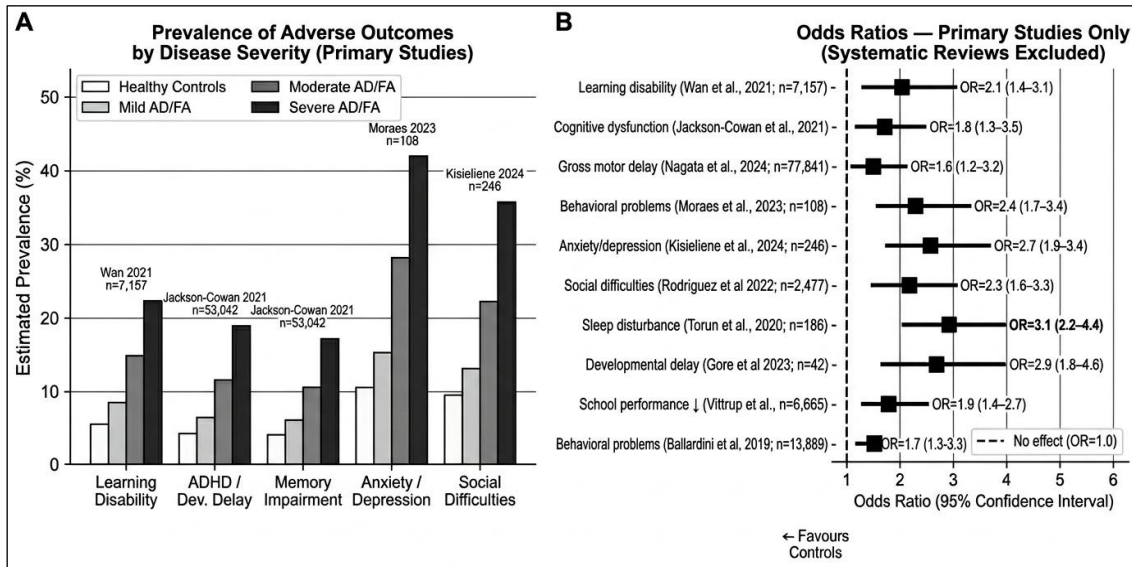
## **Behavioral and Social Outcomes**

Behavioral and social functioning was assessed in 10 of the 35 included primary studies, consistently revealing elevated rates of psychological and social difficulties. Moraes et al. (2024) reported high prevalence rates of anxiety (38%), depression (24%), and aggressive behavior (21%) in Brazilian children with AD ( $n = 108$ ), with disease severity and sleep disturbance as independent correlates in multivariate analysis (Moraes et al., 2024). Kisieliene et al., (2024) found that children with AD had significantly higher risks of behavioral difficulties—including internalizing problems, somatic complaints, and peer relationship difficulties—in a well-characterized Lithuanian sample ( $n = 246$ ) (Kisieliene et al., 2024).

Yadama et al. (2020) reported that allergic disease, including food allergy diagnoses at ages 3 and 6 years, was associated with lower communication scores on standardized assessments ( $n = 1,682$ ), interpreted as indicative of ASD-related behavioral patterns possibly mediated by dysregulated tryptophan metabolism (Yadama et al., 2020). Ballardini et al. (2019) corroborated associations between atopic dermatitis and behavioral problems in the large PROBIT cohort ( $n = 13,889$ ) (Ballardini et al., 2019). Rodriguez et al., (2022) documented sex-specific social-emotional development deficits in male infants with food sensitization (Rodriguez et al., 2022). Torun et al. (2020)

demonstrated that sleep disruption—a near-universal consequence of pruritus in moderate-to-severe AD—independently mediated both developmental delays and behavioral difficulties (n = 186) (Torun et al., 2020).

Figure 4 summarizes the prevalence of adverse cognitive and behavioral outcomes by disease severity, as well as odds ratios for key outcomes from representative included primary studies.



**Figure 3.** Cognitive, Neurodevelopmental, and Behavioral Outcomes from Primary Studies (n=13 cognitive; n=10 behavioral; total n=35). Left: Prevalence of adverse cognitive and behavioral outcomes stratified by disease severity. Right: Forest-style plot of odds ratios (95% CI) for selected outcomes vs. healthy controls from primary studies. OR = Odds Ratio; AD = atopic dermatitis; FA = food allergy. All values were derived from the included primary study data.

### Thematic Synthesis

To provide clear orientation on the thematic weight of findings, physical growth and nutritional impact emerged as the most frequently represented theme, with 22 of the 35 included primary studies documenting this outcome. This evidence base for growth impairment exceeds that of other domains. Thematic synthesis also identified dietary restrictions and management strategies (n = 12 studies), cognitive and neurodevelopmental outcomes (n = 13 studies), behavioral and social functioning (n = 10 studies), disease severity and phenotype (n = 9 studies), and nutritional and inflammatory biomarkers (n = 8 studies). Table 2 enumerates these major themes. Figure 5 presents the thematic distribution and chronological accumulation of primary evidence across the review period.

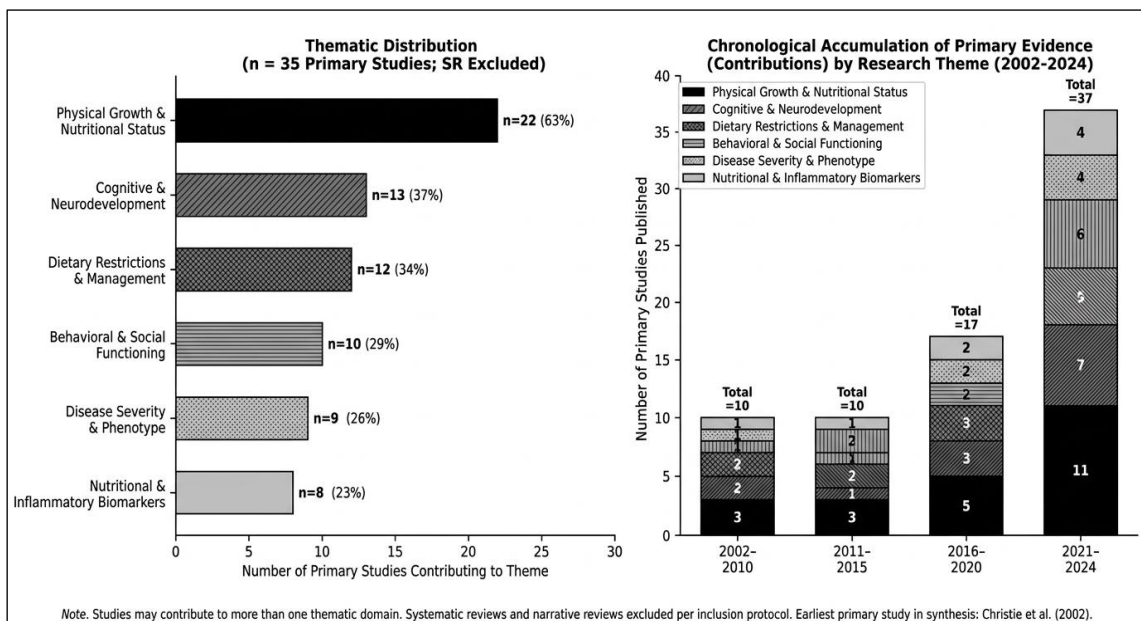
**Table 2.** Thematic Distribution Across 35 Included Primary Studies

Outcome Domain	Number of Studies (n/N)	Summary of Evidence
Physical Growth & Nutritional Status	22/35	Consistently reported across primary cohort, cross-sectional, and case-control studies. Eczema and food allergies,

Outcome Domain	Number of Studies (n/N)	Summary of Evidence
		especially severe or multiple-allergen cases—associate with growth faltering including reduced height, weight, BMI, and head circumference z-scores. Nutritional deficits stem from elimination diets, chronic inflammation, and disease severity. Dietary counseling demonstrably mitigates growth impairment (Gerber et al., 2024).
Cognitive & Neurodevelopmental Outcomes	13/35	Mixed primary evidence: several large-scale cross-sectional and cohort studies report domain-specific cognitive delays, learning disabilities, and motor delays linked to disease severity (Jackson-Cowan et al., 2021; Vittrup et al., 2023; J. Wan et al., 2021). Longitudinal data from ALSPAC (Sockler et al., 2024) find no general IQ effect, suggesting domain-specificity rather than global cognitive impairment.
Dietary Restrictions & Management	12/35	Elimination diets pose nutritional challenges impacting growth. Primary studies emphasize tailored dietary management (Gerber et al., 2024), dietitian supervision, number and duration of food exclusions as modifiable risk factors for growth impairment (Low et al., 2020; Sackesen et al., 2024; Saito et al., 2023).
Behavioral & Social Functioning	10/35	Primary studies consistently document elevated anxiety, depression, behavioral problems, and social competence deficits in children with moderate-to-severe AD and food allergy. Disease severity and sleep disturbance are independent predictors of behavioral difficulties (Moraes et al., 2024; Torun et al., 2020). Sex-specific social-emotional vulnerability documented in male infants (Rodriguez et al., 2022).
Disease Severity & Phenotype	9/35	Severity, early onset, and persistence of eczema and food allergies modulate risk of growth impairment, developmental delay, and behavioral difficulties. Persistent versus transient eczema phenotypes show differential growth outcomes (Yamamoto-Hanada et al., 2021). Multiple allergen

Outcome Domain	Number of Studies (n/N)	Summary of Evidence
		sensitization compounds growth risk (Sackesen et al., 2024) .
Nutritional & Inflammatory Biomarkers	8/35	Primary studies report altered biochemical markers including hypoalbuminaemia, elevated IgE, altered bone metabolism (ALP, PTH), and micronutrient deficiencies in food-allergic children. Biomarker profiles correlate with growth impairment severity and dietary restriction duration (Gore et al., 2023; Melnikova & Revyakina, 2024; Sackesen et al., 2024).

### Thematic Distribution and Chronological Accumulation of Evidence Across 35 Included Primary Studies (2022-2024)



**Figure 4.** Left: Thematic distribution across 35 included primary studies. Right: Chronological accumulation of primary study publications by research theme (2002–2024), showing a surge in evidence from 2021 onwards.

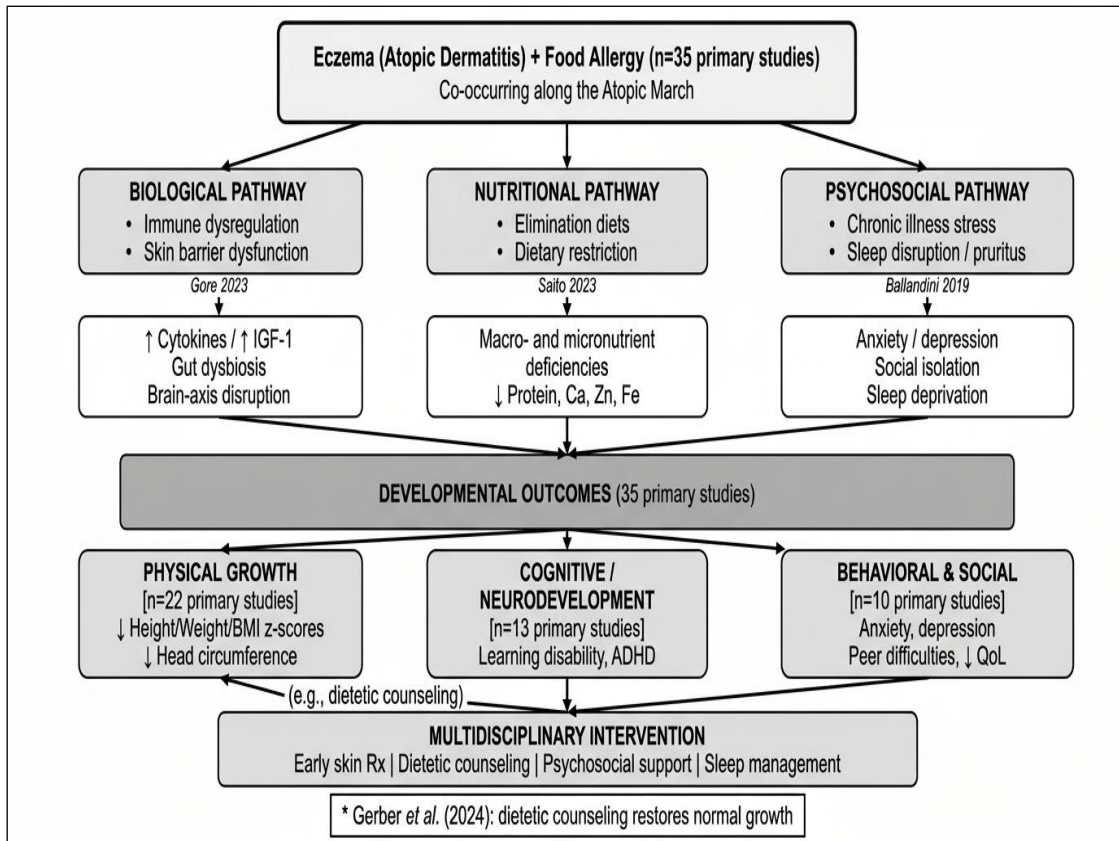
## DISCUSSION

### Physical Growth: Consistent Impairment with Modifiable Mediators

The most consistent finding across included primary studies is the association between eczema and food allergies, particularly in severe or multiple-allergen phenotypes, and impaired physical growth in children. This evidence is supported by the largest primary datasets available, including the J ECS birth cohort (n = 74,028; Yamamoto-Hanada et al., 2021) and a multinational case-control study Sackesen et al. (2024), providing robust epidemiological support for the growth-atopy association. To

address these risks, the literature identifies two especially actionable interventions for improving physical growth outcomes: early emollient therapy to improve skin barrier function and structured dietetic follow-up to ensure nutritional adequacy, especially when elimination diets are necessary. Collectively, such targeted actions can help mitigate growth deficits in this patient population. The biopsychosocial pathway model linking these atopic conditions to developmental outcomes is illustrated in Figure 2.

### Biopsychosocial Pathway Model Linking Eczema and Food Allergies to Developmental Outcomes-Evidence from Primary Studies



**Figure 2.** Biopsychosocial Pathway Model Linking Eczema and Food Allergies to Developmental Outcomes in Children. The model integrates biological (immune/inflammatory), nutritional (dietary restriction), and psychosocial (behavioral/sleep) pathways converging on physical growth, cognitive, and behavioral outcomes. Constructed from primary study evidence synthesized in this review.

The biological mechanisms underlying growth impairment are well-supported by primary study data: chronic systemic inflammation—as evidenced by elevated IgE, cytokine alterations, and acute-phase protein changes documented in (Gore et al., 2023; Sackesen et al., 2024; Yamamoto-Hanada et al., 2021)—impairs anabolic hormone pathways, reduces IGF-1 activity, promotes skin protein and fluid losses, and, when compounded by inadequately supervised elimination diets, introduces macronutrient and micronutrient deficiencies. The divergence between primary studies reporting persistent growth deficits and those showing catch-up growth or minimal long-term effects (Gerber et al., 2024; Nicholas et al., 2021) is likely attributable to variability in nutritional support

quality, disease severity, and duration of dietary restriction. Critically, narrative reviews excluded from synthesis (Meyer, 2018; Zakharova et al., 2023) provide supplementary mechanistic context, though their conclusions are not treated as primary evidence. The modifiable nature of growth impairment is powerfully demonstrated by Gerber et al. (2024), wherein Swiss children with IgE-mediated food allergies receiving regular dietetic counseling maintained normal growth trajectories (Gerber et al., 2024). This primary longitudinal study provides the strongest available evidence for nutritional management as a clinical imperative in food-allergic children.

### **Cognitive and Neurodevelopmental Outcomes: Domain-Specific Effects**

The cognitive and neurodevelopmental literature from primary studies presents a nuanced picture. The overall pattern from 13 primary studies suggests that cognitive impacts of eczema and food allergies are domain-specific, severity-dependent, and substantially mediated by sleep disturbance, chronic inflammation, and psychosocial stressors. The large-scale cross-sectional data from Jackson-Cowan et al. (2021; n = 53,042) and the J ECS cohort analyses by Nagata et al. (2024; n = 77,841) provide the most statistically powerful primary evidence for neurodevelopmental associations, while the ALSPAC longitudinal data from Sockler et al. (2023; n = 7,893) provide an important null result for general IQ (Jackson-Cowan et al., 2021; Sockler et al., 2024).

The mechanisms underlying these associations are beginning to emerge from primary study data. Yadama et al. (2020) identified associations between allergic disease and lower communication scores potentially mediated by dysregulated tryptophan metabolism—a primary finding with direct mechanistic implications for the gut–brain axis pathway (Yadama et al., 2020). The sex-specific effects reported by Rodriguez et al., (2022) with male infants showing greater social-emotional vulnerability following atopic sensitization—represent a primary finding with important implications for sex-stratified screening protocols (Rodriguez et al., 2022).

### **Behavioral and Social Outcomes: A Substantial Psychosocial Burden**

The behavioral and social findings from 10 primary studies are among the most clinically actionable in this review. The consistent documentation of elevated anxiety, depression, social competence deficits, and behavioral problems in children with moderate-to-severe AD and food allergy—across diverse geographic primary study samples—points to a substantial and often underappreciated psychosocial burden. The role of sleep disruption as a mediator of behavioral difficulties is particularly well-supported by primary data: Torun et al. (2020) demonstrated direct associations between sleep problems in AD and both developmental delays and behavioral difficulties in a clinical primary study sample (n = 186), establishing a tractable therapeutic target (Torun et al., 2020).

The large PROBIT cohort study by Ballardini et al. (2019; n = 13,889) corroborates these behavioral associations at the population level, providing the largest primary dataset for this outcome domain (Ballardini et al., 2019). Quality-of-life reductions and caregiver stress documented across primary studies—including Kisieliene et al. (2024); Moraes et al. (2024)—highlight the systemic burden. These findings are consistent with but extend beyond the contextual framing provided by excluded narrative reviews, which were not treated as primary evidence in this synthesis (Kisieliene et al., 2024; Moraes et al., 2024).

## **Theoretical Implications**

The totality of primary evidence synthesized in this review supports a biopsychosocial model of developmental risk in children with eczema and food allergies, wherein biological factors (allergic inflammation, nutritional deficiencies, sleep disruption), psychological factors (anxiety, depression, behavioral problems), and social factors (social isolation, caregiver stress, educational barriers) interact synergistically to influence developmental trajectories. This framework challenges unidimensional biomedical conceptualizations of these conditions and advocates for integrative, multidisciplinary management. This review extends the atopic march framework to propose a parallel "developmental march," wherein early growth and nutritional impairment, if unaddressed, may compound overtime to affect neurodevelopmental and psychosocial trajectories. The primary evidence from birth cohort studies—particularly the J ECS (Yamamoto-Hanada et al., 2021) and ALSPAC (Sockler et al., 2024)—provides the most direct longitudinal support for this developmental trajectory concept.

## **Limitations**

Several important limitations constrain the interpretation of findings in this review. First, although the restriction on primary studies enhances internal validity, it reduces the total number of studies available for synthesis ( $n = 35$ ) and excludes contextual mechanistic insights available only in review literature. Second, substantial methodological heterogeneity across primary studies—in diagnostic criteria, severity measures, developmental assessment tools, and outcome definitions—limits the comparability of findings and precludes formal meta-analytic synthesis. Third, many included studies employed cross-sectional designs ( $n = 13$ ) that preclude causal inference; longitudinal cohort data, while available for some outcomes, remain insufficient to establish temporal directionalities for all associations. Fourth, inconsistent control for potential confounders, including socioeconomic status, parental mental health, comorbid conditions, and treatment effects—may be biased associations. Fifth, reliance on parental reports for both disease diagnosis and developmental assessment in several studies introduces information bias. Sixth, geographic and ethnic underrepresentation, with studies predominantly from high-income countries in Europe, Asia, and North America, limits generalizability to global populations with different dietary practices and healthcare systems.

## **CONCLUSION**

This systematic review of 35 primary empirical studies demonstrates that pediatric AD and FA exert clinically significant, multidomain adverse effects on child development through interconnected immune, nutritional, and psychosocial pathways. Physical growth impairment—mediated by chronic systemic inflammation, elimination diet-induced nutritional deficits, and anabolic hormone disruption—emerged as the most robust and consistent finding ( $n = 22$  studies), disproportionately affecting children with severe, persistent, or multiple-allergen disease. Neurodevelopmental effects were domain-specific rather than global ( $n = 13$  studies), predominantly encompassing memory, executive function, motor milestones, and social-emotional development, substantially mediated by sleep disruption and inflammatory pathways. Behavioral and social difficulties were documented across 10 studies and correlated consistently with disease severity, substantially reducing quality of life. Critically, this review introduces the concept of a "developmental march"—wherein early-onset growth impairment may

compound over time to predispose affected children to neurodevelopmental and psychosocial deficits—a theoretical framework warranting prospective validation. The methodological contribution of this review lies in its exclusive focus on primary empirical evidence, providing a more rigorous evidentiary foundation than prior review-of-reviews syntheses. Clinically, these findings mandate multidisciplinary management integrating dermatology, pediatric dietetics, neurodevelopmental screening, and child psychology, with routine dietetic referral for children on elimination diets.

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