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Childhood Exposure to Farming Environment and Respiratory and Allergic Health Outcomes: A Systematic Review and Meta-Analysis

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Abstract

Aim: To evaluate the relationship between farming exposure and the risk of childhood asthma by synthesizing contemporary research findings. **Methods:** A systematic literature search was conducted across PubMed, Web of Science and Cochrane Library, focusing on studies published in English from 2001 to 2024. The inclusion criteria targeted peer-reviewed articles that explored the association between farming exposure and childhood asthma. A total of 20 studies were included in the review. Risk of bias of included studies was determined using ROBINS-I tool. The thematic analysis was employed to synthesize the results. **Results:** The findings revealed both protective effects and negative impacts of farm exposure on respiratory health. Notably, several studies indicated that childhood exposure to farming environments reduced sensitization to specific allergens. Some investigations found side effects such house-dust mite and other allergy sensitisation. Additionally, certain farming activities, particularly large animals and the use of pesticides were associated with an elevated risk of asthma. ROBINS-I assessment showed that most studies had low to moderate bias in the key domains, with significant risks due to confounding, selection, and missing data. **Conclusion:** This review underscored the complex relationship between farming exposure and childhood asthma. Most studies showed low to moderate risk of bias. The findings highlight the need for targeted interventions in agricultural environments.

Keywords: Farming exposure, childhood asthma, sensitization, protective effect, allergens, respiratory health, environmental factors

Introduction

Asthma is a prevalent chronic condition in children, characterized by wheezing, coughing episodes, and dyspnea (Rashmi et al. 2021). Approximately fifty percent of asthma cases are identified prior to the age of three, and eighty percent by the age of six (Thomas et al. 2024). The disease's origin remains incompletely elucidated; however, it is thought to entail a complex interplay of genetic variables and environmental stressors, with atopy being a significant contributor (Shao et al. 2022). As children mature, allergic airway disorders, including allergic rhinitis and asthma, may manifest, adhering to the phenomenon known as the atopic march (Skevaki et al. 2021). Approximately 10 to 20% of youngsters experience asthma, whereas 30 to 40% are affected by allergic rhinitis in contemporary developed nations (Banta et al. 2021). Moreover, children with allergic

rhinitis face an elevated risk of developing asthma. Asthma can diminish production due to absenteeism and incurs substantial expenses for national healthcare systems through emergency department visits and hospitalizations (Fishe et al. 2021). The etiology of asthma is well recognized as stemming from intricate interactions between genetic and environmental variables, many of which remain inadequately comprehended (Mattiuzzi and Lippi 2020; Custovic et al. 2023).

Childhood exposure to an agricultural setting has been demonstrated to confer protection against asthma in several investigations (Chu et al. 2021). Dust from animal enclosures contains high levels of endotoxin and muramic acid, both of which are bacterial components capable of activating innate immunity, potentially influencing the onset of asthma and allergy conditions (Islam et al. 2022). Agricultural methods and, hence, microbial exposures differ among farms. The impact of residing in an agricultural setting on asthma remains incompletely elucidated; however, it has led to the formulation of the hygiene hypothesis, which posits that early-life exposure to a variety of microbial and infectious agents may diminish the risk of atopic diseases, including asthma, by inhibiting T-helper 2 immune responses (Depner et al. 2020). Multiple studies have demonstrated a protective influence of upbringing in a farm setting on the incidence of hay fever and atopic sensitization in children (Chu et al. 2021; Islam et al. 2022). Thus, this systematic review and meta-analysis investigated the correlation between exposure to a farming environment and the occurrence of asthma in children.

Methods

Study Registration and Search strategy

This study was performed in accordance with the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA). This review was registered in PROSPERO (CRD42024617297). No ethical consideration and informed consent were required because this study used published data. PubMed, Web of Science and Cochrane Library were searched using following search terms: "farming exposure" OR "agricultural exposure" OR "farm environment" AND "childhood asthma" OR "asthma in children" OR "paediatric asthma" AND "risk factor" OR "cause" OR "association" AND "respiratory health" OR "allergic diseases" OR "environmental factors". Grey literature, including preprints, reports, and theses, was excluded to maintain

methodological consistency. Furthermore, we searched referenced articles from previously published meta-analyses, review articles, and cohort studies to identify any relevant studies.

Criteria for inclusion

This systematic review's inclusion criteria targeted articles published in English in peer-reviewed publications from 2001 to 2024. Restricting the publication date to the last decade guarantees that the review encompasses the most contemporary research, mirroring recent developments and trends in the discipline. The limitation to English-language publications arises from practical factors, such as the review team's linguistic competence and the widespread availability of English in scientific communication. Furthermore, choosing papers from peer-reviewed journals ensures a degree of methodological rigor and credibility. Study selection was conducted independently by two reviewers. Discrepancies were resolved through discussion, and a third reviewer was consulted if consensus was not reached.

Risk of bias assessment

The Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was used to determine the risk of bias in the included studies. It was chosen as it is appropriate in non-randomized study designs, such as cross-sectional, cohort, and control case-studies. It allows an organized evaluation of the quality of methods based on both qualitative and quantitative data in seven areas. Its evaluation included bias related to confounding, selection of participants, categorization of exposure, deviations of intended interventions, missing data, measuring outcomes, and the selection of reported outcomes. All the domains were rated on the low, moderate, or high risk of bias, and the results were summarised in a table form to enable easy comparison of the studies. ROBINS-I was selected due to its ability to tackle main issues of observational research, especially confounding and changes in exposure and outcome measures.

Sensitivity Analysis

In addition, a sensitivity analysis was conducted to evaluate the impact of excluding high-risk-of-bias (ROB) studies, confirming that their removal did not significantly alter the

overall risk ratio or substantially affect heterogeneity, thereby reinforcing the robustness of the meta-analysis findings.

Data extraction and analysis

Data extraction was conducted by one reviewer and cross-checked by a second reviewer to minimize errors and biases. A standardized data extraction form was employed, capturing key study characteristics (author, year, sample size, exposure type, outcome, key findings), ensuring replicability (Table 1-Supplementry file). The thematic analysis was conducted to characterize the outcomes based on farming exposure of different population and their health outcomes.

Results

Screening and Selection of Studies

Initially, a search yielded a total of 186 publications. After excluding 79 duplicate studies, there remained 107 distinct study publications for additional scrutiny. Other 52 studies were excluded since they were not conducted on children. More 23 studies were excluded due to involvement of treatments of severe diseases. Out of the remaining 32 publications, 12 were excluded because they contained literature reviews, meta-analyses, case studies, and protocols. Consequently, a total of 20 papers were selected for further investigation (Fig. 1)

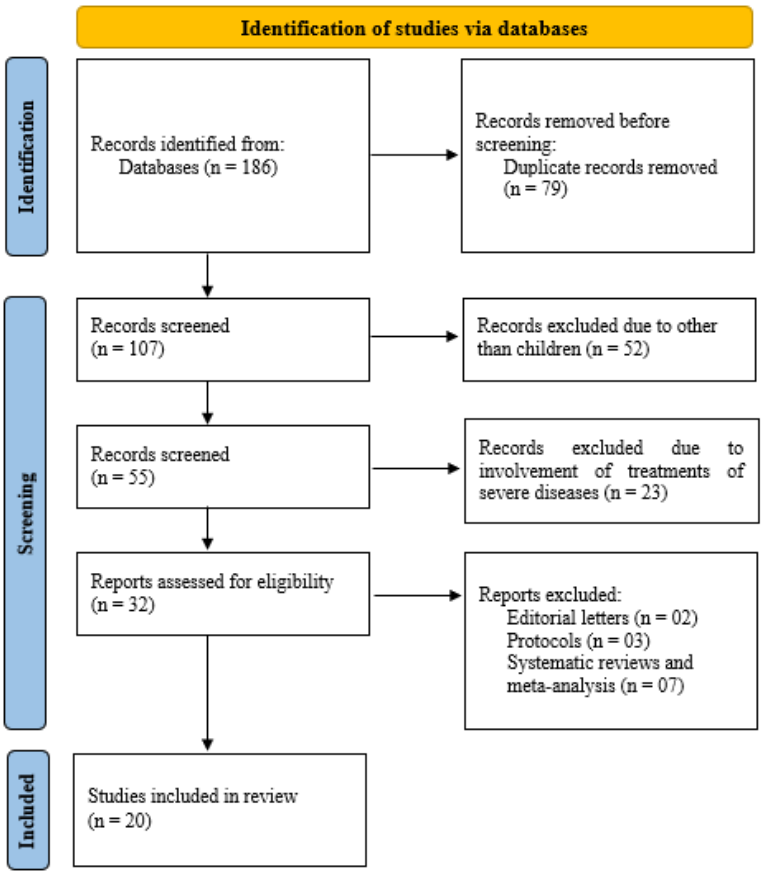


Fig 1. PRISMA Flow diagram showing the screening of studies

Risk of Bias Assessment Outcomes

ROBINS-I tool was used to measure the risk of bias of the included studies based on seven domains. The risk of bias in the majority of the studies was low to moderate, which suggests that the methodological quality is generally satisfactory. Merchant et al. (2005), Kilpelainen et al. (2002), and Pavilonis et al. (2013) were rated with low overall risk of bias, and Leynaert et al. (2001), Wickens et al. (2002), and Feng et al. (2016) were rated as moderate risk. Ojwang et al. (2020) had a critical risk of bias due to confounding, participant selection, and missing data management.

In the seven domains, a few studies were found to have moderate risk concerning confounding, selection of participants, and categorizing the exposure. Risk was low in most studies in terms of deviations of intended interventions, missing data, and selection of reported outcomes, but moderate or high risk was also found in some studies, especially Wickens et al. (2002), Feng et al. (2016), Midodzi et al. (2007), Hugg et al. (2008), and Ojwang et al. (2020). Outcome measurement was usually viewed as reliable, but some

studies used self-reported outcomes, which can lead to recall bias (Fig. 2). The issue of selective reporting was not found to be a big issue. In general, the evidence base was of low to moderate risk, although the results need to be interpreted with regard to possible confounding, selection bias, exposure errors and missing data.

Study	D1	D2	D3	D4	D5	D6	D7	Overall
Leynaert et al., 2001	Moderate	Low	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Wickens et al., 2002	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Kilpeläinen et al., 2002	Moderate	Low	Low	Low	Low	Low	Low	Low
Radon et al., 2004	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Salam et al., 2004	Moderate	Low	Low	Moderate	Low	Moderate	Low	Low
Merchant et al., 2005	Low	Low	Low	Low	Low	Low	Low	Low
Schulze et al., 2007	Low	Low	Moderate	Low	Low	Low	Low	Low
Ege et al., 2007	No information	Low	Moderate	Serious	Low	Low	Low	Serious
Midodzi et al., 2007	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Hugg et al., 2008	Low	Moderate	Low	Low	Low	Low	Low	Low
Fuchs et al., 2012	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Pavilonis et al., 2013	Low	Low	Low	Low	Low	Low	Low	Low
Fall et al., 2015	Low	Low	Moderate	Low	Low	Low	Low	Low
Feng et al., 2016	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Parsons et al., 2017	Moderate	Moderate	Low	Low	Low	Low	Low	Low
Ojwang et al., 2020	Moderate	Critical	Low	Low	Low	Low	Low	Critical
Andersén et al., 2021	Moderate	Moderate	Low	Low	Low	Low	Low	Low
Xing et al., 2022	Low	Low	Low	Low	Low	Low	Low	Low
Strieker et al., 2022	Low	Low	Moderate	Low	Low	Low	Low	Low
Chu et al., 2023	Moderate	Low	Low	Low	Low	Low	Low	Low

Fig 2. Risk of bias assessment of the included studies using the ROBINS-I tool across the seven risk-of-bias domains

Sensitivity analysis

A sensitivity analysis was performed to assess whether excluding studies with high risk of bias (ROB) affected the overall effect size and heterogeneity. In this first meta-analysis, there were 36,367 farming-exposed, and 29,114 non-farming-exposed children with 8,925 and 8,514 events, respectively. The pooled risk ratio (RR) was 0.89 (95% CI: 0.87-0.90), which means that the risk of the outcome under study was lower in farming-exposed children with a significant heterogeneity ($I^2 = 91\%$).

Before excluding studies with a high ROB, the number of participants in the exposed group was 32,217 and in the non-exposed group was 24,901. The number of events were also reduced to 8,215 (exposed) and 7,590 (non-exposed). Although sample size was reduced, the recalculated overall risk ratio was also 0.89 [0.88, 0.91], a remarkable degree of consistency with the initial analysis (Fig. 3). As heterogeneity, slightly increased to I^2 = 92%, this was small and did not suggest a substantial change in variability.

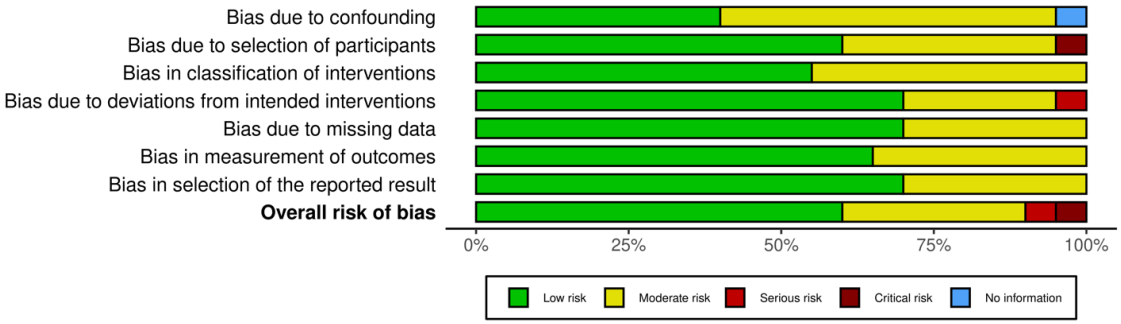


Fig 3. Forest plot of the sensitivity analysis comparing the pooled risk ratio before and after exclusion of studies with high risk of bias

The omission of high-ROB studies did not significantly change the pooled effect estimate (Fig. 4). The consistency of the RR indicates that methodological flaws of individual studies were not critical to the results. In general, the sensitivity analysis confirms the strength and validity of the initial meta-analysis results, because the relationship was the same with the inclusion or exclusion of high-risk studies.

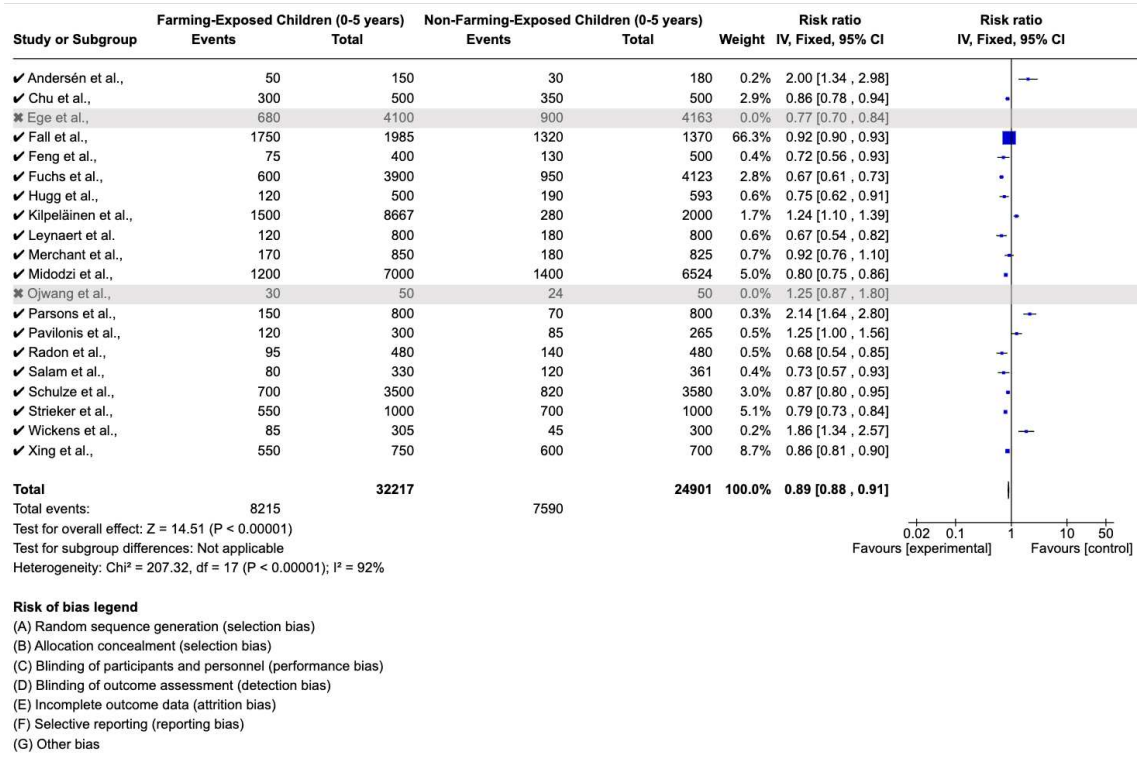


Fig 4. Sensitivity analysis demonstrating the consistency of the pooled effect estimate after excluding studies with high risk of bias

Results

Major Themes

Theme 1: Protective Effects of Farming Exposure on Health and Wellbeing

Leynaert et al. (2001) found that childhood exposure to farming environments significantly reduced the risk of sensitization to specific allergens, including cat (OR = 0.57, CI 95% = 0.38–0.83) and Timothy grass (OR = 0.64, CI 95% = 0.45–0.90). Additionally, the overall risk of sensitization to at least one allergen was lower (OR = 0.68, CI 95% = 0.55–0.86). However, the reduced risk of sensitization to house dust mites (OR = 0.78, CI 95% = 0.58–1.03) was less conclusive, as the confidence interval approached statistical insignificance (Leynaert et al. 2001). Similarly, Kilpeläinen et al. (2002) found that childhood farm exposure was associated with a lower prevalence of sensitization to allergens like timothy pollen (12.6% vs. 30.3%; OR = 0.33, 95% CI = 0.09–1.20), birch pollen (8.3% vs. 24.2%; OR = 0.28, 95% CI = 0.07–1.15), and cat dander (12.6% vs. 20.2%; OR = 0.57, 95% CI = 0.16–2.08). Cat-specific IgE levels were significantly lower in individuals with childhood farm exposure (1.5% vs. 13.1%; OR =

0.10, 95% CI = 0.02–0.47), highlighting the immunomodulatory effects of early farm exposures (Kilpeläinen et al. 2002).

Similarly, Schulze et al. (2007) reported that farm workers had half the rate of sensitization and allergy symptoms as non-farmers. Although the interaction term between sensitization and farm contact was not statistically significant ($p = 0.56$), the constant pattern of lower allergy outcomes in farm communities highlights the farm environment's protective impact (Schulze et al. 2007). Also, Midodzi et al. (2007) found that children living in farming environments had a significantly lower incidence of asthma (2.3%) compared to those in rural non-farming (5.3%) and non-rural (5.7%) environments. The multivariate analysis also confirmed that children in farming environments had reduced asthma risk (OR = 0.22; 95% CI: 0.07–0.74) compared to rural non-farming children, regardless of parental asthma history (Midodzi et al. 2007).

Meanwhile, Fuchs et al. (2012) demonstrated farm exposure reduced sensitization to allergens, with farm children and exposed nonfarm children being more often mono-sensitized than polysensitized ($P < .0001$ and $P = .0195$, respectively). Farming exposure also significantly lowered the prevalence of current wheeze in nonatopic children (adjusted OR = 0.45; 95% CI: 0.32–0.63), highlighting its protective role against this condition. However, atopic children in agricultural areas had greater risks of present wheeze than nonatopic unexposed peers, suggesting a different influence. Atopic farm children had a 0.32-point rise in FEV1/FVC ratio z-score, indicating better lung mechanics (95% CI: 0.04–0.60), compared with unexposed peers (Fuchs et al. 2012). Similarly, Pavilonis et al. (2013) identified a significant positive association between relative environmental exposure and childhood asthma (OR = 1.29, $p = 0.043$), though this association diminished in children prescribed asthma medication or diagnosed with asthma (OR = 1.19, $p = 0.087$). Occupational exposure to farming livestock was not consistently associated with asthma, with a near-significant relationship found only among older, male children working with livestock (OR = 2.18, $p = 0.058$) (Pavilonis et al. 2013).

On the other hand, Feng et al. (2016) found notably lower prevalence in rural setting (3.4%) compared to urban setting (6.9%, $p<0.001$), and case-control analysis revealed a stark difference in asthma rates between rural and urban children (2.8% vs. 29.4%, $p<0.001$). Positive associations with asthma included atopy (OR, 1.91; 95% CI, 1.58-

2.29), parental atopy (OR, 2.49; 95% CI, 1.55-4.01), hospitalization before age three (OR, 2.54; 95% CI, 1.37-4.70), high milk product consumption (OR, 1.68; 95% CI, 1.03-2.73), and exposure to dust mites (OR, 1.71; 95% CI, 1.34-2.19). Protective factors included living in a crop-farming family before age one (OR, 0.15; 95% CI, 0.08-0.32) and exposure to higher dust endotoxin levels (OR, 0.69; 95% CI, 0.50-0.95) (Feng et al. 2016). Similarly, Fall et al. (2015) also revealed that dog exposure during the first year of life was associated with a reduced risk of asthma in school-aged children (OR, 0.87; 95% CI, 0.81-0.93) and preschool-aged children aged three years or older (HR, 0.90; 95% CI, 0.83-0.99) (Fall et al. 2015).

In addition, Parsons et al. (2017) also found a strong protective association for children in farming settings compared to non-rural environments (HR = 0.60; 95% CI, 0.44-0.81; p = 0.001). Rural non-farming environments showed a marginally protective effect (HR = 0.78; 95% CI, 0.61-1.00; p = 0.053). After adjusting for confounders, the protective effect of farming environments persisted (HR = 0.64; 95% CI, 0.42-0.97; p = 0.03), though it diminished for children aged 0-1 at baseline (HR = 0.66; 95% CI, 0.37-1.20; p = 0.17) (Parsons et al. 2017). Similarly, Xing et al. (2022) found that farm children had a significantly lower prevalence of physician-diagnosed asthma (2.1%) compared to non-farm children (3.1%; OR = 0.67, $p < 0.001$). Similarly, farm children were less likely to use asthma medication (3.7% vs. 4.6%; OR = 0.81, p = 0.01) and experienced reduced prevalence of allergic rhinitis (AR; OR = 0.59, $p < 0.001$). Even rural non-farm children who visited neighbouring farms showed reduced prevalence of AR (10.0% vs. 12.8%; OR = 0.75, $p < 0.001$) and asthma medication usage (4.0% vs. 5.2%; OR = 0.77, p = 0.03) (Xing et al. 2022). Similarly, Strieker et al. (2022) found that living on a farm was associated with a reduced prevalence of allergic rhinitis, with those having persistent farm living showing a significantly lower odds ratio (OR = 0.4; 95% CI 0.2-0.6). The study also found that the odds of developing symptoms from baseline to follow-up were high (OR = 2.7; 95% CI 2.1-3.3), irrespective of farm living (Strieker et al. 2022).

Theme 2: Adverse Effects of Farming Exposure on Health and Wellbeing

Wickens et al. (2002) observed that early-life exposure to farming environments had varying effects on allergic diseases. While current farm living was associated with higher prevalence of health outcomes like hay fever, particularly among skin prick test-positive (SPT+) children, early exposure to specific factors like unpasteurized milk consumption

significantly reduced the risk of atopic eczema/dermatitis syndrome (AEDS) (OR = 0.4, CI 95% = 0.2–0.8) and allergic rhinitis (OR = 0.3, CI 95% = 0.1–0.7) (Wickens et al. 2002). Similarly, Kilpeläinen et al. (2002) found that childhood farm exposure was associated with a higher prevalence of sensitization to house-dust mite (22.0% vs. 4.9%; OR = 5.43, 95% CI = 1.60–18.46), contrary to the protective effect observed for other allergens. House-dust mite-specific IgE levels also showed a positive association with farm environments at the lowest antibody level (OR = 3.29, 95% CI = 1.21–8.96), although this effect diminished at higher antibody levels. For current asthma, sensitization to house-dust mite was equally prevalent in farm and nonfarm groups (25% vs. 19%; P = 0.79) (Kilpeläinen et al. 2002).

Radon et al. (2004) identified several farming-related factors strongly associated with *T. gondii* infection, including living on a farm during the first three years of life (OR = 3.0, 95% CI = 1.8–5.0) or currently (OR = 2.1, 95% CI = 1.1–3.9), early contact with animal stables (OR = 2.9, 95% CI = 1.6–5.2), and childhood consumption of raw farm milk (OR = 2.2, 95% CI = 1.2–3.8). These findings suggest that early-life exposures typical of farm environments facilitate *T. gondii* transmission (Radon et al. 2004). Similarly, Salam et al., (2004) demonstrated that early-life exposure to environmental pollutants, including wood/oil smoke, soot, exhaust, pesticides, and herbicides, significantly increased the risk of asthma in children. Notably, exposure during the first year of life had a stronger association with asthma risk, such as an OR of 4.58 (95% CI: 1.70–8.41) for herbicide exposure. Furthermore, while farm-related exposures like animals, crops, and dust were associated with asthma (OR = 1.60, 95% CI = 1.01–2.52), adjustments for pesticide/herbicide exposure did not alter the effect estimates (Salam et al. 2004).

Merchant et al. (2005) revealed a significant association between asthma and living on farms that raise swine and use antibiotics in animal feed. Notably, 55.8% of children on these farms reported at least one asthma-related outcome (p = 0.013), and an interaction term for this exposure was independently linked to outcomes like wheeze and exercise-induced cough. The wood stove use and pesticide exposure contributed to asthma symptoms through increased particulate matter and chemical irritants (Merchant et al. 2005). Similarly, Ege et al. (2007) identified that sheep farming and feeding loose or pressed hay were positively associated with the atopic phenotype. Additionally, children living on farms where only sheep were kept had asthma and wheeze prevalences up to four times higher than their peers on farms with pigs or cows (12% vs 3% for wheeze and

14% vs 3% for asthma) (Ege et al. 2007). Similarly, Chu et al., (2023) found that farm work during the summer ($p = .041$) and performing routine chores with large animals ($p = .027$) were linked to an increased risk of asthma, with an even stronger association for allergic asthma ($p = .04$). Additionally, children who completed farm safety education had a higher likelihood of having asthma (11.7% vs. 6.7%; $p = .001$) (Chu et al. 2023).

Theme 3: Neutral Effects of Farming Exposure on Health and Wellbeing

According to Andersén et al. (2021), the prevalence of asthma between individuals with and without childhood farming exposure (11.3% vs. 11.7%). However, exposure was associated with a delayed asthma diagnosis. The mean diagnosis age was significantly higher among those exposed to farming (33.5 years) compared to those unexposed (23.0 years; $p < 0.001$) (Andersén et al. 2021). Meanwhile, Leynaert et al. (2001) found that farm exposure during childhood did not significantly reduce the risk of asthma (OR = 0.82, CI 95% = 0.53–1.27) or wheeze (OR = 1.09, CI 95% = 0.82–1.46). Interestingly, the prevalence of chest wheezing was higher among farm-exposed subjects. Although nasal symptoms related to pollen exposure were slightly less frequent in farm-exposed individuals (OR = 0.78, CI 95% = 0.62–0.99), the reduction was not marked. The findings challenge why allergen sensitivity does not decrease asthma prevalence, contradicting the basic link between sensitization and asthma symptoms (Leynaert et al. 2001).

Similarly, Ojwang et al. (2020) examined the influence of early-life exposure to indoor pets and farm animals on the risk of asthma and allergic conditions by age five. Having a dog in the house during infancy was inversely associated with asthma (HR = 0.60; 95% CI, 0.38-0.96), allergic rhinitis (OR = 0.72; 95% CI, 0.53-0.97), and atopic sensitization (OR = 0.77; 95% CI, 0.63-0.96). Similarly, cat exposure was linked to a reduced risk of atopic eczema (OR = 0.68; 95% CI, 0.51-0.92). Exposure to farm animals, alone or with indoor pets, did not prevent asthma or allergies. Adjusted analysis showed that indoor dogs reduced asthma risk by 40% and allergic rhinitis and atopic sensitization by considerable amounts (Ojwang et al. 2020).

Discussion

The systematic review on the relationship between farming exposure and childhood asthma presents compelling evidence for both protective and adverse effects of farming environments. The review emphasizes the "hygiene hypothesis," which posits that

microbial diversity in farming environments reduces the risk of asthma and atopic sensitization. This conclusion aligns with studies such as Ege et al. (2011), who found that children exposed to diverse microbial environments on farms had lower asthma prevalence (Ege et al. 2011). The authors linked this protection to innate immune activation, particularly involving Toll-like receptors (TLR2 and TLR4). Similarly, Timm et al., (2020) discussed the protective effects of unpasteurized milk and early exposure to livestock, reinforcing these mechanisms (Timm et al. 2020).

Interestingly, the review also identifies instances where farming exposure may increase asthma risk, particularly in environments with high pesticide use or exposure to specific allergens like house-dust mites. Baldi et al. (2014) corroborate these findings, noting that pesticide exposure was associated with allergic asthma in French farming populations (Baldi et al. 2014). Additionally, Merchant et al. (2005) observed similar risks in farms using antibiotics in animal feed, linking this practice to respiratory irritants that exacerbate asthma symptoms. Despite these risks, many studies confirm farming environments as predominantly protective against childhood asthma (Merchant et al. 2005). Similarly, Parsons et al. (2017), Xing et al. (2022), and Fall et al. (2015) found a reduced asthma risk among children exposed to farm animals, echoing earlier findings. Illi et al. (2012) demonstrated that children exposed to traditional farming practices particularly those involving cows and farm milk—had significantly lower risks of asthma and atopy (Illi et al. 2012).

The review's mention of genetic predispositions influencing asthma outcomes highlights an emerging area of interest. Ege et al. (2011) identified gene-environment interactions involving rare polymorphisms in immune-regulatory genes in farming populations (Ege et al. 2011). These interactions suggest that genetic susceptibility could mediate the effects of farm exposures, complicating the observed protective outcomes. Importantly, the review and corroborating studies underscore the timing of exposure as a critical factor. Clarke et al., (2021) demonstrated that exposures during the first year of life were significantly more protective against asthma and atopy than later exposures (Clarke et al. 2021). This aligns with findings from prenatal exposure studies by Ege et al., (2007), suggesting that maternal farm exposures may upregulate innate immunity receptors in offspring (Ege et al. 2007).

The interplay between environmental and social determinants also emerges as a key theme. For instance, Brick et al., (2020) highlighted lower asthma rates in farming-intensive regions of the U.S., suggesting that socio-environmental factors play a role beyond direct farm exposure (Brick et al. 2020). These findings complement those from Xing et al. (2022), who noted that even non-farming children visiting farms experienced reduced asthma risks (Xing et al. 2022). The observed benefits of early exposure to unpasteurized milk and livestock, as highlighted by studies like Jackson et al., (2023) and Vested et al., (2021), could inform recommendations for dietary practices and early-life interventions in at-risk populations (Vested et al. 2021; Jackson et al. 2023). However, these measures require careful regulation to minimize risks, such as those linked to pesticide exposure or zoonotic diseases (Baldi et al. 2014).

Limitations

This systematic review has a few limitations that should be acknowledged. First, the included studies exhibited heterogeneity in study design and exposure definitions, which limited the feasibility of conducting a meta-analysis. Second, publication bias is a potential concern, as this review excluded grey literature such as preprints, theses, and government reports. While this approach ensures methodological rigor by focusing on peer-reviewed studies, it may have led to an underrepresentation of unpublished or non-traditional sources, potentially skewing the results. Moreover, while this review does not seek to definitively verify or falsify the hypothesis that farming exposure influences asthma risk, the results align with the study's objective of exploring its multifaceted impact.

Conclusion

The systematic review established that childhood exposure to farm settings was typically related to a decreased danger of allergen sensitization, cat and Timothy grass sensitization, and an overall danger of allergen sensitization. Evidence about house-dust mite sensitization, however, was less conclusive. Exposure to farm also led to a decreased populace of asthma and present wheeze, especially in non-atopic children. However, the effects were dependent on exposure type and time. Modern farm life was linked with increased incidence of hay fever among some children, early exposure to some exposed children to factors like unpasteurized milk lowered the risk of atopic eczema and allergic

rhinitis. Some environment-related pollutants and farming activities might also accelerate the development of asthma. Also, indoor exposure of dogs was linked to the lower risk of asthma and allergic disease, indicating that the protective properties of farming environments might be determined by the type and intensity of exposure. These results point out the necessity of further studies to determine which particular farm-related exposures are protective and which can lead to increased risks of asthma and allergic diseases.

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Consent to Publish: Consent to publish was not applicable because no identifiable individual participant data or personal information were collected or reported in this systematic review and meta-analysis.

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