


SYSTEMATIC REVIEW

Maternal asthma during pregnancy and risks of allergy and asthma in progeny: A systematic review and meta-analysis

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Abstract

Background: Clinical and preclinical evidence indicate that in utero maternal asthma exposure increases progeny asthma risk. Whether maternal asthma also increases the risks of progeny allergy is unclear.

Objectives: To synthesise the available evidence on the relationship between in utero exposure to maternal asthma and postnatal asthma, wheezing and allergic diseases (Prospero: CRD42020201538).

Search Strategy: We systematically searched MEDLINE [PubMed], Embase [Ovid], Web of Science, Informit Health, the Cochrane Library, CINAHL [EBSCOhost], MedNar [Deep Web Technologies], ProQuest Theses and Dissertations, Scopus [Elsevier] and Trove, to the end of 2023.

Selection Criteria: Studies reporting asthma, wheeze and/or allergic disease in progeny of women with and without asthma or with asthma classified by control, exacerbation or severity.

Data Collection and Analysis: Double screening, selection, data extraction and quality assessment were performed, using Joanna Briggs Institute (JBI) scoring.

Main Results: Of 134 non-overlapping studies, 127 were included in ≥1 meta-analysis. Maternal asthma ever was associated with greater risks of asthma (65 studies, risk ratio [95% confidence interval] 1.76 [1.57–1.96]), wheeze (35 studies, 1.59 [1.52–1.66]), food allergy (5 studies, 1.32 [1.23–1.40]), allergic rhinitis (7 studies, 1.18 [1.06–1.31]) and allergic dermatitis (14 studies, 1.17 [1.11–1.23]) ever in progeny. Asthma during the pregnancy, more severe, and uncontrolled maternal asthma were each associated with greater risks of progeny asthma.

Conclusions: Children of mothers with asthma are at increased risk for the development of allergic diseases. Whether improved maternal asthma control reduces risks of child allergy as well as asthma requires further investigation.

KEYWORDS

allergic dermatitis, allergic rhinitis, asthma, food allergy, maternal asthma, offspring, pregnancy, systematic review, wheeze

► This article includes Author Insights, a video abstract available at: <https://vimeo.com/976148053>

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1 | INTRODUCTION

Asthma is the most common respiratory condition affecting pregnancy.¹ Prevalence is variable and increasing, e.g. USA: 3.2% (1994–1998) versus 3.7%–8.4% (1997–2001),² and Australia: 12% (1995–1996)³ versus 17.1% (2008–2019).⁴ In addition to increased risks of pregnancy and neonatal complications,^{5,6} maternal asthma is associated with poor childhood respiratory health, including ~10% lower lung function,⁷ and ~3-fold increased risk of asthma.⁸ Maternal asthma also increases the risks of some allergic diseases in progeny; with an 11% higher risk of atopic dermatitis (AD), but similar risk of allergic rhinitis (AR), in one large study.⁹ However, the impacts of maternal asthma on child allergic diseases have not been systematically evaluated.

The impacts of maternal asthma on progeny outcomes are not solely genetic, with evidence for an in utero environmental contribution. In a meta-analysis of human studies, the association between maternal and child asthma was stronger than that between paternal and child asthma (OR 3.04 vs. 2.44, $p=0.037$).⁸ Furthermore, studies in mice provide direct evidence for in utero programming of asthma and allergy susceptibility by experimental maternal asthma.^{10–12} Risks of asthma and allergy may also be impacted by maternal asthma phenotype, given lower risks of asthma in children of mothers with less severe or better controlled asthma during pregnancy than in those whose mothers had severe or uncontrolled asthma.^{13,14} Furthermore, asthma exacerbation requiring medical intervention, which occurs in 2.5%–36.3% of pregnant women with asthma,¹⁵ is associated with 23% higher odds of childhood asthma by 5 years.¹⁶ The impacts of maternal asthma severity and control during pregnancy on progeny wheeze, asthma and allergy have not been systematically evaluated.

The primary aims of this systematic review were therefore to assess the relationships between maternal asthma and risks of wheezing, asthma and allergic diseases in progeny. Our secondary aims were to investigate the impact of asthma loss of control, asthma severity and asthma exacerbation during pregnancy on risks of wheezing, asthma and allergy in progeny.

2 | METHODS

2.1 | Protocol, registration, patient involvement and funding

We developed, published¹⁷ and registered a detailed protocol with the International Prospective Register of Systematic Reviews (PROSPERO; www.crd.york.ac.uk/prospero/ Reference CRD420201538) before commencing this review. Patients were not involved in the development of this research and the study had no specific funding.

2.2 | Search strategy

Our searches were performed according to protocol.¹⁷ Initial limited searching of Medline (PubMed) and Web of Science identified articles on the topic, from which we derived keywords and index terms. We used these to develop the final search for MEDLINE (PubMed) in consultation with the University Librarian (Table S1). This syntax was adapted to conduct similar searches in Embase (Ovid), Web of Science, Informit Health, the Cochrane Library, CINAHL (EBSCOhost), MedNar (Deep Web Technologies), ProQuest Theses and Dissertations, Scopus (Elsevier) and Trove (Appendix S1). We included studies published on paper or online until the end of 2023. We then searched reference lists of all included sources and relevant reviews and added identified additional sources directly for full-text screening.

2.3 | Study inclusion and exclusion

Any two of the authors independently screened each source, with disagreements decided by consensus in discussion with ≥1 other author. Publications were included for full-text screening if they were: of human subjects, primary sources, published in English, with a title/abstract including asthma, wheeze, an allergic disease or synonym as an outcome and a title/abstract mentioning pregnancy or delivery exposures (e.g. smoking during pregnancy, gestational age) or maternal asthma. Relevant studies were assessed at full-text and included for data extraction if they: were not duplicates; met the abstract criteria; were full text (not conference abstracts); were not articles reporting only trial protocols; reported outcomes analysed by exposures of interest; included relevant comparator groups; reported maternal asthma diagnosed by a physician or using clinically-accepted criteria; reported asthma, wheeze and/or allergic disease in progeny of any age diagnosed by a physician or using clinically-accepted criteria, such as The International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires; and where the full text article was able to be accessed.

2.4 | Quality assessment

Studies included for data extraction were assessed independently by two review authors for methodological quality using standardised critical appraisal instruments from the Joanna Briggs Institute; disagreements were resolved through discussion with additional author/s (Table S5: cohort studies; Table S6: case-control studies; Table S7: cross-sectional studies).¹⁸ Quality of covariate measurement or statistical analysis was noted as “adequate” if the study measured or adjusted for the following four factors most critical for asthma and allergy outcomes (Figure S1): maternal smoking in pregnancy, other maternal allergic disease, paternal allergic disease and tobacco smoke exposure

at age of outcome assessment.^{19–21} We reported these quality appraisal questions as “yes” where the study measured/adjusted for the four critical factors plus at least four of the following important factors (Figure S1): child sex, child age, maternal age, born/living in a rural area, environmental/passive tobacco smoke during pregnancy, parent income/SES, ethnicity/race and parity/birth order/siblings. We assessed questions on follow-up rates and strategies as not applicable for data linkage studies.

2.5 | Data extraction

Independent double data extraction¹⁷ was performed using author-designed fields in Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). Discrepancies were resolved through consensus. Maternal asthma during the index pregnancy (when the progeny were in utero) was reported as the exposure in only a small proportion of studies. Because asthma is a chronic disease,²² we therefore included all studies where mothers had ever had appropriately diagnosed asthma, and recorded whether the exposure to maternal asthma was during the index pregnancy or ever (previous history or during a period that included times outside pregnancy). Before data synthesis, we excluded studies with actual or potential overlap of subjects and outcomes, based on cohort, region and birth years, removing 45 studies from the systematic review (Table S1); others were able to be retained for sub-analyses only. Where the same outcomes were reported in identical cohorts, we retained the earliest publication, and where cohorts overlapped we retained the study reporting a larger sample size or more relevant exposures. Key characteristics and results of included studies comparing progeny of women with and without asthma and progeny of women with measures of asthma control/severity during pregnancy are described in Tables S2 and S3, respectively.

2.6 | Statistical analysis

Our primary aim was addressed by comparison of progeny of mothers with and without asthma. To address the secondary aim, we extracted information on asthma control, asthma severity, active versus inactive asthma and the occurrence of asthma exacerbations during pregnancy. Data from all studies was included in the meta-analysis regardless of quality assessment. Where available, confounder-adjusted data were used in the meta-analysis. Risk ratios were extracted directly from individual studies where available, or calculated from available information. As planned,¹⁷ separate analysis of progeny outcomes at different ages were conducted where ≥ 4 studies reported an outcome of interest at 0–2, 2–5, 5–10 or ≥ 10 years of age. Our search identified studies reporting the effects of maternal asthma on different wheeze trajectories and we therefore conducted posthoc analyses

with these wheeze trajectories as outcomes. Appendix S1: Supplementary methods provide additional details on statistical analyses. All analyses were performed in Stata (v17; StataCorp, College Station, Tex).

3 | RESULTS

Of the 21 083 unique articles identified from our search, 137 were included in the narrative review, with 128 included in meta-analyses (Figure S2). Only 23 studies contained information on maternal asthma during the index pregnancy. We identified 15 studies containing information on the severity or control of maternal asthma, with six included in meta-analyses.

3.1 | Asthma

Eighty-six non-overlapping studies reported asthma in the progeny of mothers with and without asthma, with 84 of these able to be included in ≥ 1 meta-analysis of this association (Figure S2), and the remaining studies summarised in Appendix S1: supplementary results. The estimated pooled risk of ever asthma was 1.76-fold higher in progeny of mothers with asthma compared to progeny of mothers without asthma (65 studies; RR 1.76; 95% CI 1.57–1.96; $p < 0.001$; $I^2 = 99.5\%$, 95% CI 95.5%–99.8%; $\tau^2 = 0.1648$; Figure 1). The distribution of variance around the estimated effect size suggested small study effects and high between-study heterogeneity (Figure S3A). We explored potential reasons for high heterogeneity in subgroup analyses. There was no significant effect of study design ($\chi^2_{(2)} = 0.70$, $p = 0.706$), or outcome prevalence ($\chi^2_{(2)} = 3.32$, $p = 0.191$), and substantial unexplained heterogeneity remained within all subgroups (Table S7). Although the effects of maternal asthma on progeny asthma differed between studies reporting unadjusted or adjusted effect estimates ($\chi^2_{(1)} = 6.18$, $p = 0.013$), substantial heterogeneity remained within each subgroup (Table S7). Maternal asthma ever was similarly associated with increased risks of current asthma in progeny at 2–5, 5–10 and ≥ 10 years of age (Figure S3B–D).

Sixteen studies reported asthma outcomes in children of mothers with and without asthma during the index pregnancy. In a pooled analysis, the risk of ever asthma was 1.71-fold higher in progeny of mothers with asthma compared to progeny of mothers without asthma during pregnancy (16 studies; RR 1.71; 95% CI 1.58–1.85; $p < 0.001$; $I^2 = 92.1\%$, 95% CI 17.8%–97.3%; $\tau^2 = 0.0125$; Figure 2).

3.2 | Wheeze

Forty-one non-overlapping studies reported wheezing in progeny of mothers with and without asthma, with 40 included in meta-analyses of this association (Figure S2), the other is summarised in Appendix S1: supplementary results. Meta-analysis of effects of pregnancy-specific maternal asthma

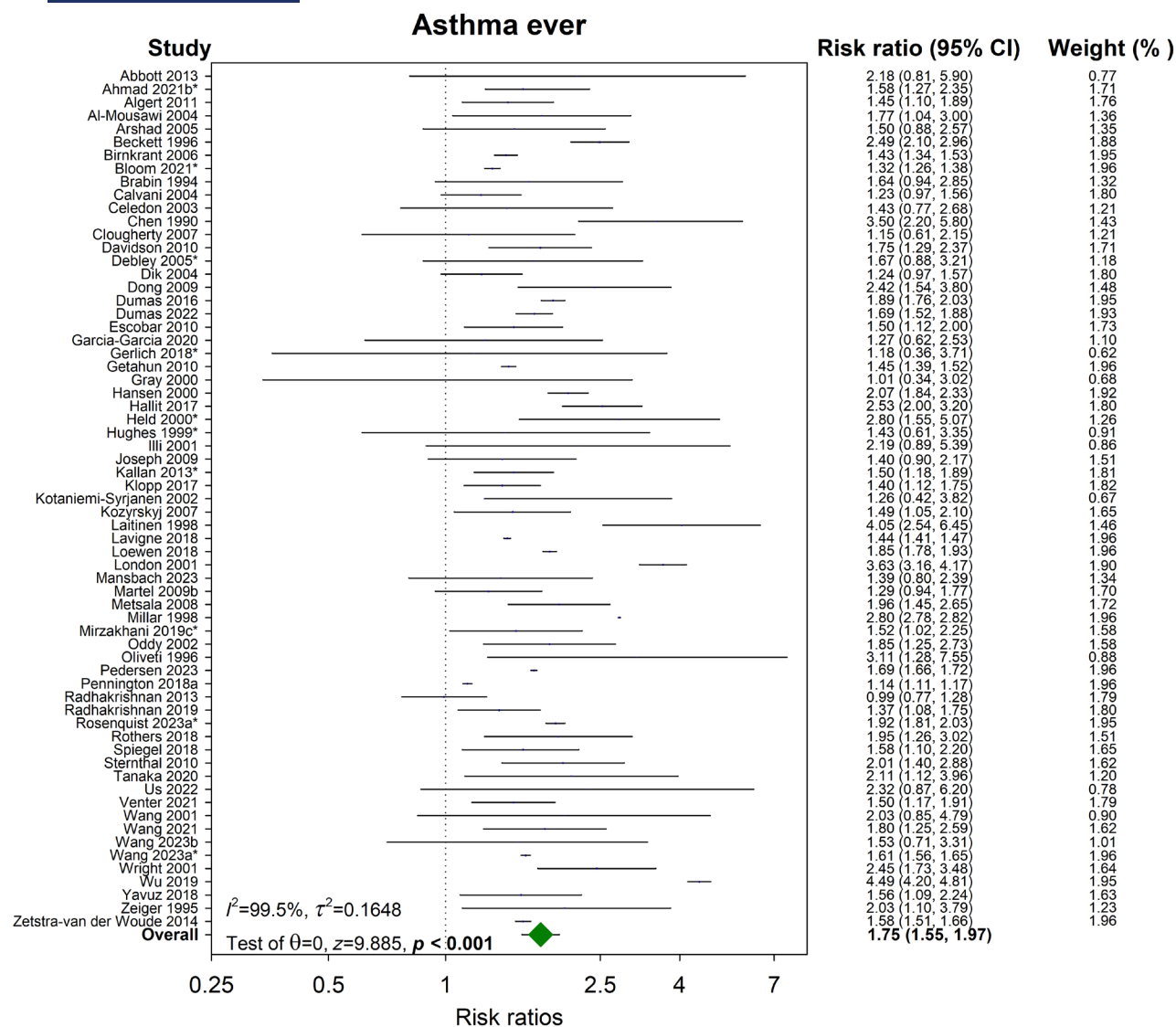


FIGURE 1 Meta-analysis of the relationship between maternal asthma and risk of asthma ever in progeny. Risk ratios and 95% CIs are relative to progeny of mothers without asthma. *Indicates studies where the exposure was maternal asthma status during the index pregnancy.

was not possible as only two studies reported this exposure (Table S3).^{23,24} In a pooled analysis, the risk of ever wheeze was 1.59-fold higher in progeny of mothers with asthma compared to progeny of mothers without asthma (36 studies; RR 1.59, 95% CI 1.52–1.66; $p<0.001$; $I^2=16.3\%$, 95% CI 0.0%–46.6%; $\tau^2=0.0020$; Figure 3). Inspection of the funnel plot did not suggest any ‘small study effects’, which may reflect reporting biases (Figure S4A). Maternal asthma was associated with increased risks of current wheeze at 0–2, 2–5, 5–10 and ≥ 10 years of age (Figure S4B–E) and of transient, intermediate/late-onset and persistent wheeze in progeny (Figure S5A–C).

3.3 | Food allergy/anaphylaxis

Five studies reported food allergy (FA) in children of mothers with and without asthma; none reported asthma during the index pregnancy as the exposure (Figure S2).

Four of these studies evaluated allergies to a range of foods from birth to early or mid-childhood,^{25–28} whereas the fifth eligible study assessed infant peanut allergy.²⁹ In a pooled analysis, risk of ever FA was 1.32-fold higher in progeny of mothers with asthma compared to progeny of mothers without asthma (5 studies; RR 1.32, 95% CI 1.23–1.40; $p=0.02$; $I^2=0.0\%$, 95% CI 0.0%–56.6%; $\tau^2=0.0000$; Figure 4A). The OR of epinephrine prescription by 7 years old, excluding children with a diagnosed venom allergy and reflecting more severe FA, was also higher in children of women with asthma than in children of women without asthma (OR 1.54, 95% CI 1.12–2.11).²⁵

3.4 | Allergic rhinitis/hayfever

Seven non-overlapping studies reported AR in 0–24-year-old progeny of mothers with and without asthma (Figure S2).

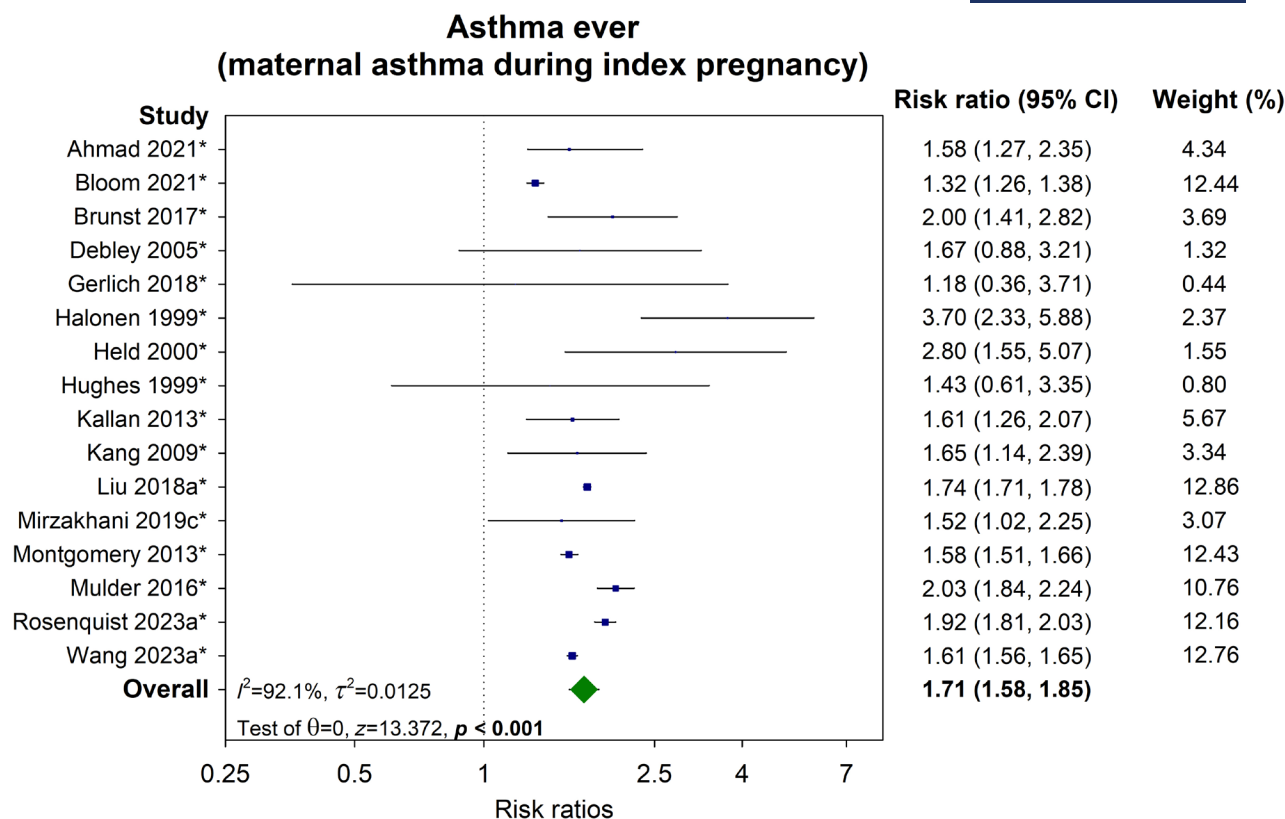


FIGURE 2 Meta-analysis of the relationship between maternal asthma during the index pregnancy and risk of asthma ever in progeny. RR (95% CI), RRs and 95% CIs relative to progeny of mothers without asthma. *Indicates studies where the exposure was maternal asthma status during the index pregnancy.

Meta-analysis of effects of pregnancy-specific maternal asthma exposure was not possible as only two studies reported this exposure (Table S3).^{24,30} In a pooled analysis, the risk of ever AR was 1.18-fold higher in progeny of mothers with asthma compared to progeny of mothers without asthma (7 studies; RR 1.18, 95% CI 1.06–1.31; $p=0.002$; $I^2=68.8\%$, 95% CI 0.0%–89.8%; $\tau^2=0.0095$; Figure 4B).

3.5 | Allergic dermatitis/eczema

Fifteen non-overlapping studies reported AD in progeny of mothers with and without asthma, with 14 of these included in meta-analyses of this association (Figure S2). A narrative summary of the remaining study is provided in Appendix S1: supplementary results. Meta-analysis of effects of pregnancy-specific maternal asthma was not possible as only two studies reported on this exposure (Table S3).^{24,31} In a pooled analysis, the risk of ever AD/eczema was 1.17-fold higher in progeny of mothers with asthma compared to progeny of mothers without asthma (14 studies; RR 1.17, 95% CI 1.11–1.23; $p<0.001$; $I^2=41.4\%$, 95% CI 0.0%–74.2%; $\tau^2=0.0023$; Figure 4C). Visual inspection of the funnel plot did not suggest the presence of so-called ‘small study effects’ (Figure S6A). The association between maternal asthma and current AD in progeny

at 0–2 years of age was not significant, albeit in only four small studies (Figure S6B).

3.6 | Severity and control of asthma during pregnancy

3.6.1 | Asthma severity

Six studies reported progeny asthma analysed by the severity of maternal asthma, in populations from Denmark,^{14,32} United Kingdom,³³ United States³⁴ and Canada^{9,13} (Table S4). We included only the larger¹³ of two studies of an overlapping Canadian cohort^{9,13} in our meta-analysis. In a pooled analysis, the risk of ever asthma was 1.23-fold higher in progeny of mothers with moderate–severe asthma compared to progeny of mothers with mild asthma (five studies; RR 1.23; 95% CI 1.12–1.35; $p<0.001$; $I^2=63.9\%$, 95% CI 0.0%–88.4%; $\tau^2=0.0062$; Figure 5A).

There was insufficient evidence to conduct meta-analyses of the relationships between maternal asthma severity and our other outcomes of interest. In a follow-up of women in the Danish Managing Asthma in Pregnancy study, the likelihood of AD by 12 years of age did not differ between children of mothers with moderate–severe compared to mild asthma ($N=571$, OR 0.77, 95% CI 0.49–1.20).³² A much

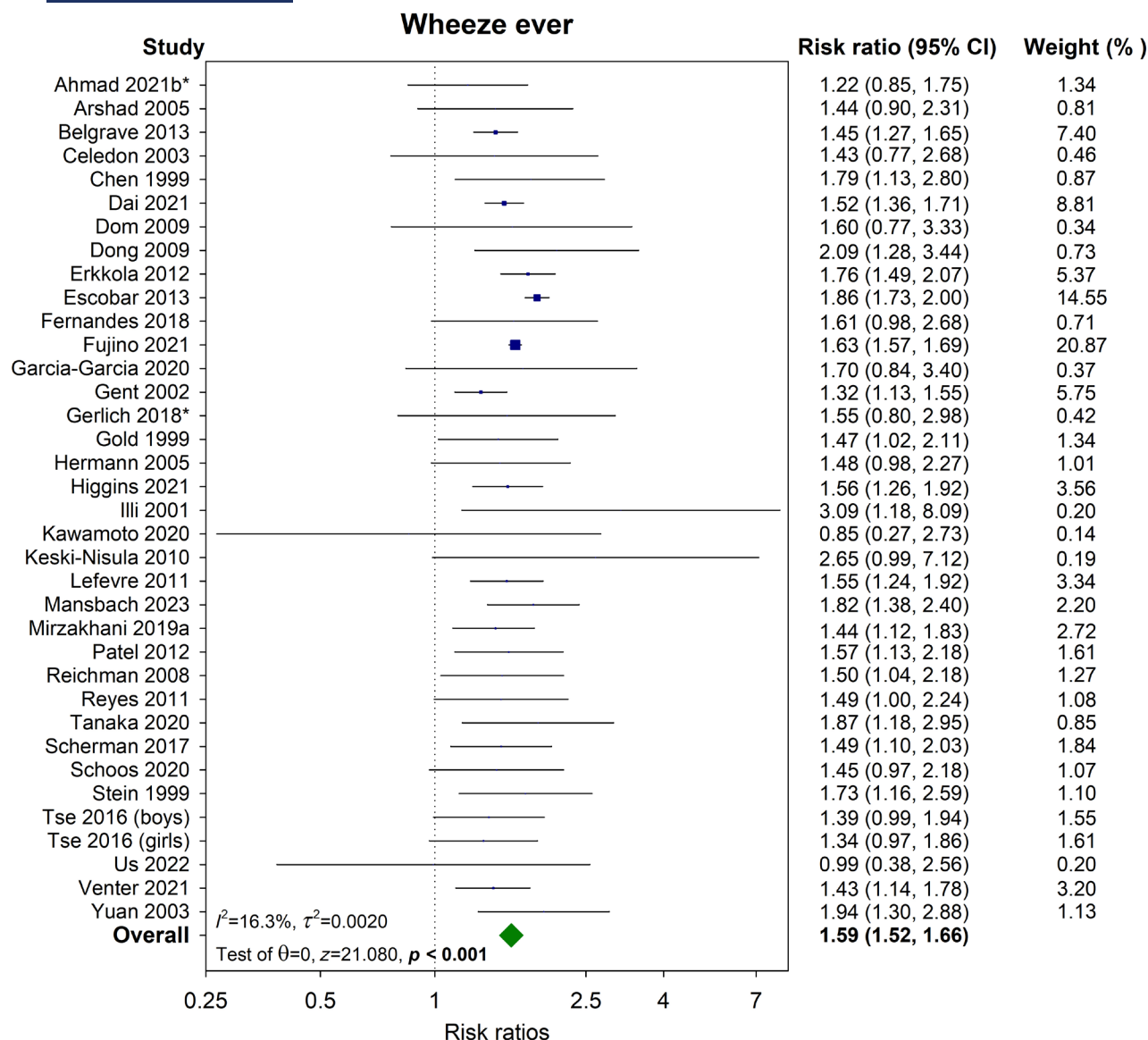


FIGURE 3 Meta-analysis of the relationship between maternal asthma and risk of wheezing ever in progeny. Risk ratios and 95% CIs are relative to progeny of mothers without asthma. *Indicates studies where the exposure was maternal asthma status during the index pregnancy.

larger Canadian study ($N=8226$) reported no differences in rates of AD and AR in progeny of women with moderate-severe asthma or mild-uncontrolled asthma compared to progeny of women with mild-controlled asthma (Table S4).⁹ No studies reported FA outcomes according to maternal asthma severity.

3.6.2 | Asthma control

Only four studies were included in meta-analysis of the relationship between maternal asthma control and asthma in progeny (Table S4) after excluding data on progeny asthma from Martel and co-authors⁹ that reported on a cohort that overlapped with the included study.¹³ In a pooled analysis, risk of ever asthma was 1.15-fold higher in progeny of women with uncontrolled

asthma compared to progeny of women with controlled asthma (four studies; RR 1.15; 95% CI 1.07–1.23; $p < 0.001$; $I^2=29.6\%$, 95% CI 0.0%–78.6%; $\tau^2=0.0015$; Figure 5B).

There was insufficient evidence to conduct meta-analysis of the relationships between maternal asthma control and our other outcomes of interest. In a Danish cohort, the likelihood of AD by 12 years old did not differ between children of mothers with uncontrolled and controlled asthma during pregnancy ($N=571$, OR 1.41, 95% CI 0.86–2.05).³² Martel and co-authors found no differences in aHR for AD and AR between children of women with uncontrolled and controlled mild asthma during pregnancy, but did not split outcomes for women with moderate-severe asthma according to asthma control.⁹ No studies reported FA outcomes according to maternal asthma control.

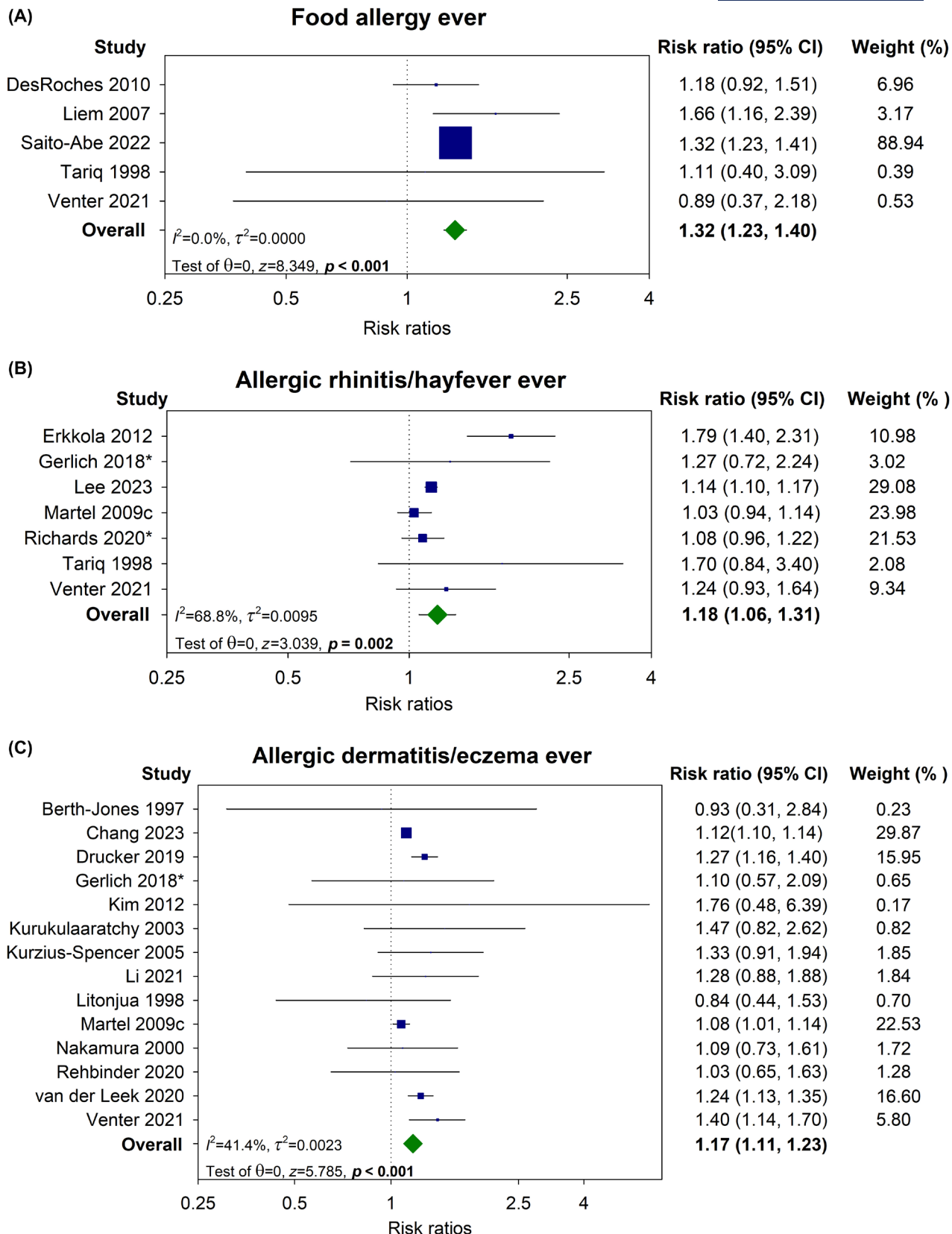


FIGURE 4 Meta-analysis of the relationship between maternal asthma and risk of (A) FA ever (B) AR ever and (C) AD ever in progeny. Risk ratios and 95% CIs are relative to progeny of mothers without asthma. *Indicates studies where the exposure was maternal asthma status during the index pregnancy.

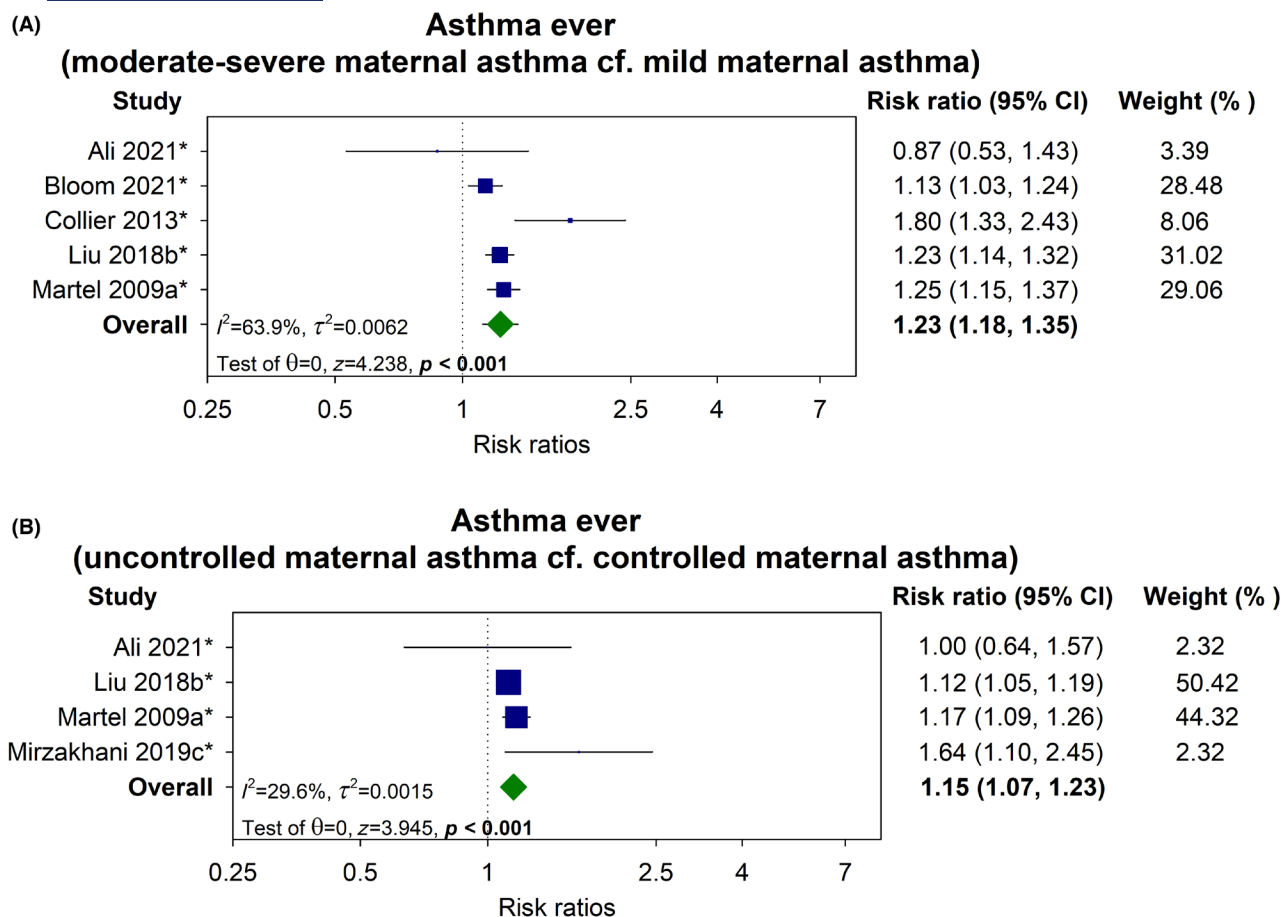


FIGURE 5 (A) Meta-analysis of the relationship between asthma severity during the index pregnancy and risk of asthma ever in progeny. RR (95% CI), RRs and 95% CIs are for progeny of mothers with moderate-severe asthma relative to progeny of mothers with mild asthma. (B) Meta-analysis of the relationship between maternal asthma control during the index pregnancy and risk of asthma ever in progeny. RR (95% CI), RRs and 95% CIs are for progeny of mothers with uncontrolled asthma relative to progeny of mothers with controlled asthma. *Indicates studies where the exposure was maternal asthma status during the index pregnancy.

3.6.3 | Exacerbations and active versus inactive asthma during pregnancy

There was insufficient data to conduct meta-analysis of effects of asthma exacerbations or of active or inactive asthma during pregnancy, on any outcomes of interest (Appendix S1: supplementary results and Table S4).

the chronic nature of asthma.²² Uncontrolled and more severe maternal asthma during the index pregnancy were also associated with increased risk of progeny asthma. There was insufficient evidence to assess impacts of maternal asthma control and severity on progeny wheeze or allergic disease, nor of asthma exacerbations or inactive vs. active asthma during pregnancy.

4 | DISCUSSION

4.1 | Main findings

This systematic review and meta-analysis strengthen the evidence that maternal asthma is associated with increased risks of asthma in progeny and demonstrates that maternal asthma is also associated with increased risk of wheeze and multiple allergic diseases (food allergy [FA], atopic dermatitis [AD] and allergic rhinitis [AR]) in progeny. Associations between maternal asthma and risks of progeny asthma were similar when the exposure was maternal asthma during the index pregnancy or as a history of asthma, consistent with

4.2 | Strengths and limitations

Strengths of this review include extensive coverage of literature, through searching multiple databases and reference lists of included papers and reviews. Most studies were of high quality¹⁸; we did not exclude any studies from analysis on the basis of study quality. Populations of women with and without asthma were comparable in most studies. Only including studies in which maternal asthma was diagnosed medically or by validated criteria, ensured the validity and consistency of the exposure measure. Similarly, assessments of the progeny outcomes were of high quality across all studies; diagnosis of allergic diseases and asthma

were restricted to medical diagnosis or validated instruments such as ISAAC survey questions.³⁵ We did not accept parent- or self-report of asthma or allergy without clinical diagnosis as a valid outcome, as parent reports of ever asthma or wheeze are only moderately correlated with equivalent medical diagnoses.³⁶ The main limitation to quality, in >95% of studies, was the lack of statistical adjustment for clinically important predictors of progeny allergy and asthma.^{19–21} Where possible, we recommend that future studies collect information on pregnancy exposures as well as paternal asthma and allergy in order to reduce confounding and improve precision of effect estimates. We were somewhat surprised by how few studies measured asthma during the index pregnancy, preventing analysis of effects of this exposure on progeny risks of wheeze and allergic diseases. Similarly, there was insufficient evidence to allow meta-analysis of associations between maternal asthma control and severity on risks of wheeze and allergic diseases in progeny. Follow-up of progeny in cohorts where maternal asthma control has been closely monitored during pregnancy, or where interventions to improve maternal asthma control in pregnancy have been tested, will be important to fill these gaps in knowledge.

4.3 | Interpretation

An interesting finding of our primary analyses is that the magnitudes of risks associated with maternal asthma ever were much stronger for progeny wheeze and asthma than for the allergic diseases of FA, AD and AR. This might suggest that maternal asthma impacts non-immune mechanisms that increase risks of asthma and wheeze only, as well as immune mechanisms that increase risks of asthma and allergy (expanded in [Appendix S1](#): supplementary discussion). Poorer lung function in children whose mothers have asthma,⁷ and perturbed lung development in fetuses of asthmatic dams in preclinical studies, are consistent with direct effects of in utero asthma exposure on lung development.³⁷

The association between maternal asthma ever and asthma ever in progeny was highly heterogenous ($I^2 = 99.7\%$), and remained high in subgroup analyses based on study design, statistical adjustment and asthma prevalence. The reasons for the variable associations between maternal and progeny asthma are therefore not entirely clear, although differing impacts of maternal asthma on different progeny asthma phenotype and severity may contribute. Ascertainment of progeny asthma varied between studies, including parent report of doctor-diagnosed asthma,³⁸ direct medical assessment,³⁹ child hospitalisation for asthma,⁴⁰ review of medical records for individual cohorts,⁴¹ and whole-of-population data linkage of birth, population and medical/prescription records.⁴² Population incidence of asthma was highly variable (1.1%–40.0%), likely reflecting study differences in population susceptibility to asthma and the asthma definition used.

If better maternal asthma control during pregnancy indeed reduces risk of progeny asthma, as our secondary analyses suggest, then programs that target improved pregnancy management of asthma might improve long-term progeny health as well as reduce risks of pregnancy complications. We acknowledge that a limitation of our analyses is that the associations between uncontrolled or severe asthma and progeny asthma may reflect genetic or environmental factors in addition to the in utero exposure to maternal asthma. For example, women who smoke during pregnancy are more likely to experience recurrent uncontrolled asthma than women who do not smoke,⁴³ and prenatal exposure to tobacco smoke is also associated with increased risk of childhood wheeze and asthma.¹⁹ Nevertheless, direct evidence that better maternal asthma control during pregnancy reduces child asthma risk is now available from the Growing Into Asthma study,⁴⁴ a follow-up to the Managing Asthma in Pregnancy cohort.⁴⁵ In this study, children of women randomised to the Fractional Exhaled Nitric Oxide (FENO)-guided asthma management group, who had better maternal asthma control, were at lower risk of developing asthma at 4–6 years old (aOR 0.39, 95% CI 0.16–0.94, $p = 0.035$).⁴⁴ Maternal use of inhaled corticosteroids during pregnancy, probably a marker of better asthma management rather than asthma severity, was also associated with lower risks of child asthma.⁴⁴ Together, these results suggest that improved management of maternal asthma during pregnancy will reduce the risks of asthma in progeny. A lack of available evidence currently prevents any conclusions about effects of improved maternal asthma control during pregnancy on risk of allergic disease in progeny.

5 | CONCLUSION

This meta-analysis adds to existing literature identifying maternal asthma as a risk factor for progeny asthma⁸ and demonstrates that maternal asthma is also a risk factor for progeny allergic disease. Importantly, the current meta-analysis, along with recent RCT outcomes,⁴⁴ suggests that improved asthma control during pregnancy may reduce inter-generational transmission of asthma, and this should be a priority in asthma prevention programs. Our findings further identify children of mothers with asthma as a high-risk group who should be prioritised for surveillance to allow early management of any emerging allergies. Children of mothers with asthma may also be a priority target population for postnatal interventions that reduce allergic disease risk.

AUTHOR CONTRIBUTIONS

AJR, AT, VLC, JLM and KLG conceived and designed the study. AJR, JLR, SJH, AT, VLC, JLM and KLG acquired and collected the data. AJR, JB and KLG analysed the data. All authors drafted and critically revised the manuscript for important intellectual content and gave final approval of the version to be published.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

ETHICS APPROVAL

Not applicable.

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REFERENCES

- Bonham CA, Patterson KC, Strek ME. Asthma outcomes and management during pregnancy. *Chest*. 2018;153(2):515–27.
- Kwon HL, Belanger K, Bracken MB. Asthma prevalence among pregnant and childbearing-aged women in the United States: estimates from national health surveys. *Ann Epidemiol*. 2003;13(5):317–24.
- Clifton VL, Engel P, Smith R, Gibson P, Brinsmead M, Giles WB. Maternal and neonatal outcomes of pregnancies complicated by asthma in an Australian population. *Aust NZ J Obstet Gynaecol*. 2009;49(6):619–26.
- Das J, Andrews C, Flenady V, Clifton VL. Maternal asthma during pregnancy and extremes of body mass index increase the risk of perinatal mortality: a retrospective cohort study. *J Asthma*. 2022;59(10):2108–16.
- Xu Z, Doust JA, Wilson LF, Dobson AJ, Dharmage SC, Mishra GD. Asthma severity and impact on perinatal outcomes: an updated systematic review and meta-analysis. *BJOG*. 2022;129(3):367–77.
- Murphy VE, Wang G, Namazy JA, Powell H, Gibson PG, Chambers C, et al. The risk of congenital malformations, perinatal mortality and neonatal hospitalisation among pregnant women with asthma: a systematic review and meta-analysis. *BJOG*. 2013;120(7):812–22.
- Turner S, Fielding S, Mullane D, Cox DW, Goldblatt J, Landau L, et al. A longitudinal study of lung function from 1 month to 18 years of age. *Thorax*. 2014;69(11):1015–20.
- Lim RH, Kobzik L, Dahl M. Risk for asthma in offspring of asthmatic mothers versus fathers: a meta-analysis. *PLoS One*. 2010;5(4):e10134.
- Martel MJ, Beauchesne MF, Malo JL, Rey E, Perreault S, Forget A, et al. Maternal asthma, its control and severity in pregnancy, and the incidence of atopic dermatitis and allergic rhinitis in the offspring. *J Pediatr*. 2009;155(5):707–713.e1.
- Hamada K, Suzuki Y, Goldman A, Ning YY, Goldsmith C, Palecanda A, et al. Allergen-independent maternal transmission of asthma susceptibility. *J Immunol*. 2003;170(4):1683–9.
- Lebold KM, Drake MG, Pincus AB, Pierce AB, Fryer AD, Jacoby DB. Unique allergic asthma phenotypes in offspring of house dust mite-exposed mice. *Am J Respir Cell Mol Biol*. 2022;67(1):89–98.
- Richgels PK, Yamani A, Chougnet CA, Lewkowich IP. Maternal house dust mite exposure during pregnancy enhances severity of house dust mite-induced asthma in murine offspring. *J Allergy Clin Immunol*. 2017;140(5):1404–1415.e9.
- Martel MJ, Rey E, Beauchesne MF, Malo JL, Perreault S, Forget A, et al. Control and severity of asthma during pregnancy are associated with asthma incidence in offspring: two-stage case-control study. *Eur Respir J*. 2009;34(3):579–87.
- Liu X, Agerbo E, Schlünssen V, Wright RJ, Li J, Munk-Olsen T. Maternal asthma severity and control during pregnancy and risk of offspring asthma. *J Allergy Clin Immunol*. 2018;141(3):886–892.e3.
- Robijn AL, Bokern MP, Jensen ME, Barker D, Baines KJ, Murphy VE. Risk factors for asthma exacerbations during pregnancy: a systematic review and meta-analysis. *Eur Respir Rev*. 2022;31(164):220039.
- Abdullah K, Zhu J, Gershon A, Dell S, To T. Effect of asthma exacerbation during pregnancy in women with asthma: a population-based cohort study. *Eur Respir J*. 2020;55(2):1901335.
- Roff AJ, Morrison JL, Tai A, Clifton VL, Gatford KL. Maternal asthma during pregnancy and risks of allergy and asthma in progeny: a systematic review protocol. *JBIM Evid Synth*. 2021;19(8):2007–13.
- Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. *JBIM manual for evidence synthesis*. JBIM; 2020. <https://doi.org/10.46658/JBIMES-24-01>
- Silvestri M, Franchi S, Pistorio A, Petecchia L, Rusconi F. Smoke exposure, wheezing, and asthma development: a systematic review and meta-analysis in unselected birth cohorts. *Pediatr Pulmonol*. 2015;50(4):353–62.
- Castro-Rodriguez JA, Forno E, Rodriguez-Martinez CE, Celedón JC. Risk and protective factors for childhood asthma: what is the evidence? *J Allergy Clin Immunol Pract*. 2016;4(6):1111–22.
- Sonnenschein-van der Voort AM, Arends LR, de Jongste JC, Annesi-Maesano I, Arshad SH, Barros H, et al. Preterm birth, infant weight gain, and childhood asthma risk: a meta-analysis of 147,000 European children. *J Allergy Clin Immunol*. 2014;133(5):1317–29.
- Miller RL, Grayson MH, Strothman K. Advances in asthma: new understandings of asthma's natural history, risk factors, underlying mechanisms, and clinical management. *J Allergy Clin Immunol*. 2021;148(6):1430–41.
- Ahmad K, Kabir E, Ormsby GM, Khanam R. Are wheezing, asthma and eczema in children associated with mother's health during pregnancy? Evidence from an Australian birth cohort. *Arch Public Health*. 2021;79(1):193.
- Gerlich J, Benecke N, Peters-Weist AS, Heinrich S, Roller D, Genuneit J, et al. Pregnancy and perinatal conditions and atopic disease prevalence in childhood and adulthood. *Allergy*. 2018;73(5):1064–74.
- Liem JJ, Kozyrskyj AL, Huq SI, Becker AB. The risk of developing food allergy in premature or low-birth-weight children. *J Allergy Clin Immunol*. 2007;119(5):1203–9.
- Tariq SM, Matthews SM, Hakim EA, Stevens M, Arshad SH, Hide DW. The prevalence of and risk factors for atopy in early childhood: a whole population birth cohort study. *J Allergy Clin Immunol*. 1998;101(5):587–93.
- Venter C, Palumbo MP, Sauder KA, Glueck DH, Liu AH, Yang IV, et al. Incidence and timing of offspring asthma, wheeze, allergic rhinitis, atopic dermatitis, and food allergy and association with maternal history of asthma and allergic rhinitis. *World Allergy Org J*. 2021;14(3):100526.

28. Saito-Abe M, Yamamoto-Hanada K, Pak K, Iwamoto S, Sato M, Miyaji Y, et al. How a family history of allergic diseases influences food allergy in children: the Japan environment and children's study. *Nutrients*. 2022;14(20):4323.
29. DesRoches A, Infante-Rivard C, Paradis L, Paradis J, Haddad E. Peanut allergy: is maternal transmission of antigens during pregnancy and breastfeeding a risk factor? *J Invest Allergol Clin Immunol*. 2010;20(4):289–94.
30. Richards M, Ferber J, Li DK, Darrow LA. Cesarean delivery and the risk of allergic rhinitis in children. *Ann Allergy Asthma Immunol*. 2020;125(3):280–286.e5.
31. Kurzius-Spencer M, Halonen M, Carla Lohman I, Martinez FD, Wright AL. Prenatal factors associated with the development of eczema in the first year of life. *Pediatr Allergy Immunol*. 2005;16(1):19–26.
32. Ali Z, Jemec GBE, Ulrik CS. Associations between maternal and environmental exposures on atopic disease in the offspring of mothers with asthma. *Immunity Inflam Dis*. 2021;9(3):862–70.
33. Bloom CI, Franklin C, Bush A, Saglani S, Quint JK. Burden of preschool wheeze and progression to asthma in the UK: population-based cohort 2007 to 2017. *J Allergy Clin Immunol*. 2021;147(5):1949–58.
34. Collier CH, Risnes K, Norwitz ER, Bracken MB, Illuzzi JL. Maternal infection in pregnancy and risk of asthma in offspring. *Matern Child Health J*. 2013;17(10):1940–50.
35. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International study of asthma and allergies in childhood (ISAAC): rationale and methods. *Eur Respir J*. 1995;8(3):483–91.
36. Korsten K, Naaktgeboren CA, Bont LJ, van der Ent CK, de Hoog MLA. Defining asthma in children: how well do parents, doctors and spirometry agree? *ERJ Open Res*. 2020;6(4):00348–2019.
37. Robinson JL, Gatford KL, Clifton VL, Morrison JL, Stark MJ. The impact of maternal asthma on the fetal lung: outcomes, mechanisms and interventions. *Paediatr Respir Rev*. 2024;51:38–45.
38. Laitinen T, Räsänen M, Kaprio J, Koskenvuo M, Laitinen LA. Importance of genetic factors in adolescent asthma: a population-based twin-family study. *Am J Respir Crit Care Med*. 1998;157(4 Pt 1):1073–8.
39. Gray L, Peat JK, Belousova E, Xuan W, Woolcock AJ. Family patterns of asthma, atopy and airway hyperresponsiveness: an epidemiological study. *Clin Exp Allergy*. 2000;30(3):393–9.
40. Debley JS, Smith JM, Redding GJ, Critchlow CW. Childhood asthma hospitalization risk after cesarean delivery in former term and pre-mature infants. *Ann Allergy Asthma Immunol*. 2005;94(2):228–33.
41. Oliveti JF, Kerckmar CM, Redline S. Pre- and perinatal risk factors for asthma in inner city African-American children. *Am J Epidemiol*. 1996;143(6):570–7.
42. Wu Q, Dalman C, Karlsson H, Lewis G, Osborn DPJ, Gardner R, et al. Childhood and parental asthma, future risk of bipolar disorder and schizophrenia spectrum disorders: a population-based cohort study. *Schizophr Bull*. 2019;45(2):360–8.
43. Grzeskowiak LE, Smith B, Roy A, Dekker GA, Clifton VL. Patterns, predictors and outcomes of asthma control and exacerbations during pregnancy: a prospective cohort study. *ERJ Open Res*. 2016;2(1):00054–2015.
44. Morten M, Collison A, Murphy VE, Barker D, Oldmeadow C, Attia J, et al. Managing asthma in pregnancy (MAP) trial: FENO levels and childhood asthma. *J Allergy Clin Immunol*. 2018;142(6):1765–1772.e4.
45. Powell H, Murphy VE, Taylor DR, Hensley MJ, McCaffery K, Giles W, et al. Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial. *Lancet*. 2011;378(9795):983–90.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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