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Early childhood obesity and the development of asthma

A Systematic review

Faculty of Medicine,
Department of Clinical Medicine
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Author:
Juho Jaatinen

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Author(s): Juho Jaatinen
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Supervisor(s): M.D, PHD. Minna Lukkarinen
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Background

Childhood overweight and obesity have been recognized as risk factors for childhood asthma. However, mixed results have been observed across different subgroups. Boys might have a higher risk than girls of developing asthma. Other factors that increase asthma risk include gut microbiota and neonatal conditions, both of which may also be linked to excess weight. Childhood weight trajectories are suggested to be a more useful tool for evaluating the risk of asthma development than isolated cross-sectional weight measurements at specific ages. This work aims to elucidate the current knowledge on two key questions related to childhood asthma and obesity.

Objective

The aim of this study was to analyze two questions related to childhood asthma and obesity: 1. Does an infant's large birth size increase the incidence of asthma, and can it be differentiated into atopic and non-atopic asthma? 2. Does early childhood obesity (obesity at two years of age) increase the incidence of asthma compared to children who become obese later in childhood (obesity at five years of age)?

Methods

This is a systematic review conducted through a literature search in the PubMed database, focusing on key findings regarding the association between childhood asthma and obesity. The literature search in PubMed was performed independently. The data from the screened articles were not independently retrieved or analyzed. The top 200 search results were screened, and three articles that met the selection criteria were included in this systematic review.

Results

Obesity and overweight are risk factors for asthma only in boys, but not in girls. Early obesity likely does not increase asthma risk if the child loses excess weight, whereas late obesity probably does. The association between birth size and asthma was inconclusive.

Key words: Childhood, obesity, early-obesity, overweight, asthma.

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1 Introduction

The incidence of two of the most common childhood medical conditions, obesity and atopic diseases, including asthma has been increasing (Reyes-Angel, 2022). In 2023, in Finland, 26% of boys and 17% of girls aged 2–16 were overweight (ISO-BMI of 25 kg/m² or higher) (THL, 2024). The prevalence of obesity (ISO-BMI of 30 kg/m² or higher) was 8% in boys and 3% in girls, while severe obesity (ISO-BMI of 35 kg/m² or higher) was observed in 1.7% of boys and 0.1% of girls (THL, 2024). In the FinnBrain Birth Cohort, 29.3% of 2-year-old boys and 16.1% of girls were overweight or obese, reflecting similar prevalence rates to those seen in the Finnish population (Lundqvist et al., 2019; Hyppänen, 2020). Childhood obesity is often persistent into adulthood (Juonala et al., 2011). Recent data on the prevalence of childhood asthma in Finland is lacking; however, the Finnish national health organization estimates that currently, 6–10% of children in Finland have asthma (THL, 2024). In the United States, childhood asthma prevalence has doubled over the past 40 years, reaching approximately 7% (CDC, 2023).

Childhood asthma is a heterogeneous disease influenced by multiple factors affecting its development. Proposed contributing factors include genetics and genomics, epigenetics, microbiome alterations, diet and nutrition, lung and airway mechanics, airway inflammation, and systemic inflammation (Han, 2014). Similarly, childhood obesity is recognized as a multifactorial condition. However, the interplay between these factors remains poorly understood, and some contributing mechanisms may still be unidentified. Obesity-related inflammation has been suggested to predispose individuals to asthma (Raj, 2013). Previous research has established that obese boys have a higher risk of developing asthma compared to their non-obese peers (Brumpton, 2013; Gilliland, 2003). Additionally, it has been shown that obese teenagers with insulin resistance have an increased risk of developing asthma (Manuel et al., 2021).

Children's asthma phenotypes also differ from those observed in adults. In adults, an obesity-driven asthma phenotype characterized by neutrophilic predominance and corticosteroid resistance has been identified; however, a similar finding has not been confirmed in children. Two cohort studies have associated high IL-6 concentrations with higher BMI and pulmonary function impairment (Reyes-Angel, 2022). A meta-analysis reported that overweight and obese children had slightly higher FEV_1 values than non-overweight children but significantly higher FVC values. This resulted in a -2.4% (95% CI: -3.0 to -1.8%) decrease in the FEV_1/FVC ratio, indicating that overweight and obese children generally exhibit slightly obstructive lung function compared to their non-overweight counterparts (Forno, 2018).

Maternal psychological distress (PD) symptoms during pregnancy have been associated with adverse child somatic outcomes, particularly atopic disorders, including wheezing and asthma (Cookson et al., 2009; Hartwig et al., 2014; Ramratnam et al., 2017). Birth by cesarean section also appears to increase a child's risk of developing asthma (Keag et al., 2018). Maternal obesity and excessive weight gain during pregnancy are also associated with an increased risk of asthma in children, suggesting that asthma risk factors may begin accumulating as early as the intrauterine stage (Forno et al., 2014). It is well known that neonatal conditions and early weight gain can affect metabolism throughout an individual's lifetime (Keag et al., 2018; Rosa et al., 2018). Therefore, when evaluating a child's risk factors for asthma, gestational and neonatal influences should be carefully considered.

Therefore, studying the effects of early-life conditions and early weight gain on the development of childhood asthma is of a significant importance. Further research on the connection between these two major health hazards, childhood obesity and asthma is essential, not only for the young individuals affected but also because both conditions can have long-term consequences on a child's health. Additionally, they contribute to a substantial socioeconomic, healthcare, and family-life burden for the coming decades. This study aims to elucidate the current knowledge on the relationship between early childhood obesity and asthma.

2 Methods

2.1 Search strategy

A literature search was conducted in October 2024 using the MeSH terms (infan OR child OR neonatal*) AND (obesity* OR overweight* OR growth*) AND (asthma*) in the PubMed database. Only articles published between 2014 and 2024 were included, and the search was limited to meta-analyses, reviews, and systematic reviews. A total of 635 records were identified through PubMed.

2.2 Selection criteria

The top 200 search results were included in this research. A total of 39 records were excluded because they were not written in English, were redacted, or full-text access was not available through the University of Turku subscriptions. The remaining 161 records were screened by reviewing at least the abstract, leading to the exclusion of 109 records that were not relevant to this research. A total of 52 articles were fully read and analyzed, of which 25 contained relevant information for this study. The primary exclusion criteria were that the study did not focus on children or addressed only obesity or asthma, but not both.

The inclusion criteria for this review were twofold: First, only meta-analyses, systematic reviews, and reviews that analyzed cohort studies on the childhood asthma-obesity connection were included. A key criterion was that asthma was not present at baseline in any of the cohort studies included in the selected articles. This criterion excluded all but three studies (Table 1). Due to the limited number of studies available, a meta-analysis from 2013 is also comprehensively discussed in the text, even though it falls outside the scope of this review (2014–2024). Additionally, cohort studies with weight trajectories found in one of the included studies are thoroughly discussed in this review.

Secondly, all other studies (n=22) that contained some relevant information are selectively reviewed in this text. These articles mostly lacked cohort data and were therefore deemed less valuable than the studies included in the table. No separate table was created for these additional 22 studies.

3 Results

Reference (first author, journal, year)	*N (total participants: studies)*	*Study type & selection criteria*	Age of the children at baseline and Follow-up peridod	BMI measurement or how obesity is defined	Males (%; n)	Outcome measurement (How asthma was defined)	N (outcome) and % of total	Key results (Asthma overall) OR (95% CL)	Overal risk of bias assesment
Chang C-L, Ali GB, Pham J, et al. Childhood body mass index trajectories and asthma and allergies: A systematic review. Clin Exp Allergy. 2023;53: 911-929. doi:10.1111/cea.14366	**37,690** from **11** studies	Systematic review of longitudinal cohort studies	**Baseline**: Birth - 5 years: **Follow** up age: 4-58 years	**BMI measurement**: Parent reported (n = 3), Health or school records (n = 4), Research centre measurement (n = 4), Physicians or other health personnel (n = 1). **Obesity definition**: (BMI z-score n = 6), BMI (n = 2), BMI percentile (n = 2)	Not available	Parent reported (n = 7), Physician diagnosed (n = 2), self reported (n = 2)	N/A	Ali et al., 2021 <u>persistent high weigh trajectory</u> and prevalent asthma at 18 years (**OR = 2.42**, 95% CI 1.11–5.28). Nanishi et al., 2022: <u>persistent obesity</u> and current asthma at 5 years (**OR = 2.55**, 95% CI 1.07 - 6.09). Ziyab et al., 2014 <u>Early persistent obesity</u> and asthma prevalent at 18 years (**OR = 2.15**, 95% CI 1.33–. 3.49). Chen et al. 2017: <u>Persistent overweight</u> and incident asthma at 12 years (**OR = 1.54**, 95% CI 1.05–2.26)	High heterogeneity and risk of bias across studies
Shan L-S, Zhou Q-L and Shang Y-X (2020) Bidirectional Association Between Asthma and Obesity During Childhood and Adolescence: A Systematic Review and Meta-Analysis. Front. Pediatr. 8:576858. doi: 10.3389/fped.2020.576858	**1,112,758** from **6** studies (obesity - asthma**).** **28,494** from **3** studies (obesity - asthma)	Systematic review and meta-analysis of prospective cohort studies	**Baseline**: 2 - 7 years: **Follow up** 1-12 years	**BMI Measurement:** n/a**. Obesity definition**: BMI ≥ 95th percentile (CDC growth charts).	Obesity - asthma. **50,45%**; 561,361. Obesity - asthma: **51,01%**; 14,536	Parent reported (n = 2), Physician diagnosed (n = 3), self reported (n = 1),	74,066 children developed incident asthma (6 studies).	RR of obesity and physician diagnosed asthma <u>both sexes</u> **1.39** (95% CI 1.28 - 1.50; **p < 0.001**). <u>Boys</u> RR **1.53** (95% CI 1.17 - 1.99; **p = 0.002**), <u>girls</u> RR **1.17** (95% CI 0.79 - 1.72; **p = 0.434**). RR of early-onset asthma and childhood obesity <u>both sexes</u> **1.47** (95% CI 1.25 - 1.72; **p < 0.001**)	High heterogeneity and risk of bias across studies
Deng X, Ma J, Yuan Y, Zhang Z, Niu W. Association between overweight or obesity and the risk for childhood asthma and wheeze: An updated meta-analysis on 18 articles and 73 252 children. Pediatric Obesity. 2019;14:e12532. https://doi.org/10.1111/ijpo.12532	**73,252** from **18** studies	Meta-analysis of prospective cohort studies	**Baseline**: 0 - 15.5 years: **Follow up** 1 - 18 years	**BMI Measurement:** n/a**. Obesity definition**: US criteria (n = 8), Age- and gender specific threshold in Taiwan (n = 2), The international obesity task force standards (n = 4), UK Criteria (n = 2), WHO criteria (n = 2)	**48,46%**; 35,499 (one study only had female patients)	Parent reported (n = 7), Physician diagnosed (n = 8), mixed (n = 3),	N/A	OR obesity or overweight and asthma **1.30** (95% CI 1.23 – 1.39; **p < 0.001**). OR Obesity **1.40** (95% CI 1.29 – 1.52; **p < 0.001**). OR overweight **1.22** (95% CI 1.14 – 1.31; **p < 0.001**). Obese or overweight girls OR **1.34** (95% CI 1.16 – 1.56; **p < 0.001**), boys OR **1.27** (95% CI 1.15 – 1.40; **p < 0.001**)	Begg funel plot seemed apparently symmetric. Egger test indicated none and marginal evidence of puvblication bias

Table 1.

3.1 Study Selection and Characteristics

Out of the top 200 selected results from a total of 635, three studies were chosen for the main table. Two were meta-analyses, and one was a systematic review. All analyzed cohort studies. The selected articles included: A 2020 meta-analysis, which included 1,112,758 children across nine studies. A 2019 meta-analysis, which included 72,252 children across 18 studies. A 2023 systematic review, which included 37,690 children across 11 studies.

3.2 Childhood obesity-asthma association at some point in childhood

Three separate prospective meta-analyses on the association between childhood obesity and asthma yielded somewhat mixed results when compared to non-obese or non-overweight controls. The age of the children in these studies ranged from birth to 18 years. Asthma type was not specified in these meta-analyses, and all three included only prospective studies in which asthma was not present at baseline.

A 2020 meta-analysis, which included 1,112,758 children across nine studies, reported that 74,066 of them developed asthma. The study concluded that the overall relative risk (RR) of obesity being associated with physician-diagnosed asthma for both sexes was 1.39 (95% CI: 1.28–1.50; $p < 0.001$). Boys had a statistically significant RR of 1.53 (95% CI: 1.17–1.99; $p = 0.002$), whereas no significant association was observed in girls (RR: 1.17; 95% CI: 1.79–1.72; $p = 0.434$). This meta-analysis did not include overweight children, as obesity was defined as being at or above the 95th percentile in the CDC weight charts. The age range of the children varied from 2 to 17 years. Interestingly, the same article conducted a separate meta-analysis, which concluded that early-onset asthma increases the risk of developing childhood obesity, with an RR of 1.47 for both sexes (95% CI: 1.25–1.72; $p < 0.001$) (Shan et al., 2020).

A 2019 meta-analysis, which included 72,252 children across 18 studies, found that the overall odds ratio (OR) for the association between obesity or overweight and asthma was 1.30 (95% CI: 1.23–1.39; $p < 0.001$). Obese children had a higher OR of 1.40 (95% CI: 1.29–1.52; $p < 0.001$) compared to overweight children, who had an OR of 1.22 (95% CI: 1.14–1.31; $p < 0.001$). Interestingly, obese or overweight girls had a slightly higher OR of 1.34 (95% CI: 1.16–1.56; $p < 0.001$) compared to boys, who had an OR of 1.27 (95% CI: 1.15–1.40; $p < 0.001$). This meta-analysis also included parent-reported asthma cases, which showed a higher OR of

1.45 (95% CI: 1.05–2.01; $p = 0.024$) compared to physician-diagnosed asthma, which had an OR of 1.29 (95% CI: 1.21–1.38; $p < 0.001$). However, gender-specific data on the differences between parent-reported and physician-diagnosed asthma were not available. Obesity was primarily defined using U.S. criteria, and the age range of the children varied from birth to 18 years (Deng et al., 2019).

A 2013 meta-analysis, which included 18,760 children across six studies, found that the overall relative risk (RR) for asthma in overweight or obese children was 1.19 (95% CI: 1.03–1.37; $p = 0.02$). The RR was even higher in obese children, at 2.02 (95% CI: 1.16–3.50; $p = 0.1$).
The association between obesity and asthma was strongest in obese boys (RR: 2.47; 95% CI: 1.57–3.87; $p < 0.001$) and was statistically significant. However, in obese girls, no statistically significant association was observed (RR: 1.25; 95% CI: 1.15–1.40; $p = 0.63$). Similar findings were reported when accounting for overweight children, with overweight boys having an RR of 1.57 (95% CI: 1.23–2.00; $p < 0.001$), while overweight girls had an RR of 0.85 (95% CI: 0.45–1.78; $p = 0.66$). When comparing incidence differences between sexes, a significant difference was found between obese boys and girls ($p = 0.04$), but not among overweight children ($p = 0.62$). Asthma was primarily defined as physician-diagnosed, although some cases of unspecified asthma were also included. Obesity and overweight were defined using age- and sex-specific BMI, with overweight classified as above the 85th percentile and obesity as above the 95th percentile. The children's ages ranged from 5 to 18 years (Chen et al., 2013).

In conclusion, all three meta-analyses found a statistically significant association between being overweight or obese and an increased risk of developing asthma in boys compared to non-overweight controls. Additionally, one meta-analysis that compared overweight and obese children found a higher risk of asthma development in obese boys than in overweight boys, suggesting that the degree of excess weight may independently contribute to asthma risk. Only one of the three meta-analyses found a statistically significant increased risk of asthma in overweight and obese girls compared to non-overweight controls. Notably, this meta-analysis also included studies that accepted parent-reported asthma cases, whereas the other two primarily considered physician-diagnosed asthma.

3.3 Weight Trajectories – The Most Accurate Method for Evaluating the Asthma-Obesity Association

A recent systematic review combined five prospective cohort studies, including a total of 20,895 children, to compare weight trajectories from birth up to 25 months and asthma incidence at 10 years of age (Chang et al., 2023). One study included only physician-diagnosed asthma cases, while the others used parent-reported asthma as the outcome measure. Obesity measurement was parent-reported in two studies, assessed in a research center or by other health professionals in two studies, and both methods were used in one study. The determination of weight trajectories varied across studies, making direct comparisons challenging. The included studies, their weight trajectories, and the odds ratios (OR) for asthma incidence were as follows:

Ali et al. 2021. BMI age range was 0-2 years. Outcome was:

1. Prevalent asthma at 12 years of age

- Average: baseline
- Below average: OR = 1.36 (0.66, 2.83)
- Persistently low: OR = 1.16 (0.45, 2.98)
- Early low and catch-up: OR = **2.01 (0.90, 4.44)**
- Persistently high: OR = 1.31 (0.54, 3.12)

2. Prevalent asthma at 18 years of age

- Average: baseline
- Below average: OR = 1.81 (0.92, 3.56)
- Persistently low: OR = 0.52 (0.18, 1.54)
- Early low and catch-up: OR = 2.23 (1.04, 4.82)
- Persistently high: OR = **2.42 (1.11, 5.28)**

Nanishi et al. 2021. BMI age range was 0-3 years. Outcome was current asthma at 5 years of age:

- Normative: baseline
- Persistent low growth: OR = 1.03 (0.67,1.58)
- Transient overweight: OR = 1.29 (0.82, 2.02)

- Late-onset overweight: OR = 1.35 (0.83, 2.22)
- Persistent obesity: OR = **2.55 (1.07, 6.09)**

Rzehak et al. 2013. BMI age range was 0-6 years. Outcome was incident asthma within 6 years:

- Normative growth: baseline
- Rapid growth only up to 2 years: HR = 1.27 (1.06, 1.51)
- Persistent rapid growth up to 6 years of age: HR = 1.24 (0.62, 2.47)

Wadden et al. 2018. BMI age range was 0-10 years. Outcome was persistent asthma between 0-10 years:

1. Female:

- Stable BMI: baseline
- Decreasing BMI: OR = 0.67 (0.08, 5.51)
- Increasing BMI: OR = **4.09 (1.04, 16.15)**

2. Male:

- Stable BMI: baseline
- Decreasing BMI: OR = 0.81 (0.17, 3.86)
- Increasing BMI: OR = 0.80 (0.26, 2.44)

Lovinsky-Desir et. all 2021. BMI age range was 0-10 years of age. Outcome was prevalent asthma at 10 years:

- Flat: baseline
- Linear gain: OR = 1.15 (0.69, 1.93)
- Rapid gain: **OR = 1.19 (0.66, 2.17)**

The risk of bias due to confounding was deemed high in all included studies. Additionally, weight trajectories and their definitions varied across studies. However, five out of six studies reported a high asthma incidence in children with a persistent weight gain trajectory, where a child's weight increased immediately after birth and remained above average throughout the observation period. One study found a correlation between increasing weight and asthma incidence in girls but not in boys.

3.4 Obesity at birth

I was unable to find studies that identified cohorts of children considered obese or overweight at birth and compared their asthma incidence. Even in studies that identified children as obese at an early age (approximately six months), these children were measured to have a normative weight at birth.

3.5 Obesity at or before two years (early obesity)

A 2016 meta-analysis, which included 24 birth cohorts and 12,511 children, found that infant weight gain during the first year (per SDS), adjusted for gestational age and birth weight, was associated with an increased incidence of childhood asthma (OR: 1.27; 95% CI: 1.21–1.34) (Den Dekker et al., 2016). This study did not differentiate between obese and overweight children; instead, all weight gain was considered collectively.

Nanishi et al. analyzed a birth cohort of 880 infants hospitalized for bronchiolitis (median age: 3 months) in a multicenter study conducted in the USA. Weight was measured at 0, 6, 12, 18, 24, 30, and 36 months of age. The outcome measure was asthma development by age 5. Children were categorized into five weight groups based on weight development. All categories were classified as having a normal weight at birth (BMIz between -1 and 0). Odds ratios were adjusted for eight potential confounders: sex, race/ethnicity, prematurity, history of eczema, cigarette smoke exposure at home, parental history of asthma, parental history of eczema, and allergic sensitization. Additionally, potential patient clustering within hospitals was accounted for in the analysis. The **persistent obesity category** (n=29) included children who were classified as obese (BMI-for-age above the 95th percentile) at every weight measurement after 6 months. This category had the highest odds ratio (OR) for asthma: **2.55 (95% CI: 1.07–6.09, p = 0.03)**. Laboratory data showed that only one child had blood eosinophilia (above 4%), but 41% were classified as allergic (specific IgE sensitization), which was twice the incidence observed in the normative growth profile. The **late-onset overweight category** (n=141) included children who maintained a normal weight until 12 months but became overweight

(BMI-for-age above the 85th percentile but below the obesity threshold) afterward. This group had an OR of 1.35 (95% CI: 0.83–2.22). Lastly, the **transient overweight category** (n=181) included children who were obese or overweight between 6 and 24 months but returned to a normal weight by 36 months. This group had an asthma OR of 1.29 (95% CI: 0.82–2.02). The **normative weight growth profile** was used as the baseline, while the **persistent low growth profile** had an OR of 1.03 (95% CI: 0.67–1.58). Blood eosinophilia and allergic IgE sensitization were similar across all weight profiles, except in the **persistent obesity category**, where the incidence was notably higher.

Nanishi M, Fujiogi M, Stevenson M, et al. Association of Growth Trajectory Profiles with asthma development in infants hospitalized with bronchiolitis. J Allergy Clin Immunol Pract. 2022;10(3):723-31. e5. https://doi.org/10.1016/j.jaip.2021.11.001	***OR (95% CI; p-value) asthma at 12 years***
Normative weight trajectory (33%)	Baseline
Persistent low weight growth trajectory (27%)	1.03 (0.67 - 1.58; p = 0.91)
Transient overweight trajectory (21%)	1.29 (0.82 - 2.02; p = 0.27)
Late-onset overweight trajectory (16 %)	1.35 (0.83 - 2.22; p = 0.23)
Persistent obesity weight trajectory (3%)	**2.55** (1.07 - 6.09; p = **0.03**)

Table 2.

Ali et al. analyzed a cohort of 620 infants with a family history of allergic diseases. Data were retrieved from the *Melbourne Atopy Cohort Study*, which initially began as a randomized controlled trial (RCT) to evaluate the impact of three different infant formulas on the incidence of allergic diseases. Weight and height were measured at 18 time points from birth to 24 months, and then again at 12 and 18 years. Parents reported asthma status at 12 years, while participants self-reported their asthma status at 18 years. Children were categorized into five weight trajectory groups based on weight development. Only in the **persistent high-weight trajectory group** (n=90) were children classified as overweight (BMIz-score ≥ +1) at some point. Odds ratios (ORs) were adjusted for multiple confounders, including sex, maternal age, paternal income and occupation, maternal asthma status, education, smoking status, breastfeeding, bronchitis, upper respiratory tract infection, RCT treatment arm, number of siblings, and age at solid food introduction. The **persistent high-weight trajectory group** had the highest OR for asthma at 18 years: **2.42 (95% CI: 1.11–5.28)**. Notably, the **early-low and catch-up weight**

group had a nearly identical OR of **2.23 (95% CI: 1.03–4.82)**. In this weight group, children were considered small at birth (average BMIz = -1), but by 24 months, their weight had caught up to match the average weight group (BMIz close to 0).

Ali et al. Infant body mass index trajectories and asthma and lung function. J Allergy Clin immunol Volume 148, Number 3, https://doi.org/10.1016/j.jaci.2021.02.020	***OR (95% CI) asthma at 12 years***	***OR (95% CI) asthma at 18 years***
Average weight trajectory (24.9%)	Baseline	Baseline
Below-average weight trajectory (29.4%)	1.36 (0.66 - 2.83)	1.81 (0.92 - 3.56)
Persistently low weight trajectory (13.6%)	1.16 (0.45 - 2.98)	0.52 (0.18 - 1.54)
Early-low and catch-up weight trajectory (17.6 %)	**2.01** (0.90 - 4.44)	**2.23** (1.03 - 4.82)
Persistently high weight trajectory (14.5%)	1.31 (0.54 - 3.12)	**2.42** (1.11 - 5.28)

Table 3.

Rzehak et al. analyzed data from 12,050 subjects across eight European birth cohorts (Belgium, Germany, Denmark, Spain, and the Netherlands). BMI measurements followed WHO standards. BMI data from birth were available for all subjects (n = 12,050), with subsequent measurements taken annually from ages 1 to 6. The number of available BMI data points between ages 1 and 6 varied from 3,356 to 10,323 subjects. Children were categorized into three different weight trajectories, with physician-diagnosed (incident) asthma at any point within six years as the outcome. Hazard ratios (HRs) were adjusted for birth weight, weight-for-length at birth, gestational age, sex, maternal smoking during pregnancy, breastfeeding, and family history of asthma or allergies. The **normative growth group** (51.2% of subjects) served as the reference group. In the two other weight trajectory groups, the **"rapid growth only up to 2 years" group** (47.3% of subjects) had an HR of **1.27 (95% CI: 1.06–1.51)**, while the **"persistent rapid growth up to 6 years" group** (only 1.5% of subjects) had an HR of **1.24 (95% CI: 0.62–2.47)**. These two weight groups showed nearly identical weight development patterns and percentages of overweight (14.9% vs. 18.6%) and obese (1.1% vs. 1.7%) children in the first two years. The average BMI at 2 years was also identical (BMI-SDS +1) in both groups. However, after age 2, these weight trajectories began to diverge. In the **"rapid growth only up to 2 years" group**, BMI-SDS gradually decreased, and between ages 4 to 6, the average BMI-SDS ranged between +0.5 and 0. In contrast, in the **"persistent rapid weight growth up to 6 years" group**, the average BMI-SDS remained significantly higher, reaching nearly **+2.5 between ages 4 and 6**. The study authors noted that the differences between obesity before and after 2 years of age could not be evaluated due to the limited statistical power caused by the small sample size in the **persistent rapid weight growth up to 6 years** group.

Rzehak et al. Body mass index trajectory classes and incident asthma in childhood: Results from 8 European Birth Cohorts - a Global Allergy and Asthma European Network iniative. J Allergy Clin Immunol 2013;131:1528-36. http://dx.doi.org/10.1016/j.jaci.2013.01.001	***HR (95% CI) Incident asthma within 6 years of age***
Normative weight trajectory (51.2 %)	Baseline
Persistent rapid weight growth trajectory (1.5 %)	1.242 (0.62 - 2.47)
Rapid weight growth only up to 2 years of age weight trajectory (47.3 %)	1.267 (1.06 - 1.51)

Table 4.

Ziyab et al. (2014) identified an early transient weight trajectory in which children were overweight at one year of age but later experienced weight reduction and were classified as having a normative weight at and after four years. This group had a similar asthma incidence (OR: 1.01; 95% CI: 0.65–1.58, p = 0.97) to the normative weight trajectory, which served as the baseline. This study is further discussed in Chapter 3.6 (Late Obesity).

3.6 Obesity after two years (late obesity)

Ziyab et al. analyzed a birth cohort of 1,456 infants from the *Isle of Wight Birth Cohort* (UK). BMIz data were available at ages 1, 4, 10, and 18 years. The outcome was asthma, defined as a history of physician-diagnosed asthma plus at least one episode of wheezing or asthma treatment in the previous 12 months. Confounders included sex, birth weight, gestational age at birth, maternal age at delivery, maternal education, breastfeeding, and socioeconomic status. Children were categorized into four weight trajectory groups, with the **normative weight trajectory group** (n = 866) serving as the baseline.

- In the **early transient overweight group** (n = 163), children were classified as overweight at 1 year of age but not thereafter. The relative risk (RR) of asthma in this group was 1.01 (95% CI: 0.65–1.58, p = 0.97), indicating no significant association.
- In the **early persistent obesity group** (n = 48), children had a normative weight at 1 year but became overweight or obese in later years. The asthma RR in this group was **2.15 (95% CI: 1.33–3.49, p = 0.001)**. Notably, the classification of this weight

group differed from the methods used in the study, meaning that this group aligns more closely with the late obesity category.

- In the **delayed overweight group**, children had a normative weight at ages 1 and 4 but became overweight at 10 and 18 years. The asthma RR in this group was **1.70 (95% CI: 1.22–2.38, p = 0.002)**.

Ziyab AH, Karmaus W, Kurukulaaratchy RJ, et al. J Epidemiol Community Health 2014;68:934–941. doi:10.1136/jech-2014-203808	***RR (95% CI; p-value) Asthma at 18 years of age***
Normative weight trajectory (71,4 %)	Baseline
Early persistent obesity weight trajectory (3,9 %)	**2.15** (1.33 - 3.49; p = **0.001**)
Delayed overweight trajectory (11,5 %)	**1.70** (1.22 - 2.38; p = **0.002**)
Early transient overweight trajectory (13,1 %)	1.01 (0.65 - 1.58; p = 0.968)

Table 5.

Chen et al. analyzed data from 4,422 children in two cohorts from the *Taiwan Children Health Study*, a longitudinal study. BMI data were measured yearly from ages 6 to 11 in both cohorts, and height and weight data were retrospectively retrieved from participants' elementary school health records. Obesity was defined as an age- and sex-specific BMI at or above the 95th percentile, while overweight was classified as a BMI between the 85th and 95th percentiles, according to WHO criteria. Multiple asthma-related outcomes were assessed: 1. Active asthma at 12 years. 2. Exercise-induced asthma at 12 years. 3. Incident asthma between ages 12 and 18 and 4. Incident exercise-induced asthma between ages 12 and 18. Children were categorized into four weight trajectory groups based on BMI development:

- **Persistent Overweight Category (30.1%)** – The average BMIz was approximately +1.5 between ages 6 and 11.
- **Declining Obesity Category (2.6%)** – Children had the highest BMIz, starting from +3.5 and declining to approximately +2.0.
- **Rapid Growth Category (19.9%)** – At age 6, the BMIz was similar to the **Normative Weight Category (47.7%)**, but children in this group experienced rapid weight gain, primarily between ages 7 and 11, with BMIz increasing from 0 to approximately +1.0.

Children in the **Persistent Overweight Category** had the highest incidence of asthma, except for incident exercise-induced asthma between ages 12 and 18, where the **Declining Obesity Category** had the highest hazard ratio (HR). The authors also compared different obesity criteria (IOTF, WHO, and Taiwanese standards) and found notable differences in obesity and overweight classifications across these definitions.

Chen Y-C, Liou T-H, Chen P-C, et al. Growth trajectories and asthma/rhinitis in children: a longitudinal study in Taiwan. Eur Respir J 2017; 49: 1600741 [https://doi.org/10.1183/13993003.00741-2016]	***OR (95th CI) Active asthma at 12 years***	***OR (95th CI) Exercise-induced asthma at 12 years***	**HR (95th CI) incident asthma between 12 to 18 years**	**HR (95th CI) Incident exercise-induced asthma between 12 to 18 years**
Normative weight class 1 (47.4%)	Baseline	Baseline	Baseline	Baseline
Rapid weight growth class 2 (19.9%)	1.29 (0.82 - 2.02)	1.12 (0.77 - 1.61)	1.77 (0.75 - 4.15)	0.90 (0.60 - 1.35)
Persistently overweight class 3 (30.1%)	**1.54** (1.05 - 2.26)	**1.42** (1.04 - 1.93)	**2.47** (1.18 - 5.12)	1.40 (1.01 - 1.95)
Declining obesity weight class 4 (2.6%)	0.85 (0.25 - 2.87)	0.96 (0.37 - 2.44)	1.82 (0.38 - 8.63)	**1.68** (0.83 - 3.40)

Table 6.

Wadden et al. analyzed 571,790 males and 549,230 females in prospective cohort study of children aged 0-2 years who were followed every two years for eight years in the National Longitudinal Survey of Children and Youths (NLSCY; Canada). Worth mentioning is that due to the large sizes of these weight groups, at no point the average BMI at any weight trajectory was above 65th percentile, meaning that average child's weight at all weight groups were considered normative weight at all time. Children were divided to three weight trajectory groups: stable BMI (41%, reference), Decreasing BMI (13%), Increasing BMI (46%). Confounders were: premature delivery, parent smoking status, family income, parent history of asthma, parents education and socio-economic-status. Outcome was persistent or transient asthma (from questionnaires). Females in the increasing BMI trajectory group had OR = 4.09 (95% CI; 1.04 - 16.15, p = 0.04) for persistent asthma, while males in increasing weight trajectory had OR 0.80 (95% CI; 0.17 – 3.86, p= 0.79). Increasing BMI trajectory was not significantly associated with risk of transient asthma for either sex. Decreasing weight trajectory was without statistic significance in both sexes and in both asthma phenotypes.

Wadden et al. analyzed data from 571,790 males and 549,230 females in a prospective cohort study of children aged 0–2 years, who were followed every two years for eight years as part of the *National Longitudinal Survey of Children and Youths* (NLSCY; Canada). Notably, due to the large sample sizes in these weight groups, the average BMI at any weight trajectory never exceeded the 65th percentile, meaning that all groups were considered to have a normative weight throughout the study period. Children were categorized into three weight trajectory groups: **Stable BMI** (41%) – Used as the reference group. **Decreasing BMI** (13%). **Increasing BMI** (46%) Confounders included premature delivery, parental smoking status, family income, parental history of asthma, parental education, and socioeconomic status. The study's primary outcome was persistent or transient asthma, as reported through questionnaires. Among females in the **increasing BMI trajectory group**, the odds ratio (OR) for persistent asthma was **4.09 (95% CI: 1.04–16.15, p = 0.04)**. In contrast, males in the increasing BMI trajectory group had an OR of 0.80 (95% CI: 0.17–3.86, p = 0.79), indicating no significant association. The increasing BMI trajectory was not significantly associated with transient asthma for either sex. Additionally, the **decreasing BMI trajectory** showed no statistically significant association with asthma risk in either sex or asthma phenotype.

Wadden et al. Sex-Specific Association between Childhood BMI Trajectories and Asthma Phenotypes. Hindawi International Journal of Pediatrics Volume 2018, Article ID 9057435, 9 pages https://doi.org/10.1155/2018/9057435	***OR (95% CI; p-value) Persistent Asthma (Females)***	***OR (95% CI; p-value) Persistent Asthma (Males)***	***OR (95% CI; p-value) Transient Asthma (Females)***	***OR (95% CI; p-value) Transient Asthma (Males)***
Stable BMI trajectory (41 %)	Baseline	Baseline	Baseline	Baseline
Decreasing BMI trajactory (13 %)	0.67 (0.08 - 5.51; p = 0.71)	0.81 (0.17 - 3.86; p = 0.79)	1.46 (0.43 - 4.95; p = 0.52)	0.67 (0.29 - 1.53; p = 0.33)
Increasing BMI trajectory (46%)	**4.09** (1.04 - 16.15; p = **0.0442**)	0.80 (0.26 - 2.44; p = 0.68)	1.56 (0.82 - 2.95; p = 0.17)	0.75 (0.45 - 1.23; p = 0.25)

Table 7.

Lovinsky-Desir et al. analyzed Birth Cohort (URECA, USA) of 609 predominantly black and latino children, that had 418 children with asthma data available. Height and weight was measured at birth, 3 months and after that once a year until 10 years of age. Obesity was defined as a BMI z-score over 1.64 (WHO criteria). Outcome was asthma at age 10 defined using a pre-specified algorithm that included parent-reported physician diagnosis, symptoms, healthcare utilization, use of asthma medications in the previous year, spirometry with reversibility and bronchial hyper-responsiveness assessed by methacholine challenge. Confounders were: sex, ethnicity, maternal asthma, smoking during pregnancy, gestational age, family income at birth, maternal education, maternal allergic sensitization. Children were divided to three weight trajectories. Flat weight growth category (n=329) was used as a baseline and had stable and normative weight from birth until 10 years of age. In Rapid weight gain category (n = 81) had most weight gain in first 2 to 3 years after which weight gain leveled. In Linear weight gain category (n = 102) average BMI at 2 years was nearly similar to Flat weight category and most weight gain was between ages 4 to 10. In this study researchers concluded that asthma incidence differences in weight trajectories did not have statistical power.

Lovinsky-Desir et al. analyzed data from the *Urban Environment and Childhood Asthma* (URECA) birth cohort in the USA, which included 609 predominantly Black and Latino children, with asthma data available for 418 participants. Height and weight were measured at birth, at 3 months, and then annually until age 10. Obesity was defined as a BMI z-score above 1.64, according to WHO criteria. The primary outcome was asthma at age 10, determined using a pre-specified algorithm that included: Parent-reported physician diagnosis, Symptoms, Healthcare utilization, Use of asthma medications in the previous year, Spirometry with reversibility, Bronchial hyperresponsiveness assessed via methacholine challenge. Confounders included sex, ethnicity, maternal asthma, smoking during pregnancy, gestational age, family income at birth, maternal education, and maternal allergic sensitization. Children were classified into three **weight trajectory groups**:

- **Flat Weight Growth Category** (n = 329) – Used as the baseline group, characterized by stable, normative weight from birth to 10 years.
- **Rapid Weight Gain Category** (n = 81) – Exhibited the most weight gain within the first 2 to 3 years, after which weight gain stabilized.
- **Linear Weight Gain Category** (n = 102) – Had an average BMI at 2 years similar to the Flat Weight Growth Category, with most weight gain occurring between ages 4 to 10.

Researchers concluded that the differences in asthma incidence among the weight trajectory groups lacked statistical power and could not establish a significant association.

Lovinsky-Desir et al. Trajectories of Adiposity Indicators and Association with Asthma and Lung Function in Urban Minority Children. J Allergy Clin Immunol. 2021 November ; 148(5): 1219–1226.e7. doi:10.1016/j.jaci.2021.06.015.	*Asthma Incidence (%) P-value = 0.77*
Flat weight trajectory (n = 329, 64,3%)	22,80 %
Linear weight gain trajectory (n = 102, 19,9%)	28,40 %
Rapid weight gain trajectory (n = 81, 15,8%)	24,70 %

Table 8.

4 Discussion

4.1 Gender differences and excess weight that matters

Three meta-analyses have established that obese boys have a statistically significant elevated risk of developing asthma (Shan et al., 2020; Deng et al., 2019; Chen et al., 2013). However, only one of the three meta-analyses (Deng et al., 2019) found that obese girls also had an increased risk of asthma, whereas the other two did not establish a statistically significant association between obesity and asthma in girls. The definitions of obesity and asthma diagnosis varied widely across studies, making direct comparisons difficult, even within meta-analyses. The sole meta-analysis that found an association between obesity and asthma in girls also noted that parent-reported asthma incidence was higher than physician-diagnosed asthma. In contrast, the other two meta-analyses primarily included only physician-diagnosed asthma cases. Further research is needed to determine whether the observed link between obesity and asthma in girls could be influenced by parental over-reporting of lower respiratory tract symptoms as asthma. Additionally, the Deng et al. (2019) meta-analysis was the only one to include early obesity cases (children classified as obese before the age of 2). Further research is needed to evaluate whether the association between obesity and asthma in girls could be explained by transient early obesity, where a child is obese or overweight between birth and two years but not thereafter. Furthermore, two meta-analyses (Deng et al., 2019; Chen et al.,

2013) found that overweight but not obese boys also had an elevated risk of asthma. Both studies also established that obese boys had a higher asthma incidence than overweight boys, suggesting that asthma risk may increase proportionally with excess weight. However, further research is needed to confirm this association. Finally, one meta-analysis (Shan et al., 2020) separately concluded that early-onset asthma increases the risk of childhood obesity, suggesting that the relationship between asthma and obesity may be bidirectional.

This suggests that more specific subgroups, beyond just gender and obesity or overweight status, may be needed to accurately categorize the association between asthma and obesity—or the lack thereof.

4.2 Early Obesity and Asthma Association

In this study, early obesity is defined as obesity occurring before the age of two years. One meta-analysis found that infant weight gain (per SDS) in the first year was associated with an increased risk of childhood asthma, even in the absence of overweight or obesity (Den Dekker et al., 2016). Three cohort studies that categorized children into different weight trajectories from birth until 2–3 years established that early obesity increases asthma risk, at least when the child remains obese beyond two years (Nanishi et al., 2022; Ali et al., 2021; Rzehak et al., 2013). However, one study did not find a statistically significant elevated risk of asthma (OR: 1.29; 95% CI: 0.82–2.02, $p = 0.27$) in children who were obese early but had a normative weight afterward (Nanishi et al., 2022). Similarly, another study found no increased asthma risk in a group with early obesity that normalized later (OR: 1.01; 95% CI: 0.65–1.58, $p = 0.97$) (Ziyab et al., 2014). One study did establish an increased asthma risk in children with rapid weight gain in the first two years, followed by normative weight growth. However, this study did not classify children as obese or overweight, and only 14.9% of children in this group were overweight, while just 1.1% were obese (Rzehak, 2013). Notably, I was unable to find any studies that included children classified as obese at birth and analyzed their asthma risk.

This suggests that any weight gain exceeding normative growth in the first two years of life may increase asthma risk, regardless of whether the child is classified as overweight or obese. Additionally, persistent obesity before and after two years of age is very likely to further increase asthma risk. However, two studies found no elevated asthma risk in children who were overweight or obese before the age of two but not thereafter. Due to the limited evidence, these findings remain inconclusive, and further research is needed before any definitive conclusions can be drawn about the association between early obesity and asthma.

4.3 Late Obesity and Asthma Association

Two out of the three meta-analyses that established an increased risk of asthma in obese boys included only cohorts where children were at least two years old at baseline. This strongly suggests that late-onset obesity increases asthma risk, at least in boys. Additionally, two separate cohort studies examined in more detail in this study also established this association, specifically in persistent obesity (Ziyab et al., 2014; Chen et al., 2017). One study further found an increased asthma risk in children following a delayed overweight trajectory, where children had a normative weight from ages 1 to 4 but became overweight after age 10 (Chen et al., 2017). Conversely, one study found a link between an increasing BMI trajectory and asthma in girls but not in boys(Wadden et al., 2018). However, in this study, the increasing BMI trajectory consisted mostly of children with a normative weight, which could suggest that girls are more sensitive to weight gain, regardless of whether they are classified as overweight or obese

4.4 Strenghts and limitations

No two studies included in this review used the same criteria for overweight, obesity, asthma, or weight trajectories, making direct comparisons challenging. However, I identified multiple high-quality studies that largely reached similar conclusions. The differences observed between studies were not alarmingly large and may be explained by variations in research design and methodology. Nevertheless, the overall conclusions of this review should be interpreted with caution. Further research is still needed to establish a more definitive understanding of the association between childhood obesity and asthma.

4.5 Conclusions

The association between childhood asthma and obesity is a complex issue, with these conditions potentially having a two-way influence on each other, further complicating studies on this topic. Weight trajectories, which categorize children based on their weight development and gender, should be considered the gold standard for identifying children at the highest risk for asthma.

These trajectories should consist of five distinct weight trajectory groups to ensure that each group is sufficiently large to have scientific power, while still allowing for the identification of all relevant scenarios. These weight trajectory groups should include:

1. **Normative weight** as the baseline
2. **Persistent low weight**
3. **Transient early overweight** (overweight or obese before age two, but with normative weight afterward)
4. **Persistent overweight**
5. **Late-onset overweight**

Overweight or obesity should be defined using international standards, such as those set by the International Obesity Task Force (IOTF) or the World Health Organization (WHO).
The asthma outcome should be based solely on physician-diagnosed cases, though parent-reported or questionnaire-based diagnoses can be included separately. When considering confounding factors, neonatal conditions should also be taken into account.

All of these factors require a long timeframe before measurable effects can be observed. Therefore, studying the effects of neonatal conditions and early-life weight gain on the development of asthma at a later age requires a sufficiently large birth cohort with a long follow-up period and careful consideration of multiple confounding factors. However, few studies have been conducted with this specific design, which may explain why the association between these factors is still not sufficiently understood.

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