RESEARCH
Review

Childhood Overweight/Obesity and Asthma: Is There a Link? A Systematic Review of Recent Epidemiologic Evidence

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ARTICLE INFORMATION

Article history:
Accepted 22 August 2012

Keywords
Asthma
Obesity
Overweight
Children

2212-2672/$36.00
doi: 10.1016/j.jand.2012.08.025

ABSTRACT

Asthma and overweight/obesity prevalence are both increasing worldwide. Overweight/obesity has been suggested as a risk factor for developing asthma. The aim of this review is to present and evaluate recent publications that help answer the question: "Is increased body weight (at least overweight status) related to asthma in children?" A systematic review of epidemiologic literature was carried out using the MEDLINE database. Epidemiologic studies on young human subjects (ie, infants, children, and adolescents), published in English during the period 2006-2011 were included. A comprehensive literature search yielded 434 studies for further consideration. Forty-eight studies fulfilled the review's eligibility criteria. Two researchers applied the MOOSE Guidelines for Meta-Analysis and Systematic Reviews of Observational Studies on all identified studies. Current evidence supports a weak yet significant association between high body weight and asthma. New information indicates that central obesity in children increases asthma risk. Also, the link between high body weight and asthma may be stronger in nonallergic asthma. There are mixed results about the importance of sex. Although the nature of the association between overweight/obese status and asthma remains unclear, prospective studies point that high body weight precedes asthma symptoms. These data add weight to the importance of preventing and treating a high body weight against asthma outcomes. Available research in children has not studied adequately the influence of weight change (either gain or loss) on asthma symptoms, an area of clinical importance. Beyond energy control, the role of diet as a possible inflammatory stimulus warrants further investigation. Limited data seem to favor the promotion of breastfeeding in attenuating the overweight/obesity–asthma relationship. Finally, future research should include weight intervention studies assessing various measures of body fat in relation to well-defined asthma outcomes.
J Acad Nutr Diet. 2013;113:77-105.

OVERWEIGHT/OBESITY AND ASTHMA ARE TWO OF the most significant pediatric health problems worldwide.[1] During the past 20 years, the simultaneous increase in the prevalence of both has raised the possibility that the two may be causally linked.[2] Overweight/obese asthma may constitute a unique asthma type that is more difficult to manage. It is more resistant to available steroid treatments, requires higher medication use, and is associated with more frequent hospitalizations in comparison to asthma in normal-weight children.[3-5] It has been projected that even small changes in mean population body mass index (BMI) may translate into significant increases or decreases in asthma incidence in all ages.[6] The problem of a high body weight (at least overweight status) appears on a continuum, and the extreme high end of it is obesity. In the related literature, there is frequent reference to the obesity–asthma link, but unless otherwise stated, the entire range of high body weight (overweight and obesity) is the focus of investigation.

Approximately 32% of children (aged 2 through 19 years) in the United States are either overweight or at risk for becoming overweight.[7] The overweight/obesity epidemic has been related mostly to an obesogenic environment that encourages excessive energy intakes and sedentary lifestyles.[7]

Asthma affects about 9.1% or approximately 6.7 million children (aged 0 to 17 years) in the United States.[8] The high asthma prevalence has been attributed to urbanization characterized by air pollution, environmental tobacco smoke, smaller family size, decreased exposure to infectious agents,

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and undesirable dietary or other lifestyle changes.[2] Observational studies have associated higher intakes of fruits and vegetables, antioxidant nutrients, vitamin D, and fatty acids (mainly n-3 fatty acid) with decreased incidence of asthma symptoms.[9,10] Few investigations[11,12] have looked into energy intake, and expenditure (all of which are determinants of energy balance and body weight). Resting energy expenditure is similar between children with and without asthma but estimated energy intake exceeds resting energy expenditure only in children with asthma when compared with healthy counterparts.[12]

In the past, an association between high body weight and asthma has been reported in adult and pediatric populations.[13] A majority of this evidence is descriptive. Until 2006, more than 25 cross-sectional, case-control, and prospective pediatric studies supported a positive association between high body weight and asthma.[13-16] This association, although uniformly evident, is weak, with odds ratios of around 2.5 in general population cohorts and odds ratios of up to nine in specific subgroups.[17] Longitudinal investigations (until 2006) agree that overweight or obese children experience more asthma symptoms when compared with normal-weight children.[17-21] These longitudinal studies also suggest that high body weight precedes asthma or its worsening. In 2006, Flaherman and Rutherford[14] in a meta-analysis of nine studies (1990-2004) revealed that the effect of high birth weight (>3.8 kg) on subsequent asthma has a pooled relative ratio of 1.2 (95% CI 1.1 to 1.3).[14] This analysis also suggested that more than 100,000 American children aged 5 to 14 years experience asthma each year as a result of being overweight or obese. In adults too, a meta-analysis of prospective studies suggested that the odds of incident asthma for overweight or obese individuals are increased by 50%.[6] The reverse has been shown as well; that is, asthma can lead to obesity in children.[22]

A direct relationship between high body weight and asthma has yet to be established. Possible explanations for a relationship between a high body weight and asthma include a common genetic background, comorbidities, mechanical changes associated with high body weight, changes in airway hyperresponsiveness, changes in physical activity and diet, increased insulin resistance, and systemic inflammation.[3,23-30]

A proposed hypothesis is that a high body weight, as a state of low-grade inflammation, exacerbates airway inflammation, which contributes to the development of asthma.[3] A typical Western diet may act as an inflammatory stimulus. If inflammation is a mechanism linking high body weight and asthma, it is reasonable that diet plays some role. A typical Western eating pattern—high in energy-dense foods such as animal fats and processed sugars, and low in whole unprocessed plant foods—may be obesogenic due to its energy surplus but also because it produces inflammatory biochemical signals.

Past reviews[3,13,15,31] have described epidemiologic and/or metabolic evidence on the obesity–asthma link in children, but new epidemiologic pediatric reports have become available. The aim of this review is to summarize and evaluate the most recent epidemiologic research that describes the relationship of a high body weight and asthma in children. Also, emerging priorities are briefly presented, along with implications for clinical management and public health measures.

METHODS

A systematic review of the existing literature on the link between high body weight (at least overweight) and asthma in childhood was carried out. We posed the following review question: "Is high body weight related to asthma in children?" A review protocol was drawn up following standards outlined by the MOOSE Guidelines for Meta-Analysis and Systematic Reviews of Observational Studies.[32] The literature was assessed by manual and electronic means. The review was undertaken using the computer database of the US National Library of Medicine Medline for the years 2006-2011, with the help of PubMed interface. Key words that were used for retrieving studies were: *asthma*, *obesity*, *overweight*, *adiposity*, *body weight*, *body fat*, *body mass index* or *BMI*, *infants*, *children*, and *adolescents*. Retrieved studies were checked against a list of eligibility criteria, and the references of each study were checked manually to find additional studies that may meet the eligibility criteria. Inclusion criteria were defined a priori. These criteria were: reference to human beings, publication in the English language, study was published between 2006 and 2011, epidemiologic studies (of any design), reference to association between high body weight (described as high body weight or overweight or obesity), and asthma in children and adolescents (aged 0 to 19 years). Studies that did not meet these criteria were excluded from the review. Evidence was extracted systematically for each included study by two researchers separately, using a standardized data extraction form. The data extracted from each study were: study main characteristics, study population, method of asthma diagnosis, weight status measure, diet and/or nutrition measures, measures of effect, and confidence intervals for each outcome. Studies were classified as cross-sectional, case-control, and prospective studies.

RESULTS

Figure 1 demonstrates the numbers of studies identified and selected in each phase of the research. Manual searching of bibliographies provided two additional studies that met the broad eligibility criteria. Ultimately, 48 studies qualified for inclusion. The main characteristics of these studies are provided in Tables 1 through 3. The systematic review included 31 cohort cross-sectional investigations[33-63] (Table 1), four case-control studies[64-67] (Table 2), and 13 prospective cohort studies[68-80] (Table 3).

Ten studies[44,49,53,64,65,67,69,79-81] assessed asthma by physician diagnosis, the most rigorous method to identify children with asthma. Twenty investigations[34,37,40-42,45-47,51,57,59,62,63,70-76] utilized some form of self-reported diagnosis of asthma by a health professional or other self-report of asthma symptoms. The validated International Study of Asthma and Allergies in Childhood questionnaire[82,83] was used by 19 studies.[34,37,39-41,43,48,50,52,54-56,58,60,61,68,73,77,78] Most studies used BMI as the main anthropometric variable to determine weight status, although there was some variation in how the categories of BMI were set up. Methods of BMI categorization included BMI as a continuous variable, standard deviation scores of BMI (BMI *z* scores by sex and age), BMI quartiles or other fractionation, and percentiles specific for sex and age. Studies that evaluated infants used age-appropriate measures such as birth weight, and weight for length *z* score.[84] The reference data to establish a cutoff point for either overweight

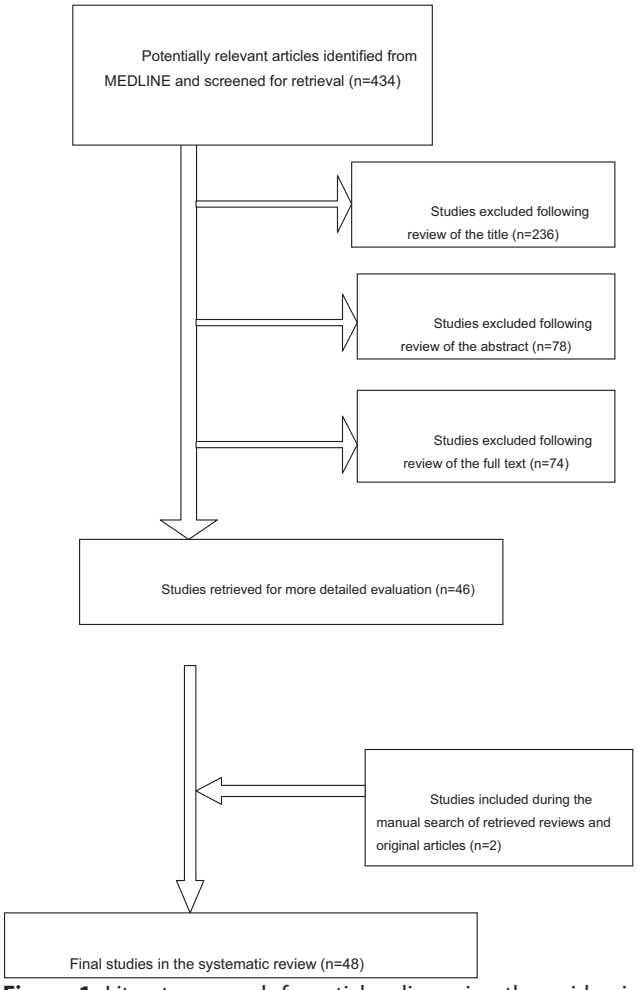

Figure 1. Literature search for articles discussing the epidemiologic link between overweight/obesity and asthma in children.

or obese status differed utilizing two predominant methods, either the International Obesity Task Force[85] or the Centers for Disease Control and Prevention cut points.[84] The Task Force developed cutoff points that correspond to the widely accepted adult cut points of 25 for overweight and 30 for obesity.[85] The Centers for Disease Control and Prevention, on the other hand, has established the 85th percentile of the BMI reference as a cutoff point for pediatric overweight, and the 95th percentile for obesity.[84]

Cross-Sectional Studies

Out of the 31 evaluated cross-sectional studies (Table 1), 30[33-43,45-63] reported an increase in the prevalence of asthma symptoms in relation to overweight or obese status or increasing body weight status in either the total sample and/or in a specific sex,[37,38,46,49-51,55,57-59,61-63] race (black),[46] or other subgroup (nonatopic [ie, nonallergic] children).[45,55,57] Odds ratio (OR) values were reported at <2.0 with few exceptions.

Five studies[34,37,41,52,60] isolated the relationship between obesity and asthma but not overweight status and asthma. In one of these studies,[34] children diagnosed with asthma were more likely than children without asthma to have higher triglyceride levels and acanthosis nigricans regardless of BMI percentile.

In several investigations, differences by sex were examined. In two studies, the association between high body weight (at least overweight status as defined by each reviewed study) and asthma was evident only in female subjects but not in male subjects[50,51] and the opposite was true in five other reports.[37,46,47,59,61] In one study,[58] increasing body weight was associated with asthma symptoms in boys and not in girls. After stratification by sex, seven studies showed significant associations between asthma symptoms and high body weight in both female and male subjects separately.[38,49,52,55,57,62,63] In one study, there was no evidence of effect modification by sex.[41]

In addition to reporting a positive relationship between body weight and asthma symptoms in boys, Hong and colleagues[61] concluded that frequent intake of fresh seafood, fresh fruits, and vegetables was associated with reduced prevalence of current asthma symptoms and was also associated with decreased BMI.

One cross-sectional investigation indicated as a secondary important finding that a shorter duration of breastfeeding (<2 months) combined with at least overweight status (BMI *z* score ≥1)[86] was significantly associated with asthma (prevalence ratio 1.53, 95% CI 1.11 to 2.09).[36]

Case-Control Studies

Among the four recent case-control studies,[64-67] three[64-66] did not identify an association between high body weight (at least overweight status) and asthma symptoms (Table 2). Only one case-control study[67] showed that BMI was significantly higher in patients with asthma compared with healthy subjects ($P<0.002$).

The case-control study by Henkin and colleagues[65] assessed the medical records of 94 Asian-American children with and without asthma. The BMI of children with asthma before and after the asthma diagnosis was compared with the BMI of the control group children. Even after adjustment for various confounders such as atopic dermatitis, allergic rhinitis, food allergies, and other allergies, the OR using BMI >85% percentile for cases vs controls was not significant: 0.92 (95% CI 0.40 to 2.20).

In the most recent and largest case-control study, which included 1,123 US children,[64] overweight status (BMI percentile ≥85th)[84] was not associated with asthma (OR 1.03, 95% CI 0.59 to 1.79). However, when central obesity was assessed by waist circumference (high-weight stratum: ≥85th waist circumference percentile), waist/height ratio (high-weight stratum: ≥85th waist/height ratio percentile), and conicity index (an index of abdominal obesity calculated as waist circumference (m)/0.109×square root (weight [kg]/height [m]) (high-weight stratum: ≥85th conicity index percentile), central obesity was significantly associated with asthma, asthma severity, lower lung function, and reduced atopy in children with asthma. In the final structural equation model, for each unit increase in waist circumference, the OR for asthma was significantly increased by about threefold (OR 2.95). Also, in boys, waist:height ratio was positively associated with asthma (OR 2.43).[64]

Mai and colleagues[66] showed that asthma was not associated with either overweight (≥85th BMI percentile)[84] or ex-

Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Cibella and colleagues, 2011[33]	School-based cross-sectional cohort survey	N=708 Italian children, 10-16 y	n=84 (11.9)	ISAAC[d] questionnaire	BMI[e] Classified according to BMI percentiles developed from the sample Overweight-obese (>85th BMI percentile) Nonoverweight-obese (≤85th BMI percentile)	Not reported		None reported	(+) Asthma ever were significantly more frequent among overweight-obese than in nonoverweight-obese (P=0.0008) Overweight-obese status was not associated with increased eNO[f] concentrations
Cottrell and colleagues, 2011[34]	Community-based cross-sectional cohort survey	N=17,944 US children, 4-12 y	n=2,521 (14.1)	Self-report of medical provider-diagnosed asthma	BMI Classified according to CDC[g84] Overweight (≥85th and ≤94.9th BMI percentile) Obese (≥95th BMI and ≤98.9th BMI percentile) Morbidly obese (>99th BMI percentile)	Not reported		None reported	(+) Overall, asthma and BMI were significantly correlated (P=0.02). As a general trend, the asthma prevalence rate increased as children's BMI percentile increased Asthma prevalence in obese and morbidly obese children was significantly higher than in children with healthy BMI (P<0.001), whereas simple overweight status did not increase asthma risk (P=0.82) Regardless of BMI percentile children diagnosed with asthma were more likely than children without asthma to have higher triglyceride levels and acanthosis nigricans as a marker of developing insulin resistance
Ziaei Kajbaf and colleagues, 2011[35]	School-based cross-sectional cohort survey	N=903 Iranian children, 7-11 y	n=79 (8.7)	ISAAC	BMI Classified according to IOTF[h85] Overweight (≥85th and <95th BMI percentile) Obese (≥95th BMI percentile)	Not reported		None reported	(+) Current asthma was positively associated with BMI (P<0.001) Obesity and overweight were not associated with eczema and allergic rhinoconjuctivitis suggesting that overweight/obesity is not related to atopic asthma

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Matos and colleagues, 2011[36]	Community-based cross sectional cohort survey	N=1,129 Brazilian children, 4-12 y	n=257 (22.8)	ISAAC	BMI Classified according to WHO[i86] Overweight/obesity (BMI z-score ≥ +1)	PR 1.34 (asthma) PR 1.35 (FEV1[j]: FVC[k] ratio)	1.07-1.67 1.11-1.61	Age, sex, birth weight, parental history of asthma, breastfeeding, number of children under 5 y in the household, mother's educational level, infection by parasites	(+) There was a positive association between the occurrence of overweight/obesity and asthma symptoms Overweight/obese children had less respiratory capacity, as measured in lower FEV1:FVC ratio A short-duration of breastfeeding (<2 months) combined with overweight/obesity was significantly associated with asthma
Suglia and colleauges, 2011[37]	Community-based cross sectional cohort survey	N=1,815 US children, approximately 3 y	n=181 (10)	Parent-reported physician-diagnosed asthma	BMI Classified according to CDC[84] Overweight (≥85th and <95th BMI percentile) Obese (≥95th BMI percentile)	NS[l] (asthma) Boys OR 1.7 (asthma) Girls NS (asthma) OR 2.26 (asthma)	 1.0-3.0 1.5-3.3	Sociodemographic factors, home social factors, home environmental factors	(+) There is a relationship between asthma and obesity in children as young as 3 y A relationship between overweight and asthma was only present in boys No social or home environmental factors contributed significantly to the relationship between overweight/obesity and asthma
Suh and colleagues, 2011[38]	School-based cross-sectional cohort survey	N=25,322 Korean children, ages 8-11 y	n= not reported (4.9)	ISAAC questionnaire	BMI, based on reported body weight and height Classified according to Korean growth charts BMI for age percentiles divided in quartiles 51st-75th percentile >75th percentile	Girls OR 1.05 (wheeze) Boys OR 1.22 (wheeze) Girls OR 1.49 (wheeze) Boys OR 1.45 (wheeze)	 0.97-1.14 1.13-1.31 1.40-1.59 1.37-1.54	None reported	(+) The lowest and highest BMI quartiles are positively associated with the prevalence of wheeze in both girls and boys The association between the prevalence of wheeze and highest BMI quartile was positive in all residential areas: metropolitan, provincial, rural, and industrial

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Tanaka and colleagues, 2011[39]	School-based cross-sectional cohort survey	N=24,399 Japanese children, ages 6-15 y	n=not reported (7.6)	ISAAC questionnaire	BMI (reported) Classified according to BMI percentiles developed from the sample Percentile categories:			Sex, age, region of residence, number of siblings, smoking in the household, physical activity, paternal and maternal history of allergic disorders, paternal and maternal educational levels	(+) Being in one of the higher 2 percentile groups was significantly positively associated with the prevalence of asthma A U-shaped relationship between BMI and asthma was noted
					>95th BMI percentile	OR 1.46 (asthma)	1.17-1.81		
					>65th-95th BMI percentile	OR 1.26 (asthma)	1.11-1.43		
					>35th-65th BMI percentile (reference category)	1.00			
					5th-35th BMI percentile	OR 1.15 (asthma)	1.01-1.30		
					>5th BMI percentile	OR 1.38 (asthma)	1.09-1.72		
Vangeepuram and colleagues, 2011[40]	Community-based cross-sectional study	N=505 ethnic minority children in the US, ages 6-8 y	n=131 (25.9)	Self-report of doctor-diagnosed asthma	BMI Classified according to CDC[84] Percent body fat (>30% used as a cutoff to describe elevated body fat) Waist circumference (>90th waist circumference percentile was classified as abdominal obesity according to the recent National Health and Nutrition Examination Survey)[128] BMI ($Q^{m}1-Q5$) Q5 vs Q1+Q2			Age in months, race/ethnicity, and sex	(+) There was a significant association between increased body size and asthma diagnosis, regardless of the measurement examined even after inclusion of ethnicity in the models
					Percent body fat (Q1-Q5)	PR 1.63 (asthma)	1.12-2.39		
					Q5 vs Q1+Q2	PR 1.50 (asthma)	1.02-2.21		
					Waist circumference percentile (Q1-Q5)	PR 1.56 (asthma)	1.04-2.34		
					Q5 vs Q1+Q2				

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Yao and colleagues, 2011[41]	School-based cross-sectional cohort survey	N=5,351 Taiwanese children, ages 4-18 y	n=not reported (9.8)	Self-report of doctor-diagnosed asthma and ISAAC questionnaire	BMI Classified according to IOTF[85] Overweight (≥85th and <95th BMI percentile)	OR 1.26 (wheeze ever) NS (current wheeze) NS (diagnosed asthma)	1.05-1.50	Age, sex	(+) Obesity is associated with a greater prevalence of asthma in children with no evidence of a significant modulation by sex
					Obese (≥95th BMI percentile)	OR 1.60 (wheeze ever) OR 1.80 (current wheeze) OR 1.52 (diagnosed asthma)	1.25-2.04 1.31-2.48 1.13-2.06		
					BMI Obesity vs normal weight	OR 1.57 (current wheeze)	1.14-2.18		
					Overweight vs normal weight	NS (current wheeze)			
Noonan and colleagues, 2010[42]	School-based cross-sectional cohort survey	N=1,852 American Indian children, 4th-12th grade	n=176 (9.5)	Self-report of doctor-diagnosed current or past asthma	BMI Classified according to CDC[84] Overweight and obesity vs normal weight	OR 1.73 (current asthma)	1.20, 2.50	Reservation site and family history of asthma	(+) Current asthma was positively associated with BMI
Okabe and colleagues, 2010[43]	Cross-sectional cohort survey	N=139,117 Japanese children, ages 6-7 y, 13-14 y, and 16-17 y	n=14,257 (10.2)	ISAAC questionnaire	BMI Classified according to the reference values for Japanese children obtained during 1978-1981 Overweight (≥90th BMI percentile)	6-7y: OR 1.24 (asthma) 13-14 y: OR 1.31 (asthma) 16-17 y: OR 1.32 (asthma)	1.15-1.34 1.21-1.42 1.22-1.44	Geographic region, sex	(+) Obesity was associated positively with current asthma
Vazquez-Nava and colleagues, 2010[44]	Cross-sectional cohort survey	N=1,160 Mexican children, 4-5 y	n=61 (5.3)	Physician diagnosed	BMI Classified according to CDC[84] Overweight (≥85th and <95th BMI percentile) Obese (≥95th BMI percentile)	NS (asthma diagnosis) NS (asthma diagnosis)		Sex, smoking parents in the home	(No association) Lack of association between overweight, obesity, and asthma diagnosis in preschool children

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Visness and colleagues, 2010[45]	Cross-sectional cohort survey, National Health and Nutrition Examination Survey, 1999-2006	N=16,074 US children, ages 2-19 y (representative sample)	n=1,544 (9.6)	Self-report of doctor-diagnosed current asthma	BMI Classified according to CDC[84] Overweight (≥85th-<95th BMI percentile) Obese (≥95th BMI percentile)	OR 1.32 (current asthma) OR 1.68 (current asthma) Nonatopic children: OR 2.46 (current asthma) Atopic children: OR 1.34 (current asthma)	1.08-1.60 1.33-2.12 1.21-5.02 0.70-2.57	Survey year, age, race/ethnicity, poverty income ratio, household smoking, physical activity	(+) Overweight/obesity was significantly associated with current asthma In obese children, the association was stronger in nonatopic children
Whitrow and colleagues, 2010[46]	School-based cross-sectional cohort survey	N=6,643 children from the UK, ages 11-13 y (80% ethnic minorities)	n=207 (3.12)	Self-report	BMI Classified according to the 1990 British growth reference curves[129] BMI percentile (as continuous variable)	Black African OR 1.15 (asthma) Black African boys OR 1.55 (asthma)	1.13-2.13 1.01-1.31	Sex, country of birth, parental history of asthma, grandparents' history of asthma, parental smoking, socioeconomic status, psychological well-being, age, family type, mother and father employment status, number of siblings, parental and grandparental generational status	(+) Increasing BMI was associated with reporting of asthma for black Africans. There was a significant interaction between BMI and sex for black Africans. The association between BMI and asthma was significant in boys
Ahmad and colleagues, 2009[47]	Cross-sectional cohort survey, National Survey of Children's Health	N=102,353 US children, ages 0-17 y	n=12,795 (12.5)	Self-report of doctor-diagnosed asthma	BMI Classified according to CDC[84] Obese (≥95th BMI percentile)	0-6 y: OR 1.101 (asthma) 7-12 y: OR 1.331 (asthma) 13-17 y: OR 1.414 (asthma)	0.905-1.339 1.159-1.528 1.190-1.680	Structural and behavioral factors	(+) Obesity was significantly associated with childhood asthma
Chu and colleagues, 2009[48]	Cross-sectional survey	N=14,654 Taiwanese adolescents, ages 13-16 y	n=1,829 (12.5%)	ISAAC questionnaire	BMI Classified according to CDC[84] BMI (as continuous variable)	OR 1.034 (asthma)	1.022-1.048	Sex, age, family, or self-reported tobacco smoking, exercise, incense burning	(+) Increasing BMI was an independent factor that predicted ISAAC-identified asthma

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
He and colleagues, 2009[49]	Cross-sectional cohort survey	N=2,179 Chinese children, 10 y	n=46 (2.1)	Physician diagnosed	BMI Classified according to reference data for Chinese children[130]			District, age, allergy, parental history of asthma and allergy, physical activity, and passive smoking	(+) BMI was positively associated with respiratory symptoms
					Overweight BMI (Girls: 8 y: ≥18.1 and <19.9, 9 y: ≥19.0 and <21.0, 10 y: ≥20.0 and <22.1, 11 y: 21.1 and <23.3, 12 y: 21.9 and <24.5, 13 y: ≥22.6 and <25.6;	Girls: OR 2.46 (phlegm with cold) OR 2.91 (cough without cold)	 1.25-4.85 1.05-8.08		
					Boys: 8 y: ≥18.1 and <20.3, 9 y: ≥18.9 and <21.4, 10 y: ≥20.3 and <23.6, 11 y: ≥20.3 and <23.6, 12 y ≥21.0 and <24.7, 13 y: ≥21.9 and <25.7)	Boys: OR 1.60 (cough with cold)	 1.01-2.55		
					Obese BMI (Girls: 8 y: ≥ 19.9, 9 y: ≥21.0, 10 y: ≥22.1, 11 y: ≥23.3, 12 y: ≥24.5, 13 y: ≥25.6;	Girls: OR 3.82 (wheezing) OR 8.75 (wheezing with cold)	 1.28-11.42 2.11-36.34		
					Boys: 8 y: ≥ 20,3, 9 y: ≥21.4, 10 y: ≥22.5, 11 y: ≥23.6, 12 y: ≥24.7, 13 y: ≥25.7)	Boys: OR 1.69 (phlegm with cold)	 1.04-2.87		
Kuschnir and colleagues, 2009[50]	Cross-sectional survey	N=2,858 Brazilian adolescents, ages 13-14 y	n=381 (13.3)	ISAAC questionnaire	BMI Classified according to CDC[84]			Sedentary lifestyle, smoking mother and presence of dog in the domicile	(+ and no association) A positive association was found between asthma and overweight, exclusively among girls
					Overweight/obese (≥85th BMI percentile)	Girls: OR 1.51 (asthma) Boys: NS (asthma)	 1.07-2.13		

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Spathopoulos and colleagues, 2009[51]	Cross-sectional survey	N=2,715 Greek children, ages 6-11 y	n=117 (4.31)	Questionnaire for lung health and atopy	BMI Classified according to growth charts for Greek children BMI as continuous variable	OR 2.17 (asthma) Girls: OR 2.73 (asthma) Boys: NS (asthma)	1.22-3.87 1.09-6.85	Sex, age, and height	(+ and no association) High BMI (overweight and obesity) was a strong independent predictor for asthma and atopy. The effect of BMI was significant in girls but not in boys
Tai and colleagues, 2009[52]	Cross-sectional cohort survey	N=1,509 Australian children, 4-5 y	n=358 (23.7)	ISAAC questionnaire	BMI Classified according to the IOTF BMI cutoff points for children)[85] Overweight Obese	 NS OR 2.75 (current wheezing) OR 2.96 (asthma ever) OR 1.34 (wheeze ever)	 1.55-4.87 1.84-4.75 1.08-1.66	Sex	(+) A positive association between asthma symptoms and obesity in preschoolers was identified
Tsai and Tsai, 2009[53]	Cross-sectional cohort survey	N=1,329 Taiwanese children from Kaohsiung, ages 11-12 y	n=77 (12.4) boys, n=64 (9.5) girls	Physician-diagnosed asthma	BMI Classified according to reference data for Taiwanese children[131] At risk for overweight (85th-94th BMI percentile) Overweight (≥95th BMI percentile)	 OR 1.93 (asthma) OR 1.78 (asthma)	 1.20-3.09 1.08-2.91	Diagnosed allergy, passive smoking, chemical vapor, and mold wall/furniture	(+) Children who were at risk of overweight or were overweight had increased risk of asthma
Corbo and colleagues, 2008[54]	Cross sectional cohort survey	N=20,016 children from Italy	n=1,575 (7.9) current wheezing and 1,343 (6.7) current asthma	ISAAC questionnaire	BMI (based on reported weight and height) Classified according to Q1 to Q5 BMI Q5 vs Q1	 OR 1.47 (wheeze) OR 1.61 (asthma)	 1.20-1.82 1.28-2.01	Sex, study area, parental education, parental smoking, parental asthma or rhinitis, questionnaire respondent, season of data collection, presence of mold in children's bedroom	(+) High weight increased independently the odds of asthma in children

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Garcia-Marcos and colleagues, 2008[55]	Cross-sectional study	N=17,145 children from Spain, ages 6-7 y	n=1,379 (8.0) current occasional asthma n=390 (2.3)	ISAAC questionnaire	BMI (based on reported weight and height) Classified according to the IOTF BMI cutoff points for children[85]			Age, older and younger siblings, exercise, mother's education, truck traffic, cat or dog during the first year of life, and smoking father or mother	(+ and −) Obesity was a risk factor for asthma Obesity increased the odds for current occasional asthma and current severe asthma Also, obesity increased the odds for current severe asthma without rhinoconjuctivitis (nonatopy), both for girls and boys Obesity did not increase the odds for current severe asthma with rhinoconjuctivitis (atopy)
					BMI as continuous variable	OR 1.38 (asthma) OR 1.25 (current occassional asthma) OR 1.87 (current severe asthma)	1.18-1.62 1.04-1.50 1.40-2.49		
					Obese Girls				
						OR 2.99 (current severe asthma without rhinoconjuctivitis)	1.68-5.32		
					Boys				
						OR 1.92 (current severe asthma without rhinoconjuctivitis)	1.13-3.25		
Garcia-Marcos and colleagues, 2008[56]	Cross-sectional cohort survey	N=931 children from Spain, ages 6-8 y	n=85 (9.1) current active asthma, n=44 (4.7) occasional mild asthma	ISAAC questionnaire	BMI Percent body fat Sum of four skinfolds Classified according to percent body fat (obese was >30% girls, 25% boys)			Age, asthma in the mother and father, and sex	(+) Using different methods to define weight status, body weight increased the odds of clinically active asthma
					BMI quartiles; Highest quartile compared with lowest	OR 2.03 (asthma)	1.05-3.91		
					Percent body fat quartiles; Highest quartile compared with lowest	OR 2.28 (asthma)	1.11-4.68		
					Sum of four skinfolds; Highest quartile compared to lowest	OR 2.33 (asthma)	1.16-4.64		

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Sithole and colleagues, 2008[57]	School-based cross-sectional cohort survey	N=3,804 Canadian children, ages 10-11 y	n=814 (21.4)	Parent-reported doctor-diagnosed asthma or bronchitis	BMI BMI As continuous variable	OR 1.06 (asthma) Non-atopic girls OR 1.06 (asthma) Atopic girls OR 1.05 (asthma) Non-atopic boys OR 1.05 (asthma) Atopic boys OR 1.04 (asthma)	1.03-1.09 1.02-1.10 1.01-1.10 1.02-1.08 1.01-1.07	Allergies, sex, and socioeconomic factors	(+) A linear association was revealed between BMI and asthma in girls and boys. The underlying mechanisms are not likely to involve atopic immune responses
Priftis and colleagues, 2007[58]	Cross-sectional cohort survey	N=700 Greek children, ages 10-12 y	n=74 (10.6)	ISAAC questionnaire	Weight (per 5 kg)	Boys OR 1.13 (asthma symptoms) Girls: NS	 1.02-1.25	None reported	(+ and no association) In multiple logistic regression analysis, increasing body weight (per 5 kg) was positively associated with asthma symptoms in boys but not girls
Tsai and Tsai, 2007[59]	Cross-sectional cohort survey	N=2,218 Taiwanese children from Taipei, ages 11-12 y	n=217 (9.8) doctor-diagnosed asthma n=357 (16.1) suspected asthma	Questionnaire on respiratory symptoms including self-report of doctor-diagnosed asthma	BMI Classified according to reference data for Taiwanese children[131] At risk for overweight (85th-94th BMI percentile) Overweight (≥95th BMI percentile) Girls NS (suspected asthma) Boys OR 1.56 (suspected asthma)	 OR 1.53 (exercise induced-wheezing) OR 1.43 (exercise induced-cough) OR 1.47 (persistent cough) OR 1.62 (wheezing with cold) OR 1.52 (dyspnea associated with wheezing) OR 1.80 (exercise induced-wheezing) OR 1.94 (exercise-induced cough)	 1.16-2.02 1.09-1.87 1.08-2.00 1.17-2.25 1.11-2.10 1.37-2.38 1.47-2.55	Residential districts, sex, and physician-diagnosed allergy	(+ and no association) Overweight or at risk for overweight was positively associated with an increased risk of asthma symptoms. Also, overweight status increased the risk of suspected asthma in boys, but not in girls

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Cassol and colleagues, 2006[60]	Cross-sectional cohort survey	N=4,010 children from Southern Brazil, ages 13-14 y	n=642 (16)	ISAAC questionnaire	BMI Classified according to CDC[84] Overweight (≥85th and <95th BMI percentile) Obese (≥95th BMI percentile)	 OR 1.28 (wheeze ever) OR 1.36 (wheezing with exercise) OR 1.29 (asthma ever) OR 1.55 (severe asthma)	 1.08-1.52 1.11-1.66 1.03-1.62 1.12-2.14	None reported	(+) There was a positive association between obesity and prevalence of asthma symptoms and asthma severity
Hong and colleagues, 2006[61]	Cross-sectional cohort survey	N=24,260 children from Korea, ages 6-12 y	n=1,395 (5.75)	ISAAC questionnaire	BMI BMI quartiles; Highest quartile compared with lowest	 Girls NS Boys OR 1.610 (current wheeze)	 1.274-2.033	Age, birth weight, breastfeeding, parental asthma, parental smoking, socioeconomic status, and exercise	(+ and no association) BMI may increase the odds of developing asthma symptoms in boys but not in girls Frequent intake of fresh seafood, fresh fruits, and vegetables was associated with reduced prevalence of current asthma symptoms and was also associated with decreased BMI
Jones and colleagues, 2006[62]	Cross-sectional school-based cohort survey, 2003 Youth Risk Behavior Survey	N=13,222US students, attending grades 9-12	n=2,129 (16.1)	Self-reported physician or nurse diagnosed asthma	BMI (reported weight and height) classified according to CDC[84] Overweight (≥95th BMI percentile)	 OR 1.4 (current asthma) Girls OR 1.5 (current asthma) Boys OR 1.3 (current asthma)	 1.1-1.6 1.1-2.0 1.1-1.6	Sex, race/ethnicity, and grade	(+) There was an increased risk of asthma associated with being overweight in all children together, and separately when analyzed by sex

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Table 1. Cross-sectional studies of overweight/obesity and asthma prevalence among children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of high body weight status	OR[a] or RR[b] or PR[c] estimate	95% CI	Adjusted for	Outcome(s)
Kwon and colleagues, 2006[63]	Cross-sectional cohort survey	N=853 Black and Hispanic children, ages 2-11 y	n=194 (22.7)	Parent/guardian-reported diagnosis of asthma and asthma-related symptoms or emergency care in the previous 12 mo	BMI Classified according to CDC[84]			Age, race, ethnicity, household smoking	(+) Being at risk for overweight increases the odds for asthma
						Boys			A U-shaped curve was observed for boys and a linear trend was observed for girls when examining BMI percentile vs the probability of having asthma
					Underweight (≤5th BMI percentile)	OR 2.9	1.1-7.7		
					Normal (≥6th and ≤84th BMI percentile)	OR 1.0			
						Girls			
					At risk of overweight (≥85th and ≤94th BMI percentile)	OR 2.6	1.4-5.0		
						Boys			
						NS			
						Girls			
					Overweight (≥95th BMI percentile)	OR 2.1	1.2-3.8		
						Boys			
						OR 2.4	1.4-4.3		

[a]OR=odds ratio.
[b]RR=relative ratio.
[c]PR=prevalence ratio.
[d]ISAAC=International Study of Asthma and Allergies in Childhood.
[e]BMI=body mass index.
[f]eNO=exhaled nitric oxide.
[g]CDC=Centers for Disease Control and Prevention.
[h]IOTF=International Obesity Task Force.
[i]WHO=World Health Organization.
[j]FEV1=forced expiratory volume in 1 second.
[k]FVC=forced vital capacity.
[l]NS=not significant.
[m]Q=quintile.

clusive breastfeeding <12 weeks in the absence of each other condition. Only the combination of both exclusive breastfeeding <12 weeks and overweight (≥85th BMI percentile)[84] revealed a significant association with asthma (OR 1.81, 95% CI 1.11 to 2.95), after adjustment for sex, maternal asthma, paternal asthma, aboriginal origin, passive smoking at birth, residence location, and family income. By studying the same cohort, Mai and colleagues[87] reported that girls with asthma had 3.6 times increased odds of having a combination of infrequent milk consumption (never or occasionally or once or twice per week) and being overweight (≥85th BMI percentile)[84] than girls without asthma (OR 3.64, 95% CI 1.18 to 11.24).

Prospective Studies

The findings of 13 prospective studies in young populations that have investigated the influence of overweight/obesity on asthma appear in Table 3.[68-80] Out of these 13 studies, 12 supported that overweight/obesity increased asthma symptoms later in life.[68-78,80]

In a birth cohort study[69] of 285 full-term children who were at high-risk for asthma (based on parental history), the association between body weight and asthma was influenced by age. A high body weight (>85th weight for length percentile)[84] at age 1 year was associated with a lower rate of asthma at age 6 years (P=0.02) and 8 years (P=0.04). In the same study,[69] late onset of overweight status (>85th BMI percentile)[84] (ie, being overweight at age 5 years but not at age 1 year) was associated with a higher risk for asthma at ages 6 and 8 years.

In 3,582 participants of the Cardiovascular Risk in Young Finns Study[70] followed from childhood to young adulthood (1980 to 2001), asthma was associated with obesity in subjects once they became adults but not during younger ages. At ages 24 to 39 years, but not earlier, BMI as a continuous variable was independently associated with asthma (OR 1.05, 95% CI 1.01 to 1.09). This investigation[70] also reported on the association between leptin, asthma, and BMI. Higher leptin concentrations were identified only in obese adults with asthma compared with adults without asthma or obesity but not in the two other younger pediatric age groups of the cohort.[70]

Burgess and colleagues[74] followed 753 individuals for 25 years where childhood higher BMI—defined as at least overweight status according to the International Obesity Task Force BMI cutoff points for children[85]—predicted adult-onset current asthma in female subjects but not before.

In the Prevention and Incidence of Asthma and Allergy birth cohort study,[71] 3,756 Dutch infants were followed up to age 8 years. Children with a baseline high BMI—defined as a BMI standard deviation score >85th percentile using the reference growth curves of the Dutch Fourth Nationwide Growth Study[88]—were at an increased risk for dyspnea and bronchial hyper-responsiveness at 8 years. In the same study,[71] an early-life high BMI was not important as long as the child achieved a normal weight—BMI standard deviation score ≤85th percentile[88]—later in life (age 6 to 7 years).

The Northern Finland Birth Cohort study,[72] a longitudinal cohort that included 9,479 subjects, showed that childhood asthma was associated with a high birth weight (>4,510 g). In 195 Swiss healthy infants[75] who were followed from birth for 12 months every week for respiratory symptoms, birth weight was a potent predictor of wheeze (incidence risk ratio 2.67, 95% CI 1.43 to 4.98). In another prospective birth cohort, Taveras and colleagues[73] found that each 1-unit increment in 6-month weight-for-length z score[84] was associated at age 3 years with greater odds of recurrent wheezing (OR 1.46, 95% CI 1.11 to 1.91) and any wheezing (OR 1.23, 95% CI 1.03 to 1.48). In a Korean birth cohort, Jeong and colleagues[68] reported that the highest BMI tertile at age 3 years increased the odds for asthma diagnosis (OR 4.28, 95% CI 1.17 to 15.57). Also, children in the lowest birth weight tertile combined with the highest BMI tertile at age 3 years displayed a very high OR (OR 16.35, 95% CI 1.66 to 160.57) for chronic respiratory illness (ie, symptoms exceeding 3 months).

Only one prospective study by Mamun and colleagues[76] investigated the effect of weight change, defined as change in BMI z score, on the future odds of incident asthma. The study[76] included almost 3,000 Australian children, measured at age 5 years and 14 years. The z scores of BMI at age 5 years and 14 years were subtracted from each other to determine the change in BMI z score between the two time points (baseline was age 5 years and follow-up was at age 14 years). The change in BMI z score in children without asthma from age 5 years to age 14 years was −0.025, and in children with asthma +0.093 (P=0.004). A positive difference of BMI z score from age 5 to 14 years was significantly associated with increased odds of asthma symptoms in adolescence (OR 1.13, 95% CI 1.02 to 1.25). Once the same analysis was conducted separately by sex, the same association remained significant only in boys (OR 1.22, 95% CI 1.06 to 1.41), and not in girls (OR 1.07, 95% CI 0.92 to 1.24). Given that this study[76] adjusted data for diet and physical activity, the authors concluded that obesity, and not related lifestyle factors, are associated with asthma.

The burden of overweight/obesity on asthma was also observed in boys but not in girls in a Brazilian birth-cohort study of 4,452 children assessed as infants and, re-evaluated at age 11 years,[77] and in a US-based longitudinal investigation of 4,393 children—asthma-free at baseline—followed for 14 years.[80] Similar findings were evident only in girls but not in boys in a study of 2,399 Norwegian adolescents, evaluated at ages 13 to 15 years (baseline), and 17 to 19 years (follow-up).[78]

Finally, Eneli and colleagues[79] presented the only prospective study that did not find any direct association between BMI and prevalence of asthma and airway hyper-responsiveness. In the same study, a secondary observation was a significant interaction (P for interaction=0.01) between high BMI (highest quintile of BMI at age 4 years) and a short breastfeeding period (<8 weeks) on increasing the prevalence of airway hyper-responsiveness.[79] Specifically, when children had been breastfed for <8 weeks and were in the highest quintile of BMI at age 4 years, they were more likely to have airway hyper-responsiveness at age 10 years (27.7%) compared with children in the lower four quintiles of BMI.

DISCUSSION

This review summarizes recent epidemiologic evidence (ie, studies published between 2006 and 2011) on the association between high body weight (at least overweight status) and asthma in children. As is often the case with systematic reviews, our analysis is limited by the quality and quantity of

Table 2. Case-control studies of overweight/obesity and asthma in children and adolescents

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	OR[a] estimate	95% CI	Adjusted for	Outcome(s)
Musaad and colleagues, 2009[64]	Case-control study	N=1,123 US children, ages 5-18 y	n=469 (41.76) cases	Physician-diagnosed asthma	BMI[b] Classified according to CDC[c84] Waist circumference Waist/height ratio Conicity index BMI percentiles (High-weight stratum: ≥85th BMI percentile) Waist circumference percentiles (high-weight stratum: ≥85th waist circumference percentile) Waist/height ratio percentiles (boys) (high-weight stratum: ≥85th waist/height ratio percentile) Conicity Index percentiles (High-weight stratum: ≥85th conicity index percentile)	 NS OR 2.95 (asthma) OR 2.43 (asthma) OR 2.63 (asthma)	 3.55[d] 2.07[d] 1.19-5.82	Age group, sex, and parental education	(No association and +) BMI percentiles were not related to asthma Central obesity was associated with asthma, asthma severity, lower lung function, and reduced atopy in children
Henkin and colleagues, 2008[65]	Case-control medical record review study	N=188 Asian American children	n=94 (50) cases	Physician-diagnosed asthma	BMI Classified according to CDC[84] Overweight (≥86th and <95th BMI percentile) Obese (≥95th BMI percentile)	 NS[e] NS	 	Atopic dermatitis, allergic rhinitis, and other allergies	(No association) Neither overweight nor obesity were related to asthma in Asian immigrant children
Mai and colleagues, 2007[66]	Nested case-control study	N=723 Canadian children, ages 8-10 y	n=246 (34.02) cases	Physician-diagnosed asthma	BMI Classified according to CDC84 Overweight/obese (≥85th BMI percentile)	 NS	 	Sex, parental asthma, aboriginal origin, passive smoking at birth, residence, family income	(No association) Overweight/obesity was not associated with asthma diagnosis. Exclusive breast-feeding <12 wk plus overweight was significantly associated with asthma. This association appeared to be strong in children whose mothers had asthma and also in boys In the same cohort,[87] infrequent milk consumption plus being overweight increased the odds for asthma in girls

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Table 2. Case-control studies of overweight/obesity and asthma in children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	OR[a] estimate	95% CI	Adjusted for	Outcome(s)
Mansell, 2006 and colleagues[67]	Case-control study	N=216 adolescents, ages 12-18 y	n=134 (62.04) cases	Physician-diagnosed asthma	BMI classified according to CDC[84] Overweight (>85th BMI percentile) and Nonoverweight (<85th BMI percentile)	Not reported		None reported	(+) BMI was higher in asthmatics compared with healthy subjects $P<0.002$ There was a positive relationship between overweight and airway flow limitation but not asthma severity

[a]OR=odds ratio.
[b]BMI=body mass index
[c]CDC=Centers for Disease Control and Prevention.
[d]Estimated coefficient/standard error of the estimate in the final (reduced) structural equation model.
[e]NS=not significant.

the primary investigations. Many cross-sectional, case-control, and longitudinal studies were identified but none of the publications included interventions. The results overwhelmingly supported a positive relationship between overweight/obesity and asthma in children.

Cross-Sectional Surveys and Case-Control Studies Show a Weak Link between High Body Weight (at Least Overweight Status) and Asthma in Children

Thirty-one cross-sectional surveys (Table 1) and four case-control studies (Table 2) were identified. Cross-sectional studies[34-36,38-63] included a large number of children (>466,000 subjects). Because of the cross-sectional design, causality cannot be implied. In five studies[34,37,41,52,60] an association was identified between asthma and obese status but not overweight. The majority of evidence exhibited a positive association between a high body weight (at least overweight status) and asthma across a variety of countries, and ages. The volume of this evidence supports that a high body weight (at least overweight status) may be significant in asthma development and that the relationship is not restricted between obesity and asthma. Although the chance of publication bias cannot be excluded, it is possible that the prevalence of both disease entities (overweight/obesity and asthma) have reached a necessary threshold level in recent years that a relationship between the two is more easily detected throughout a variety of pediatric populations. The strength of the association was low, with an OR <2.0; yet, ORs of up to 8.75 were reported in specific population subgroups.[49]

In terms of the role of sex, although some studies in adults favor an association in women compared with men,[13] epidemiologic studies in children provide mixed results (Table 1).

One case-control study[67] showed a positive relationship between increasing BMI and asthma by comparing adolescents with and without asthma. The three other available case-control studies [64-66] did not support a relationship between BMI and asthma (Table 2). However, the case-control study by Musaad and colleagues[64] is the first to report a positive association between central obesity and asthma. The importance of central obesity and body fat distribution is an area that deserves further attention. Musaad and colleagues[64] also demonstrated that central obesity was associated with asthma severity, lower lung function, and reduced atopy in children. One more study[60] showed an increase in asthma severity with obesity (≥95th BMI percentile)[84] in a cohort of >4,000 children and adolescents. On the contrary, Mansell and colleagues[67] found no influence of BMI on asthma severity scores in adolescents, although their sample size was very small (n=216).

Methodologic limitations of analyzed cross sectional and case-control studies included self-reported data, different definitions used for assessing pediatric overweight and obesity, and lack of controlling for confounding factors such as physical activity and diet. With the exception of four investigations,[34,39,57,63] results did not distinguish underweight subjects from normal weight subjects, although the prevalence of asthma may increase at both extremes of pediatric BMI.[39,63] If there is an increased prevalence of asthma in underweight children that is not taken into account, the size of the effect of the overweight/obesity–asthma relationship may be underestimated. Future research should address these limitations.

Table 3. Prospective studies of overweight/obesity and asthma in children and adolescents

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	HR[a] or OR[b] or other estimate	95% CI	Adjusted for	Outcome(s)
Jeong and colleagues, 2010[68]	Prospective birth cohort study	N=422 Korean children, from birth to 3 y	Not reported (5.5) (age 3 y)	ISAAC[c] questionnaire	Birth weight Classified according to tertiles BMI[d] Classified according to tertiles BMI tertiles, at 3 y Lowest tertile Middle tertile (reference) Highest tertile Birth weight tertiles Lowest tertile Middle tertile (reference) Highest tertile	NS[e] OR 1.00 OR 4.28 (asthma at 3 y) NS (asthma at 3 y) BMI tertiles, at 3 y Highest tertile OR 16.35 (chronic respiratory illness) Middle tertile OR 1.00 (chronic respiratory illness) Lowest tertile NS (chronic respiratory illness)	1.17-15.57 1.66-160.57	Sex, gestational age, household income, mother's employment, prenatal or postnatal environmental tobacco smoke exposure, and family history of allergic disease	(+) The prevalence of asthma increased significantly with an increase in BMI quartiles at age 3 y Children initially in the lowest birth weight tertile but at age 3 y in the highest BMI tertile had higher risk of chronic respiratory illness (symptoms for >3 mo) compared with those who remained in the middle tertile
Zhang and colleagues, 2010[69]	Prospective birth cohort study, The Childhood Origin of Asthma cohort	N=285 full-term US high-risk children, from birth to 8 y	n=259 (91) (age 6 y) n=238 (84) (age 8 y)	One or more of the following: 1. physician-diagnosed asthma; 2. use of albuterol for coughing or wheezing episodes (prescribed by physician); 3. use of a daily controller medication: 4. step-up plan, including use of albuterol or short-term use of inhaled corticosteroids during illness; and 5. use of prednisone for asthma exacerbation	Height/length Weight BMI All classified according to CDC[f84] Weight for length percentiles (for age ≤2 y) BMI percentiles (for age ≥3 y) Overweight status (>85th percentile) at age 1 y at age 5 y but not age 1 y	NS (at age 6 y) (asthma) NS (at age 8 y) (asthma) OR 5.78 (at age 6 y) (asthma)	Not reported	Sex, maternal asthma, environmental factors during the first year (eg, breast-feeding, dog and cat ownership, smoke exposure, day care attendance and having older children in the household), and wheezing with rhinovirus infection, and birth weight	(− and +) Association between weight and childhood asthma changes with age. High body weight at age 1 y was associated with a decreased risk of asthma and better lung function at ages 6 and 8 y in children with a parental history of asthma or atopy. In contrast, becoming overweight and obese beyond infancy might be a potential risk factor for asthma

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Table 3. Prospective studies of overweight/obesity and asthma in children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	HR[a] or OR[b] or other estimate	95% CI	Adjusted for	Outcome(s)
Jartti and colleagues, 2009[70]	Prospective cohort study, The Cardiovascular Risk in Young Finns Study	N=3,582 (3-18 y in 1980), n=2, 764 (9-24 y in 1986), and n=2,620 (24-39 y in 2001) Finnish children and adolescents	n=64 (1.8) (3-18 y in 1980) n=101 (3.7) (9-24 y in 1986) n=121 (4.6) (24-39 y in 2001)	Parent-reported physician-diagnosed asthma	BMI Classified according to IOTF[g][85] BMI as continuous variable	NS (3-18 y in 1980) (asthma) NS (9-24 y in 1986) (asthma) OR 1.05 (24-39 y in 2001) (asthma)	1.01-1.09	None reported	(No association during childhood, + association during adulthood) Asthma was linked with obesity in adults, but not in younger ages Higher leptin concentrations were identified in obese asthmatic adults compared to non-obese asthmatic adults but not in the younger groups
Scholtens and colleagues, 2009[71]	Birth cohort study, the Prevention and Incidence of Asthma and Allergy	N=3,756 Dutch children, evaluated at age 8 y	n=275 (7.3) wheezed at age 8 y n=361 (9.6) had dyspnea at age 8 y	Questionnaire on asthma symptoms based on parental reporting	BMI Classified according to reference data for Dutch children[88] BMI-for-age SDS[h] Persistent high BMI (>85th BMI SDS percentile at 3-5 y and at 6-7 y) during childhood or high BMI (>85th BMI SDS percentile) at 6-7 y	OR 1.68 (at age 8 y) (dyspnea) OR 1.66 (at age 8 y) (measured bronchial hyperresponiveness)	1.18-2.39 1.10-2.52	Maternal allergy, paternal allergy, maternal education, maternal smoking during pregnancy, smoking in the house at 8 years, sex, mode of delivery, the child's birth weight, and breast-feeding duration	(+ and no association) Children with a current high BMI were at increased risk to have dyspnea and bronchial hyperresponsiveness at 8 y. A high BMI at an earlier age was not related to an increased risk if the child achieved a normal weight at 6-7 y.
Remes and colleagues, 2008[72]	The Northern Finland Birth Cohort 1986, a longitudinal cohort	N=9,479 subjects from Finland; from birth to age 16 y	n=489 (5.2)	Self-report of doctor-diagnosed asthma	Birth weight High birth weight (>4,510 g) vs reference birth weight (2,500-3,340 g)	Atopic subjects OR 2.40	1.33-4.32	Unadjusted results were reported because potential confounders did not change results	(+) Childhood asthma was associated with high birth weight. This association was mostly explained by an increased risk of atopy

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Table 3. Prospective studies of overweight/obesity and asthma in children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	HR[a] or OR[b] or other estimate	95% CI	Adjusted for	Outcome(s)
Taveras and colleagues, 2008[73]	Project Viva, a prospective cohort study of children	N=932 children from the US; from 6 mo to 3 y	n=not reported (current asthma: 13%), (recurrent wheezing:14%)	Parents' report of doctor-diagnosed asthma, and wheeze	Weight for length *z* scores Classification according to CDC[84] Weight for length *z* scores (at 6 mo)	OR 1.46 (at age 3 y) (recurrent wheezing) OR 1.23 (at age 3 y) (any wheezing) OR 1.22 (at age 3 y) (current asthma)	1.11-1.91 1.03-1.48 0.94-1.59	Birth weight, sex, age, race/ethnicity, passive exposure to smoke, mother's prepregnancy BMI, vitamin D intake during pregnancy, breastfeeding status at 6 mo, father's BMI, household income, No. of children <12 y living in the household, and parental history of asthma	(+) Each one unit increment in 6-mo weight-for-length *z* score had a greater risk of recurrent wheezing, and any wheezing at 3 y. A weaker association was observed between 6-mo weight-for-length *z* score and current asthma
Burgess and colleagues, 2007[74]	The Tasmanian Asthma Survey, a prospective cohort study	N=753 asthma-free children from Tasmania, Australia; evaluated at age 7 y (baseline)	n=81 (10.8), age 32 y	Parent-, and self-reported asthma	For adult ages: BMI (from self-reported height and weight) For childhood ages: BMI (from measured height and weight) BMI *z* score (at age 7 y) BMI for childhood classified according to IOTF[85] BMI z-score (at age 7 y) Quartile 1 Quartile 2 Quartile 3 Quartile 4 Trend Overweight (at age 7 y)	Girls (asthma onset after age 21 y) OR 1.00 OR 0.76 OR 1.70 OR 3.86 OR 1.73 OR 3.05 Boys (asthma onset after age 21 y) NS	0.16-3.51 0.46-6.29 1.20-12.42 1.17-2.17 1.28-7.29	Adjustment did not alter results; presented results are without adjustment	(+ and no association) Higher body mass index in nonasthmatic young girls at age 7 y predicts risk of current asthma developing in adult life. No associations were seen in boys
Latzin and colleagues, 2007[75]	Birth cohort of healthy infants	N=195 Swiss infants, evaluated at birth and during the first 12 mo of life by weekly telephone follow-up	n=41 (21) (wheeze at least once)	Parent reported respiratory symptoms	Birth weight (per kg) As a continuous variable	IRR[i] 2.67 (wheeze)	1.43-4.98	Boy, one older sibling, ≥2 older siblings, nursery care, maternal allergic rhinitis, maternal smoking in pregnancy, maternal asthma	(+) Multivariable regression analysis showed that in the first year of life high birth weight was a strong determinant of wheeze

(continued on next page)

Table 3. Prospective studies of overweight/obesity and asthma in children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	HR[a] or OR[b] or other estimate	95% CI	Adjusted for	Outcome(s)
Mamun and colleagues, 2007[76]	Birth cohort of mothers and children	N=2,911 Australian children, evaluated at age 5 y and 14 y	n=348 (272 with symptoms of asthma + 76 with bronchitis) at age 5 y (12.0%)	Questionnaire on lung health based on maternal reporting	BMI Classified according to IOTF[85] BMI *z*-score (at age 5 y), as continuous variable BMI *z*-score (at age 15 y) as continuous variable Change in BMI *z*-score (from age 5 to 14 y) as continuous variable	OR 1.13 (symptoms of asthma or bronchitis)	1.02-1.25	Birth weight, maternal age at birth, mothers level of education, gross family income around pregnancy, maternal smoking during pregnancy, duration of breast feeding, diet, sports, watching television and puberty	(+) Increase in BMI *z* score between ages 5 and 14 y was associated with increased risk of asthma symptoms in adolescence
Menezes and colleagues, 2007[77]	Prospective birth cohort study	N=4,452 children from Brazil, followed from birth to the age of 11 y	n=601 (13.5)	ISAAC questionnaire	BMI Triceps and subscapular skinfolds All classified according to WHO[j132] Obese (>85th BMI percentile and >90th triceps and subscapular skinfolds percentile)	Girls NS (wheeze) Boys OR 1.38 (wheeze)	 not reported	None reported	(+ and no association) Obesity was associated with an increased risk of wheezing in boys but not in girls
Tollefsen and colleagues, 2007[78]	Longitudinal study, phase 1 and 2	N=2,399 Norwegian adolescents, evaluated at ages 13-15 y (baseline), and 17-19 y (follow-up)	n=94 girls (7.3% girls) and 66 boys (5.9% boys) evaluated at ages 13-15 y (baseline), and 161 girls (12.5% of girls) and 72 boys (6.5% of boys) at ages 17-19 y (follow-up)	ISAAC questionnaire	BMI Classified according to IOTF[85], for ages <18 y	Girls NS (incident current wheeze) Boys NS (incident current wheeze) Girls OR 2.4 (persistent current wheeze) Boys NS (persistent current wheeze)	 1.3-4.6	Self-reported current smoking, environmental smoking and low physical activity, and measured overweight at baseline	(+ and no association) Overweight status was associated with an increased risk of persistent current wheezing in girls but not in boys

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Table 3. Prospective studies of overweight/obesity and asthma in children and adolescents *(continued)*

Reference	Type of study	Sample	Asthma frequency (% of study population)	Asthma diagnosis	Anthropometric measure; definition of weight status	HR[a] or OR[b] or other estimate	95% CI	Adjusted for	Outcome(s)
Eneli and colleagues, 2006[79]	Longitudinal community-based study	N=536 German children	n=17 (3.1%)	Physician-diagnosed asthma	BMI Classified according to CDC[84] BMI *z* score quintiles	 NS (asthma) NS (airway hyperresponsiveness)		Birth weight breastfeeding, sex, parental atopy, and environmental smoke exposure	(No association) There was no association between BMI and prevalence of asthma, and airway hyperresponsiveness. When children had been breastfed for less than 8 wk and were in the highest quintile of BMI at age 4, they were more likely to have airway hyperresponsiveness at age 10 (27.7%), compared with children in the lower four quintiles of BMI
Mannino and colleagues, 2006[80]	Prospective birth cohort study, National Longitudinal Survey of Youth	N=4,393 US asthma-free children at baseline followed for up to 14 y	n=218 (5.0)	Physician-diagnosed asthma	BMI Classified according to CDC[84] High body mass (≥85th BMI percentile)	 Girls NS (asthma) Boys HR 2.4 (asthma)	 1.4-4.4	None reported	(+ and no association) Boys but not girls with high body masses were at an increased risk for developing asthma

[a]HR=hazard ratio.
[b]OR=odds ratio.
[c]ISAAC=International Study of Asthma and Allergies in Childhood.
[d]BMI=body mass index.
[e]NS=not significant.
[f]CDC=Centers for Disease Control and Prevention.
[g]IOTF=International Obesity Task Force.
[h]SDS=standard deviation score.
[i]IRR=incidence risk ratio.
[j]WHO=World Health Organization.

Longitudinal Research in Children Supports the Hypothesis that High Body Weight (at Least Overweight Status) Leads to Asthma

Recent prospective evidence (that incorporates >39,000 subjects) favors the hypothesis that high body weight (at least overweight status) causes asthma later in life (Table 3). Out of 13 studies, 12[68-78,80] reported a positive association between high body weight (at least overweight status) and the subsequent development of asthma symptoms, including studies that provided subgroup analyses (ie, specific sex).

Among prospective studies, all birth cohorts[68,69,71-73,75,77,80] supported the overweight/obesity–asthma link. This accumulating data is important because it strengthens the hypothesis that high body weight status is a risk factor for asthma early in life when most asthma develops.[89] It is not clear whether the relationship of infant adiposity and early life asthma symptoms extend to asthma that persists later. The study by Remes and colleagues[72] who followed children from birth until age 16 years seems to support this. Longer follow-up periods in birth cohort studies are needed to clarify this.

The reported ORs or hazard ratios ranged from 1.1 to a little over 5.5. The heterogeneity in effect size may be in part due to the influence of sex in the overweight/obesity–asthma relationship. Not all prospective studies[70,72,76] controlled for sex. It is also possible that the differences found in the various studies are due to different stages of sexual maturation. Sexual maturation during puberty is a risk factor for the onset of asthma.[90] Puberty status was taken into account by only one prospective study[76] (Table 3).

Published longitudinal pediatric studies have not addressed the possible importance of duration of overweight/obese status on asthma development. Recent research suggests a positive association between childhood BMI and reduced lung function in overweight and obese adult women due to an interaction effect between age and BMI.[91] In another study, obesity duration is associated with pulmonary function impairment in obese subjects of various ages (8 to 76 years).[92] On the same issue of high body weight duration, in prepubertal children,[93] overweight/obesity induces reduction of upper airway flow but without any proinflammatory airway changes attributed to overweight/obesity. It may be that in children or adolescents, evidence of inflammation is not present or not easily detected. On the contrary, in a study of 490 children with mild persistent asthma, the influence of obesity on asthma symptoms is reduced with increasing age, and yet reduction in lung function persists.[94] Taken together, these data[91-94] suggest that age and duration of high body weight may be important. It could be argued that in young ages, obesity-related inflammation or other factors might not have reached their full harmful potential and a possible involvement of the respiratory system might require a long history of overweight/obesity.

Another consideration is whether age of asthma onset modifies the association between obesity and asthma. Longitudinal studies in children so far have not investigated this parameter (Table 2). One study of children with asthma[95] showed that in early onset of asthma (<12 years) but not late (≥12 years) there is a significant association between increasing BMI and duration of asthma. In a retrospective study of adults[96] a significant association was found between age of asthma onset and obesity. However, the association was sex-dependent in that male subjects were at increased odds of obesity if diagnosed with asthma during puberty and female subjects were at increased odds for obesity if diagnosed with asthma after age 20 years.

Further investigation is needed into the role of sex, age, age of asthma onset, sexual maturation, and duration of high body weight in the development of asthma.

High Body Weight and Nonatopic (Nonallergic) Asthma

Three studies[35,45,57] revealed that nonatopic (ie, nonallergic) asthma is more strongly affected by high body weight. Also, in one study central obesity was associated with reduced atopy in children.[64] Researching the specific influence of high body weight (at least overweight) on atopic and nonatopic asthma may provide a clearer understanding as to why we are seeing a variation in effect size in the different studies.

Nonatopic asthma involves an interleukin-8 inflammatory pathway characterized by high neutrophil production. It is triggered by bacteria, viruses, pollutants, and dietary components such as saturated and n-6 polyunsaturated fatty acids.[97,98] In adult patients with asthma,[99] a high-fat meal increases neutrophilic airway inflammation, with the effect being the highest when a meal high in *trans* fatty acid is consumed. The details of this pathway in relation to a high body weight are yet to be investigated.

Body Composition and Central Obesity in Asthma

BMI is a practical and widely used measure of weight status in children and adults, yet BMI may not be the ideal or the only measure to assess the influence of a high body weight (at least overweight status) on respiratory health, including asthma. For example, in one pediatric longitudinal study,[69] a high BMI (at least overweight status: >85th weight for length percentile)[84] in infancy was associated with reduced risk of asthma and improved lung function in childhood. In the same study,[69] the development of overweight/obesity (>85th BMI percentile)[84] at age 5 years was associated with increased risk of asthma and decreased lung function at ages 6 and 8 years. These results appear conflicting at first glance. BMI reflects total body mass, which in childhood undergoes continuous change due to the growth process. During the first months of life, an infant is characterized by rapid growth, and a higher BMI may not necessarily reflect higher fat mass but increased deposition of lean mass instead. Increased lean mass is associated with improved respiratory health.[91] In contrast, the development of high BMI (at least overweight status: >85th weight for length percentile)[84] at age 5 years, which corresponds fairly well with the critical period of adiposity rebound, is likely to reflect a higher than desirable fat mass. This is one possible explanation as to why a high BMI at 12 months may protect against asthma but a high BMI at age 5 years may not.

Epidemiologic research in this review did not assess body composition in detail. Two cross-sectional studies of children aged 6 to 8 years[40,56] found that BMI, percent body fat, sum of skinfold thicknesses, and waist circumference produced relatively comparable results when analyzing the relation between high body weight (as defined by each examined measure) (see Table 1) and asthma; but these studies were not

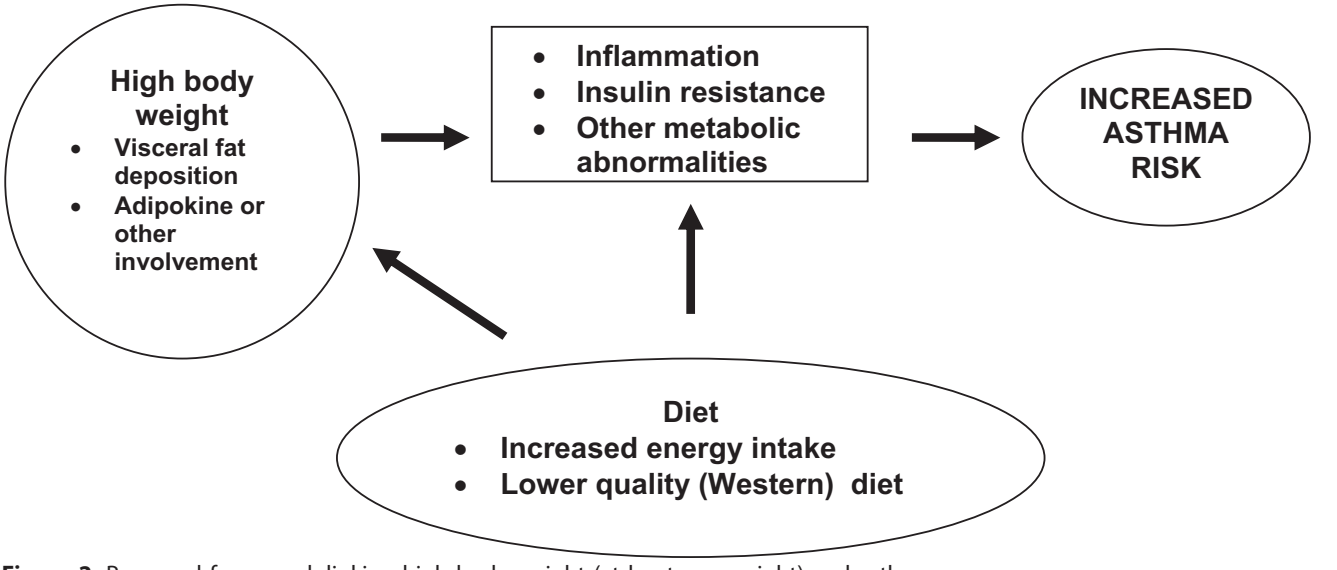

Figure 2. Proposed framework linking high body weight (at least overweight) and asthma.

longitudinal and by definition they could not compare the different body composition methods at different ages. Body composition studies in adults have shown that fat mass is inversely related to lung function.[91] Also, in one pediatric clinical study that studied the effect of asthma medication,[100] body weight and height between children with asthma and healthy children was not different at baseline but percent body fat was significantly higher in children with asthma. Studies that assess body composition—besides BMI—are needed to investigate the development and progression of overweight/obese asthma throughout life.

Central body fat distribution may be another avenue to study, in lieu of its possible connection with inflammation and insulin resistance (Figure 2). However, central obesity has rarely been evaluated in relation to asthma in studies of children. In the case-control study by Musaad and colleagues,[64] BMI percentiles were not associated with asthma in children but central obesity was. In the same study, central obesity was associated with asthma severity, reduced lung function, and reduced atopy. One more study of ethnic minority children[40] showed that central obesity was associated with asthma even after inclusion of ethnicity in the models. There is corroborating data from adult subjects that central obesity is significantly associated with an increased risk of nonatopic asthma only.[101] The causal pathway is unknown, but this information suggests the involvement of different pathophysiologic mechanisms requiring further investigation.

In future research, additional anthropometric and body composition measures related to fat distribution and body fat should be measured. These measurements may include waist circumference, waist-to-hip ratio, percent body fat, skinfold thicknesses, or conicity index to more accurately estimate potential health risk.

Overweight/Obesity, Asthma, and Inflammation

A state of higher systemic inflammation may be key in unraveling the details of the overweight/obesity–asthma relationship.[3]

Chronic systemic inflammation that is characteristic of a high body weight status may worsen airway inflammation and lead to asthma. The exact details of this putative mechanism have not been described yet.

In one cross-sectional study,[33] that measured exhaled nitric oxide (eNO), as a measure of airway inflammation, eNO was not related to overweight/obese status (>85th BMI percentile of the studied population sample). Also, in a clinical pediatric study[102] eNO was not related to systemic inflammatory markers, and there were no differences in eNO between obese (≥95th BMI percentile)[84] and normal weight (<85th BMI percentile) children with asthma. In contrast, in a study of 153 children with asthma with normal BMI values (>25th and <75th BMI percentile) as well as lung function variables,[103] BMI was negatively related with bronchial reversibility induced by administering a bronchodilator medication. Because bronchial reversibility is related to bronchial inflammation, this finding might underline a link between overweight and airway inflammation in children. In adults,[104] also, there is significant increase in airway inflammation in obese compared with nonobese people with asthma. Furthermore, airway inflammation is positively associated with total plasma saturated fatty acids and negatively with monounsaturated fatty acids.[104] Frequent intake of fresh seafood, fresh fruits, and fresh vegetables was associated with reduced prevalence of current asthma symptoms and was also associated with decreased BMI in children.[61] Although a single cross-sectional study[61] cannot reveal whether increased intake of fruits or vegetables is directly responsible for the reduced risk of development of asthma symptoms through lower BMI, there might be some relationship among food intake, BMI, and asthma symptoms prevalence. The connection with dietary intake needs to be explored more and such findings point to the possible benefits of a diet that has anti-inflammatory properties (Figure 2).

Another area of interest connecting obesity, asthma, and inflammation is leukotrienes. Leukotriene molecules are lipid mediators with inflammatory properties that contribute to many aspects of airway inflammation and asthma pathogenesis. Obese adults who receive leukotriene receptor antago-

nists (montelukast) experience greater clinical improvement than normal weight subjects, which suggests that leukotrienes are likely to play a bigger role in mediating asthma symptoms in obese patients with asthma.[105] Significant reduction in leukotriene production has been observed in relation to fish oil supplementation in adults,[106] and low fish intake may be a predictor of poor respiratory health in children.[107] Hence, this area is worth investigating further.

It is possible that obesity-related molecules such as adipokines act as important mediators of inflammation in the obesity–asthma link.[108,109] Adiponectin and leptin are two energy-regulating adipokines released by fat tissue that may be involved in systemic or airway inflammation affecting asthma. Adiponectin has anti-inflammatory properties and is lower in overweight and obese individuals than normal weight peers. Low adiponectin has been associated with asthma in adults[110] and children.[111] Adiponectin is positively associated with asthma control, and negatively with asthma symptoms, even after controlling for BMI.[102,108] This means that a high body weight is not solely responsible for the influence of adiponectin on asthma but other metabolic or other unaccounted factors are also involved.

Leptin is proinflammatory, and is increased in people with asthma who are obese vs people with asthma who are not obese of all ages.[102,104] In children with asthma, being a girl and at-least-overweight status predicts a higher serum leptin concentration.[109] Serum leptin concentration has been associated with clinical severity of asthma, but independent of BMI.[112] Also, leptin increases the odds of a child with asthma to experience exercise-induced bronchodilation, an asthma symptom, regardless of the child's BMI.[102,104] One case-control study that matched children for age, sex, and BMI,[30] showed significant increases in the blood concentrations of the adipokines interleukin-6, interleukin-4, interleukin-5, and leptin in asthma case subjects vs healthy control subjects despite the similar BMI between case and control subjects. As in the case of adiponectin, other significant unaccounted factors besides high body weight may be important. Only one longitudinal study[70] (Table 3) reported on the association between leptin, asthma, and BMI in three age groups and found higher leptin concentrations only in obese adults with asthma compared with nonobese adults with asthma but not in the two other younger pediatric age groups of the cohort. The possibility of inadequate power could not be excluded in this study.[70]

Adiponectin, leptin, and other adipokines should be studied further to fully understand their role in the development of pediatric asthma. It is uncertain whether adipokine alterations precede or are a consequence of respiratory disease like asthma, and how adipokines may influence the relationship between obesity and asthma. Longitudinal studies with adequate power and weight intervention studies in children and adolescents will help resolve such open questions.

Overweight/Obesity, Asthma, and Metabolic Abnormalities

A high body weight status has frequently been associated with hypertriglyceridemia, hypercholesterolemia, and insulin resistance; problems that can also influence unfavorably the health of the respiratory tract.[113] Because dyslipidemia and hyperinsulinemia are involved in the development of airway inflammation, it is possible that early abnormalities in lipid or glucose metabolism are involved in pediatric asthma. In a small clinical study of children with asthma,[114] obese children (≥95th BMI percentile)[84] were diagnosed with a significantly higher prevalence of metabolic syndrome in comparison to nonobese peers (<95th BMI percentile). Using a different study design, Del-Rio-Navarro and colleagues[115] showed that adolescent boys who were obese (≥95th BMI percentile)[84] and also had mild persistent asthma had a significantly higher prevalence of metabolic syndrome than obese boys without asthma. Arshi and colleagues[30] showed a significantly higher level of insulin resistance in children with asthma compared with healthy controls of similar BMI. These findings agree with results from the first epidemiologic study that took into account metabolic abnormalities[34] (Table 1). In this large cross-sectional study of approximately 18,000 American children,[34] hypertriglyceridemia and insulin resistance were positively associated with asthma even after controlling for BMI.

These new studies extend our knowledge to show that the presence of overweight/obesity may accompany underlying metabolic abnormalities in asthma, but not always. Screening for and correcting problems of dylsipidemia and insulin resistance may be an important consideration in children with asthma regardless of body weight status. The specific influence of metabolic abnormalities on asthma and body weight is still uncertain and will need to be addressed in prospective studies.

Overweight/Obesity, Asthma, and Weight Loss

A small number of adult weight loss studies has focused on patients with asthma.[116-122] Although limited by their small sample sizes, these weight-loss studies have uniformly reported improvement in lung function or asthma symptoms and reduced medication requirements following weight decrease.[117,123,124] One older pediatric study showed improvement in asthma outcomes once weight loss was achieved by bariatric surgery in adolescents.[125] Recent publications did not include any pediatric interventions. This is an area where research is needed because the natural history of asthma in young ages differs from that of adult onset asthma.[126]

Future intervention trials should investigate potential mediators (eg, influence of adipokines, hormones, physical activity level, and diet composition) and moderators (eg, sociodemographic characteristics and comorbidities) of the intervention effects.

In the absence of intervention studies, weight change studies are valuable. One prospective investigation[76] reported that a positive change in weight status from childhood to adolescence increased the odds of asthma development during adolescence. In a randomized drug trial for asthma treatment,[127] infant weight-gain rate was not associated with asthma symptoms, but infants with a slow weight-gain rate had fewer exacerbations. If future studies confirm that weight change pattern is associated with asthma diagnosis or related aspects, appropriate weight-related interventions could be developed with asthma prevention as a primary objective.[127]

In Pursuit of Identifying Interactions: Short Breastfeeding May Be Critical

Three studies[36,66,79] looked into the possible role of breastfeeding in the relationship between overweight/obesity and asthma. All three are in agreement that a short breastfeeding period (<2 months) combined with overweight status (as defined by each study) interact to increase the odds of asthma development. One more study indicated that infrequent milk consumption in addition to overweight status increased odds for asthma development in girls.[87] Identifying significant lifestyle interactions that influence the relation between overweight/obesity and asthma may contribute to the development of more effective public health strategies.

CONCLUSIONS

Methodologic rigor and consistency in disease classification for both asthma and high body weight (overweight and obesity) are important to help us better understand underlying associations. Despite design limitations, a multitude of recent epidemiologic investigations support an association between high body weight (at least overweight status) and asthma in children. Cross-sectional studies almost uniformly suggest a weak yet significant relationship. Also, prospective studies support that a high body weight precedes asthma. The link between high body weight (at least overweight status) and asthma may be stronger in nonallergic asthma. New research indicates that pediatric central obesity is associated with asthma, asthma severity, and lower lung function. There are no weight intervention studies in children that take into account asthma outcomes. This is a gap in the available literature. Adequately powered randomized controlled trials can definitively demonstrate the benefit of body weight normalization in relation to asthma.

There is very limited information on how inflammation and insulin resistance might influence asthma in the presence of a high body weight. Emerging research reveals that metabolic abnormalities are more prevalent in children with asthma than in healthy children, but these abnormalities may not always be a function of BMI. A Western-type diet has often been described as an inflammatory stimulus, yet the mechanisms linking dietary pattern, high body weight, and asthma have not been explored. Relevant pediatric interventions are needed to offer answers on this topic.

Although future studies will expand our knowledge, food and nutrition practitioners should recommend that children consume a varied and balanced diet as a way to achieve and maintain a healthy weight and overall health. Clinicians can play an important role in helping correct energy excess by counseling for age-appropriate weight maintenance/weight loss. Monitoring should include follow-up of weight status and measures of central obesity. Screening for and correcting problems of dylsipidemia and insulin resistance may be an important consideration in children with asthma regardless of body weight status. Finally, available data thus far seem to favor a breastfeeding period >2 months as a way to ameliorate the overweight/obesity–asthma relationship.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.