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Obesity, Asthma, and Exercise in Child and Adolescent Health

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Abstract

Obesity increases the risk of asthma throughout life but the underlying mechanisms linking these all too common threats to child health are poorly understood. Acute bouts of exercise, aerobic fitness, and levels of physical activity clearly play a role in the pathogenesis and/or management of both childhood obesity and asthma. Moreover, both obesity and physical inactivity are associated with asthma symptomatology and response to therapy (a particularly challenging feature of obesity-related asthma). In this article, we review current understandings of the link between physical activity, aerobic fitness and the asthma-obesity link in children and adolescents (e.g., the impact of chronic low-grade inflammation, lung mechanics, and direct effects of metabolic health on the lung). Gaps in our knowledge regarding the physiological mechanisms linking asthma, obesity and exercise are often compounded by imprecise estimations of adiposity and challenges of assessing aerobic fitness in children. Addressing these gaps could lead to practical interventions and clinical approaches that could mitigate the profound health care crisis of the increasing comorbidity of asthma, physical inactivity, and obesity in children.

Keywords

Obesity; asthma; body mass index; nutrition; physical activity; comorbidities; systemic inflammation

INTRODUCTION

The prevalence of asthma and obesity, common chronic illnesses in children, has increased dramatically over the past few decades in a parallel manner (3;86). It is alarming that the increase in these two conditions, both of which are modulated by levels of physical activity, continues despite heightened awareness in both the medical community and general public. It is clear that there are economic and health impacts of childhood asthma and obesity in the short and long term as both conditions tend to persist across the lifespan (6;26;38;40). The number of obese and asthmatic children will continue to increase until clinicians, in

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partnership with families, schools, and local communities, develop new methods of addressing this problem.

In this review, we will discuss what is known and delineate the gaps in our understanding of the physiological mechanisms linking obesity and asthma. We will expand on the possible role of physical activity and aerobic fitness, which is currently not well delineated, in the obesity-related asthma link.

SCOPE OF THE PROBLEM: EPIDEMIOLOGICAL PERSPECTIVE

Numerous epidemiological studies have investigated the relationship between asthma and obesity (22;46;76). The preponderance of studies indicates that obesity is a risk factor for the development of asthma throughout the lifespan. Additionally, maternal overweight/obesity excessive weight gain during pregnancy as well as both high and low birth weight appears to increase the risk of asthma in childhood (14;44). We have summarized the results of systematic reviews evaluating the relationship between body mass index (BMI=weight/height^2) and asthma among children in Table 1(18;30;39;70;84). Overall, there is a positive association between BMI and asthma or asthma-like symptoms in children, with the relative risk ranging from 1.19 to 1.35 in overweight and from 1.5 to 2.02 in obese children. This relationship may be modified by such factors as sex, race, ethnicity, age of onset, and duration of obesity. A few investigators have examined the possible effect of sex and pubertal status on the asthma-obesity connection; however, the results have been mixed (17;18;76). One systematic review and meta-analysis by Chen et al evaluated the sex difference on the relationship between obesity and asthma risk and found that obese boys had a significantly increased risk of asthma (RR 2.47; 95% CI 1.57, 3.87) compared to obese females (RR 1.25; 95% CI 0.51, 3.03) (18). However, other studies have shown the obesity-asthma link to be stronger in girls (17;51;109). These inconsistencies may be partly explained by age and/or pubertal status because of the varying range of ages included in studies ranging from birth to 19 years. The relationship between sex and asthma depends on age with boys being more affected with asthma during childhood and girls being more affected with asthma during adolescence and adulthood (29;78). Only one study has included pubertal status and they found that increased risk of asthma related to obesity was only significant in girls (17). Lastly, while patients with asthma may be at increased risk of becoming overweight or obese due to avoidance of physical activity (47;69) or side effects of medications (25), the longitudinal studies show that obesity antecedes the development of asthma.

THE EXERCISE-OBESITY-ASTHMA PARADOX

One of the challenges facing researchers attempting to delineate the link between exercise, body weight, and asthma is the fact that acute bouts of exercise are a common trigger of bronchoconstriction in both adults and children with asthma. Consequently, children and adolescents diagnosed with asthma face reduced participation in organized, school-based physical education and may self-limit their spontaneous participation in exercise in daily life (47;69). In contrast, there is a growing body of literature, both in animal models and in human studies, linking the biological mechanisms that contribute to aerobic fitness with

those that reduce asthma symptomatology (56;57;88;102). Thus, just as obesity itself can contribute to physical inactivity in children and adolescents (110), the comorbidities of asthma and obesity will likely further sedentary behaviors in affected individuals and worsen asthma symptoms and cause treatment challenges (7;16;45;62;63).

Aerobic fitness and physical activity are essential components in both the diagnosis and treatment of the obese child and adolescent, and in those who have asthma (23;33;60;72). Despite this, evidence-based guidelines do not yet exist on how best to assess and track aerobic fitness in this population. Recently, Hansen and coworkers (58) reviewed a number of studies focused on assessing aerobic fitness from cardiopulmonary exercise tests (CPET) in obese adolescents. They were unable to find consensus among these studies, and reached the following conclusion, *"whether cardiopulmonary anomalies during maximal exercise testing would occur in obese adolescents remains uncertain. Studies are therefore warranted to examine the cardiopulmonary response during maximal exercise testing in obese adolescents."* Thus, an obstacle in attempting to identify key factors in the asthma-obesity connection has been the lack of precision in the quantification of aerobic fitness.

In children, only a handful of prospective studies examining weight status and the risk of asthma have accounted for physical activity levels, typically by subjective measures (17;46;61;75;93;109). Paradoxically, Vlaski found that the risk of asthma was increased in relation to both increased television watching as well as vigorous physical activity children 13-14 years of age (80;114). However, there was a stronger association between sedentary behavior and asthma symptoms compared to the association of frequent physical activity and asthma symptoms. The investigators concluded that asthma symptoms triggered by physical activity were secondary to a sedentary lifestyle and poor aerobic fitness (114).

A 10-year prospective study found that physical aerobic fitness was associated with a reduced risk for development of asthma (55). More recently, Chen et al. found that central obesity most accurately predicts asthma in a group of school aged children in Taiwan. Furthermore, low aerobic fitness and high screen times increased the risk of central obesity but did not appear to be a link in the relationship between obesity and asthma (19). Aerobic fitness in this study was assessed using an 800 m run; a field test that relies on technique and motivation and therefore the results may not accurately reflect aerobic fitness. While most of the studies reviewed examined the role of physical activity, obesity, and the risk of developing asthma, there are additional questions regarding the role of physical activity, aerobic fitness, obesity, and the risk of asthma morbidity in those with established asthma.

THE EFFECT OF OBESITY ON ASTHMA

Relationship between obesity and asthma outcomes

Several studies in adults suggest that obesity-related asthma is associated with worse quality of life, poor asthma control, and increased healthcare utilization compared to non-obese asthmatics (85;106). The effect of obesity on asthma in children is less well established and findings have been inconsistent, as summarized in Table 2. Given the variable nature of asthma symptoms over time and the limitations of cross-sectional studies, we chose to highlight only longitudinal studies in children. A word of caution is warranted regarding the

perception of poor asthma control in obese children, as one study reported increased dyspnea, increased health care utilization, and nocturnal awakening that were not accompanied by evidence of airway obstruction, thus putting in question whether or not this was due to asthma (94). Additional factors including sex, race, and ethnicity may influence this relationship (11). Lastly, studies in both adults and children have shown that obesity is associated with decreased effectiveness of inhaled corticosteroids, the mainstay of therapy, compared to normal weight asthmatics (12;15;43;104).

Obesity, asthma and exercise-induced bronchoconstriction

Exercise-induced bronchoconstriction (EIB), defined as airway narrowing or obstruction associated with exercise, occurs in the majority of children with asthma, even though the pathophysiology is not fully understood (90;103;116). Overweight and obesity in adults was associated with higher odds of reporting exercise as an asthma trigger compared to normal weight (118). Studies in children with no prior history of asthma show that obesity may contribute to increased frequency of EIB(111) or greater degree of bronchospasm following exercise testing (50;67). Studies investigating EIB in children with asthma found that EIB severity was increased in children with both asthma and obesity compared to the normal weight asthmatics (5;71). Baek et al. found that maximum decreases in percentage of FEV_1 and recovery after exercise challenge were positively correlated with serum leptin levels [leptin reflects adiposity (35)] and negatively associated with serum adiponectin levels [adiponectin is inversely correlated with adiposity (36;83)] in children with asthma, suggesting that adipokines may play a role in augmenting EIB in asthmatics (5). Furthermore, van Leeuwen et al. showed that dietary weight loss in overweight and obese children with asthma led to significant reductions in severity of EIB and recovery, as well as improvements in quality of life (112).

THE DEVELOPMENT OF THE OBESE ASTHMATIC CHILD–POSSIBLE MECHANISMS

There is clearly an epidemiological link between asthma and obesity, and it is no surprise that despite the clear connection, the mechanisms of this relationship remain elusive. Asthma and obesity are both complex conditions, not single disease entities. Asthma has genetic and environmental mechanisms which can be exacerbated in a given individual by biological factors (e.g., puberty, exposure to allergens) or behavioral and lifestyle factors (e.g., smoking, stress). Similarly, the propensity for childhood obesity has both genetic and environmental mechanisms, all of which can be modulated by lifestyle and behavior. In the following, we present three likely, and possibly interrelated, pathways of interaction between asthma and obesity based on current understandings of each of these separate conditions.

Mechanism 1: Stress and inflammation

Our first speculation rests on one of the key common features of both asthma and obesity, chronic inflammation. We hypothesize that stress-related alterations in the immuno-inflammatory pathway associated with low-grade systemic inflammation from obesity activate key immune cells or the pulmonary epithelium and render an individual susceptible to additional factors or a “second hit”. A “second hit” includes typical asthma triggers, such

as atopy, environment (such as pollutant exposure), diet, and comorbidities (such as gastro-esophageal reflux disease and obstructive sleep apnea), which in turn results in the development of obesity-related asthma. Finally, in a child with a genetic predisposition for asthma/allergy, the onset of obesity might trigger sufficient inflammatory activation to hasten the development of frank disease.

The last decade has seen major advances in our understanding of the pathophysiology of obesity. Adipose cells produce a variety of metabolically active mediators, many of which are pro-inflammatory. The low-grade inflammatory state associated with obesity has been postulated to be the link between obesity and chronic diseases, including asthma. However, most studies have failed to show an association between obesity and increased airway inflammation via conventional biomarkers, suggesting that there may be alternate pathways (73;101;107).

In obesity, blood monocytes and adipose tissue macrophages (MACs) expand and take on a pro-inflammatory "M1 or classical phenotype," with the activated macrophage elaborating biologically active cytokines and chemokines, such as IL-6, IL-1β and TNFα, as well as adipokines, including leptin and adiponectin (77). Additionally, alveolar macrophages may exhibit a unique phenotype in overweight/obese asthmatics. In *in vitro* experiments, the alveolar MACS response to lipopolysaccharide antigens was most robust in overweight/obese asthmatics, and exposure to high levels of leptin, elevated in obese asthmatic airways, enhanced this pro inflammatory state (73). Additionally, studies performed on blood monocytes and airway macrophages show a reduction in clearance of apoptotic inflammatory cells, which was associated with altered inflammation and reduced glucocorticoid responsiveness (37).

We are only beginning to understand the complex relationship among obesity-mediated inflammation and asthma in the obese asthmatic child; however, improved physical activity and aerobic fitness may mitigate the impact of obesity on asthma by the ability of regular exercise to attenuate chronic low grade inflammation (21).

Mechanism 2: Lung Mechanics

In adults, the effect of obesity on lung function results in a restrictive pattern characterized by reduced lung volumes, gas flow, and respiratory compliance. These impairments lead to rapid and shallow breathing occurring near the lung closing volume (9;10;95). With increased airway smooth muscle mass (common in asthma), airway smooth muscle fails to lengthen during deep inspiration resulting in hyper-responsiveness (87). Potential impacts of obesity on airway smooth muscle include both static (decreases in functional residual capacity) and dynamic (decreased tidal volumes) mechanical factors predisposing obese individuals towards airway hyper-reactivity (100). While the results of various broncho-provocation studies in obese asthmatics are mixed, exercise appears to consistently induce bronchoconstriction that is more severe in obese asthmatics compared to normal weight asthmatics (5;71).

The effect of obesity on lung function in children is not yet fully understood. For example, spirometry may be unaffected in overweight/obese children compared to healthy weight

children (91) or shows a relationship between increased airway obstruction with increasing BMI (68;105). Additionally, static lung volumes may be reduced in overweight/obese children similar to adults (66;91).

The presence of asthma leads to increased airway resistance, V/Q (ventilation-to-perfusion) mismatch at high intensity exercise (59). Additionally, obesity increases the work of breathing from both obstructive and restrictive alterations leading to increases in O_2 cost of exercise and reduced exercise tolerance (96;97). Conceivably, the combination of asthma and obesity would lead to further impairments in exercise tolerance, lung function, and increased work of breathing, particularly at high-intensity exercise. Lastly, the timing and duration of obesity in growing children (that is, the age of onset of obesity and its duration during growth and development) should be considered as early factors that affect lung growth and airway remodeling (100).

Mechanism 3: Direct Effects of Metabolic Syndrome on the Lung in Susceptible Individuals

There is emerging research that suggests that relationships between insulin resistance and dyslipidemia, markers of metabolic syndrome, and asthma risk are independent of BMI (24;82). Others suggest that metabolic syndrome and obesity interact synergistically to worsen asthma health (20). Forno et al found that insulin resistance and dyslipidemia were associated with decreased lung function in overweight and obese adolescents (42).

Dyslipidemia is thought to affect alveolar cholesterol homeostasis, important for surfactant production and lung growth (52). Recently Rastogi et al. called attention to the relationship between metabolic and lung health in obese asthmatic adolescents (92). They reported that reduced high-density lipoproteins (HDL), associated with obesity, appeared to negatively affect lung function in obese asthmatics, potentially through monocyte activation. In a study of overweight and obese children, exercise was demonstrated to increase HDL (34). Furthermore, data in adults suggests that there may be a dose response relationship between exercise and improved HDL (28). These studies suggest that approaches to improving metabolic health through physical activity could be useful in this population.

Improved aerobic fitness through physical activity and exercise could play a role in each of the putative mechanisms by: 1. lowering inflammation; 2. increasing tidal volumes (117); 3. reducing effects of metabolic syndrome, resulting in reduced asthma symptoms in obese children and adolescents. There is a growing body of literature indicating that exercise training and improved aerobic fitness improve asthma symptomatology even in non-obese children. This may result from the ability of repeated exercise to downregulate the inflammatory response to exercise (48). Alternatively, as children become more fit, the ventilation requirement at high work rates may lessen and, thereby, reduce some of the heat and water loss attributed to exercise induced bronchoconstriction (57;79).

Physical activity is thought to protect against the development of chronic diseases as well as for treatment of chronic conditions, in part by anti-inflammatory effects. Possible mechanisms for the anti-inflammatory effects of exercise include reduction in visceral fat mass, increased production and release of anti-inflammatory cytokines (i.e. IL-1RA), down-

regulation of toll-like receptor expression, reduced numbers of pro-inflammatory monocytes, and increased regulatory T cells (49;89).

OBSTACLES IN IDENTIFYING THE GAPS OF KNOWLEDGE; LINKING OBESITY AND ASTHMA

Imprecise estimation of adiposity is an obstacle to studying obese asthma in children. Most prominent is the difficulty in defining obesity in the context of the growing child. Per Centers for Disease Control and Prevention's (CDC) growth charts, a child's weight status is determined by BMI percentiles per age and sex; overweight is defined as BMI ≥85th and <95th percentile, and obese is BMI ≥95th percentile. While BMI is the most commonly used biomarker for obesity (27), there is an increasing body of literature demonstrating that this measurement is at best a limited indicator of the relative amount of body fat (115). A recent meta-analysis reveals that BMI may fail to identify as many as 25% of children with excess body fat (64). Additionally, there are complex growth-related shifts in fat distribution independent of BMI that occur during childhood (81). The finding of a high BMI in a child cannot, by itself, distinguish increased muscle mass in a physically fit child from the sedentary child whose percent body fat is excessively high.

Other measures of body composition include waist circumference, waist/hip ratios, skin fold thickness, and dual-energy X-ray absorptiometry (DXA). Several studies indicate that central obesity, in particular, is associated with a higher risk of asthma compared to BMI. Most recently, Guibas et al. found that waist circumference, not BMI, was positively correlated with asthma in children ages 2–5, while BMI was appropriate in older children, suggesting that alternative measures of adiposity may be useful in different age groups (54). Other measures of adiposity may also be helpful as one study found that while there were no differences in BMI, the asthmatic boys and girls had significantly higher fat mass percentage compared to controls (113).

With regard to asthma severity and/or control, additional adiposity measures including DXA did not add additional value in relating adiposity (by BMI) to asthma control among inner-city adolescents or to asthma severity/control and atopy among Puerto-Rican children (41;68).

Clearly, much work is needed to harmonize the various and sometimes conflicting biomarkers of obesity in children. A further obstacle lies in the identification and definition of asthma that varies among studies including self-reported asthma or related symptoms, physician diagnosis, and clinical phenotyping including pulmonary function testing and broncho-provocation testing. In the meantime, clinicians should continue using BMI as a screen for adiposity and consider including additional measures such as waist circumference to broaden our understanding of the obesity-asthma link, as well as following National Asthma Education and Prevention Program's (NAEPP) guidelines for the diagnosis of asthma (1).

Assessing aerobic fitness in pediatric populations, typically using CPET, has been shown to have substantial discrepancies with lack of common terminology, standard protocols, and

calibration (4). Measuring aerobic fitness in children is complicated because muscle and fat mass and hormonal regulation of metabolism and growth change rapidly in children and adolescents (32;53;108). Consequently, any physiological variable derived from CPET must be scaled to some index of body size and maturational status. In the obese child, body fat (virtually metabolically inactive during exercise) may obscure the effect of the metabolically active muscle tissue when CPET is normalized to body mass.

Traditional CPET in both children and adults relies on some assessment of peak or maximal oxygen uptake using protocols in which the effort performed increases progressively and is highly dependent on the willingness of each child to continue exercise at relatively high work rates when dyspnea, muscle fatigue, and other stress sensations are commonly experienced (8;99). It is not surprising that the plateau in oxygen uptake, the classical physiologic proof that VO_2max had been reached, is found in relatively small proportions of normal-weight or obese children and adolescents (13). Several studies suggest that obese children and adolescents perceive high-intensity exercise differently than normal-weight controls. These studies highlight the difficulty in quantifying cardiorespiratory aerobic fitness, particularly in pediatric populations, that could lead to further insight into the role of aerobic fitness in the obesity-related asthma link.

THERAPEUTIC APPROACHES

Optimizing body composition and improving aerobic fitness

There have been relatively few prospective studies evaluating the effect of exercise training on asthma outcomes in children. A recent systematic review showed that exercise training was associated with: 1) improvement of multiple asthma outcomes (including days without asthma symptoms); 2) increased FEV_1; 3) reduced bronchial hyper-responsiveness; 4) better exercise capacity; and 5) improved quality of life (31). Rasmussen et al. showed that lack of aerobic fitness in early childhood was weakly correlated with the development of asthma during adolescence, while high physical aerobic fitness reduced the risk after adjusting for sex, age, and BMI (55). Scott et al. investigated the role of exercise in obese asthmatic adults and found that the exercise group maintained a stable weight with a significant decrease in eosinophilic airway inflammation in sputum (98). Previous and ongoing studies targeting obese asthmatics have primarily focused on weight loss through dietary and/or exercise interventions. Little attention has been paid to whether the intervention had actually improved aerobic fitness. In the first large-scale randomized controlled trial of 330 obese adults with uncontrolled asthma, there was modest weight reduction and increases in daily activity; however, there were no significant differences in asthma outcomes (74). One limitation of the study was the lack of objective measures of aerobic fitness and physical activity, and whether improving aerobic fitness levels impacts asthma outcomes.

Weight reduction programs

Several studies have reported the effects of weight loss on asthma after surgical or dietary interventions leading to improvement in asthma, including lung function, quality of life, and asthma control. A few studies have specifically focused on the impact of weight-loss interventions in obese-asthmatic children (2;65;112) suggesting improvements in lung

function, inflammatory biomarkers, and exercise-induced bronchoconstriction. However, these studies have several limitations, including small sample sizes and short follow-up time. Further studies should also address better strategies to improve compliance and achieve long-term sustainability that can be applied to the clinical setting.

SUMMARY

Despite the complexity of mechanisms that possibly link obesity and asthma, data are emerging to support the idea that children with obesity are more susceptible to a whole host of factors that can lead to obesity-related asthma. The combination of obesity and reduced physical activity, each of which can stimulate inflammation, can lead to a vicious cycle of further reductions in physical activity and aerobic fitness in the obese asthmatic child. Could improving aerobic fitness alone lead to improved asthma outcomes in obese asthmatic children even in the absence of weight loss? While we continue to investigate the specific mechanism(s) linking obesity and asthma, it is clear that we need a better understanding of the role of aerobic fitness on the development of the obese-asthmatic, as well as the role of obesity and aerobic fitness in modulating disease in individuals with established asthma.

For the practicing clinician, if asthma is found in the obese child, we suggest that management should include, first and foremost, the recognition that this may be a unique group of patients which could make asthma control challenging and necessitates following NAEPP guidelines closely and titrating medications as needed. In addition, we would advocate a more comprehensive approach to the obese asthmatic child including screening for obesity-related co-morbidities, attention to nutrition, physical activity, and aerobic fitness as well as close follow-up.

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Abbreviations

BMI	body mass index
CPET	cardiopulmonary exercise testing
FENO	fractional exhaled nitric oxide
ICS	inhaled corticosteroid
LABA	long acting beta agonist
MAC	macrophages
OSA	obstructive sleep apnea

Reference List

1. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. J Allergy Clin Immunol. 2007 Nov; 120(5 Suppl):S94–138. [PubMed: 17983880]
2. Abd El-Kader MS, Al-Jiffri O, Ashmawy EM. Impact of weight loss on markers of systemic inflammation in obese Saudi children with asthma. Afr Health Sci. 2013 Sep; 13(3):682–8. [PubMed: 24250307]
3. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. NCHS Data Brief. 2012 May.(94):1–8.
4. Ashish N, Bamman MM, Cerny FJ, Cooper DM, D'Hemecourt P, Eisenmann JC, et al. The clinical translation gap in child health exercise research: a call for disruptive innovation. Clin Transl Sci. 2015 Feb; 8(1):67–76. [PubMed: 25109386]
5. Baek HS, Kim YD, Shin JH, Kim JH, Oh JW, Lee HB. Serum leptin and adiponectin levels correlate with exercise-induced bronchoconstriction in children with asthma. Ann Allergy Asthma Immunol. 2011 Jul; 107(1):14–21. [PubMed: 21704880]
6. Barnett SB, Nurmagambetov TA. Costs of asthma in the United States: 2002-2007. J Allergy Clin Immunol. 2011 Jan; 127(1):145–52. [PubMed: 21211649]
7. Beckett WS, Jacobs DR Jr, Yu X, Iribarren C, Williams OD. Asthma is associated with weight gain in females but not males, independent of physical activity. Am J Respir Crit Care Med. 2001 Dec 1; 164(11):2045–50. [PubMed: 11739133]
8. Belanger K, Breithaupt P, Ferraro ZM, Barrowman N, Rutherford J, Hadjiyannakis S, et al. Do obese children perceive submaximal and maximal exertion differently? Clin Med Insights Pediatr. 2013; 7:35–40. [PubMed: 24052695]
9. Beuther DA, Sutherland ER. Obesity and pulmonary function testing. J Allergy Clin Immunol. 2005 May; 115(5):1100–1. [PubMed: 15867878]
10. Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. Am J Respir Crit Care Med. 2006 Jul 15; 174(2):112–9. [PubMed: 16627866]
11. Borrell LN, Nguyen EA, Roth LA, Oh SS, Tcheurekdjian H, Sen S, et al. Childhood obesity and asthma control in the GALA II and SAGE II studies. Am J Respir Crit Care Med. 2013 Apr 1; 187(7):697–702. [PubMed: 23392439]
12. Boulet LP, Franssen E. Influence of obesity on response to fluticasone with or without salmeterol in moderate asthma. Respir Med. 2007 Nov; 101(11):2240–7. [PubMed: 17686624]
13. Breithaupt P, Adamo KB, Colley RC. The HALO submaximal treadmill protocol to measure cardiorespiratory fitness in obese children and youth: a proof of principle study. Appl Physiol Nutr Metab. 2012 Apr; 37(2):308–14. [PubMed: 22452609]
14. Bruske I, Flexeder C, Heinrich J. Body mass index and the incidence of asthma in children. Curr Opin Allergy Clin Immunol. 2014 Apr; 14(2):155–60. [PubMed: 24500295]
15. Camargo CA Jr, Boulet LP, Sutherland ER, Busse WW, Yancey SW, Emmett AH, et al. Body mass index and response to asthma therapy: fluticasone propionate/salmeterol versus montelukast. J Asthma. 2010 Feb; 47(1):76–82. [PubMed: 20100025]
16. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. Arch Intern Med. 1999 Nov 22; 159(21):2582–8. [PubMed: 10573048]
17. Castro-Rodriguez JA, Holberg CJ, Morgan WJ, Wright AL, Martinez FD. Increased incidence of asthmalike symptoms in girls who become overweight or obese during the school years. Am J Respir Crit Care Med. 2001 May; 163(6):1344–9. [PubMed: 11371399]
18. Chen YC, Dong GH, Lin KC, Lee YL. Gender difference of childhood overweight and obesity in predicting the risk of incident asthma: a systematic review and meta-analysis. Obes Rev. 2013 Mar; 14(3):222–31. [PubMed: 23145849]
19. Chen YC, Tu YK, Huang KC, Chen PC, Chu DC, Lee YL. Pathway from central obesity to childhood asthma. Physical fitness and sedentary time are leading factors. Am J Respir Crit Care Med. 2014 May 15; 189(10):1194–203. [PubMed: 24669757]

20. Chen YC, Tung KY, Tsai CH, Su MW, Wang PC, Chen CH, et al. Lipid profiles in children with and without asthma: interaction of asthma and obesity on hyperlipidemia. Diabetes Metab Syndr. 2013 Jan; 7(1):20–5. [PubMed: 23517791]
21. Chen YW, Apostolakis S, Lip GY. Exercise-induced changes in inflammatory processes: Implications for thrombogenesis in cardiovascular disease. Ann Med. 2014 Nov; 46(7):439–55. [PubMed: 25012964]
22. Chinn S, Rona RJ. Can the increase in body mass index explain the rising trend in asthma in children? Thorax. 2001 Nov; 56(11):845–50. [PubMed: 11641508]
23. Conn VS, Hafdahl A, Phillips LJ, Ruppar TM, Chase JA. Impact of physical activity interventions on anthropometric outcomes: systematic review and meta-analysis. J Prim Prev. 2014 Aug; 35(4): 203–15. [PubMed: 24852179]
24. Cottrell L, Neal WA, Ice C, Perez MK, Piedimonte G. Metabolic abnormalities in children with asthma. Am J Respir Crit Care Med. 2011 Feb 15; 183(4):441–8. [PubMed: 20851922]
25. Dahl R. Systemic side effects of inhaled corticosteroids in patients with asthma. Respir Med. 2006 Aug; 100(8):1307–17. [PubMed: 16412623]
26. Daniels SR. The consequences of childhood overweight and obesity. Future Child. 2006; 16(1):47–67. [PubMed: 16532658]
27. Dietz WH, Bellizzi MC. Introduction: the use of body mass index to assess obesity in children. Am J Clin Nutr. 1999 Jul; 70(1):123S–5S. [PubMed: 10419414]
28. Drygas W, Kostka T, Jegier A, Kunski H. Long-term effects of different physical activity levels on coronary heart disease risk factors in middle-aged men. Int J Sports Med. 2000 May; 21(4):235–41. [PubMed: 10853693]
29. Eagan TM, Bakke PS, Eide GE, Gulsvik A. Incidence of asthma and respiratory symptoms by sex, age and smoking in a community study. Eur Respir J. 2002 Apr; 19(4):599–605. [PubMed: 11998986]
30. Egan KB, Ettinger AS, Bracken MB. Childhood body mass index and subsequent physician-diagnosed asthma: a systematic review and meta-analysis of prospective cohort studies. BMC Pediatr. 2013 Aug 13.13(1):121. [PubMed: 23941287]
31. Eichenberger PA, Diener SN, Kofmehl R, Spengler CM. Effects of exercise training on airway hyperreactivity in asthma: a systematic review and meta-analysis. Sports Med. 2013 Nov; 43(11): 1157–70. [PubMed: 23846823]
32. Eliakim A, Barstow TJ, Brasel JA, Ajie H, Lee WN, Renslo R, et al. Effect of exercise training on energy expenditure, muscle volume, and maximal oxygen uptake in female adolescents. J Pediatr. 1996 Oct; 129(4):537–43. [PubMed: 8859260]
33. Escalante Y, Saavedra JM, Garcia-Hermoso A, Dominguez AM. Improvement of the lipid profile with exercise in obese children: a systematic review. Prev Med. 2012 May; 54(5):293–301. [PubMed: 22387009]
34. Escalante Y, Saavedra JM, Garcia-Hermoso A, Dominguez AM. Improvement of the lipid profile with exercise in obese children: a systematic review. Prev Med. 2012 May; 54(5):293–301. [PubMed: 22387009]
35. Fantuzzi G. Adipose tissue, adipokines, and inflammation. J Allergy Clin Immunol. 2005 May; 115(5):911–9. [PubMed: 15867843]
36. Fantuzzi G. Adipose tissue, adipokines, and inflammation. J Allergy Clin Immunol. 2005 May; 115(5):911–9. [PubMed: 15867843]
37. Fernandez-Boyanapalli R, Goleva E, Kolakowski C, Min E, Day B, Leung DY, et al. Obesity impairs apoptotic cell clearance in asthma. J Allergy Clin Immunol. 2013 Apr; 131(4):1041–7, 1047. [PubMed: 23154082]
38. Finkelstein EA, Graham WC, Malhotra R. Lifetime Direct Medical Costs of Childhood Obesity. Pediatrics. 2014 Apr 7.
39. Flaherman V, Rutherford GW. A meta-analysis of the effect of high weight on asthma. Arch Dis Child. 2006 Apr; 91(4):334–9. [PubMed: 16428358]
40. Fletcher JM, Green JC, Neidell MJ. Long term effects of childhood asthma on adult health. J Health Econ. 2010 May; 29(3):377–87. [PubMed: 20394999]

41. Forno E, Acosta-Perez E, Brehm JM, Han YY, Alvarez M, Colon-Semidey A, et al. Obesity and adiposity indicators, asthma, and atopy in Puerto Rican children. J Allergy Clin Immunol. 2014 May; 133(5):1308–14, 1314. [PubMed: 24290290]
42. Forno E, Han YY, Muzumdar RH, Celedon JC. Insulin resistance, metabolic syndrome, and lung function in US adolescents with and without asthma. J Allergy Clin Immunol. 2015 Aug; 136(2): 304–11. [PubMed: 25748066]
43. Forno E, Lescher R, Strunk R, Weiss S, Fuhlbrigge A, Celedon JC. Decreased response to inhaled steroids in overweight and obese asthmatic children. J Allergy Clin Immunol. 2011 Mar; 127(3): 741–9. [PubMed: 21377042]
44. Forno E, Young OM, Kumar R, Simhan H, Celedon JC. Maternal Obesity in Pregnancy, Gestational Weight Gain, and Risk of Childhood Asthma. Pediatrics. 2014 Jul 21.
45. Garcia-Aymerich J, Varraso R, Anto JM, Camargo CA Jr. Prospective study of physical activity and risk of asthma exacerbations in older women. Am J Respir Crit Care Med. 2009 Jun 1; 179(11):999–1003. [PubMed: 19246716]
46. Gilliland FD, Berhane K, Islam T, McConnell R, Gauderman WJ, Gilliland SS, et al. Obesity and the risk of newly diagnosed asthma in school-age children. Am J Epidemiol. 2003 Sep 1; 158(5): 406–15. [PubMed: 12936895]
47. Glazebrook C, McPherson AC, Macdonald IA, Swift JA, Ramsay C, Newbould R, et al. Asthma as a barrier to children's physical activity: implications for body mass index and mental health. Pediatrics. 2006 Dec; 118(6):2443–9. [PubMed: 17142530]
48. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol. 2011 Sep; 11(9):607–15. [PubMed: 21818123]
49. Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol. 2011 Sep; 11(9):607–15. [PubMed: 21818123]
50. Gokbel H, Atas S. Exercise-induced bronchospasm in nonasthmatic obese and nonobese boys. J Sports Med Phys Fitness. 1999 Dec; 39(4):361–4. [PubMed: 10726439]
51. Gold DR, Damokosh AI, Dockery DW, Berkey CS. Body-mass index as a predictor of incident asthma in a prospective cohort of children. Pediatr Pulmonol. 2003 Dec; 36(6):514–21. [PubMed: 14618644]
52. Gowdy KM, Fessler MB. Emerging roles for cholesterol and lipoproteins in lung disease. Pulm Pharmacol Ther. 2013 Aug; 26(4):430–7. [PubMed: 22706330]
53. Graves LE, Batterham AM, Foweather L, McWhannell N, Hopkins ND, Boddy LM, et al. Scaling of peak oxygen uptake in children: a comparison of three body size index models. Med Sci Sports Exerc. 2013 Dec; 45(12):2341–5. [PubMed: 23698249]
54. Guibas GV, Manios Y, Xepapadaki P, Moschonis G, Douladiris N, Mavrogianni C, et al. The obesity-asthma link in different ages and the role of body mass index in its investigation: findings from the Genesis and Healthy Growth Studies. Allergy. 2013 Oct; 68(10):1298–305. [PubMed: 24053597]
55. Guldberg-Moller J, Hancox B, Mikkelsen D, Hansen HS, Rasmussen F. Physical fitness and amount of asthma and asthma-like symptoms from childhood to adulthood. Clin Respir J. 2014 Apr 11.
56. Haas F, Pasierski S, Levine N, Bishop M, Axen K, Pineda H, et al. Effect of aerobic training on forced expiratory airflow in exercising asthmatic humans. J Appl Physiol (1985). 1987 Sep; 63(3): 1230–5. [PubMed: 3654468]
57. Hallstrand TS, Bates PW, Schoene RB. Aerobic conditioning in mild asthma decreases the hyperpnea of exercise and improves exercise and ventilatory capacity. Chest. 2000 Nov; 118(5): 1460–9. [PubMed: 11083702]
58. Hansen D, Marinus N, Remans M, Courtois I, Cools F, Calsius J, et al. Exercise tolerance in obese vs. lean adolescents: a systematic review and meta-analysis. Obes Rev. 2014 Nov; 15(11):894–904. [PubMed: 25132188]

59. Haverkamp HC, Dempsey JA, Miller JD, Romer LM, Pegelow DF, Rodman JR, et al. Gas exchange during exercise in habitually active asthmatic subjects. J Appl Physiol (1985). 2005 Nov; 99(5):1938–50. [PubMed: 16024529]
60. Hills AP, Dengel DR, Lubans DR. Supporting public health priorities: recommendations for physical education and physical activity promotion in schools. Prog Cardiovasc Dis. 2015 Jan; 57(4):368–74. [PubMed: 25269062]
61. Ho WC, Lin YS, Caffrey JL, Lin MH, Hsu HT, Myers L, et al. Higher body mass index may induce asthma among adolescents with pre-asthmatic symptoms: a prospective cohort study. BMC Public Health. 2011; 11:542. [PubMed: 21740558]
62. Huovinen E, Kaprio J, Koskenvuo M. Factors associated to lifestyle and risk of adult onset asthma. Respir Med. 2003 Mar; 97(3):273–80. [PubMed: 12645835]
63. Huovinen E, Kaprio J, Laitinen LA, Koskenvuo M. Social predictors of adult asthma: a co-twin case-control study. Thorax. 2001 Mar; 56(3):234–6. [PubMed: 11182018]
64. Javed A, Jumean M, Murad MH, Okorodudu D, Kumar S, Somers VK, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity in children and adolescents: a systematic review and meta-analysis. Pediatr Obes. 2014 Jun 25.
65. Jensen ME, Gibson PG, Collins CE, Hilton JM, Wood LG. Diet-induced weight loss in obese children with asthma: a randomized controlled trial. Clin Exp Allergy. 2013 Jul; 43(7):775–84. [PubMed: 23786284]
66. Jensen ME, Gibson PG, Collins CE, Wood LG. Airway and systemic inflammation in obese children with asthma. Eur Respir J. 2013 Oct; 42(4):1012–9. [PubMed: 23349447]
67. Kaplan TA, Montana E. Exercise-induced bronchospasm in nonasthmatic obese children. Clin Pediatr (Phila). 1993 Apr; 32(4):220–5. [PubMed: 8462234]
68. Kattan M, Kumar R, Bloomberg GR, Mitchell HE, Calatroni A, Gergen PJ, et al. Asthma control, adiposity, and adipokines among inner-city adolescents. J Allergy Clin Immunol. 2010 Mar; 125(3):584–92. [PubMed: 20226295]
69. Lang DM, Butz AM, Duggan AK, Serwint JR. Physical activity in urban school-aged children with asthma. Pediatrics. 2004 Apr; 113(4):e341–e346. [PubMed: 15060265]
70. Liu PC, Kieckhefer GM, Gau BS. A systematic review of the association between obesity and asthma in children. J Adv Nurs. 2013 Jul; 69(7):1446–65. [PubMed: 23560878]
71. Lopes WA, Radominski RB, Rosario Filho NA, Leite N. Exercise-induced bronchospasm in obese adolescents. Allergol Immunopathol (Madr). 2009 Jul; 37(4):175–9. [PubMed: 19783347]
72. Lucas SR, Platts-Mills TA. Physical activity and exercise in asthma: relevance to etiology and treatment. J Allergy Clin Immunol. 2005 May; 115(5):928–34. [PubMed: 15867847]
73. Lugogo NL, Hollingsworth JW, Howell DL, Que LG, Francisco D, Church TD, et al. Alveolar macrophages from overweight/obese subjects with asthma demonstrate a proinflammatory phenotype. Am J Respir Crit Care Med. 2012 Sep 1; 186(5):404–11. [PubMed: 22773729]
74. Ma J, Strub P, Xiao L, Lavori PW, Camargo CA Jr, Wilson SR, et al. Behavioral weight loss and physical activity intervention in obese adults with asthma. A randomized trial. Ann Am Thorac Soc. 2015 Jan; 12(1):1–11. [PubMed: 25496399]
75. Mamun AA, Lawlor DA, Alati R, O'Callaghan MJ, Williams GM, Najman JM. Increasing body mass index from age 5 to 14 years predicts asthma among adolescents: evidence from a birth cohort study. Int J Obes (Lond). 2007 Apr; 31(4):578–83. [PubMed: 17384659]
76. Mannino DM, Mott J, Ferdinands JM, Camargo CA, Friedman M, Greves HM, et al. Boys with high body masses have an increased risk of developing asthma: findings from the National Longitudinal Survey of Youth (NLSY). Int J Obes (Lond). 2006 Jan; 30(1):6–13. [PubMed: 16344843]
77. Mathis D, Shoelson SE. Immunometabolism: an emerging frontier. Nat Rev Immunol. 2011 Feb. 11(2):81. [PubMed: 21469396]
78. Maziak W, Behrens T, Brasky TM, Duhme H, Rzehak P, Weiland SK, et al. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Munster, Germany. Allergy. 2003 Jul; 58(7):572–9. [PubMed: 12823113]

79. Meyer A, Gunther S, Volmer T, Taube K, Baumann HJ. A 12-month, moderate-intensity exercise training program improves fitness and quality of life in adults with asthma: a controlled trial. BMC Pulm Med. 2015; 15:56. [PubMed: 25947010]
80. Mitchell EA, Beasley R, Bjorksten B, Crane J, Garcia-Marcos L, Keil U. The association between BMI, vigorous physical activity and television viewing and the risk of symptoms of asthma, rhinoconjunctivitis and eczema in children and adolescents: ISAAC Phase Three. Clin Exp Allergy. 2013 Jan; 43(1):73–84. [PubMed: 23278882]
81. Moreno LA, Fleta J, Sarria A, Rodriguez G, Gil C, Bueno M. Secular changes in body fat patterning in children and adolescents of Zaragoza (Spain), 1980-1995. Int J Obes Relat Metab Disord. 2001 Nov; 25(11):1656–60. [PubMed: 11753587]
82. Morishita R, Franco MD, Souza FI, Sole D, Puccini RF, Strufaldi MW. Body mass index, adipokines and insulin resistance in asthmatic children and adolescents. J Asthma. 2015 Nov.2:1–24.
83. Nemet D, Wang P, Funahashi T, Matsuzawa Y, Tanaka S, Engelman L, et al. Adipocytokines, body composition, and fitness in children. Pediatr Res. 2003 Jan; 53(1):148–52. [PubMed: 12508095]
84. Noal RB, Menezes AM, Macedo SE, Dumith SC. Childhood body mass index and risk of asthma in adolescence: a systematic review. Obes Rev. 2011 Feb; 12(2):93–104. [PubMed: 20406414]
85. Novosad S, Khan S, Wolfe B, Khan A. Role of obesity in asthma control, the obesity-asthma phenotype. J Allergy (Cairo). 2013; 2013:538642. [PubMed: 23710195]
86. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. JAMA. 2012 Feb 1; 307(5):483–90. [PubMed: 22253364]
87. Oliver MN, Fabry B, Marinkovic A, Mijailovich SM, Butler JP, Fredberg JJ. Airway hyperresponsiveness, remodeling, and smooth muscle mass: right answer, wrong reason? Am J Respir Cell Mol Biol. 2007 Sep; 37(3):264–72. [PubMed: 17463392]
88. Pastva A, Estell K, Schoeb TR, Atkinson TP, Schwiebert LM. Aerobic exercise attenuates airway inflammatory responses in a mouse model of atopic asthma. J Immunol. 2004 Apr 1; 172(7):4520–6. [PubMed: 15034069]
89. Petersen AM, Pedersen BK. The anti-inflammatory effect of exercise. J Appl Physiol (1985). 2005 Apr; 98(4):1154–62. [PubMed: 15772055]
90. Randolph C. Pediatric exercise-induced bronchoconstriction: contemporary developments in epidemiology, pathogenesis, presentation, diagnosis, and therapy. Curr Allergy Asthma Rep. 2013 Dec; 13(6):662–71. [PubMed: 23925985]
91. Rastogi D, Canfield SM, Andrade A, Isasi CR, Hall CB, Rubinstein A, et al. Obesity-associated asthma in children: a distinct entity. Chest. 2012 Apr; 141(4):895–905. [PubMed: 21980061]
92. Rastogi D, Fraser S, Oh J, Huber AM, Schulman Y, Bhagtani RH, et al. Inflammation, Metabolic Dysregulation, and Pulmonary Function among Obese Urban Adolescents with Asthma. Am J Respir Crit Care Med. 2015 Jan 15; 191(2):149–60. [PubMed: 25457349]
93. Romieu I, Mannino DM, Redd SC, McGeehin MA. Dietary intake, physical activity, body mass index, and childhood asthma in the Third National Health And Nutrition Survey (NHANES III). Pediatr Pulmonol. 2004 Jul; 38(1):31–42. [PubMed: 15170871]
94. Sah PK, Gerald TW, Demuth KA, Whitlock DR, Brown SD, Fitzpatrick AM. Poor asthma control in obese children may be overestimated because of enhanced perception of dyspnea. J Allergy Clin Immunol Pract. 2013 Jan; 1(1):39–45. [PubMed: 23646295]
95. Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. J Appl Physiol (1985). 2010 Jan; 108(1):206–11. [PubMed: 19875713]
96. Salvadego D, Lazzer S, Busti C, Galli R, Agosti F, Lafortuna C, et al. Gas exchange kinetics in obese adolescents. Inferences on exercise tolerance and prescription. Am J Physiol Regul Integr Comp Physiol. 2010 Nov; 299(5):R1298–R1305. [PubMed: 20686169]
97. Salvadego D, Sartorio A, Agosti F, Tringali G, Patrizi A, Mauro AL, et al. Acute respiratory muscle unloading by normoxic helium-O(2) breathing reduces the O(2) cost of cycling and perceived exertion in obese adolescents. Eur J Appl Physiol. 2015 Jan; 115(1):99–109. [PubMed: 25213005]

98. Scott HA, Gibson PG, Garg ML, Pretto JJ, Morgan PJ, Callister R, et al. Dietary restriction and exercise improve airway inflammation and clinical outcomes in overweight and obese asthma: a randomized trial. Clin Exp Allergy. 2013 Jan; 43(1):36–49. [PubMed: 23278879]

99. Shim YM, Burnette A, Lucas S, Herring RC, Weltman J, Patrie JT, et al. Physical deconditioning as a cause of breathlessness among obese adolescents with a diagnosis of asthma. PLoS ONE. 2013; 8(4):e61022. [PubMed: 23637784]

100. Shore SA, Fredberg JJ. Obesity, smooth muscle, and airway hyperresponsiveness. J Allergy Clin Immunol. 2005 May; 115(5):925–7. [PubMed: 15867846]

101. Sideleva O, Dixon AE. The many faces of asthma in obesity. J Cell Biochem. 2014 Mar; 115(3): 421–6. [PubMed: 24115053]

102. Silva RA, Almeida FM, Olivo CR, Saraiva-Romanholo BM, Martins MA, Carvalho CR. Airway remodeling is reversed by aerobic training in a murine model of chronic asthma. Scand J Med Sci Sports. 2015 Jun; 25(3):e258–e266. [PubMed: 25156656]

103. Storms WW. Review of exercise-induced asthma. Med Sci Sports Exerc. 2003 Sep; 35(9):1464–70. [PubMed: 12972863]

104. Sutherland ER, Goleva E, Strand M, Beuther DA, Leung DY. Body mass and glucocorticoid response in asthma. Am J Respir Crit Care Med. 2008 Oct 1; 178(7):682–7. [PubMed: 18635892]

105. Tantisira KG, Litonjua AA, Weiss ST, Fuhlbrigge AL. Association of body mass with pulmonary function in the Childhood Asthma Management Program (CAMP). Thorax. 2003 Dec; 58(12): 1036–41. [PubMed: 14645968]

106. Taylor B, Mannino D, Brown C, Crocker D, Twum-Baah N, Holguin F. Body mass index and asthma severity in the National Asthma Survey. Thorax. 2008 Jan; 63(1):14–20. [PubMed: 18156567]

107. Todd DC, Armstrong S, D'Silva L, Allen CJ, Hargreave FE, Parameswaran K. Effect of obesity on airway inflammation: a cross-sectional analysis of body mass index and sputum cell counts. Clin Exp Allergy. 2007 Jul; 37(7):1049–54. [PubMed: 17581198]

108. Tolfrey K, Barker A, Thom JM, Morse CI, Narici MV, Batterham AM. Scaling of maximal oxygen uptake by lower leg muscle volume in boys and men. J Appl Physiol (1985). 2006 Jun; 100(6):1851–6. [PubMed: 16484361]

109. Tollefsen E, Langhammer A, Romundstad P, Bjermer L, Johnsen R, Holmen TL. Female gender is associated with higher incidence and more stable respiratory symptoms during adolescence. Respir Med. 2007 May; 101(5):896–902. [PubMed: 17084607]

110. Trost SG, Kerr LM, Ward DS, Pate RR. Physical activity and determinants of physical activity in obese and non-obese children. Int J Obes Relat Metab Disord. 2001 Jun; 25(6):822–9. [PubMed: 11439296]

111. Ulger Z, Demir E, Tanac R, Goksen D, Gulen F, Darcan S, et al. The effect of childhood obesity on respiratory function tests and airway hyperresponsiveness. Turk J Pediatr. 2006 Jan; 48(1):43–50. [PubMed: 16562785]

112. van Leeuwen JC, Hoogstrate M, Duiverman EJ, Thio BJ. Effects of dietary induced weight loss on exercise-induced bronchoconstriction in overweight and obese children. Pediatr Pulmonol. 2013 Oct 25.

113. Varekova R, Vareka I. How to estimate overweight in pubescent asthmatics? Adv Med Sci. 2013; 58(2):331–7. [PubMed: 24285129]

114. Vlaski E, Stavric K, Seckova L, Kimovska M, Isjanovska R. Influence of physical activity and television-watching time on asthma and allergic rhinitis among young adolescents: preventive or aggravating? Allergol Immunopathol (Madr). 2008 Sep; 36(5):247–53. [PubMed: 19080795]

115. Wang Y. Epidemiology of childhood obesity–methodological aspects and guidelines: what is new? Int J Obes Relat Metab Disord. 2004 Nov; 28(Suppl 3):S21–S28. [PubMed: 15543215]

116. Wanrooij VH, Willeboordse M, Dompeling E, van de Kant KD. Exercise training in children with asthma: a systematic review. Br J Sports Med. 2014 Jul; 48(13):1024–31. [PubMed: 23525551]

117. Wasserman K. Breathing during exercise. N Engl J Med. 1978 Apr 6; 298(14):780–5. [PubMed: 628413]

118. Wright A, Lavoie KL, Jacob A, Rizk A, Bacon SL. Effect of body mass index on self-reported exercise-triggered asthma. Phys Sportsmed. 2010 Dec; 38(4):61–6.

Highlights

1. Asthma and exercise are mechanistically related.
2. Obesity is associated with both physical inactivity and asthma.
3. Obesity is a chronic inflammatory disease.
4. The response to inhaled corticosteroids may be blunted in this population.
5. Management should involve assessment of physical activity, nutrition and comorbidities.

Table 1

Systematic Reviews: obesity and risk of developing asthma in children

Authors	# and type of studies, time period	Outcome	Summary of Findings	Sex Differences
Egan et al (30)	6 prospective cohort studies 2001-2012	BMI and physician diagnosed incident asthma	Overweight RR 1.35 (95% CI 1.15,1.58) Obesity RR 1.50 (95% CI 1.22,1.83)	Sex differences; obese boys RR 1.40 (95% CI 1.01, 1.93); obese girls RR 1.53 (95% CI 1.09, 2.14)
Chen et al (19)	6 prospective cohort studies 2001-2012	BMI and incident asthma, gender differences	Overweight RR 1.19 (95% CI 1.03,1.37) Obesity RR 2.02 (95% CI 1.16,3.50)	Sex differences; obese boys RR 2.47 (95% CI 1.57, 3.87), obese girls RR 1.25 (95% CI 0.51, 3.03)
Liu et al (73)	35 studies; 4 longitudinal 2001-2006	BMI and asthma	27/35 studies with positive association between overweight/ obesity and asthmatic symptoms 3/4 longitudinal studies-higher BMI predicted future new asthma or asthma-like symptoms	Link between obesity and asthma is more prominent in girls
Noal et al (87)	10 longitudinal studies 2001-2007	Nutritional status and incidence or persistence of asthma	8/10 studies had positive associations between overweight/ obesity and asthma	3/10 studies with positive associations found only in boys, 3/10 only in girls
Flaherman et al (39)	4 longitudinal cohort studies (childhood) 9 longitudinal cohort studies (birth weight) 1997-2004	Body weight at birth or during childhood and future asthma	Childhood: pooled RR 1.5 (95% CI 1.2, 1.8) Birth weight: pooled RR 1.2 (95% CI 1.1, 1.3)	Insufficient power to subset analysis by sex

RR: Relative Risk

CI: Confidence Interval

Table 2

Relationship of obesity to asthma severity/control and healthcare utilization

Authors	Study details	Summary of Findings
Black et al (11)	Retrospective cohort; 2007-2011; 623358 children 6-19 years; Kaiser	↑ healthcare utilization, exacerbations and SABA use in obese
Quinto et al (93)	Retrospective cohort; 2004-2008; 32321 children 5-17 years, Kaiser	↑ SABA and OCS usage in overweight/obese
Michelson et al (82)	Retrospective cohort; 2001-2004;10140 children 0-19 years, NHANES	↑ SABA and steroids among overweight/obese No difference in healthcare utilization
Lang et al (71)	*Post-hoc* analysis of RCT; 490 children 6-17 years	↑ symptoms in adolescent females ↓ symptoms in 6-11 y females
Kattan et al (69)	*Post-hoc* analysis of RCT; 368 children 12-20 years	↑ symptoms among obese girls No difference in asthma control or exacerbations
Lang et al (72)	*Post-hoc* analysis of RCT;306 children ages 6-17 years	No difference in asthma control or exacerbations by BMI

SABA- short acting beta agonist use

OCS- oral corticosteroids