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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/ height²) 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 obesityasthma 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 FEV1 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 immunoinflammatory 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 gastroesophageal 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-1 β and TNF α , 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 bronchoprovocation 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 ^{595th} 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 innercity 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 VO₂max 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 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	

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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)	<i>Post-hoc</i> 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