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Overweight, obesity, and lung function in children and adults – a meta-analysis

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Abstract

Background—There is conflicting evidence on the effect of obesity on lung function in adults and children with and without asthma. We aimed to evaluate the relation between overweight or obesity and lung function, and whether such relationship varies by age, sex, or asthma status.

Methods—We searched PubMed, Scopus, CINAHL, Cochrane, and EMBASE for all studies (in English) reporting on obesity status (by BMI) and lung function, from 2005 to 2017. Main outcomes were FEV1, FVC, FEV1/FVC, FEF₂₅₋₇₅, TLC, RV, and FRC. Random-effects models were used to calculate the pooled risk estimates; each study was weighed by the inverse effect size variance. For each outcome, we compared overweight or obese ("obese") subjects with those of normal weight.

Results—All measures of lung function were decreased among obese subjects. Obese adults showed a pattern (lower FEV₁, FVC, TLC, and RV) different from obese children (more pronounced FEV_1/FVC deficit with unchanged FEV_1 or FVC). There were also seemingly different patterns by asthma status, in that subjects without asthma had more marked decreases in FEV_1 , TLC, RV and FRC than subjects with asthma. Subjects who were obese (as compared to overweight) had even further decreased FEV_1 , FVC, TLC, RV, and FRC.

Conclusion—Obesity is detrimental to lung function, but specific patterns differ between children and adults. Physicians should be aware of adverse effects of obesity on lung function, and weight-control should be considered in the management of airway disease among the obese.

Keywords

Obesity; childhood obesity; lung function; asthma; meta-analysis

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INTRODUCTION

The worldwide epidemic of obesity is a major public health problem, particularly in industrialized countries. Obesity is associated with numerous complications, including multiple detrimental effects on the respiratory system¹. Several plausible mechanisms have been proposed to explain the observed association between obesity and respiratory symptoms, such as decreased total respiratory system compliance, increased airway resistance, reduced lung volumes, and altered ventilation and gas exchange^{2, 3}. Overweight and obesity have also been associated with higher incidence of asthma⁴, asthma morbidity, and resistance to therapy⁵. Evidence shows that weight gain precedes the development of asthma symptoms⁶ and that obese individuals have later decreases in lung function⁷. Conversely, weight loss results in improvement of asthma-related health outcomes in adults 8, 9.

In adults, an inverse association between BMI and lung volumes indicates that obesity leads to a restrictive lung deficit^{10, 11}. However, some studies have also reported slightly lower FEV₁/FVC in adults with asthma¹². On the other hand, several studies in children have reported that increased BMI is associated with normal –or even increasing– FEV₁ and FVC but low FEV₁/FVC, consistent with either an obstructive deficit or airway dysanapsis^{13, 14}, with some reports showing differences by sex¹⁵. Yet other studies have shown findings in children that may be suggestive of a restrictive deficit, which may be more similar to findings reported in adults^{16–18}. Such inconsistencies may partly be due to differences among study populations and outcome measures. More importantly, they suggest that the association between obesity and lung function may differ between children and adults. In this meta-analysis, we aim to further elucidate the relationship between overweight or obesity and lung function, and whether such relationship differs by age group or by asthma status.

METHODS

We prospectively registered the protocol for this meta-analysis on 10/07/2015 at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015023193.

Search and selection criteria

We searched PubMed, Scopus, CINAHL, and the Cochrane Database for all studies reporting obesity status and lung function in human subjects, published in English from 2005 (standardization of spirometry¹⁹) to January of 2017, using the following keywords: ("Body Mass Index" OR "BMI" OR "percent body fat" OR "body fat distribution" OR "Waist Circumference" OR "Obesity" OR "Overweight" OR "Waist-hip ratio" OR "Adiposity" OR "abdominal obesity") AND [("FEV1" OR "FVC" OR "FEV₁/FVC" OR "FEF2575" OR "PEFR" OR "TLC" OR "RV/TLC" OR "FRC" OR "lung function" OR "spirometry") NOT ("cystic fibrosis" OR "COPD" OR "cancer")].

Inclusion criteria were: 1) observational studies of children or adults with assessments of obesity and lung function; or 2) baseline data from experimental studies focused on obesity and lung function. Exclusion criteria were: 1) studies focused on cystic fibrosis or chronic

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obstructive pulmonary disease (COPD); 2) studies that included diseases or therapies that may affect the lung function of subjects (e.g. cancer, radiotherapy); and 3) obesity secondary to specific diseases (e.g. hypothyroidism, hypertension) or medical treatments. Our primary outcomes were spirometry measures (FEV₁, FVC, FEV₁/FVC, and FEF₂₅₋₇₅). Secondary outcomes were measures of lung volume (TLC, RV, RV/TLC, and FRC). Study subjects were classified as "normal weight (reference group)", "overweight", or "obese" by BMI (z-score in children and kg/m² in adults). Central or abdominal obesity was defined by waist circumference (WC) or waist-to-hip ratio (WHR).

Data abstraction and data analysis

The study was performed following the recommendations for reporting meta-analyses of observational studies by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group²⁰ and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines²¹. Titles, abstracts, contexts, and citations were independently assessed and analyzed by two investigators (YYH and JM). Disagreements were resolved through a mediator (EF).

For all outcomes analyzed, we calculated the pooled β coefficients (weighted mean difference [WMD]) and 95% confidence intervals (CI) using random-effects models to address the heterogeneity across the included studies. Each study was weighted by its inverse effect size variance. Some studies were included more than once when they had several comparisons (e.g. overweight vs. normal weight, and obese vs. normal weight) or strata (e.g. males and females, children [18 years] and adults [>18 years]). Egger's test and funnel plots with pseudo 95% CI were used to examine small-study effects and publication bias. When possible, meta-regression was performed to explore potential sources of heterogeneity and test whether certain characteristics (e.g. age-group, sex distribution) modify the effect of obesity on lung function; meta-regression was performed only when 10 studies reported a specific characteristic. All analyses were performed using STATA v13 (StataCorp, College Station, TX).

RESULTS

A total of 1327 articles were initially identified (Figure 1). After removal of duplicates and non-relevant studies, 379 studies were evaluated. Based on full-text screening, the authors agreed on 328 of 379 articles (inter-reader $\kappa = 86.5\%$). After arbitration, and based on inclusion and exclusion criteria, a total of 62 studies were included for meta-analysis. Because very few studies reported WC or WHR, only studies using BMI to define overweight/obesity were included.

Forced expiratory volume in 1 second (FEV₁)

When analyzing all selected studies (44 studies, n=23,460 subjects)^{12, 15–18, 22–60}, overweight/obese subjects had 2.2% lower percent-predicted FEV₁ [WMD –2.2, 95% CI= -2.6 to -1.8] than subjects of normal weight (Table 1). The decrement was significant in adults (WMD –2.4%, 95% CI= -2.9 to -1.9]) but not in children (-0.8%, 95% CI= -2.3 to 0.6], Figure 2); and more pronounced among overweight/obese subjects without asthma

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(-3.9%, 95% CI=-7.1 to -0.7) than in those with asthma (-1.4% [-1.9, -0.9])(Supplemental Figure E1). Similar results were found when analyzing adults only by asthma status: overweight/obese adults with asthma had 1.7% (95% CI= -2.3 to -1.2) lower FEV₁; while those without asthma had 6.9% (95% CI= -11.1 to -2.8) lower FEV₁ (Table 1). These results were driven mainly by obesity (-2.5%, 95% CI= -3.4 to -1.5%) in subjects with asthma and -5.3% (95% CI= -8.8 to -1.8) in those without) rather than by overweight (non-significant; data not shown).

When analyzing studies that reported FEV₁ as an absolute value (liters)^{61–69}, overweight/ obese children had 410 mL [95% CI= 280mL to 540mL] higher FEV₁, while overweight/ obese adults had 150mL [95% CI= -260mL to -40mL] lower FEV₁ (Supplemental Figure E2).

Forced vital capacity (FVC)

In 30 studies included (n=16,913), percent-predicted FVC decreased by 2.2% [95% CI= -3.7 to -0.6%] among overweight/obese subjects compared to those of normal weight 15-18, 23-29, 32-34, 36, 37, 39, 40, 45, 46, 48, 50, 52-59. The decrement was significant in adults (-4.6% [95% CI= -6.9 to -2.2%]) but not in children (Figure 3); and more pronounced among obese subjects (-3.2% [95% CI= -5.2 to -1.2%] than in overweight subjects (Supplemental Figure E3). When stratifying by asthma status, FVC decreased further in adults without asthma (-7.5% [95% CI= -11.4 to -3.7%]) than in those with asthma (-3.2% [95% CI= -6.0 to -0.4%]). Among studies that reported FVC as absolute value (liters)^{51, 61-70}, overweight/obese children had an increased FVC (250mL [95% CI= 190mL to 300mL]), while overweight/obese adults had a decreased FVC (-140mL [95% CI= -250mL to -40mL], data not shown).

FEV₁/FVC

For all 34 studies combined (n=28,494), FEV₁/FVC was 1.5% [95% CI= -1.9 to -1.2%] lower among overweight/obese subjects¹², 15–18, 23–29, 31, 34, 35, 38, 40, 45, 47, 48, 50, 53, 55, 57, 59, 61–63, 66–71 (Table 1). The

decrement was more pronounced in children (-2.4%, [95% CI= -3.0 to -1.8%]) than in adults (-1.0% [95% CI= -1.4 to -0.6%]) (Figure 4); and it was similar in subjects with (-1.5% [95% CI= -1.9 to -1.0%]) and without asthma (-1.6% [95% CI= -2.3 to -0.8%]) (Table 1). When reviewing twelve studies that reported FEV₁/FVC as percent of predicted, 10, 32, 33, 36, 37, 39, 44, 54, 56,58, 60, 72, 73 FEV₁/FVC was lower among overweight/obese children (-1.7% [95% CI= -3.2 to -0.2%]) but slightly increased among overweight/obese adults (1.3% [95% CI= 0.01 to 2.6%], data not shown).

Maximum mid-expiratory flow (MMEF or FEF₂₅₋₇₅)

Percent-predicted FEF₂₅₋₇₅ was significantly decreased (-5.4% [95% CI= -7.3 to -3.5%]) among overweight/obese subjects in 16 studies (n=13,627)

16-18, 28, 32, 33, 43, 45, 46, 50-52, 54, 55, 58, 74. The decrement was significant in children (-4.7% [95% CI= -6.9 to -2.6%]) but not in adults (Supplemental Figure E4). It was significant only subjects with asthma (-3.2%, [-6.3 to -0.1%]); and after stratifying by weight, it was

similarly decreased in overweight (-4.8%, [95% CI= -7.2 to -2.4%]) and obese (-4.6%, [95% CI= -8.1 to -1.2%]) subjects (Table 1).

Total lung capacity (TLC)

Overall, overweight/obese subjects had 4.2% [95% CI= -5.4 to -3.0%] lower percentpredicted TLC based on 16 studies (n=2,678)^{10, 23–25, 31–33, 35, 38, 40, 41, 46, 50, 51, 53, 73}, with similar findings in children (-3.7% [95% CI= -5.8 to -1.5%]) and adults (-4.4% [95% CI= -5.7 to -3.0%], Figure 5). The decrease was more pronounced in subjects without asthma (-4.8% [95% CI= -7.1 to -2.5%]) than among those with asthma (-3.3% [95% CI= -5.1 to -1.5%], Supplemental Figure E5); and in the obese (-5.4% [95% CI= -7.0 to -3.9%]) than in the overweight (-2.0% [95% CI= -4.1 to 0.1%], Supplemental Figure E6).

Residual volume (RV)

In 12 studies combined (n=2,085), overweight/obese subjects had 6.6% [95% CI= -9.3 to -3.8%] lower percent-predicted RV^{10, 23–25, 31–33, 35, 38, 41, 50, 73}. The decrement in RV was significant in adults (-5.4% [95% CI= -8.2 to -2.7%]) (Table 1); only one study reported RV in children⁵⁰, and thus no pooled analysis was performed. The effect was more pronounced in subjects without asthma (-7.6% [95% CI= -11.7 to -3.5%]) than in those with asthma (Figure 6), and in the obese (-7.4% [-11.6 to -3.2%]) than in the overweight (Table 1). Four studies reported **RV/TLC ratio** measures^{10, 40, 50, 73}; there was no significant change in RV/TLC by overweight/obesity (data not shown).

Functional residual capacity (FRC)

Overall, percent-predicted FRC was significantly lower among overweight/obese subjects than in those normal weight $(-17.1\% [-25.2, -9.0], 9 \text{ studies}, n=1,235)^{10}, 23, 24, 31, 35, 38, 41, 50, 73$. The decrement was more pronounced in subjects without asthma (-23.2% [-30.3, -16.1], Figure 7); and in the obese (-21.2% [-30.9%, -11.5], Supplemental Figure E7).

Assessment of publication bias and meta-regression

Egger tests showed no evidence of publication bias in any of the measures, except for RV (p=0.003, Supplemental Figure E8). There was marked heterogeneity (I²>70%) in all outcomes and analyses, except for TLC in children (I²=0%). Meta-regression analyses showed that age and sex distributions explain part of this heterogeneity. Studies with higher proportion of males showed a more pronounced effect of obesity on FEV₁ (β =-0.09, p=0.019) in adults, and on FEV₁/FVC in subjects with asthma (β =-0.04, p=0.002). Studies with higher mean age showed a more significant effect of obesity on FVC (β =-0.17, p=0.013) in all subjects, and FEV₁/FVC in all subjects (β =0.06, p=0.005) (Supplemental Figure E9).

DISCUSSION

In this meta-analysis, overweight/obesity is shown to be detrimental to lung function across age groups, regardless of asthma status. However, these detrimental effects differ between adults and children: obese adults have a more pronounced decline in FEV₁, FVC, TLC, and

RV; whereas obese children show a more pronounced decline in FEV_1/FVC and FEF_{25-75} . Likewise, more marked decrements in FEV_1 , TLC, RV and FRC were found in subjects without asthma than in those with asthma. Compared to overweight subjects, the obese also had more marked decrements in FEV_1 , FVC, TLC, RV, and FRC.

FEV₁, the most frequently used spirometric index, is a function of airway resistance and total lung compliance. Overweight or obesity^{12, 24, 25, 27, 28, 34–37, 39–42, 56, 58 was significantly associated with lower FEV₁ in the overall meta-analysis. However, the effect differed by age, with results driven by adults and no significant association in children. In fact, only a few individual studies reported a decreased FEV₁ in overweight/obese children^{16–18, 45, 56, 58}, and the pooled analysis of studies reporting FEV₁ in liters showed that overweight/obese children had slightly higher absolute values. On the contrary, very few studies have shown an increased FEV₁ in overweight adults^{23, 30} compared to adults of normal weight.}

FVC, the total volume of air exhaled with maximally forced effort from a maximal inspiration, reflects the total compliance from both the lung and chest wall. Similar to FEV₁, overweight or obesity ^{24–28}, ³³, ³⁴, ³⁶, ³⁷, ³⁹, ⁴⁰, ⁶⁷ was negatively associated with FVC in adults, but there was no significant association in children. Likewise, our pooled analysis of studies reporting absolute FVC showed a slight increase in FVC in overweight^{46, 66} or obese^{15, 52, 66} children. Thus, overweight/obesity is associated with lower FEV₁ and FVC in adults, but with either normal or higher FEV₁ and FVC in children. We have recently reported that overweight/obese children have increased risk of airway dysanapsis¹⁴, a phenomenon in which an asymmetrical growth of the lungs and airways lead to higher FEV₁ and FVC but with a more pronounced effect on FVC. Subjects with dysanapsis thus have a low FEV₁/FVC ratio but normal or supranormal FEV₁ and FVC. We found an increase in FEV1 that appeared to be larger than the increase in FVC (WMD 410 mL vs 250 mL), but the current analysis is based on published study means rather than individual-level data, and thus we were not able to directly assess the association between obesity and dysanapsis.

Interestingly, the effect sizes for FEV1 and FVC were much larger among subjects without asthma than among those with asthma, suggesting that obesity may have stronger effects on FEV₁ and FVC in healthy subjects. Although the reasons for this are beyond the scope of this analysis, mean FEV1 and FVC in all included studies was markedly higher among non-asthmatics than among asthmatics (see Supplementary Table E1), and thus we hypothesize that the effect of obesity is more readily apparent in subjects without asthma because of their normal lung function, whereas subjects with asthma already have lower lung function due to their disease, and thus the effect of obesity may not be as prominent.

In contrast to FEV₁ and FVC, the overall decrease of **FEV₁/FVC** among overweight or obese subjects was more pronounced in children than in adults. Similar results were observed for **FEF₂₅₋₇₅**, which is the mean forced expiratory flow between 25% and 75% of the FVC: FEF₂₅₋₇₅ decreased significantly among overweight or obese children^{16, 17, 45, 52, 58, 74} with an overall 5.4% decrement, but there was no significant associations in adults. Only one individual study reported a 9% decrease in FEF₂₅₋₇₅ in asthmatic overweight adults²⁸. FEF₂₅₋₇₅ can be highly variable and thus should be

interpreted with caution, but it has been correlated with bronchodilator responsiveness in asthmatic children with normal FEV₁, suggesting clinically relevant reversible airflow obstruction⁷⁵. Interestingly, the declines in FEV₁/FVC and FEF₂₅₋₇₅ were similar between overweight and obesity.

The effects of obesity on lung volumes have been better studied in adults. TLC is often used to identify a restrictive ventilatory deficit⁷⁶. While TLC may be preserved in most obese subjects, other than those with morbid obesity or with excessive central adiposity⁷⁷, our results indicate a reduction in TLC overall, with several individual studies showing that overweight or obesity diminished TLC both in adults^{10, 23–25, 33, 35, 40, 41} and -to a lesser degree- in children⁵¹. A more pronounced decrement in TLC was reported in obesity than in overweight, and in non-asthmatics than among asthmatics. Similarly, we observed that obesity was associated with lower RV in adults, and this association was seen both in asthmatics^{23–25, 32, 33, 50} and non-asthmatics^{10, 35, 38, 40, 41, 50, 51}. Obesity was also associated with lower FRC among adults, which may be secondary to changes in the elastic properties of the chest wall that can lead to reduced airway caliber and increased airways resistance⁷⁸. FRC was decreased only in overweight or obese non-asthmatics (~23.2% lower compared to normal weight asthmatics), but not in asthmatics, suggesting again that obesity may have a more noticeable detrimental effect on lung volumes in otherwise healthy individuals. Only one study reported RV and FRC in children, and we were thus unable to perform a pooled analysis.

Strengths and limitations

To the best of our knowledge, this is the first meta-analysis to encompass all published studies on obesity and lung function. Because of large sample size, we were able to stratify the analysis by age group, asthma, and weight category. We were also able to perform meta-regression to evaluate potential effect modifiers such as age or gender.

We also recognize several limitations. First, few studies of obesity and lung function have used indices other than BMI (e.g. percent body fat, waist-to-hip ratio, etc.), and thus we had to focus on BMI. Future efforts should aim to determine whether adiposity distribution has different effects on lung function. Second, most studies included in the analysis were cross-sectional, and thus a causal relationship between overweight or obesity and lung function cannot be determined. Third, most studies reported joint findings for males and females, and we could thus only evaluate the potential effect of sex by using the proportions from each individual study. Given the small number of studies reporting details on smoking, atopy and race/ethnicity, we were unable to assess whether these factors modify the effect of obesity on lung function; moreover, we had no data on pubertal status and thus could not assess whether it constitutes an effect modifier among children. Because we did not have individual-level data for these studies, we were unable to perform more detailed analyses, including the association between obesity and airway dysanapsis. Finally, we had insufficient data on RV and FRC among children to perform a pooled analysis of these measures.

Conclusion

Overweight and obesity have significant effects on lung function, including spirometric parameters and lung volumes. Overall, this association is observed regardless of age group and asthma status. However, specific patterns differed between children and adults. While obesity affected lung function in subjects with asthma, subjects without asthma had even more pronounced reductions –particularly for lung volumes. Physicians should be aware of the adverse effects of obesity on lung function, and weight control should be considered in the management of airway diseases among obese individuals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

95% CI	95% confedence interval
BMI	Body mass index
FEF ₂₅₋₇₅	Forced expiratory flow between 25 th and 75 th of the forced vital capacity
FEV1	Forced expiratory volume in the 1 st second
FRC	Functional residual capacity
FVC	Forced vital capacity
RV	Residual volume
TLC	Total lung capacity
WC	Waist circumference
WHR	Waist-to-hip ratio
WMD	Weighted mean difference

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What is known about the topic?

Overweight and obesity are associated with changes in lung function in children, adolescents, and adults. However, there is some conflicting evidence on whether these changes differ by age group, sex, or asthma status.

What does this article add to our knowledge?

We provide comprehensive pooled estimates of the effect of obesity on lung function, stratified by age group (pediatrics vs. adults) and asthma status. Moreover, we use meta-regression to evaluate the role of age and gender in these associations.

How does this study impact current management guidelines?

Detrimental changes in lung function constitute yet another complication of obesity. These changes differ by age, sex, and asthma status; clinicians should take these characteristics into account when evaluating obesity and lung function.

Additional records identified Studies identified by in other sources (n=19) initial PubMed search Scopus (n=1) (n=1308) • CINAHL (n=16) • Cochrane (n=2) • Excluded studies (n=948) Examined studies by title and abstract Studies that were duplicates (n=1327) or not relevant to proposed study aims Full-text articles were evaluated for eligibility Full-text articles excluded (n=317) (n=379) Full-text were not available or in ٠ other languages (n=54) Insufficient data on exposure or • outcome measures (n=227) Subjects with other respiratory к=86.5% conditions (n=21) • Review articles without original data (n=11) Studies reported the same • populations (n=4) Studies included in qualitative synthesis (n=62) Studies included in quantitative synthesis (meta-analysis) (n=62)

Figure 1. Study selection flowchart

 κ = Kappa agreement coefficient.





Forest plot for FEV_1 % pred, showing weighted mean difference (WMD) by study, for each comparison group (CompGP) vs normal-weight subjects. OV: Overweight. OB: Obese. OVOB: Overweight or obese.



Figure 3. Obesity and FVC (as percent of predicted) by age group

Forest plot for FVC %pred, showing weighted mean difference (WMD) by study, for each comparison group (CompGP) vs normal-weight subjects. OV: Overweight. OB: Obese. OVOB: Overweight or obese.





Forest plot for FEV_1/FVC , showing weighted mean difference (WMD) by study, for each comparison group (CompGP) vs normal-weight subjects. OV: Overweight. OB: Obese. OVOB: Overweight or obese.

Study		
ID	WMD (95% CI) Astr	ima CompGP
Children		
Rastogi_2015	-4.70 (-10.40, 1.00) Ast	nma 3-OB
Mansell_2006	-2.00 (-8.96, 4.96) Ast	nma 1-OV
Davidson_2014	-5.00 (-9.68, -0.32) No-	asthma 1-OV
Davidson_2014	-5.00 (-9.13, -0.87) No-	asthma 3-OB
Mendelson_2014	-3.00 (-11.42, 5.42) No-	asthma 3-OB
Rastogi_2015	-1.20 (-7.02, 4.62) No-	asthma 3-OB
Mansell_2006	-1.00 (-8.27, 6.27) No-	asthma 1-OV
Subtotal (I-squared = 0.0%, p = 0.891)	-3.68 (-5.82, -1.54)	
Adults		
Engbers_2010	-11.00 (-15.51, -6.49) Asth	nma 1-OV
Lessard_2008	-9.00 (-16.39, -1.61) Ast	nma 3-OB
Gibeon_2013	-6.10 (-6.39, -5.81) Asti	nma 3-OB
Lessard_2008	-6.00 (-14.03, 2.03) Astr	nma 3-OB
Deesomchok_2010	-4.00 (-9.03, 1.03) Asti	nma 3-OB
Farah_2011	-3.00 (-4.86, -1.14) Asti	nma 3-OB
Gibeon_2013	-2.80 (-3.13, -2.47) Asti	nma 1-OV
Sutherland_2008	-2.50 (-5.84, 0.84) Ast	nma 3-OB
Farah_2011	2.00 (-0.41, 4.41) Astr	nma 1-OV
Sutherland_2008	2.90 (-0.56, 6.36) Astr	nma 1-OV
Steier_2014	-15.80 (-29.46, -2.14) No-	asthma 3-OB
Watson_2005	-14.00 (-17.30, -10.70) No-	asthma 3-OB
Pellegrino_2014	-12.00 (-15.91, -8.09) No-	asthma 3-OB
Jones_2006	-10.60 (-14.25, -6.95) No-	asthma 3-OB
Jones_2006	-6.70 (-9.36, -4.04) No-	asthma 3-OB
Jones_2006	-5.60 (-8.17, -3.03) No-	asthma 3-OB
Pellegrino_2014	-5.00 (-9.57, -0.43) No-	asthma 1-OV
Essalhi_2013	-4.00 (-9.73, 1.73) No-	asthma 3-OB
Mehari_2015	-2.36 (-6.40, 1.68) No-	asthma 3-OB
Jones_2006	-1.80 (-4.47, 0.87) No-	asthma 1-OV
Mehari_2015	-0.22 (-5.20, 4.76) No-	asthma 3-OB
Mehari_2015	1.06 (-2.25, 4.37) No-	asthma 1-OV
Mehari_2015	2.54 (-1.77, 6.85) No-	asthma 3-OB
Subtotal (I-squared = 94.0%, p = 0.000)	-4.36 (-5.71, -3.02)	
NOTE: Weights are from random effects analysis		
	1	
-29.5 -15 -5 0 5 1	5 29.5	
WMD: Weighted mean difference	e (TLC %pred)	
	(,spied)	



Forest plot for TLC % pred, showing weighted mean difference (WMD) by study, for each comparison group (CompGP) vs normal-weight subjects. OV: Overweight. OB: Obese. OVOB: Overweight or obese.

Study		
ID	WMD (95% CI) AgeGP C	ompGP
Asthma		
Lessard_2008	-35.00 (-51.81, -18.19) Adults 3-	-OB
Rastogi_2015	-30.00 (-45.96, -14.04) Children 3-	-OB
Engbers_2010	-28.00 (-32.93, -23.07) Adults 1-	-OV
Deesomchok_2010	-13.00 (-26.26, 0.26) Adults 3-	-OB
Gibeon_2013	-5.10 (-5.94, -4.26) Adults 1-	-OV
Lessard_2008	-2.00 (-17.69, 13.69) Adults 3-	-OB
Gibeon_2013	-0.60 (-1.33, 0.13) Adults 3-	-OB
Farah_2011	0.00 (-5.41, 5.41) Adults 1-	-OV
Farah_2011	0.00 (-5.82, 5.82) Adults 3-	-OB
Sutherland_2008	10.70 (3.15, 18.25) Adults 1-	-OV
Sutherland_2008	13.40 (6.45, 20.35) Adults 3-	-OB
Subtotal (I-squared = 95.6%, p = 0.000)	-5.31 (-9.36, -1.25)	
No-asthma		
Rastogi_2015	-35.90 (-51.80, -20.00) Children 3-	-OB
Pellegrino_2014	-20.00 (-26.05, -13.95) Adults 3-	-OB
Jones_2006	-12.20 (-18.27, -6.13) Adults 3-	-OB
Pellegrino_2014	-12.00 (-18.16, -5.84) Adults 1-	-OV
Jones_2006	-8.10 (-13.17, -3.03) Adults 3-	-OB
Jones_2006	-7.20 (-11.86, -2.54) Adults 3-	-OB
Essalhi_2013	-7.00 (-18.03, 4.03) Adults 3-	-OB
Jones_2006	-6.00 (-11.19, -0.81) Adults 1-	-OV
Mehari_2015	-5.58 (-16.11, 4.95) Adults 3-	-OB
Watson_2005	-1.00 (-5.50, 3.50) Adults 3-	-OB
Mehari_2015	-0.03 (-9.12, 9.06) Adults 3-	-OB
Mehari_2015	2.06 (-6.19, 10.31) Adults 1-	-OV
Mehari_2015	5.27 (-4.72, 15.26) Adults 3-	-OB
Subtotal (I-squared = 78.4%, p = 0.000)	-7.60 (-11.68, -3.51)	
NOTE: Weights are from random effects analysis		
	T T T T	
-51.8 -45 -35 -25 -15 -5 0 5 15	25 35 45 51.8	
WMD: Weighted mean difference	(RV %pred)	

Figure 6. Obesity and RV (as percent of predicted) by asthma status

Forest plot for RV %pred, showing weighted mean difference (WMD) by study, for each comparison group (CompGP) vs normal-weight subjects. OV: Overweight. OB: Obese. OVOB: Overweight or obese.

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Study		
ID	WMD (95% CI) AgeGP Co	ompGP
Asthma		
Engbers_2010	-27.00 (-34.30, -19.70) Adults 1-	-OV
Rastogi_2015	-19.70 (-28.63, -10.77) Children 3-	-OB
Farah_2011	-7.00 (-11.33, -2.67) Adults 3-	-OB
Farah_2011	7.00 (1.43, 12.57) Adults 1-	-OV
Sutherland_2008	10.70 (6.98, 14.42) Adults 3-	-OB
Sutherland_2008	11.50 (6.83, 16.17) Adults 1-	-OV
Subtotal (I-squared = 96.4%, p = 0.000)	-3.74 (-15.02, 7.55)	
No-asthma		
Watson_2005	-41.00 (-44.30, -37.70) Adults 3-	-OB
Pellegrino_2014	-40.00 (-45.67, -34.33) Adults 3-	-OB
Jones_2006	-36.50 (-41.34, -31.66) Adults 3-	-OB
Jones_2006	-30.90 (-35.31, -26.49) Adults 3-	-OB
Essalhi_2013	-27.00 (-34.75, -19.25) Adults 3-	-OB
Jones_2006	-24.80 (-28.93, -20.67) Adults 3-	-OB
Pellegrino_2014	-23.00 (-29.42, -16.58) Adults 1-	-OV
Mehari_2015	-19.59 (-25.30, -13.88) Adults 3-	-OB
Rastogi_2015	-17.60 (-25.50, -9.70) Children 3-	-OB
Mehari_2015	-14.34 (-19.30, -9.38) Adults 3-	-OB
Jones_2006	-13.90 (-18.34, -9.46) Adults 1-	-OV
Mehari_2015	-7.73 (-13.47, -1.99) Adults 3-	-OB
Mehari_2015	-4.38 (-8.73, -0.03) Adults 1-	-OV
Subtotal (I-squared = 96.2%, p = 0.000)	-23.17 (-30.26, -16.07)	
NOTE: Weights are from random effects analysis		
-45.7 -35 -25 -15 -5 0 5	5 15 25 35 45.7	
WMD: Weighted mean dif	ference (FRC %pred)	

Figure 7. Obesity and FRC (as percent of predicted) by asthma status

Forest plot for FRC % pred, showing weighted mean difference (WMD) by study, for each comparison group (CompGP) vs normal-weight subjects. OV: Overweight. OB: Obese. OVOB: Overweight or obese.

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	FEV1 (%pred)	FVC (%pred)	FEV ₁ /FVC (%)	FEF ₂₅₋₇₅ (%pred)	TLC (%pred)	RV (%pred)	FRC (%pred)
All	-2.2 (-2.6, -1.8)	-2.2 (-3.7, -0.6)	-1.5 (-1.9, -1.2)	-5.4 (-7.3, -3.5)	-4.2 (-5.4, -3.0)	-6.6 (-9.3, -3.8)	-17.1 (-25.2, -9.0)
By age							
Adult	-2.4 (-2.9, -1.9)	-4.6 (-6.9, -2.2)	$-1.0 \; (-1.4, -0.6)^{*}$	-3.3 (-10.1, 3.6)	-4.4 (-5.7, -3.0)	-5.4 (-8.2, -2.7)	-16.9 (-25.4, -8.2)
Child	-0.8 (-2.3, +0.6)	0.3 (-1.7, +2.3)	-2.4 (-3.0, -1.8)*	-4.7 (-6.9, -2.6)	-3.7 (-5.8, -1.5)	-33.0 (-44.2, -21.7) []]	$-18.5 (-24.4, -12.6)^{I}$
By asthma							
Asthma	-1.4 (-1.9, -0.9)	-1.7 (-3.7, +0.3)	$-1.5 \ (-1.9, -1.0)$	-3.2 (-6.3, -0.1)	-3.3 (-5.1, -1.5)	-5.3 (-9.4, -1.3)	-3.7 (-15.0, +7.6)
No asthma	-3.9 (-7.1, -0.7)	-2.8 (-7.8, +2.3)	-1.6 (-2.3, -0.8)	-4.4(-10.0, +1.2)	-4.8 (-7.1, -2.5)	$-7.6 \ (-11.7, -3.5)$	$-23.2\ (-30.3, -16.1)$
By age and asthma							
Adult, asthma	$-1.7 \left(-2.3, -1.2\right)^{*}$	-3.2 (-6.0, -0.4)	-1.2 (-1.8, -0.6)	$-3.3 \left(-10.1, +3.6\right)$	-3.3 (-5.2, -1.4)	-4.1 (-8.2, -0.1)	$-0.7 \left(-12.5, +11.0 ight)^{*}$
Adult, no asthma	-6.9 (-11.1, -2.8)*	-7.5 (-11.4, -3.7)	-0.9 (-1.9, +0.1)	ł	-5.3 (-8.2, -2.4)	-6.5 (-10.2, -2.7)	$-23.6 \ (-31.1, -16.1)^{*}$
Child, asthma	0.4 (-1.2, +2.0)	$0.4 \ (-0.6, +1.5)$	-1.8 (-2.4, -1.3)	-2.5 (-6.6, +1.5)	$-3.6\left(-8.0, +0.8\right)$	ł	:
Child, no asthma	-0.9(-5.4, +3.6)	2.8 (-6.8, +12.5)	-2.8 (-3.9, -1.8)	-4.4 (-10.0, +1.2)	-3.7 (-6.2, -1.3)	ł	ł
By weight group							
Overweight	0.37 (-1.7, +0.9)	-0.3 (-1.8, +1.2)	-1.2 (-1.9, -0.6)	-4.8 (-7.2, -2.4)	-2.0 (-4.1, +0.1)	-5.8 (-12.9, +1.4)	-8.2 (-19.7, +3.4)
Obese	-3.9 (-4.8, -2.9)	-3.2 (-5.2, -1.2)	-1.7 (-2.5, -0.9)	-4.6 (-8.1, -1.2)	-5.4 (-7.0, -3.9)	-7.4 (-11.6, -3.2)	-21.2 (-30.9, -11.5)
Shown are weighted m	ean differences (WMD)	s) for overweight/obes	se vs normal weight. S	Significant WMDs in t	oold.		
* WMDs are significan	tly different between th	e groups (e.g. WMD f	or adult vs. child, or a	asthma vs. no asthma).			

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 I Only one study and thus only that study's effect size reported (not a pooled estimate).