

Overweight, Obesity and Incident Asthma: A Meta-analysis of Prospective  
Epidemiologic Studies

David A. Beuther, MD<sup>1,2</sup> and E. Rand Sutherland, MD, MPH<sup>1,2</sup>

Department of Medicine

<sup>1</sup>National Jewish Medical and Research Center, Denver, CO

<sup>2</sup>University of Colorado at Denver and Health Sciences Center, Denver, CO

Correspondence and Reprint Requests To:

E. Rand Sutherland, MD, MPH

National Jewish Medical and Research Center

1400 Jackson Street, J220

Denver, CO 80206

Phone: 303-398-1081

Fax: 303-398-1780

Email: sutherlande@njc.org

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## **Abstract**

**Rationale:** Although obesity has been implicated as an asthma risk factor, there is heterogeneity in the published literature regarding its role in asthma incidence, particularly in men.

**Objectives:** To quantify the relationship between categories of body mass index (BMI) and incident asthma in adults and to evaluate the impact of gender on this relationship.

**Methods:** Online bibliographic databases were searched for prospective studies evaluating BMI and incident asthma in adults. Independent observers extracted data regarding annualized asthma incidence from studies meeting predetermined criteria, within defined categories of normal weight (BMI<25), overweight (BMI 25-29.9) and obesity (BMI≥30). Data were analyzed by inverse-variance-weighted random-effects meta-analysis. Stratified analysis between BMI categories and within gender was performed.

**Results:** Seven studies (subject n=333,102) met inclusion criteria. Compared with normal weight, overweight and obesity (BMI≥25) conferred increased odds of incident asthma, with an odds ratio of 1.51 (95% confidence interval [1.27-1.80]). A dose-response effect of elevated BMI on asthma incidence was observed; the odds ratio for incident asthma for normal weight versus overweight was 1.38 [1.17-1.62] and was further elevated for normal weight versus obesity 1.92 [1.43-2.59], p<0.0001 for the trend. A similar increase in the odds of incident asthma due to overweight and obesity was observed in both men (1.46 [1.05-2.02]) and women (1.68 [1.45-1.94]), p=0.232 for the comparison.

**Conclusions:** Overweight and obesity are associated with a dose-dependent increase in the odds of incident asthma in both men and women, suggesting asthma incidence could be reduced by interventions targeting overweight and obesity.

Abstract word count: 248

Key words: Risk factors, epidemiology, body weight, respiratory tract diseases

## Introduction

The increasing prevalence of both asthma and obesity has suggested an association between the two conditions (1). Age-adjusted prevalence data from the National Health and Nutrition Examination Survey (NHANES) show that 65% of U.S. adults are either overweight or obese, with an increase of 10% from 1988-94 to 1999-2000 (2, 3). While asthma is less prevalent than obesity, it currently affects approximately 7% of the adult U.S. population (4).

Many cross-sectional epidemiologic investigations have shown a modest association between obesity and prevalent asthma (5-8), and a comprehensive qualitative review of this literature has been published (9). Using differing definitions of obesity, the relative risk of asthma in obesity ranges from 1.0 (no effect) to 3.0, and some studies have shown this risk to be greater in women than in men. The strength of these studies is their ability to examine large numbers of subjects, and some have characterized obesity objectively using measured height and weight (5, 7, 8). However, even though these reports frequently control for confounding by socioeconomic status, age, activity levels, and diet, causation in the obesity-asthma relationship cannot be determined conclusively from cross-sectional data alone. While many investigators have interpreted these data to suggest that obesity increases the risk of asthma, one cannot rule out that asthma may contribute to obesity, perhaps due to inactivity or side effects of systemic corticosteroids.

Prospective epidemiologic studies have the advantage of clarifying the direction of this relationship and have suggested that antecedent obesity leads to an increase in the incidence of a new diagnosis of asthma. For example, Camargo and colleagues

showed that in a group of women participating in the Nurses' Health Study, the relative risk for incident asthma increased with increasing body mass index (BMI), up to 2.7 for a BMI $\geq$ 30 (p for trend <0.001) (10). However, there is heterogeneity in the magnitude and significance of this relationship across studies. Reported odds or risk ratios for incident asthma in obese or extreme obese compared to normal-weight individuals range from 1.0 to 3.5. While these studies are all prospective adult investigations utilizing reported or measured BMI at baseline and self-reported new diagnosis of asthma or asthma symptoms, there are differences in duration of follow-up, study size, gender distribution, age distribution, range of BMI, and other variables that could explain some of the differences in point estimates. For example, the role of gender in the obesity-asthma relationship is controversial, and there is considerable heterogeneity among studies reporting incidence data stratified by gender, with some demonstrating that the relationship between obesity and asthma is significant and similar for men and women (11, 12), with others failing to show a significant relationship in men (5, 13) or reporting that the relationship in men is weaker than in women (14), and still others demonstrating significant findings only in men (15).

The primary objectives of this meta-analysis were 1) to determine a precise numerical estimate of the impact of overweight and obesity on the annual odds of developing asthma in adults, 2) to determine whether there is a dose-response effect of elevated BMI on asthma incidence, and 3) to determine whether gender alters the odds of incident asthma in overweight or obese adults. We hypothesized that overweight and obesity would increase the odds of incident asthma in a dose-dependent manner, and

that this effect would be more pronounced in women than men. Some of the results of this study have been reported previously in the form of an abstract (16).

**Methods** (word count: 494)

This meta-analysis was conducted and reported according to recommendations of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group (17). Targeted studies were those in which the relationship between body mass index and incident asthma was evaluated. MEDLINE, Cumulative Index to Nursing & Allied Health Literature (CINAHL), International Pharmaceutical Abstracts (IPA), and all EBM reviews (Cochrane Database of Systematic Reviews, ACP Journal Club, Database of Abstracts of Reviews of Effects, and Cochrane Central Register of Controlled Trials) were searched between a date range of 1966 to May, 2006, crossing keywords “overweight” and “asthma,” “obesity” and “asthma,” “body mass index” and “asthma,” “body weight” and “asthma,” and “anthropometry” and “asthma.” Reference lists were searched for additional articles and discussions were held with experts in the area of investigation in attempts to identify additional published or unpublished data.

Two investigators independently reviewed each study. Pre-determined inclusion criteria included 1) adult subjects, 2) primary outcome of incident asthma, 3) use of body mass index as a measure of overweight or obesity, 4) minimum 1 year follow-up, 5) follow-up of at least 70%, and 6) data that could be categorized by standard ranges of BMI obtained at study inception. It was anticipated that all studies would use either new self-reported, physician-diagnosed asthma or new symptoms and/or medication use compatible with asthma as the criteria for incident asthma diagnosis. Normal weight

was defined as BMI<25, overweight was defined as BMI between 25 and 29.9, and obesity was defined as BMI≥30. Study data sources were examined to ensure that every included data set was unique.

Data were extracted into contingency tables to facilitate calculation of odds of incident asthma over the study period. To standardize the differing follow-up periods between studies, asthma incidence data were expressed in an annualized fashion by assuming a constant rate of incident asthma over the follow-up period and then dividing the number of new asthma cases by the number of years of follow-up. These contingency tables were then used to further stratify asthma incidence in three BMI and two gender categories. Specific comparisons were made to allow determination of odds ratios comparing overweight subjects with normal weight subjects, obese subjects with normal weight subjects and overweight *and* obese subjects with normal weight subjects. These comparisons were performed in men and women separately.

Stata™ 7.0 (Stata Corporation, College Station, TX) (18) was used to generate summary odds ratios using inverse variance-weighted random-effects meta-analysis (19, 20). Random effects methodology was chosen to account for both within-study and between-study variation. Heterogeneity of data was evaluated using the *Q* statistic (19). Summary odds ratios were represented as a point estimate and 95% confidence intervals on a forest plot (21), and publication bias was evaluated (22, 23). A plan was established *a priori* to perform sensitivity analyses in the case of identified issues relating to study quality, if necessary, rather than apply weights to studies in the meta-analysis based simply on quality scoring criteria (17).

## Results

The systematic search (Figure 1) yielded 2006 total references, of which 1569 were unique. Using the pre-specified inclusion criteria, a title review rejected 1474 references, yielding 95 candidate abstracts. A subsequent abstract review rejected 82 of these references, yielding 13 candidate studies. After each of these studies was reviewed in its entirety, seven (10-15, 24) were found to meet the pre-specified inclusion criteria.

A total of 333,102 unique subjects were included in the analysis (Table 1). Study populations included were well-characterized cohorts in the United States, Canada, and Europe. Two studies included only women (10, 24). One of the seven articles stratified BMI by decile (24) and attempts to obtain primary data for categorization according to the aforementioned criteria were unsuccessful. Because one of the BMI decile cut-offs in this paper approximated 25 (24.62), this article was included in an analysis that grouped overweight and obesity into a single category ( $BMI \geq 25$ ). All included studies were entirely observational and of similar design, thus quantitative measures of quality were not used to weight the studies in the meta-analysis (17).

Antecedent obesity was associated with significantly increased annual odds of a new diagnosis of asthma. The summary odds ratio for one-year incident asthma in overweight and obese versus normal-weight men and women was 1.51 [1.27-1.80] (Table 2, Figure 2). A dose-response effect to this relationship was observed, with increasing BMI being associated with increasing odds of incident asthma (Table 2), such that the annual odds of incident asthma in overweight versus normal weight individuals was 1.38 [1.17-1.62], with the annual odds of incident asthma in obese

versus normal weight individuals being further increased at 1.92 [1.43-2.95] (Table 2, Figure 3), with a  $p < 0.0001$  for this trend.

Gender did not appear to be a significant modifier of the strength of relationship between overweight and obesity and asthma incidence. Comparing overweight and obese subjects with normal weight subjects, the odds of asthma over 1 year of follow-up were 1.46 [1.05-2.02] for men and 1.68 [1.45-1.94] for women (Table 2, Figure 4), with a  $p = 0.2$  for the comparison. The dose-response relationship between increasing BMI and odds of incident asthma remained evident when stratified by gender (Table 2).

There was no evidence of significant publication bias (Egger  $p = 0.09$ ).

## **Discussion**

This meta-analysis has provided a precise estimate of the odds of incident asthma for individuals who are overweight or obese, suggesting that the odds of incident asthma are increased 50% in overweight or obese individuals as a whole. Our findings also demonstrate a clear dose-response relationship between BMI and asthma, suggesting that asthma risk increases further as body weight increases. Additionally, we have shown female gender does not appear to disproportionately impact upon the obesity–asthma relationship, given that the odds of incident asthma in overweight or obese men and women were similar.

On the basis of these findings, overweight and obesity appear to be significant risk factors for asthma, and if they can be considered to be modifiable risk factors, interventions which effect weight loss could also be associated with a decrease in asthma incidence. As an example, survey data suggest that two-thirds of the adult U.S.

population of 220 million is overweight or obese (2). Assuming that approximately 12% of these overweight or obese individuals already have asthma (25, 26), and assuming that 6% of the remaining adult population has asthma, approximately 200 million U.S. adults are free of asthma but at risk of developing it at any given time. Studies suggest that new asthma cases in the general adult population occur at a rate of approximately 0.5% per year (27, 28), and presumably this rate is influenced by contributions from both the lean and overweight/obese subgroups of the population in the ratio described above (1 lean:2 obese/overweight). If significant weight loss could be achieved in the population of overweight and obese individuals (admittedly a difficult task), it could be estimated that the number of new asthma cases in US adults might fall by as much as 250,000 per year (from 0.5% to 0.375% per year). If these rates of increase can also be extrapolated to the pediatric population, where the annual incidence of asthma is as much as five times higher (24 per 1000 person-years (29)), the effect of even small changes in mean population BMI would appear to translate into significant increases or decreases in asthma incidence in both children and adults.

The findings of this analysis must be considered in context of a number of potential limitations. First, many of the studies included in this meta-analysis relied upon self-reported, rather than measured, weight and height to determine BMI. If there were large and systematic differences in reporting of weight and height by sex or BMI, then these results could be confounded by a classification bias. We believe this is unlikely to have affected our results. Of the seven studies included in this analysis, two (11, 14) used measured and not self-reported height and weight, and found that the relationship between obesity and asthma was significant, and was similar between men and women,

consistent with our results. In addition, a recent study by Hu and colleagues validated self-reported with measured weight among 184 participants in the Nurses' Health Study (30). Self-reported weight was highly correlated with measured weight ( $r=0.96$ ; mean measured weight was 1.4 kg greater than self-reported weight). Reassuringly, this analysis was performed in a study cohort included in this meta-analysis (10).

Additionally, BMI may not be the best measure of adiposity, particularly when looking at the effect of obesity on lung disease. There may be sex differences in muscle mass and body fat distribution that could make BMI a misleading indicator of the degree of adiposity, and measures of abdominal adiposity are better predictors of alteration in pulmonary function than body weight or BMI (31, 32). However, while future research in obesity and lung disease may benefit from the use of alternative measures of adiposity, for practical purposes, we were constrained to use BMI, as it is by far the most commonly used measure of obesity in this literature.

It is possible that asthma may be over-diagnosed in an obese population, or that the phenotype of asthma seen with overweight and obesity is unique with regard to clinically-meaningful parameters such as the nature or perception of symptoms, specific physiologic impairments (33), or response to therapy (34). Although the data on which our analysis is based do not allow evaluation of these factors in the combined study population, previous reports suggest that asthma associated with obesity may differ phenotypically from asthma in individuals of normal weight. Obesity, in the absence of asthma, causes physiologic impairments in lung function including reduction in lung volumes (35), chest wall restriction (36), and increased oxygen cost of breathing (37), and contributes to co-morbid conditions such as gastroesophageal reflux (38, 39) and

sleep apnea, which can result in dyspnea and wheezing that might be mistaken for asthma by patients and clinicians (33, 40). It has also been reported that while lung volumes are reduced and asthma symptoms are increased in obesity, airflow obstruction and airway hyperresponsiveness are not altered (41). Weight loss studies have shown improvements in lung function and asthma symptoms (42) but not necessarily airflow obstruction or airway hyperresponsiveness (43). These reports cast some doubt on the validity of self-reported asthma (even if “physician-diagnosed”) in large epidemiologic studies. It is reasonable to believe that some of these patients with “asthma” may have respiratory symptoms due to obesity, but may not meet rigorous objective physiologic criteria for asthma (40). This type of classification bias is difficult to address in a large epidemiologic investigation, without having independent clinical and physiologic data for each subject, and may have falsely inflated the number of new cases of asthma in obese subjects, leading to an overestimate of the odds ratio, a phenomenon which might also contribute to the overdiagnosis of asthma in reports in which conclusions are drawn from epidemiologic data using self-reported asthma as the primary criterion for diagnosing asthma, without supporting physiologic evaluation.

Alternatively, the calculated odds ratios may have been underestimated due to the grouping together of underweight and normal-weight subjects. Underweight has been shown to be a risk factor for asthma, with the relationship between asthma risk and BMI having a J-shape such that very low BMI has also been reported to be associated with elevated asthma risk (15). By defining “normal” BMI as  $<25$ , we potentially included underweight individuals with a high incidence of asthma in the “normal” group, which elevates the group’s asthma incidence and diminishes the

relative odds of asthma due to obesity. Since three of the seven studies included BMI < 20 in their “normal” group, we were unable to rigorously exclude underweight individuals in our analysis.

While the effect of obesity on asthma in this study was statistically significant, and there was a clear dose-response relationship, the magnitude of the effect was modest, even if one assumes that all newly reported cases of asthma in these studies are really asthma and not obesity-associated respiratory symptoms. However, in order to standardize data for our analysis, we determined the number of new cases of asthma per year; thus the increased odds are elevated even over a relatively short time frame with regard to duration of overweight and/or obesity in many patients, and when multiplied over many years are likely to be clinically significant.

Obesity is a well-established risk factor for diabetes, hypertension, sleep apnea, stroke, cardiovascular disease, arthritis, cancer, and many other diseases (44, 45). Our findings support adding asthma to this list, and should provide yet one more piece of information to compel obese individuals to lose weight and to support the aggressive implementation of public health measures to support the attainment of this goal.

## References

1. Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. *Am J Respir Crit Care Med* 2006;174:112-9.
2. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among U.S. children, adolescents, and adults, 1999-2002. *JAMA* 2004;291:2847-50.
3. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960-1994. *Int J Obes Relat Metab Disord* 1998;22:39-47.
4. Schiller JS, Bernadel L. Summary health statistics for the U.S. population: National Health Interview Survey, 2002. *Vital Health Stat 10* 2004;1-101.
5. 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;164:2045-50.
6. Chen Y, Dales R, Krewski D, Breithaupt K. Increased effects of smoking and obesity on asthma among female Canadians: the National Population Health Survey, 1994-1995. *Am J Epidemiol* 1999;150:255-62.
7. Guerra S, Sherrill DL, Bobadilla A, Martinez FD, Barbee RA. The relation of body mass index to asthma, chronic bronchitis, and emphysema. *Chest* 2002;122:1256-63.
8. Shaheen SO, Sterne JA, Montgomery SM, Azima H. Birth weight, body mass index and asthma in young adults. *Thorax* 1999;54:396-402.
9. Ford ES. The epidemiology of obesity and asthma. *J Allergy Clin Immunol* 2005;115:897-909.

10. 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;159:2582-8.
11. Ford ES, Mannino DM, Redd SC, Mokdad AH, Mott JA. Body mass index and asthma incidence among USA adults. *Eur Respir J* 2004;24:740-4.
12. Gunnbjornsdottir MI, Omenaas E, Gislason T, Norrman E, Olin AC, Jogi R, Jensen EJ, Lindberg E, Bjornsson E, Franklin K, Janson C, Gulsvik A, Laerum B, Svanes C, Toren K, Tunsater A, Lillienberg L, Gislason D, Blondal T, Bjornsdottir US, Jorundsdottir KB, Talvik R, Forsberg B, Franklin K, Lundback B, Soderberg M, Ledin MC, Boman G, Norback D, Wieslander G, Spetz-Nystrom U, Cashelunge KS, Ryden E. Obesity and nocturnal gastro-oesophageal reflux are related to onset of asthma and respiratory symptoms. *Eur Respir J* 2004;24:116-21.
13. Chen Y, Dales R, Tang M, Krewski D. Obesity may increase the incidence of asthma in women but not in men: longitudinal observations from the Canadian National Population Health Surveys. *Am J Epidemiol* 2002;155:191-7.
14. Nystad W, Meyer HE, Nafstad P, Tverdal A, Engeland A. Body mass index in relation to adult asthma among 135,000 Norwegian men and women. *Am J Epidemiol* 2004;160:969-76.
15. Huovinen E, Kaprio J, Koskenvuo M. Factors associated to lifestyle and risk of adult onset asthma. *Respir Med* 2003;97:273-80.
16. Beuther DA, Sutherland ER. Obesity, overweight and the odds of incident asthma: a meta-analysis. *Proc Am Thorac Soc* 2006;3:A527.

17. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008-12.
18. Sterne JAC, Bradburn MJ, Egger M. Meta-analysis in Stata. In: Egger M, Altman DG and Smith GD, editors. Systematic reviews in health care: meta-analysis in context. London, UK: BMJ Publishing Group; 2001. p. 347-372.
19. Cochran WG. The combination of estimates from different experiments. *Biometrics* 1954;10:101-129.
20. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-88.
21. Light RJ, Singer JD, Willett JB. The visual presentation and interpretation of meta-analysis. In: Cooper H and Hedges LV, editors. The handbook of research synthesis. New York, NY: Russell Sage Foundation; 1994. p. 439-454.
22. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;50:1088-101.
23. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629-34.
24. Romieu I, Avenel V, Leynaert B, Kauffmann F, Clavel-Chapelon F. Body mass index, change in body silhouette, and risk of asthma in the E3N cohort study. *Am J Epidemiol* 2003;158:165-74.

25. Kim S, Camargo CA, Jr. Sex-race differences in the relationship between obesity and asthma: the behavioral risk factor surveillance system, 2000. *Ann Epidemiol* 2003;13:666-73.
26. Luder E, Ehrlich RI, Lou WY, Melnik TA, Kattan M. Body mass index and the risk of asthma in adults. *Respir Med* 2004;98:29-37.
27. Huovinen E, Kaprio J, Laitinen LA, Koskenvuo M. Incidence and prevalence of asthma among adult Finnish men and women of the Finnish Twin Cohort from 1975 to 1990, and their relation to hay fever and chronic bronchitis. *Chest* 1999;115:928-36.
28. Sama SR, Hunt PR, Cirillo CI, Marx A, Rosiello RA, Henneberger PK, Milton DK. A longitudinal study of adult-onset asthma incidence among HMO members. *Environ Health* 2003;2:10.
29. Gilliland FD, Berhane K, Islam T, McConnell R, Gauderman WJ, Gilliland SS, Avol E, Peters JM. Obesity and the risk of newly diagnosed asthma in school-age children. *Am J Epidemiol* 2003;158:406-15.
30. Hu FB, Willett WC, Li T, Stampfer MJ, Colditz GA, Manson JE. Adiposity as compared with physical activity in predicting mortality among women. *N Engl J Med* 2004;351:2694-703.
31. Ochs-Balcom HM, Grant BJ, Muti P, Sempos CT, Freudenheim JL, Trevisan M, Cassano PA, Iacoviello L, Schunemann HJ. Pulmonary function and abdominal adiposity in the general population. *Chest* 2006;129:853-62.
32. Larsson I, Henning B, Lindroos AK, Naslund I, Sjostrom CD, Sjostrom L. Optimized predictions of absolute and relative amounts of body fat from weight, height, other anthropometric predictors, and age. *Am J Clin Nutr* 2006;83:252-9.

33. Beuther DA, Sutherland ER. Obesity and pulmonary function testing. *J Allergy Clin Immunol* 2005;115:1100-1.
34. Peters-Golden M, Swern A, Bird SS, Hustad CM, Grant E, Edelman JM. Influence of body mass index on the response to asthma controller agents. *Eur Respir J* 2006;27:495-503.
35. Biring MS, Lewis MI, Liu JT, Mohsenifar Z. Pulmonary physiologic changes of morbid obesity. *Am J Med Sci* 1999;318:293-7.
36. Naimark A, Cherniack RM. Compliance of the respiratory system and its components in health and obesity. *J Appl Physiol* 1960;15:377-82.
37. Cournand A, Richards DW, Jr., Bader RA, Bader ME, Fishman AP. The oxygen cost of breathing. *Trans Assoc Am Physicians* 1954;67:162-73.
38. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med* 2005;143:199-211.
39. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA, Jr. Body-mass index and symptoms of gastroesophageal reflux in women. *N Engl J Med* 2006;354:2340-8.
40. Sin DD, Jones RL, Man SF. Obesity is a risk factor for dyspnea but not for airflow obstruction. *Arch Intern Med* 2002;162:1477-81.
41. Schachter LM, Salome CM, Peat JK, Woolcock AJ. Obesity is a risk for asthma and wheeze but not airway hyperresponsiveness. *Thorax* 2001;56:4-8.

42. Hakala K, Stenius-Aarniala B, Sovijarvi A. Effects of weight loss on peak flow variability, airways obstruction, and lung volumes in obese patients with asthma. *Chest* 2000;118:1315-21.
43. Aaron SD, Fergusson D, Dent R, Chen Y, Vandemheen KL, Dales RE. Effect of weight reduction on respiratory function and airway reactivity in obese women. *Chest* 2004;125:2046-52.
44. Overweight, obesity, and health risk. National Task Force on the Prevention and Treatment of Obesity. *Arch Intern Med* 2000;160:898-904.
45. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA* 1999;282:1523-9.

## Figure Legends

Figure 1: Results of systematic literature search.

Figure 2: Point estimate for the summary odds of incident asthma at 1 year of follow-up, comparing obese and overweight men and women vs. normal-weight men and women.

Figure 3: Point estimates for the summary odds of incident asthma at 1 year of follow-up, comparing overweight men and women vs. normal-weight men and women (top panel) and obese men and women vs. normal-weight men and women (bottom panel). Increasing BMI is associated with an increased odds of incident asthma at 1 year of follow-up.

Figure 4: Point estimate for the summary odds of incident asthma at 1 year of follow-up, comparing overweight and obese men vs. normal-weight men (top panel) and overweight and obese women vs. normal-weight women (bottom panel).

Study	Population	N	Time	Reported OR, RR BMI>30	Annualized OR BMI>30
Camargo <sup>10</sup>	Nurses' Health II	85911	4 yr		
	Men	0		n/a	n/a
	Women	85911		2.7 [2.3-3.1]	2.5 [2.0-3.2]
Chen <sup>13</sup>	Canadian NPHS	9149	2 yr		
	Men	4266		1.0	0.7 [0.2-2.1]
	Women	4883		1.9 [1.1-3.4]	2.1 [1.2-4.0]
Ford <sup>11</sup>	NHANES I	9546	10 yr		
	Men	3621		1.5 [0.9-2.6]*	1.6 [0.3-8.8]
	Women	5925		1.4 [1.0-1.9]*	1.4 [0.5-4.1]
Gunnbjörnsdóttir <sup>12</sup>	ECRHS	16191	7.9 yr <sup>†</sup>		
	Men	7604		2.1 [1.4-3.2]*	2.2 [0.7-6.7]
	Women	8587		1.6 [1.1-2.1]*	1.4 [0.6-3.7]
Huovinen <sup>15</sup>	Finnish Twin Cohort	9671	9 yr		
	Men	4449		3.5 [1.6-7.7]	4.4 [0.6-33]
	Women	5222		2.3 [0.9-6.1]	4.5 [0.7-31]
Nystad <sup>14</sup>	Norwegian Health Surveys	135405	21 yr <sup>†</sup>		
	Men	66723		1.8 [1.4-2.3]	2.3 [0.9-6.3]
	Women	68682		2.0 [1.7-2.4]	1.9 [1.0-3.7]
Romieu <sup>24</sup>	French E3N Cohort	67229	3 yr		
	Men	0		n/a	n/a
	Women	67229		2.2 [1.4-3.2]**	1.4 [1.0-2.2]

Table 1: Included Studies

\*Study did not report this comparison, so primary data were extracted into a 2x2 table comparing BMI>30 to BMI<25, and OR was calculated. \*\*Reported OR comparing BMI≥27 to the reference BMI category 20.2-21.4. †Mean follow-up.

BMI = Body Mass Index; NPHS = National Population Health Survey; NHANES = National Health and Nutrition Examination Survey; ECRHS = European Community Respiratory Health Survey.

Comparison	Total	Men	Women
Overweight vs. Normal BMI	1.38 [1.17-1.62] p<0.001	1.44 [1.01-2.04] p=0.042	1.42 [1.18-1.72] p<0.001
Obese vs. Normal BMI	1.92 [1.43-2.59] p<0.001	1.63 [0.92-2.89] p=0.094	2.30 [1.88-2.82] p<0.001
Overweight and Obese (BMI≥25) vs. Normal BMI	1.51 [1.27-1.80] p<0.001	1.46 [1.05-2.02] p=0.025	1.68 [1.45-1.94] p<0.001
Obese vs. Overweight	1.49 [1.20-1.85] p<0.001	1.17 [0.66-2.07] p=0.590	1.58 [1.25-1.99] p<0.001

Table 2: Odds [95% CI] of incident asthma after 1 year of follow up in various categories of body mass index (BMI), in aggregate and stratified by gender

Figure 1

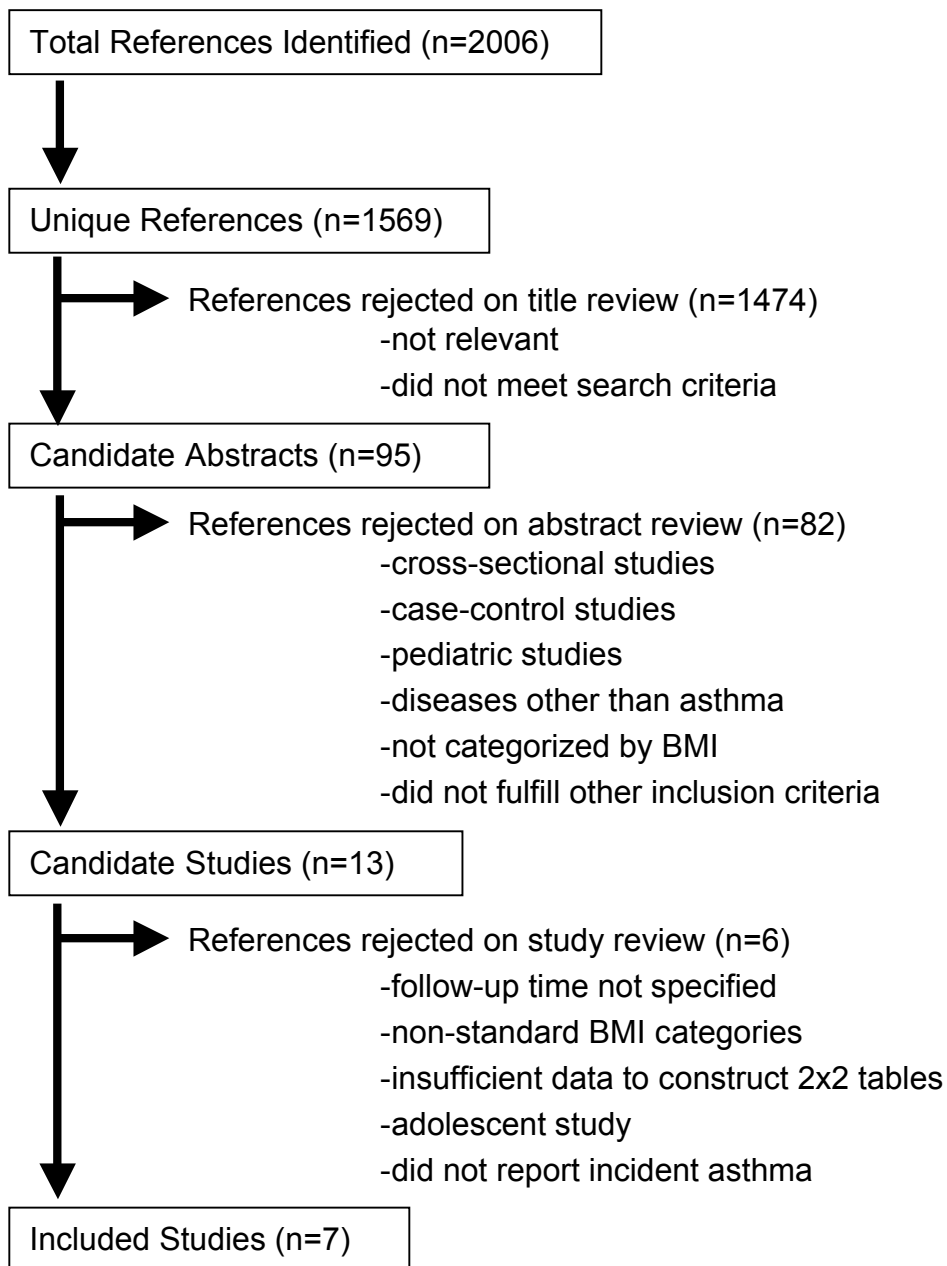


Figure 2

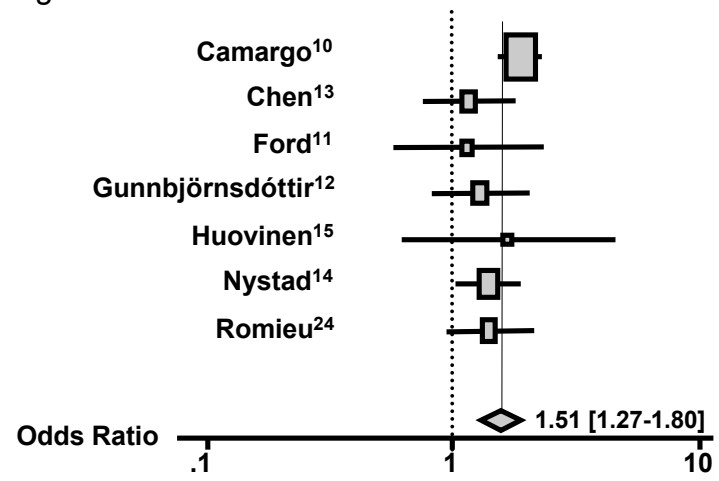


Figure 3

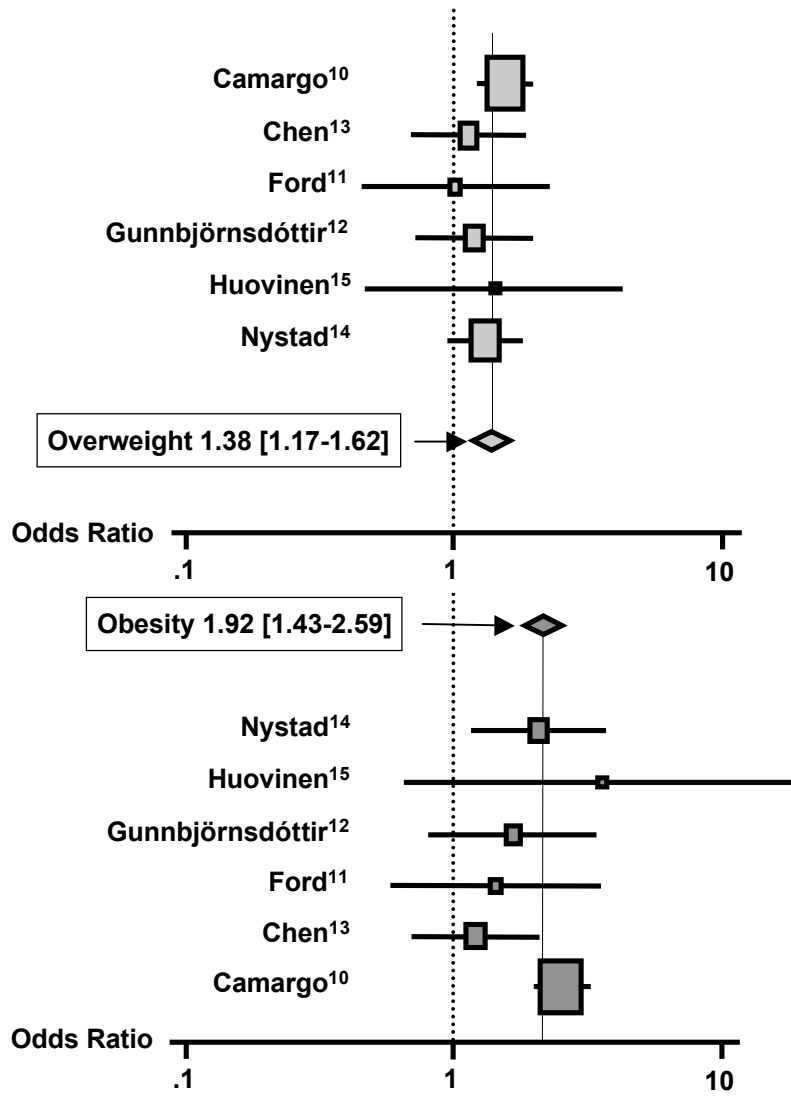


Figure 4

