American Journal of
EPIDEMIOLOGY

Volume 155
Number 3
February 1, 2002

Sponsored by the Society for Epidemiologic Research
Published by Oxford University Press

ORIGINAL CONTRIBUTIONS

Obesity May Increase the Incidence of Asthma in Women but Not in Men: Longitudinal Observations from the Canadian National Population Health Surveys

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To investigate the possibility of gender specificity for the effect of body mass index (BMI) on development of asthma, the authors used the longitudinal data from the first and second cycles of the National Population Health Survey, conducted in Canada in 1994–1995 and 1996–1997, respectively. Data from 9,149 subjects (4,266 men and 4,883 women) aged 20–64 years who reported no asthma at baseline were used in this analysis. The 2-year cumulative incidence of asthma was estimated by using a bootstrap procedure to take sampling weights and design effects into account. During the 2-year study period, 1.6% of the men and 2.9% of the women developed asthma. Average changes in body weight and BMI over the 2-year observation period were relatively small and were not associated with asthma incidence. However, baseline BMI was a significant predictor for asthma incidence in women. The adjusted odds ratio for women whose baseline BMI was at least 30.0 kg/m^2 versus 20.0–24.9 kg/m^2 was 1.9 (95% confidence interval: 1.1, 3.4), whereas the corresponding odds ratio of 1.1 (95% confidence interval: 0.3, 3.6) for men was not significantly different from unity. The authors concluded that obesity was related to development of asthma in women but not in men. *Am J Epidemiol* 2002;155:191–7.

asthma; body mass index; incidence; longitudinal studies; lung; obesity; sex

Editor's Note: *An invited commentary on this paper appears on page 198, and the authors' response is on page 201.*

Obesity and asthma are two important population health issues in Canada as well as in other industrialized countries. The prevalence of obesity has increased worldwide, reaching epidemic proportions in many industrialized countries (1). In Canada, nearly 60 percent of men and 40 percent of women are overweight as defined by a body mass index (BMI) of at least 25 kg/m^2 (2). There has been little change in the prevalence of obesity, defined as a BMI of more than 30 kg/m^2, over the past two decades (3). Obesity is associated with an increased risk of many diseases including diabetes, hypertension, coronary artery disease, and cancer. It is a cause of restrictive lung disease and has recently been associated with asthma (2, 4, 5).

Asthma is an important cause of morbidity and increased health care costs (6). Among the 17,605 subjects who participated in the Canadian National Population Health Survey (NPHS) in 1994–1995, the prevalence of physician-diagnosed asthma was approximately 10 percent for adolescents and young adults and 5 percent for adults (2). Asthma is a common cause of hospital admission. During the period from fiscal years 1994–1995 to 1996–1997, the hospital separation rate for asthma in Canada among children less than 15 years of age was 3 per 1,000 (7), and asthma accounted for 3 percent of total hospitalizations of the Canadian population (unpublished data). In 1990, the indirect and direct costs of asthma in Canada totaled an estimated Can $600 million (8), with the corresponding figure for the United States being approximately US $6.2 billion (9).

Received for publication January 25, 2001, and accepted for publication May 9, 2001.

Abbreviations: BMI, body mass index; CI, confidence interval; NPHS, National Population Health Survey.

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Several recent studies have demonstrated an association between relative body weight and asthma. Using cross-sectional data from the first cycle of the Canadian NPHS, Chen et al. (2) found that BMI was linearly related to the prevalence of asthma in women but not in men. Similarly, for British subjects at least 26 years of age, Shaheen et al. (10) observed an association between BMI and asthma restricted to females. However, cross-sectional studies do not allow determination of the directionality of the BMI-asthma association. A longitudinal analysis by Camargo et al. (11) of questionnaire data from the Nurses' Health Study in the United States demonstrated that increased BMI was associated with an increased risk of developing asthma. However, this study, which was confined to women, could not determine whether the effect of BMI on the development of asthma was modified by gender. The present investigation used longitudinal data from the NPHS to address this issue.

MATERIALS AND METHODS

This analysis was based on the longitudinal data from the first and second cycles of the NPHS, conducted by Statistics Canada (Ottawa, Ontario) in 1994–1995 and 1996–1997, respectively. The two cycles of the NPHS provided information on a panel of people who were followed over a 2-year period. The design and execution of the baseline survey have been detailed elsewhere (12). In brief, the target population included household residents in all 10 provinces, excluding Indian Reserves, Canadian Forces Bases, and some remote areas of Quebec and Ontario. The NPHS used a two-stage stratified sampling design to draw a representative sample of approximately 19,600 households, with a national response rate of 88 percent. In all provinces except Quebec, the Labour Force Survey design was used to draw the sample. In Quebec, the Enquête sociale et de santé conducted by Santé Quebec in 1992–1993, with a two-stage design similar to that of the Labour Force Survey, was used. In each household, all members were asked to complete a short general questionnaire, and one person was randomly selected for a more in-depth interview. The survey included questions related to the determinants of health, health status, and use of health services (2).

The second cycle of the NPHS was conducted in 1996–1997 by using similar methodology, including a longitudinal component. The longitudinal panel was defined as every selected household member who had completed at least the general questionnaire in the first cycle (13). Of 17,276 eligible subjects, 16,168 (94 percent) participated, and 15,670 provided both general and in-depth health information for both the 1994–1995 and 1996–1997 surveys (14).

In this analysis, we excluded subjects less than 20 years of age or more than 64 years of age in the baseline survey who were not asked to provide information on body weight. We also excluded those who either had reported having asthma in the first cycle or did not respond to questions about asthma in the first and/or second cycles. The present analysis was then based on 9,149 subjects (4,266 men and 4,883 women).

Respondents who answered the following question affirmatively were considered to have asthma: "Do you have asthma diagnosed by a health professional?" Incident asthma cases were those who reported no asthma in the first cycle but reported having asthma in the second cycle.

Self-reported body weight and height were recorded for subjects aged 20–64 years at baseline. For these subjects, BMI values at baseline and at follow-up were calculated from the equation BMI = weight(kg)/height(m)^2 and were grouped into the following four categories: <20.0, 20.0–24.9, 25.0–29.9, and ≥30.0. We also calculated odds ratios for persons with a BMI of 28.0 kg/m^2 or more, a cut-point set by Statistics Canada. Weight change (BMI change) during the 2-year study period was determined by subtracting weight (BMI) at baseline from weight (BMI) at follow-up.

In both cycles, current smokers were respondents who reported smoking cigarettes every day at the time of the survey. Former smokers were those who reported smoking cigarettes daily in the past but were not smoking at the time of the survey. Otherwise, subjects were classified as nonsmokers. Smoking status did not change dramatically during the 2-year study period, with a great majority of the subjects (87.6 percent of the men and 88.8 percent of the women) remaining in the same smoking categories (nonsmoking, former smoking, and current smoking) in the 1994–1995 and 1996–1997 surveys. The present analysis was based on smoking status at baseline (NPHS 1994–1995).

Subjects were also grouped according to other baseline variables. Subjects in the low education category had not proceeded beyond secondary school; the high education category included subjects who had been admitted to college or university, as well as those with a postsecondary school certificate or diploma. Subjects were classified into low-, middle-, and high-income groups based on total household income adjusted for number of household members (2). A positive history of allergy was defined by an affirmative response to either of the following questions: "Do you have any food allergies diagnosed by a health professional?" or "Do you have other allergies diagnosed by a health professional?" Other variables included in the analysis were age (20–29, 30–39, 40–49, or 50–64 years), immigrant status (yes, no), household size (1, 2, 3, or ≥4 people), number of bedrooms (<3, ≥3), any pets at home (yes, no), regular drinking (yes, no), and regular exercise (yes, no). A regular drinker was defined as a person who drank alcoholic beverages at least once a month. A regular exerciser was defined as a person who engaged in physical activities that lasted more than 15 minutes at least 12 times a month.

The relations between the weight variables and asthma were examined for men and women separately. We calculated the 2-year cumulative incidence of asthma and corresponding 95 percent confidence intervals according to various risk factors. Logistic regression models were used to evaluate the associations between weight variables and cumulative incidence of asthma, taking other important variables into consideration. Model parameters were esti-

mated by using the method of maximum likelihood and were tested for significance by using the Wald statistic.

The NPHS used a complex survey design incorporating stratification, multiple stages of selection, and unequal probabilities of selection of respondents. The effect of the complex survey design on variance estimates is represented by the design effect, defined as the ratio of the estimated variance taking into account the nature of the survey design to a comparable estimate of variance based on a simple random sample of the target population (15, 16). In the present analysis, the Rao-Wu bootstrap method (17, 18) was used for variance estimation to take both the population weights and design effects into consideration. First, bootstrap weights were calculated by using the Rao-Wu bootstrap approach provided to us by Statistics Canada. In each stratum, clusters were used as the resampling units, including all observations within each cluster. Within stratum h, $n_h - 1$ of n_h clusters were randomly selected with replacement, and the bootstrap weight $w^*_{hik} = [n_h/(n_h - 1)]\, m^*_{hi}\, w_{hik}$ was calculated, where m^*_h denotes the number of times that the h_ith cluster was selected, and w_{hik} denotes the original survey weight. If a cluster was not selected ($m^*_{hi} = 0$), then the bootstrap weight (w^*_{hik}) of the observations in the cluster was zero.

A total of 500 bootstrap samples were provided for the 1994–1996 longitudinal panel, permitting calculation of 500 point estimates of each parameter of interest. The standard error of each parameter estimate is then given by a standard deviation of the values for the 500 bootstrap replications. SAS software macros for the bootstrap approach were developed by Statistics Canada, and the statistical analyses were conducted by using SAS software, release 6.12 (19).

RESULTS

The 2-year cumulative incidence of asthma was higher in women than in men: 2.9 percent (95 percent confidence interval (CI): 2.4, 3.5 percent) versus 1.6 percent (95 percent CI: 1.2, 2.0 percent). The average change in body weight over the 2-year period of observation was 0.7 kg for both men and women. BMI changes were 0.18 kg/m^2 for men and 0.22 kg/m^2 for women. These relatively small changes in weight and BMI were not associated with the incidence of asthma (table 1). In women but not in men, the incidence of asthma tended to be higher for those with an increased BMI at the onset of the study (table 1).

Table 2 shows the 2-year cumulative incidence of asthma stratified by other potential risk factors for asthma. These factors were considered potential confounders or modifiers of the relation between obesity and asthma incidence. In women more so than men, the incidence of asthma tended to be higher for those with pets and those who smoked and drank alcohol regularly.

A multiple logistic regression model was used to assess the independent effect of baseline BMI in women on the 2-year cumulative incidence of asthma after controlling for age, smoking, pets, immigrant status, history of allergy, income adequacy, and alcohol drinking. The adjusted odds ratio for women with a baseline BMI of at least 30 kg/m^2

TABLE 1. Two-year cumulative incidence (%) and 95% confidence intervals for asthma, according to body mass index and weight change, among subjects aged 20–64 years at baseline based on longitudinal observations from the National Population Health Surveys, Canada, 1994–1996

	Men				Women			
	No.	Cases (no.)	%*	95% CI†	No.	Cases (no.)	%	95% CI
Weight change (kg)								
−2 or less	1,111	11	0.8	0.2, 1.4	1,199	35	3.1	1.6, 4.5
−1 to 1	1,397	12	1.4	0.4, 2.3	1,569	36	2.1	1.3, 2.9
2 to 4	1,030	15	1.6	0.6, 2.6	1,044	29	2.8	1.6, 4.1
5 or more	670	11	1.5	0.5, 2.5	704	21	2.5	1.2, 3.8
Unknown	58	0	0.0	0.0, 0.0	367	6	2.2	0.2, 4.2
Body mass index change (kg/m^2)								
−1.1 or less	714	7	0.7	0.1, 1.3	819	23	2.9	1.1, 4.6
−1.0 to −0.4	644	5	0.8	0.0, 1.7	647	15	2.4	1.1, 3.7
−0.3 to 0.3	892	11	1.9	0.5, 3.2	849	20	2.0	0.9, 3.1
0.4 to 1.0	864	11	1.5	0.4, 2.7	806	19	2.7	1.3, 4.0
1.1 or more	989	13	1.2	0.4, 2.1	1,209	36	2.5	1.6, 3.4
Unknown	163	2	1.4	0.7, 3.6	553	14	3.2	1.3, 5.1
Body mass index at baseline (kg/m^2)								
<20.0	126	2	1.5	0.0, 3.6	563	11	1.6	0.5, 2.6
20.0 to 24.9	1,565	17	1.5	0.7, 2.3	2,190	49	2.4	1.6, 3.2
25.0 to 29.9	1,378	20	1.1	0.5, 1.7	1,277	34	2.6	1.6, 3.6
≥30.0	1,172	10	1.5	0.4, 2.6	649	29	3.9	2.2, 5.6
Unknown	25	0	0.0	0.0, 0.0	204	4	2.8	0.0, 5.9

* The incidence estimates were weighted to the general population.
† 95% CI, 95% bootstrap confidence interval.

TABLE 2. Two-year cumulative incidence (%) and 95% confidence intervals for asthma, according to various risk factors, among subjects aged 20–64 years at baseline based on longitudinal observations from the National Population Health Surveys, Canada, 1994–1996

	Men				Women			
	No.	Cases (no.)	%*	95% CI†	No.	Cases (no.)	%	95% CI
Age (years)								
20–29	969	17	1.8	0.8, 2.8	1,097	43	3.6	2.4, 4.9
30–39	1,233	10	0.9	0.3, 1.4	1,473	31	2.2	1.1, 3.2
40–49	1,028	9	1.5	0.4, 2.6	1,092	28	2.4	1.4, 3.3
50–64	1,036	13	1.2	0.4, 2.0	1,221	25	2.3	1.2, 3.3
Size of household (no. of persons)								
1	783	10	1.4	0.4, 2.3	750	23	3.3	1.9, 4.8
2	1,255	14	1.3	0.5, 2.1	1,554	48	3.5	2.3, 4.7
3	893	14	1.8	0.7, 3.0	1,111	33	3.2	2.0, 4.4
≥4	1,335	11	1.0	0.3, 1.7	1,468	23	1.3	0.7, 1.9
No. of bedrooms								
<3	1,374	21	1.5	0.7, 2.3	1,576	45	2.9	1.9, 3.8
≥3	2,892	28	1.2	0.7, 1.7	3,302	82	2.4	1.8, 3.1
Unknown	0	0			5	0		
Pets at home								
Yes	2,013	19	1.2	0.5, 1.8	2,452	74	3.2	2.4, 4.1
No	2,252	30	1.4	0.8, 2.0	2,429	53	1.9	1.3, 2.5
Unknown	1	0			2	0		
Any allergy								
Yes	633	17	3.0	1.3, 4.6	1,073	52	4.9	3.3, 6.4
No	3,633	32	1.0	0.6, 1.4	3,810	75	1.9	1.4, 2.5
Immigrant								
Yes	570	6	0.9	0.1, 1.6	650	11	1.5	0.2, 2.9
No	3,693	43	1.4	0.9, 1.9	4,232	116	2.8	2.2, 3.4
Unknown	3	0			1	0		
Educational level								
Low	1,645	18	1.1	0.4, 1.7	1,854	41	2.0	1.2, 2.8
High	2,616	31	1.4	0.9, 2.0	3,024	86	2.9	2.1, 3.6
Unknown	5	0			5	0		
Income adequacy								
Low	637	9	1.2	0.4, 2.1	1,009	28	2.5	1.3, 3.6
Middle	1,124	15	1.0	0.4, 1.7	1,354	33	1.9	1.2, 2.7
High	2,335	23	1.3	0.7, 1.9	2,343	61	2.9	2.1, 3.7
Unknown	170	2	2.4	0.0, 5.9	177	5	2.9	0.0, 6.1
Smoking status								
Nonsmoker	1,682	20	1.2	0.6, 1.8	2,358	45	1.7	1.1, 2.2
Former smoker	1,182	9	0.9	0.1, 1.7	1,150	33	3.5	1.9, 5.0
Smoker	1,401	20	1.8	0.8, 2.8	1,374	49	3.6	2.4, 4.7
Unknown	1	0			1	0		
Regular alcohol drinking								
Yes	3,131	38	1.5	1.0, 2.0	2,530	73	3.4	2.5, 4.3
No	1,128	11	0.7	0.2, 1.3	2,352	54	1.6	1.1, 2.1
Unknown	7	0			1	0		
Regular exercise								
Yes	2,131	25	1.4	0.8, 2.1	2,634	64	2.3	1.7, 3.0
No	1,879	21	1.1	0.6, 1.7	2,159	61	2.8	2.0, 3.7
Unknown	256	3	1.5	0.0, 3.3	90	2	2.2	0.0, 5.6

* The incidence estimates were weighted to the general population.
† 95% CI, 95% bootstrap confidence interval.

compared with 20.0–24.9 kg/m^2 was 1.9 (95 percent CI: 1.1, 3.4) (table 3), whereas the corresponding odds ratio for men approached unity (data not shown). The adjusted odds ratio for women with a baseline BMI of at least 28 kg/m^2, the cutpoint used by Statistics Canada, compared with 20.0–24.9 kg/m^2 was 1.9 (95 percent CI: 1.1, 3.1).

TABLE 3. Unadjusted and adjusted* odds ratios and 95% confidence intervals for 2-year cumulative incidence of asthma in relation to women's body mass index at baseline, National Population Health Surveys, Canada, 1994–1996

Body mass index (kg/m²)	Unadjusted		Adjusted	
	OR†	95% CI†	OR	95% CI
<20.0	0.64	0.26, 1.60	0.62	0.24, 1.62
20.0–24.9	1.00		1.00	
25.0–29.9	1.10	0.65, 1.87	1.25	0.72, 2.18
≥30.0	1.65	0.93, 2.93	1.92	1.09, 3.41

* Adjusted for age, smoking, pet(s) at home, immigrant status, history of allergy, income adequacy, and alcohol drinking.
† OR, odds ratio; CI, confidence interval.

DISCUSSION

Based on longitudinal data from a representative sample of the Canadian population, our analyses suggest that women have an elevated incidence of asthma as compared with men and that increased BMI may increase the risk of developing asthma for women but not for men. The increased risk of asthma for women is also supported by Canadian national hospitalization data, which indicate that women were more likely to be admitted to hospital for asthma and to stay at hospital longer compared with men (unpublished data). Several recent cross-sectional studies have documented a significant association between BMI and asthma in women but not in men. Chen et al. (2) found that, based on data from the 1994–1995 NPHS, BMI values were positively associated with the prevalence of asthma in women only. The adjusted odds ratio was 1.52 for women whose BMI was 28.0 kg/m^2 or more versus 20.0–24.9 kg/m^2. Shaheen et al. (10) found that the odds ratios for the prevalence of asthma among 8,960 British adults were higher for overweight women but not men. For women 26 years of age, odds ratios were 1.51 for those whose BMI was 25.0–29.9 kg/m^2 and 1.84 for those whose BMI was at least 30.0 kg/m^2 compared with those whose BMI was less than 25.0 kg/m^2. Luder and Melnik (20) recently reported a similar gender-related association between BMI and physician-diagnosed asthma based on data from 5,527 adults aged 18 years or more living in New York State. Again, BMI was positively associated with asthma in women but not in men.

One limitation of the aforementioned prevalence studies is the inability to determine whether asthma preceded obesity or obesity preceded asthma, thus weakening the argument that asthma causes obesity. A longitudinal analysis of data from a prospective cohort study of female registered nurses in the US Nurses' Health Study provided the first evidence that obesity preceded asthma. Over a 4-year period, Camargo et al. (11) studied 85,911 female registered nurses aged 26–46 years and found a strong association between obesity and the risk of developing adult-onset asthma. Both BMI at baseline and weight gain after 18 years of age were strongly associated with an increased risk of asthma. However, the issue of gender specificity could not be addressed since men were not included in the study.

In contrast to the findings for adults, associations between obesity and asthma are inconsistent for children and adolescents (21). Some studies demonstrated that BMI was positively associated with wheezing (22, 23) and bronchial hyperresponsiveness (22) in girls but not in boys, whereas another study found BMI to be associated with asthma in both boys and girls (24). Some earlier studies found that asthmatic children weigh more than nonasthmatic children (25, 26), whereas other studies found no association between BMI and childhood asthma, despite their findings of positive associations for several other respiratory ailments (27–29).

Apart from a causal association between obesity and asthma, particularly in adults, there are several other explanations. Firstly, a factor associated with both obesity and asthma, such as diet or (sedentary) lifestyle, may confound the obesity-asthma association. Obstructive sleep apnea and gastroesophageal reflux disease can be possible risk factors for asthma development that are related to obesity. Secondly, Stenius-Aarniala et al. (30) elegantly demonstrated the detrimental effects of obesity on respiratory symptoms and function. These effects may increase the risk of asthma being diagnosed. However, these arguments are unable to explain the observed gender specificity.

One plausible hypothesis is that female sex hormones play an important role in the etiology of asthma and that these hormones are influenced by obesity (2,10,11). The following observations are consistent with this possibility: Sex hormonal changes begin at puberty, with adult hormone levels being attained by approximately 16 years of age (31). Although boys are at substantially higher risk of asthma than girls are (32–34), the incidence of asthma is higher in women than in men (35–37), and prevalence does not differ markedly between men and women (2, 36). Similarly, the rate of hospital admission for asthma is higher for prepubertal males than females but is lower for adult males than females (38). Airway responsiveness, a defining characteristic of asthma, may be greater in women than in men (39).

To some extent, these epidemiologic observations are consistent with the documented influence of sex hormones, including progesterone and estrogen, on mechanisms that may influence asthma. Progesterone upregulates beta$_2$ receptors. The luteal phase increase in progesterone and estradiol is associated with an increased density of beta$_2$ adrenoreceptors on lymphocytes (40). Forty micrograms of exogenously administered progesterone have been shown to cause an eightfold increase in the bronchorelaxant effect of the catecholamine isoprenaline (41). One hypothesis is that obesity reduces progesterone levels, which reduces beta$_2$ adrenoreceptor function, which in turn reduces bronchial smooth muscle relaxation. In support of this hypothesis is the observation that weight loss increases progesterone level and adrenoreceptor density (42). After studying 20 obese hyperandrogenic women, Wahrenberg et al. (43) found that a mean weight loss of 8 pounds (3.63 kg) was associated with a five- to sevenfold increase in noradrenaline and terbutaline sensitivity, with a twofold increase in beta$_2$-receptor density as measured by radioligand binding.

Estrogen may have different effects on asthma. The Nurses' Health Study showed that postmenopausal estrogen use was associated with an increased incidence of asthma and

that there was a dose-response relation between asthma incidence and the current dose and duration of use of estrogen (44). BMI has been shown to be positively associated with plasma estrogen and estrone sulfate levels in postmenopausal women (45). Relevant to the lack of association between BMI and asthma in men, Leenen et al. (46) reported that visceral fat accumulation, determined by magnetic resonance imaging, was associated with sex hormone alterations in women but not in men. Our analysis was limited by a lack of sex hormone data. The interrelations between asthma, obesity, and sex hormones warrant further study.

One major limitation of the present analysis is the diagnosis of asthma. Although a universally accepted definition of asthma remains to be established, there is no question that bronchial hyperresponsiveness and reversible airway narrowing are key features of the disease. Unfortunately, it is not practical to measure these characteristics in large-scale epidemiologic studies. As in most epidemiologic studies, the asthma definition used here was based on self-reported, physician-diagnosed asthma. The persons who reported having no asthma at baseline but reported having asthma at follow-up were considered incident cases during the 2-year study period, without additional verification.

Identification of incident cases of asthma in this manner may be crude; however, we could not find reasons that this would have an important impact on our conclusions. Firstly, Camargo et al. (11) reported substantially more information on the characteristics surrounding the diagnosis of asthma and found that stricter criteria led to stronger associations between BMI and asthma (11). Secondly, the disease definition we used contains the components essential to the definition in the original American Thoracic Society (47) Standardization Project questionnaire, which inquired "Have you ever had asthma?" and "Was it confirmed by a doctor?" These questions have been used in various epidemiologic studies, and they have been validated. In the present study, our definition was based on self-reported asthma and diagnosis by a health care professional. Thirdly, one study has demonstrated that various definitions of asthma have little influence on the observed incidences, and the data have shown an incidence of 1.2 percent for "ever had asthma," 1.1 percent for "asthma diagnosed by a physician," and 1.3 percent for "current use of asthma drugs." Even if the definition used had a small influence on the observed incidence of asthma, the choice of definition would be less likely to create an observed gender difference in asthma incidence in our study (35).

In addition, the follow-up period for our study was relatively short. Since the incidence of asthma was lower for men than for women, one could argue that there was insufficient statistical power to detect an association between BMI and asthma incidence in men. However, the data did not show an increasing trend in the incidence of asthma with increasing BMI at baseline for men. Another limitation is a lack of measures of adiposity other than body weight and BMI. BMI may not be an equivalent measure of fatness in men and women. The fact that men tend to have more muscle mass and women more fat mass may also contribute to the apparent gender-specific relation between obesity and asthma.

In summary, we found obesity to be a risk factor for asthma in women but not in men. The reproducibility of these findings in other populations, the lack of known confounding variables, and the existence of a biologically plausible explanatory mechanism all support an argument for a causal association. Evidence for causality would be strengthened by objectively measuring changes in asthma severity and female sex hormone levels during periods of weight gain or loss.

ACKNOWLEDGMENTS

This research was supported by a National Health Research and Development Program grant (6606-06-1998/2640023). Dr. Yue Chen is a Canadian Institutes of Health Research Investigator Award recipient.

The authors thank Colette Koeune of Statistics Canada for her assistance with remote access to the NPHS longitudinal data.

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