Case-by-Case Assessment of Adult-Onset Asthma Attributable to Occupational Exposures Among Members of a Health Maintenance Organization

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Objective: *In a general population of employed persons with health insurance, what proportion of adult-onset asthma is caused by occupational exposures?* ***Method:*** *We conducted a 2-year prospective study to identify adult-onset asthma among health maintenance organization (HMO) members. Telephone interviews regarding occupational exposures, symptoms, medication use, and triggers were used to assess likelihood of work-related asthma for each case. Weighted estimating equations were used to adjust the proportion of asthma attributable to workplace exposures for factors associated with interview participation.* ***Results:*** *Overall, 29% (95% confidence interval, 25–34%) of adult-onset asthma was attributable to workplace exposures; 26% (21–30%) and 22% (18–27%) of cases had asthma attributable to occupational irritant and sensitizer exposures, respectively.* ***Conclusions:*** *Occupational exposures, including irritants, are important causes of adult-onset asthma.* (J Occup Environ Med. *2006;48:400–407*)

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Relatively few community-based studies have been conducted to provide an overall measure of the fraction (occupational attributable fraction) of cases that arise as a result of occupational exposures.[1–6] This study prospectively identified adult-onset asthma cases in the adult members of a health maintenance organization (HMO) based in central Massachusetts. The analyses in this article were designed to measure the proportion of cases that were likely to have work-related asthma based on expert exposure scores and work-related symptoms and asthma medication use. Estimates of the proportion of asthma that is work-related range from 1% to 6% based on physician case reports of occupational asthma up to 36% in community-based studies of asthma risk.[4,7,8] Few studies have reported on the occupational-attributable fraction of asthma in the United States.[9]

Occupational-attributable fraction can be estimated using either case-by-case methods or by risk-based methods, as recently described in a review by the American Thoracic Society.[9] The primary goal of this report is to use a case-by-case approach to estimate the proportion of incident asthma that meets an epidemiologic case definition for probable work-related or occupational asthma based on individual exposure and symptom data.[2,8,10] Our secondary goal was to evaluate potential differences between sensitizer and irritant

exposures as causes of asthma onset or reactivation in adults.

Materials and Methods

This investigation was reviewed and approved by the Fallon Institutional Review Board and the Harvard School of Public Health Human Subjects Committee.

Study Population

Fallon Clinic provides healthcare services to members of the Fallon Community Health Plan (FCHP). The Fallon Clinic is a centralized, multispecialty group practice organization that provides the full range of services to FCHP members with over 300 physicians working at more than 27 ambulatory care centers in central Massachusetts. Virtually all (99%) FCHP members are enrolled without health screening either through employer-based programs (83%) or Medicaid and Medicare contracts (16%). Thus, there are no health-based barriers to membership for employed persons and their families. FCHP is offered by approximately 3500 employers. Most of the self-pay members have converted temporarily to this status on leaving employment. In addition, the Fallon Clinic offers fee-for-service medical care to nonmembers.

Case Identification

Software to query the HMO's Oracle data warehouse of coded outpatient encounter forms and inpatient and referral claims was developed and a study algorithm was designed to sensitively identify potential cases of adult-onset asthma, as previously described.[11]

Automated searches were performed monthly and were indexed by the first day of the month from March 2000 through February 2002. Males and females ages 15 to 54 were eligible for inclusion in the study population. We excluded those 55 and over to limit the number of chronic obstructive pulmonary disease and cardiac asthma cases that would be identified as potential cases of adult-onset asthma by our computerized record searches. Identification of cases was based on a physician diagnosis of asthma with clinically significant treatment for asthma. Subjects aged 15 to 18 were included to assess risk in working teens, because this was increased in a report from Singapore.[7] All Medicare and Medicaid beneficiaries enrolled in the HMO were included in the eligible population from March 1, 2000, through September 31, 2000. Beginning on October 1, 2000, the health plan started recoding membership so that by October 1, 2001, Medicare and Medicaid patients were no longer included in our study.

Chart Review

As previously described,[11] we confirmed asthma case status for each patient identified by the automated search by manual review of each medical record (both electronic and hard-copy charts) to provide high specificity to complement the initial case identification by the computerized algorithm, which was highly sensitive. Trained research nurses performed the reviews and recorded findings in a computerized database.

We considered an adequate case-defining event to exist when a physician recorded an asthma diagnosis in the written record and there was clinically significant asthma treatment prescribed and ordered within a month of the diagnosis. A case was confirmed when a subject met any of the inclusion criteria during the index period (month during which a case was identified) without meeting any exclusion criterion during the 12 months previously.

Telephone Interview

Cases were contacted after sending them a letter that explained the study and after obtaining permission from a parent, if a minor. Every effort was then made to contact cases by phone. We hired translators to assist with non-English-speaking patients.

The 45-minute questionnaire was structured to collect detailed information in the following areas: demographics (age, gender, race, ethnicity, personal and family income, education level), smoking history, respiratory symptoms, including standard questions for use in the International Union Against Tuberculosis and Lung Disease (IUATLD)–discriminate function predictor (DFP),[12] personal and family medical history, detailed job information and household characteristics, pets, hobbies, accidental one-time exposures, and quality of life. A positive value for the IUATLD-DFP predicts bronchial hyperresponsiveness.[12] The detailed work history pertained to current job(s) (or schools) and all previous jobs held in the past year. Subjects were intentionally not told that we were investigating occupationally related asthma in an attempt to avoid participation and reporting biases. The questionnaire was designed to imply that a wide range of etiologies was being investigated.

Interviewers were trained by senior project staff and met with the project industrial hygienist every other week to review the job information that was gathered and to perfect interviewing techniques in collecting detailed job information. Interviewers were trained to gather specific descriptions of job tasks and processes, as well as names and types of chemicals and products used on the job, and general conditions of the work environment.

Work-Related Symptom Assessment

The questionnaire included standard questions that ascertained the work-relatedness of symptoms. The first question asked whether or not symptoms changed when away from work for 2 or more days. If the answer to this question was "yes," the follow-up question asked whether symptoms were better or worse when away from work. Questions were similarly posed to determine whether more or less asthma-reliever medication (β-agonist inhaler or nebulizer) was used when

away from work. Finally, open-ended questions regarding triggers for asthma were asked. For each reported trigger, cases were asked where exposure to this trigger occurred (work, home, or elsewhere). All triggers were reviewed by project staff to assess the validity of each work-related trigger.

A work-related symptom score (0–3) was assigned based on responses to these detailed questions. Subjects were assigned one point if they reported symptoms improved on "weekends, vacations, and other times away from work" and one point if they reported using less asthma medication while away from work. They were also assigned a point if they reported a trigger that occurred at work. The sum of these scores was their work-related symptom score.

Workplace Exposure Assessment

Two workplace exposure assessment experts reviewed each job described in the work history while blinded to any other information about the subjects. Therefore, the experts were blinded to the presence or absence of work-related symptoms and to whether the job being rated was held during the targeted interval relevant to the onset of asthma. Each expert rated every job based on the probability, frequency, and intensity of exposure to sensitizers and irritants, separately, on a three-point scale: zero indicated "no or low probability of exposure"; one, "likely/moderate exposure"; and two, "highly likely/significant exposure." Experts used Chan-Yeung's list of sensitizers, as edited and maintained by the Association of Occupational and Environmental Clinics, known to induce asthma to rate sensitizer exposures, and professional judgment to rate probability of exposure to irritants. Interrater agreement as analyzed by the method of Agresti was moderate, with odds ratios of agreement of 6.1 (95% confidence interval [CI], 3.9–9.4) for sensitizers and 3.8 (3.0–4.8) for irritants.

TABLE 1
Occupational Asthma Case Definition and Classification Matrix

	Work-Related Symptom Score			
Expert Exposure Rating	**0**	**1**	**2**	**3**
0	None*	Weak	Weak	Moderate
1	Weak	Moderate	Moderate	Strong
2	Weak	Moderate	Strong	Strong

*None, weak, moderate, and strong refer to the strength of evidence for occupational asthma.

Case Classification

Cases included for study had either no history of asthma or asthma that had been in remission (ie, required no significant treatment) for at least 1 year. Those who had no history of asthma, based on chart review and interview, were classified as "incident." The remaining cases who had not received active treatment for asthma in the year before the index month (reference period) and met the inclusion criteria for study were categorized as "reactivated cases" because they had some history of asthma.

Those who reported respiratory symptoms that started immediately after a high-level exposure to an irritant occurring within 3 months before the month of identification as a case and whose symptoms persisted for at least 90 days after the exposure were categorized as RADS cases. If the exposure occurred at work, the case was considered an occupational RADS case.

The remaining non-RADS cases were classified as having no, weak, moderate, or strong evidence of asthma attributable to occupation based on job and symptom scores. Job data used for classification were for jobs the case held during the month he or she was identified as a case and during the 2 previous months. Cases were classified using three separate measures of occupational exposure based on all jobs held during the relevant interval: 1) the maximum of the irritant and sensitizer scores, 2) the maximum irritant score only, and 3) the maximum sensitizer score only. The evidence for work-related asthma classification was derived from a crosstabulation of exposure score by work-related symptom score (Table 1). Cases with moderate or strong evidence or those meeting the occupational RADS-like definition were considered asthma attributable to occupational exposure as previously described.[4]

Data Analysis

Occupational attributable fraction for all interviewed cases was calculated in a complete case analysis using SAS (version 8.2; SAS Institute, Cary, NC) and the following formula: occupational attributable fraction = [occupational RADS + moderate and strong evidence cases]/interviewed cases. We then analyzed all cases (interviewed and not interviewed) using weighted estimating equations (WEE) to estimate the probability of having work-related asthma, controlling for factors that were predictive of participation in the telephone interview (age, gender, and health insurance status), minimizing any participation bias. The method is described in Zhao[13] and is implemented in R (version 1.7.1). Code is available from the authors on request. Tests for differences in occupational-attributable fraction among men and women in different age and exposure categorizations were conducted using generalized estimating equations to account for repeated measures.

Results

The study population for the 2-year period consisted of 60,384 eligible HMO members ages 15 to 54, including 54,568 members who were at risk of developing asthma. Our monthly, automated searches identified 2117 potential adult-onset asthma cases that represented 109,135 person-years of follow-up. Forty-three percent of potential cases ($n = 906$) were confirmed as adult-onset asthma cases after review of both hard copy and electronic medical records to confirm physician diagnosis and significant clinical treatment for asthma. Forty-five percent of confirmed cases ($n = 405$) were successfully interviewed.

Among cases, women were significantly more likely to participate than men (relative risk = 1.24; 95% CI, 1.03–1.49). Age and insurance status were not associated with response at the $P < 0.05$ level of statistical significance, although odds ratios suggest that cases in the youngest and oldest categories may have been more likely to respond ($P = 0.34$). Dependents and spouses and Medicare/Medicaid patients also seemed more likely to participate than subscribers directly insured through employers, but statistical significance was not attained ($P = 0.19$). However, we included all of these factors in a model for response probability using a weighted estimating equation approach to control for potential bias due to differential response rates.

The 405 interviewed asthma cases were on average 34.3 years of age (standard deviation, 12.32), 69% female, 94% white, 3% black, and 7% Hispanic (Tables 2 and 3). The source of health insurance coverage was roughly equally split between subscribers enrolled through employer plans (47%) and their spouse/dependents (50%), with an additional 3% of cases enrolled through Medicare or Medicaid.

Incident cases, as compared with reactivated cases, were significantly older (36.4 years vs 33.2 years, $P = 0.01$) and were slightly but not significantly more likely to be white than reactivated cases (96% vs 94%, $P = 0.38$) in this largely white population. Incident cases were significantly less likely to report knowing that they had a current asthma diagnosis (16% vs 81%, $P < 0.0001$) (Table 4). Reactivated cases were more likely to report allergies, chronic bronchitis,

TABLE 2
Population Demographics of Adult-Onset Asthma Cases

	Respondents				
	Incident	Reactivated	Total	Nonrespondents	All Cases
N	140	265	405	501	906
Age, n (%)					
15–17	17 (12)	48 (18)	65 (16)	57 (11)	122 (13)
18–21	12 (8)	25 (10)	37 (9)	52 (10)	89 (10)
22–29	11 (8)	33 (12)	44 (11)	65 (13)	109 (12)
30–39	36 (26)	66 (25)	102 (25)	135 (27)	237 (26)
>40	64 (46)	93 (36)	157 (39)	192 (38)	349 (39)
Gender*					
Female	96 (69)	184 (69)	280 (69)	309 (62)	589 (65)
Male	44 (31)	81 (31)	125 (31)	192 (38)	317 (35)
Source of health insurance coverage†					
Subscriber	78 (56)	111 (42)	189 (47)	257 (51)	446 (49)
Spouse/dependent	59 (42)	143 (54)	202 (50)	228 (46)	430 (47)
Medicare/Medicaid	3 (2)	11 (4)	14 (3)	16 (3)	30 (3)

*0.02 for equal response rates by gender in cases.
†0.02 for equivalent distribution of proportions among incident and reactivated cases.

TABLE 3
Population Demographics of Respondent Adult-Onset Asthma Cases

	Incident	Reactivated	Total
N	140	265	405
Race, n (%)			
White	134 (96)	248 (94)	382 (94)
Black	2 (1)	10 (4)	12 (3)
Asian	1 (1)	4 (2)	5 (1)
Other	1 (1)	2 (5)	6 (2)
Ethnicity			
Hispanic	10 (7)	18 (7)	28 (7)
Education			
Less than high school	21 (15)	49 (19)	70 (17)
High school	47 (34)	87 (33)	134 (33)
Beyond high school	39 (28)	71 (26)	108 (27)
College graduate or more	33 (24)	58 (22)	91 (22)
Family income			
<10,000	1 (<1)	2 (<1)	3 (<1)
10,000–14,999	0 (0)	1 (<1)	1 (<1)
15,000–19,999	1 (1)	5 (2)	6 (1)
20,000–24,999	3 (2)	9 (3)	12 (3)
25,000–34,999	13 (9)	24 (9)	36 (9)
35,000–49,999	27 (19)	44 (17)	71 (18)
50,000–75,000	23 (16)	39 (15)	62 (15)
>75,000	16 (11)	46 (17)	61 (15)
Refused/unknown	56 (40)	95 (36)	151 (38)

TABLE 4
Symptoms and Smoking Among Respondent Cases

All Cases	Incident (N = 140)	Reactivated (N = 265)	Total (N = 405)
IUATLD–discriminate function predictor,* n (%)	107 (76)	252 (95)‡	359 (89)
Aware of asthma diagnosis			
Aware of any asthma	29 (21)	235 (89)‡	264 (65)
Aware of current asthma diagnosis	23 (16)	212 (81)‡	235 (58)
Doctor diagnosis hayfever/allergies	47 (34)	170 (65)‡	217 (54)
Doctor diagnosis chronic bronchitis	30 (21)	90 (34)‡	120 (30)
Doctor diagnosis sinusitis	54 (39)	128 (49)†	182 (45)
Smoking			
Current smoker	30 (21)	61 (23)	91 (22)
Exsmoker	42 (30)	70 (26)	112 (28)
Never smoker	68 (49)	134 (51)	202 (50)

*Discriminate function predictor for bronchial hyperresponsiveness described by Burney et al.[12]
†$P < 0.05$.
‡$P < 0.01$ testing the null hypothesis of equal proportions among incident and reactivated cases.
IUATLD indicates International Union Against Tuberculosis and Lung Disease.

and sinusitis. Reactivated cases were also more likely to have a positive value for a set of symptoms predictive of bronchial hyperresponsiveness, the IUATLD-DFP, than were new-onset cases (95% vs 76%, $P < 0.0001$).[14]

Twenty-nine percent of all cases (Table 5) had evidence of asthma attributable to occupational exposures using work-related symptoms and the maximum expert exposure rating, without regard to type of exposure (sensitizer or irritant), to classify cases according to the method shown in Table 1. Twenty-two percent of incident cases and 27% of reactivated cases had asthma attributable to occupational exposure and work-related symptoms based on irritant exposures. This difference was not significant ($P = 0.3$). Workplace sensitizer exposures and work-related symptoms indicated asthma attributable to occupational exposure in 20% of incident cases and 23% of reactivated cases.

Table 6 presents the occupational-attributable fractions for asthma stratified by age and gender. Generally, a larger fraction of asthma in males than females was attributable to occupation. More than half (56%) of men with asthma onset or reactivation between ages 22 to 29 had asthma attributable to occupational exposures. However, only nine men in this age category participated. Males between the ages of 30 and 39 also demonstrated large occupational-attributable fractions (42% and 39%, maximum and irritant exposures, respectively). The fraction of asthma attributable to occupational irritant exposures was consistently equal or greater than the fraction attributable to sensitizer exposures across all age and gender categories ($P = 0.047$). Occupational-attributable asthma was also higher among persons aged 30 to 39 compared with persons under age 18.

Adjusted occupational-attributable fractions (Table 7) computed using weighted estimating equations to control for potential participation bias were very similar to the crude estimates. We estimate that had all cases been interviewed, 29% (95% CI = 25–34) would have had moderate or strong evidence of asthma attributable to occupational exposures. We estimate that 26% (95% CI = 21–30) and 22% (95% CI = 18–27) of all cases would have had moderate or strong evidence of work-related asthma based on work-related symptoms and expert assessment of exposures to irritants and sensitizers, respectively. These models controlled for the effects of age, gender, and health insurance status on the probability of participation. Only gender was a significant predictor of response; results from mod-

TABLE 5
Summary of the Strength of Evidence for Asthma Attributable to Occupational Exposure, March 2000–February 2002

Exposure	Evidence	Incident, n* (%)	Reactivated, n (%)	Total, n (%)
Maximum of irritant and sensitizer exposure	RADS-like cases	2 (1)	0	2 (<1)
	Strong evidence	3 (2)	10 (4)	13 (3)
	Moderate evidence	29 (21)	74 (28)	103 (25)
	Total	34 (24)†	84 (32)†	118 (29)
Irritant exposure	RADS-like cases	2 (1)	0	2 (<1)
	Strong evidence	2 (2)	7 (3)	9 (3)
	Moderate evidence	27 (19)	65 (25)	92 (25)
	Total	31 (22)	72 (27)	103 (25)
Sensitizer exposure	Strong evidence	3 (2)	8 (3)	11 (3)
	Moderate evidence	25 (18)	52 (20)	77 (19)
	Total	28 (20)	60 (23)	88 (22)

*Percent of all participating asthma cases ($n = 405$).
†$P = 0.1$, testing the null hypothesis of equal proportions among incident vs reactivated cases.

TABLE 6
Percentage of Asthma Attributable to Occupational Exposure Among Respondent Cases by Exposure, Age, and Gender (n)

	Maximum Score, % (n)		Irritant Score		Sensitizer Score	
Age	Male	Female	Male	Female	Male	Female
<18 yr	8 (28)	6 (17)	8 (27)	5 (14)	4 (13)	5 (14)
18–21	2 (22)	8 (29)	2 (22)	6 (21)	2 (22)	6 (21)
22–29	5 (56)	10 (29)	5 (56)	7 (20)	3 (33)	7 (20)
30–39	13 (42)	22 (31)	12 (39)	19 (27)	11 (36)	17 (24)
≥40	11 (24)	32 (29)	10 (22)	27 (24)	9 (20)	24 (22)
All	39 (31)	78 (28)	37 (30)	64 (23)	29 (23)	59 (21)

Probability of asthma attributable to occupational exposure was greater with irritant than with sensitizer exposure ($P = 0.047$) and for persons 30 to 39 years old compared with persons younger than 18 ($P = 0.045$). There were no significant two- or three-way interactions.

TABLE 7
Occupational-Attributable Fractions Adjusted for Odds of Response to Questionnaire

Exposure	Adjusted Attributable Fraction	95% Confidence Low	95% Confidence High
Maximum of Sensitizer and Irritant	0.29	0.25	0.34
Irritant only	0.26	0.21	0.30
Sensitizer only	0.22	0.18	0.27

Multiple Regression Model for Response to Questionnaire	Odds Ratio	95% Confidence Low	95% Confidence High
Sex			
Male	1.00		
Female	1.42	1.07	1.90
Age			
40–<55 y	1.00		
30–<40 y	0.92	0.66	1.29
22–<30 y	0.82	0.53	1.26
18–<22 y	0.83	0.51	1.36
<18y	1.41	0.89	2.24
Health insurance			
Self	1.00		
Spouse/dependent	1.05	0.77	1.43
Medicare/Medicaid	1.07	0.49	2.32

Logistic regression model was controlled for the probability of responding to the questionnaire using weighted estimating equations.

els controlling only for gender were similar.

Discussion

Our estimates of the fraction of asthma attributable to workplace exposures in this population ranged from 20% to 32% (Table 5) depending on the types of cases and exposures analyzed. Estimates from weighted estimating equations, used to control for potential participation bias, produced similar estimates of occupational-attributable fractions.

Our estimates of occupational-attributable fraction were similar to those (19–26%) from the earlier pilot study conducted in the same HMO over a 3-month period in 1996.[4] The case-by-case approach once again produced consistently higher estimates than those reported from surveillance studies.[6,15–21] This is not surprising, because surveillance data are known to frequently underascertain cases and are more useful in identification of new etiologies or clusters of cases coming from particular worksites or occupations rather than estimation of prevalence or incidence.

The American Thoracic Society recently published a statement on the occupational contribution to the burden of airways disease and summarized 21 recent asthma studies, presenting data for computation of attributable fractions.[9] The estimates were from several different types of studies, including cross-sectional studies, cohort studies using national samples, and case–control studies primarily from population-based samples. The statement reported published attributable risks and, when possible, calculated attributable fractions in one of two ways: 1) by dividing the number of work-related cases by the total number of cases or 2) estimating the excess number of cases among exposed workers as compared with those unexposed. Results ranged from 4% to 76% with a median estimate that 15% of asthma can be attributed to occupational exposure.

Blanc and Toren conducted a similar review of literature published from 1966 to 1999, obtaining 43 attributable fraction estimates from 19 different countries.[22] The reviewers' values (median 25%) derived from reexamination of the published data were significantly greater than those published by the authors of the original studies included in the review (median 9%). Subsequently, Karjalainen et al conducted a population-based study of adult-onset asthma in working adults in Finland. These researchers combined prescription data from the Medication Reimbursement Register of the Social Insurance Institution and the Register of Occupational Diseases with population census data to calculate the occupational-attributable fraction among men and women. They found the occupational-attributable fraction for occupation to be

29% in men and 17% in women.[23] These new estimates were up to five times greater than those previously reported for Finland.[6,24] Mannino reports that in studies using exposed/unexposed methodologies or interviews of incident asthma cases, between 10% and 25% of cases are occupationally related.[25]

Our estimates of the occupational-attributable fraction for asthma in central Massachusetts HMO members range from 20% to 32% and tend to be slightly higher when only irritant exposures were considered relevant as compared with estimates based only on sensitizer exposures. These estimates of occupational-attributable fraction are consistent with those reported in the ATS Statement (range, 4–76%; median, 15%), with the review by Blanc and Toren, and with several other reports.[7,9,26–29] Our estimate for males (31%) is also consistent with that reported by Karkalainen et al.[24] However, our estimate for females (28%) appears to be much higher. This finding is somewhat surprising and may represent significant differences in occupational exposure among women in central Massachusetts and Finland.

The sensitivity and specificity of our adult-onset asthma case definition, as previously reported, were very good (93–99.3% sensitive and 99.6% specific), but our cohort entirely excluded prevalent cases, including those whose asthma was exacerbated by workplace exposures.[11] So, work-aggravated asthma was not included in our estimates of disease burden.

The HMO population providing the base for this study does not include families without health insurance coverage. Persons without health insurance may be more likely to have lower-paying, blue-collar, and service jobs that may also be associated with higher levels of exposure to irritants and sensitizers. To address this question, we note that roughly half of the study population was dependents with insurance coverage through a spouse or parent. Among the dependents, one would expect there to be individuals employed in jobs that did not offer health insurance and which may also have relatively high exposures. However, dependents were not at increased risk of having asthma attributable to work (data not shown). Thus, we have no evidence that dependents had dirtier, riskier jobs, and it seems likely that our results are applicable to the broader population of central Massachusetts. However, because of the absence of the uninsured population, there is potential for underestimation. Care must be taken when generalizing beyond the study population.

Our response rates were relatively low and could allow for participation bias. Males were less likely to participate and frequently reported higher exposures than females. Therefore, to obtain unbiased estimates of attributable, we used weighted estimating equations to correct for differential response rates by gender, age, and health insurance type.

Because the invitational letters, questionnaire, and consent dialogs were specifically designed to ensure that participants were unaware of our primary focus on occupational exposures, it is unlikely that cases overreported work-related symptoms and exposures or participated based on their own perception of a work-related cause for their asthma. There was no secondary gain (ie, workers' compensation or time off work) for subjects reporting work-related symptoms. Thus, a reporting bias as noted in previous workers' compensation clinic-based studies[30] seems unlikely. In addition, exposure was not self-assessed and the experts, who assigned exposure to individual jobs, were blinded to the timing of job start and end dates relative to asthma onset and the presence of work-related symptoms. Detailed analysis has shown that the exposure classification was unbiased (data not shown).

The case-by-case assessment of evidence for occupational asthma and estimates for the fraction of asthma attributable to occupation relied on a work-related symptom and exposure crosstabulation (Table 1). Thus, reporting work-related exposure alone did not result in a case being categorized as work-related asthma. This is an important contrast to the recent report on occupational asthma in six Canadian communities.[5] In that study, any subject thought to have relevant occupational exposure based on a job-exposure matrix and a checklist of specific agents was classified as probable or possible occupational asthma without respect to work-related symptoms. Our use of combined exposure and work-related symptoms to define occupational asthma is a major factor in producing a lower estimate. Had we classified everyone with exposure to irritants or sensitizers as having occupational asthma, then we would have computed occupational attributable fractions of 49% or 42%, respectively.

There may have been subjects who developed asthma as a result of a workplace exposure who did not experience or report work-related symptoms. We would have misclassified these cases. Some proportion of the asthmatics we categorized as having asthma attributable to occupation may have reported work-related symptoms at the time of interview, but their disease may not have been work-initiated. Rather, they may have developed work exacerbation during the interval between diagnosis and interview. We may have erroneously categorized these cases. Identifying new cases of asthma as they developed reduced the chance that cases would change jobs for health reasons before inclusion in the study. Additionally, during the interview, we gathered information on all jobs held during the previous year and assigned exposure based on jobs held at the time of diagnosis. This would have improved our chances of getting a more accurate and probably greater estimate of disease burden compared

with standard cross-sectional or retrospective methods. Our design also avoided recall bias likely to result from asking about jobs and asthma events in the distant past.

We found that a major fraction of adult-onset asthma among HMO members in central Massachusetts is attributable to occupational exposure. Our estimates are likely to be relatively accurate because of the prospective study design, blinding of subjects to the main hypothesis, blinding of exposure assessment experts to symptoms and job timing, and adjustment for factors influencing participation using weighted estimating equations. Our estimates of work-related asthma are consistent with recent estimates in the literature, and higher than older estimates and surveillance studies. The prospective design of the study reduced the potential for healthy worker bias that often results in underestimates of occupational disease burden.

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