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Risk and Incidence of Asthma Attributable to Occupational Exposure Among HMO Members

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Occupational asthma may account for a significant proportion of adult-onset asthma, but incidence estimates from surveillance of physician reports and workers' compensation data (0.9 to 15/100,000) are lower than expected from community-based cross-sectional studies of asthma patients. We conducted a prospective cohort study of 79,204 health maintenance organization members between the ages of 15 and 55 at risk for asthma. Computerized files, medical records, and telephone interviews were used to identify and characterize asthma cases. Evidence for asthma attributable to occupational exposure was determined from work-related symptoms and workplace exposure. The annual incidence of clinically significant, new-onset asthma was 1.3/1,000, and increased to 3.7/1,000 when cases with reactivation of previously quiescent asthma were included. Criteria for onset of clinically significant asthma attributable to occupational exposure were met by 21% (95% CI 12–32%) of cases giving an incidence of 71/100,000 (95% CI 43–111). Physicians documented asking about work-related symptoms in 15% of charts, and recorded suggestive symptoms in three cases, but did not obtain occupational medicine consultation, diagnose occupational asthma, report to the state surveillance program, or bill workers' compensation for any of them. These data suggest that the incidence of asthma attributable to occupational exposures is significantly higher than previously reported, and accounts for a sizable proportion of adult-onset asthma. Am. J. Ind. Med. 33:1–10, 1998. *© 1998 Wiley-Liss, Inc.*

KEY WORDS: incidence; occupational asthma; reactive airways dysfunction syndrome; cohort study; health maintenance organization

INTRODUCTION

Asthma incidence, prevalence, morbidity, and mortality appear to be increasing [Anonymous, 1995; Weiss and Wagener, 1990; Yunginger et al., 1992]. Theories about why asthma is increasing include diagnostic trends, changes in ambient and indoor air pollution, diet, and immunologic susceptibility [Seaton et al., 1994; Shirakawa et al., 1997; Soutar et al., 1997]. Recent estimates put the incidence of asthma in adults between 0.5–2.5/1,000 per year [Kivity et al., 1995; McWhorter et al., 1989; Yunginger et al., 1992]. Thus, primary care physicians see patients with new-onset asthma or with reactivation of latent asthma several times each year and must consider why these patients are developing active disease. Occupational exposures may account for a significant portion of such cases [Chan-Yeung and Malo, 1995].

Environmental factors account for about 40% of asthma cases [Duffy et al., 1990]. When clinically demonstrable that new-onset asthma was caused by agents specific to the work environment, a case is conventionally classified as occupational asthma and may involve either allergic or non-allergic mechanisms [Chan-Yeung, 1995]. However, evidence is mounting that asthma is multifactorial. This is most clearly evident for childhood asthma, where environmental tobacco

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smoke, infection, and allergen exposures are among the well-documented risk factors [Martinez et al., 1992; Sporik et al., 1990]. Similarly, work-related exposure to irritants is a risk factor for asthma in adults, although asthma arising in this way may not be recognized as occupational asthma by conventional clinical criteria [Beach et al., 1996; Flodin et al., 1996]. Epidemiologically, the problem of determining the risk of asthma attributable to work-place exposures has been addressed in three ways: 1) by surveillance of clinically diagnosed and reported occupational asthma cases [Gannon and Burge, 1993; Kanerva et al., 1994; Keskinen et al., 1978; Meredith, 1993; Meredith et al., 1991; Provencher et al., 1997; Reijula et al., 1996; Rosenman et al., 1997], 2) by determining the proportion of prevalent or incident asthma meeting an epidemiologic case definition for probable occupational or work-related asthma based on individual exposure, symptom, and clinical data [Blanc, 1987; Blanc et al., 1996; Timmer and Rosenman, 1993], and 3) by determining the excess prevalence of asthma among workers in high-exposure jobs compared with controls [Ng et al., 1994; Xu and Christiani, 1993; Kogevinas et al., 1996]. The first two of these methods require clinical recognition, while the third allows a more general detection of risk, independent of clinical presentation.

This study was designed to estimate the incidence and proportion of asthma attributable to occupational exposures and to test the hypothesis that surveillance data underestimate incidence of asthma attributable to workplace exposure. We used the second of the three methods described above and applied it to incident cases. We prospectively identified members of a health maintenance organization (HMO) with onset of clinically significant physician diagnosed asthma and used a structured telephone questionnaire to identify cases meeting an epidemiologic definition of asthma attributable to occupational exposure.

METHODS

Study Population

We studied a dynamic cohort of persons ages 15 through 55. The exclusion of subjects over age 55 was designed to limit the number of chronic obstructive pulmonary disease and cardiac asthma cases captured by our computerized record search. We included subjects ages 15–18 because many persons in this age group work in service jobs associated with increased risk [Ng et al., 1994] and some have significant potential for exposure while training for hazardous work in technical schools.

All subjects must have been enrolled in the Fallon Community Health Plan for at least six months. The HMO maintains enrollment, outpatient visit, and hospitalization records with attached diagnosis codes in centralized computer records. These records include medication and other treatments administered during a visit and prescriptions filled through the HMO [Oliveria et al., 1995; Walker et al., 1995]. Data on diagnoses and services provided are entered from ''encounter forms'' completed by providers at the time of service. To facilitate recording and data entry, the common diagnosis codes for each specialty are printed on the encounter forms so that they may be circled by the provider. Annual negotiation of capitation rates between the HMO and the physicians' group practice creates significant financial incentive for complete and accurate recording of services and diagnoses on these forms. Pharmacy records are generated at the time medications are dispensed. To ensure that searches of pharmacy records were complete, an index by type of medication was developed for all relevant pulmonary medications in the clinic formulary in consultation with the pharmacy director. The organization was recently rated as both the highest quality HMO in Massachusetts by the Massachusetts Healthcare Purchaser Group and the US by *Newsweek* (June 24, 1996). In addition, the HMO has a well-established occupational medicine department.

The study was approved by institutional review boards at the Fallon Clinic and the Harvard School of Public Health. Each month for three months potential members of the cohort were determined. Then, the population at risk was defined by computerized review of records from the previous 12 months. Persons meeting any of six criteria in the 12 months before the index month were considered not at risk during the index month and were excluded. The criteria were designed to allow persons with very mild, intermittent asthma that had not required treatment during the last 12 months into the population at risk for ''clinically significant asthma,'' enabling us to detect the onset of persistent asthma in persons for whom the disease had been in remission. The criteria were: 1) diagnosis of congestive heart failure (International Classification of Diseases, Ninth Edition codes 428.0–.9), chronic obstructive lung disease (496), bronchiectasis (494), emphysema (492.0–.8), chronic bronchitis (491.0–.9), bronchitis not otherwise specified (490), pulmonary hypertension (416.0–.9), or pulmonary embolism (415.0.9); 2) a total of four or more β-agonist inhalers dispensed; 3) an emergency room visit for asthma (codes 493.0–.9); 4) hospital admission with primary diagnosis of asthma; 5) diagnosis of occupational asthma (codes 504, 506.0–.9 or 507.8); or 6) dispensed a steroid or cromolyn inhaler, theophylline, or an outpatient nebulizer treatment within the previous 12 months.

To identify patients with onset of ''clinically significant asthma,'' potential cases (subject to confirmation by chart review) were defined as persons at risk who met any one of four criteria during the index month: 1) an emergency room visit for asthma (ICD codes 493.0–.9); 2) a hospital admission with a primary diagnosis of asthma; 3) a diagnosis of occupational asthma; 4) an outpatient

diagnosis of asthma accompanied by one of the following—dispensing a minimum of 2 β-agonist inhalers, or of 1 β-agonist inhaler with theophylline, or of 1 steroid or cromolyn inhaler, or an oral steroid taper or outpatient treatment with intravenous theophylline or nebulized β-agonists.

Chart Review

We subjected the 108 potential cases identified by the computerized search to chart review. It was determined that three potential cases had a diagnosis of chronic obstructive pulmonary disease or sleep apnea, six had preexisting asthma without evidence of recent exacerbation, and 24 had been prescribed significant medication for asthma within the past year (steroids, cromolyn, theophylline). These 33 cases were excluded. One case coded as occupational asthma had exclusively neurologic symptoms from solvents and was also excluded. We included seven cases where the primary care chart could not be obtained from an outlying physician's office and one where the primary care chart did not contain a diagnosis of asthma during the index month because these subjects had received hospital treatment for asthma during the index month. Otherwise, all primary care charts contained documentation that the treating physician had made a diagnosis of asthma during the index month and that the patient had not received significant treatment for asthma in the last year. Thus, the computerized search was 97% specific for physician-diagnosed asthma and 77% specific for documented onset of significant asthma treatment during the index month.

There were two reasons that the computerized search was less than 100% specific for onset of significant treatment. Some patients, who had not seen a physician or filled a prescription for at least a year, had anti-inflammatory therapy added as stepped care in the absence of a documented acute exacerbation. In others, according to the chart, patients had been prescribed anti-inflammatory medication during the last year but, according to the computerized records, only filled the prescription during the index month. This new compliance with therapy may have indicated an exacerbation, but because it did not signify a change in documented asthma severity, they too were excluded. Thus, the chart review ensured that case identification was specific for physician-diagnosed asthma and onset of significant asthma treatment during the index month.

Additional information was abstracted regarding documentation of 1) the patient's occupation, 2) provider's asking about an association with work, pets at home, and other home or environmental exposures, 3) diagnostic tests performed, and 4) types of providers seeing the patient.

Telephone Questionnaire

Patients were contacted after obtaining permission from the primary physician and parent, if a minor, and after sending a letter explaining the study and procedures for informed consent. Patients who did not have telephones ($n = 3$), and those who requested it ($n = 2$), were mailed the questionnaire. Reasons for not interviewing patients were: physician request ($n = 2$), subjects refused ($n = 4$), could not be located ($n = 1$), and language barrier ($n = 1$).

The questionnaire included the Discriminative Function Predictor (DFP) to confirm the diagnosis of asthma [Bumey et al., 1989]. The questionnaire also included three sets of questions to ascertain the work-relatedness of respiratory symptoms. The first set asked whether the subject's breathing troubles changed when away from work for two days or more. If yes, follow-up questions asked whether the symptoms were better or worse away from work, during the day at work, and at home at the end of the work day. The second set of questions asked about work-related use of a β-agonist inhaler, using a similar two-tiered approach. Finally, the subject was asked an open-ended question about what factors worsen his/her asthma.

The subject was then asked for a detailed work history, including current job (or school), second job, and all prior jobs going back at least two years. If unemployed, subjects were asked about their last job and why the job ended. Job descriptions and names of chemicals and processes were requested. A question about high-level exposure to dust, smoke, gas, or fumes led to a series of questions designed to detect the onset of breathing difficulties after such exposures. The questionnaire also included standard questions about other medical conditions, family history, cigarette smoke [Ferris, 1978], pets, hobbies, and other home exposures (fireplace, humidifier, water damage to the home, etc.). [Brunekreef et al., 1989].

Assessment of Work-Related Symptoms

A work-related symptom score (0–3) was assigned based on responses to questions about the work-relatedness of symptoms, medication use, and asthma triggers. One point was assigned for a response indicating that symptoms improved ''on weekends, vacations and other times away from work.'' Similarly, one point was assigned if medications were used less away from work. Finally, one point was assigned if the subject mentioned workplace exposures as a cause of worsening asthma in response to the open-ended question about asthma triggers.

Assessment of Exposure at Work

The work history was evaluated independently by two industrial hygienists blinded to other information about the subjects. They rated exposure to sensitizers and irritants separately. A three-point rating scale was based on a composite judgment as to the likelihood and intensity (including both frequency and concentration) of exposure:

"0 = Low/No Exposure," "1 = Likely/Moderate Exposure," or "2 = Highly Likely/Significant Exposure." Both reviewers used as a reference the SENSOR program's list of agents associated with occupational asthma [Chan-Yeung, 1990]. The independent occupational exposure ratings showed moderate agreement; weighted kappa statistic for interobserver agreement [Fleiss, 1981; Galecki, 1994] was 0.510 for sensitizers ($P < .001$) and 0.472 for irritants ($P < .001$). The ratings of the two experts were combined to give final irritant and sensitizer scores based on the sum of scores: sum = 0, final score = 0; sum = 1 or 2, final score = 1; sum = 3 or 4, final score = 2.

TABLE I. Decision Matrix: Strength of Evidence for Asthma Attributable to Occupational Exposure

Exposure score	Work-related symptom score 0	1	2	3
0	None	Weak	Weak	Moderate
1	Weak	Moderate	Moderate	Strong
2	Weak	Moderate	Strong	Strong

Case Definitions

We classified each case according to two dimensions: 1) whether the case was new-onset asthma, and 2) whether the case was attributable to occupational exposure.

All cases included in this study either had no prior history of asthma or had not required active treatment for a period of at least one year. Those who reported onset of breathing difficulty within the year before identification and had no prior history of asthma based on the interview and chart review were classified as new-onset asthma. The remaining subjects who met the inclusion criteria (i.e., were not receiving active treatment for asthma during the year before the index month), but who had ever had a diagnosis of asthma were classified as a reactivation of mild or latent asthma. Patients who required active treatment during the previous year and who suffered an exacerbation of their asthma during the index month were excluded (as described above).

Epidemiologic case definitions for asthma attributable to occupational exposure were based on criteria used by the SENSOR program [Matte et al., 1990; Reilly et al., 1994]. RADS-like cases were those who reported symptoms starting immediately after high-level exposure to irritants occurring within three months prior to the month identified as a case. The remaining cases were classified as no, weak, moderate, or strong evidence for asthma attributable to occupational exposure using the work-related symptom score and the work-exposure score in a cross-tabulation matrix (Table I). Separate matrices were constructed for sensitizers and irritants with the final classification of evidence for each case being the higher of the two. Cases with moderate or strong evidence or meeting the definition for a RADS-like case were considered asthma attributable to occupational exposure.

All of the cases we identified as attributable to occupational exposure would, if clinically confirmed, have been eligible for workers' compensation and subject to mandatory disease reporting in Massachusetts. There is consensus that cases meeting the criteria for new-onset asthma and for asthma attributable to occupational exposure could be classified as occupational asthma. The cases of reactivated asthma attributable to occupational exposure might be classified as either occupational asthma, work-related asthma, or occupationally- or work-aggravated asthma—depending on the classification scheme and details of each case.

Data Analysis

All data were entered into SAS datasets (versions 6.11, SAS Institute, Cary, NC) and summary data were analyzed in Excel (Microsoft, Redmond, WA). Incidence was computed using the total person-time at risk. Variance was computed assuming a binomial distribution and confidence limits were determined by the exact method [Zar, 1984]. Confidence limits for the proportion of cases with asthma attributable to occupational exposures were also computed based on the exact method for the binomial probability distribution. Tests of comparisons between incident cases and reactivated cases were performed with two-sided Fisher's exact test using SAS Proc Freq.

RESULTS

The study population consisted of, on average, 87,624 people with 79,204 at risk of developing asthma. The automated search identified 108 potential cases during 237,611 person-months of follow-up over the three-month study period (Fig. 1). After chart review to confirm physician-diagnosed asthma and onset of significant treatment, 74 of these patients were included as cases and 66 (89%) completed questionnaires. The nonrespondents included four males and four females and had a similar age distribution to that of the respondents ($P = 0.44$).

Of the interviewed subjects, 60 (91%) were employed at the time they became an eligible case. Fifteen of the 18 subjects ages 15 to 18 years were gainfully employed at the time. Of the 15 high school and two vocational school student cases, only one high school student reported no gainful employment during the two years before the interview. Minority ethnic and racial groups accounted for 13% of the interviewed subjects (Table II), twice their proportion in the relevant census tracts. Most subjects (61%) did not

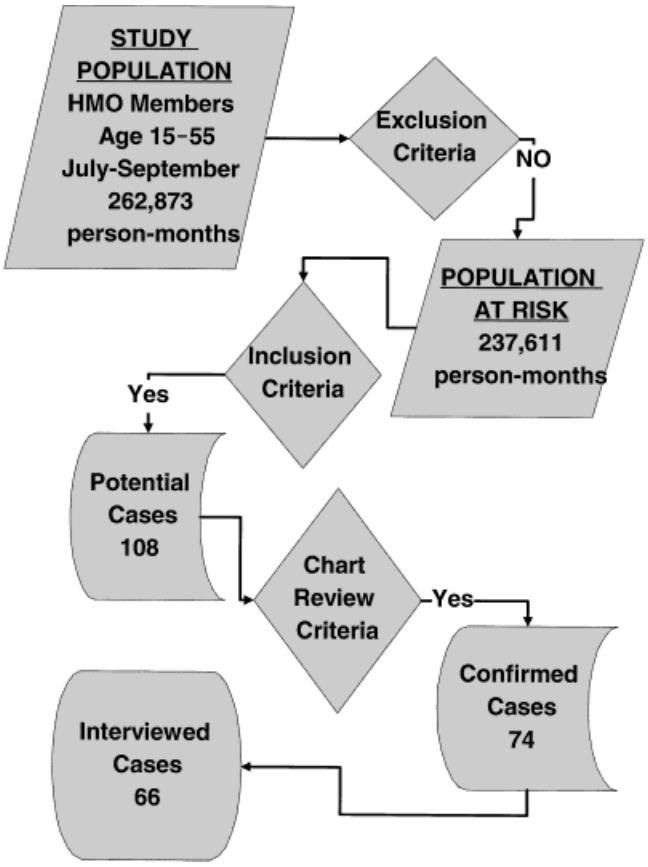

FIGURE 1. Identification of new-onset and reactivated asthma cases in a study of HMO members July–September 1995.

TABLE II. Description of Interviewed Cases in a Study of Asthma Among HMO Members, July–September, 1995

Age	15–18 (%)	18 (27)
	19–30	17 (26)
	31–55	31 (47)
Race/ethnicity	White, not Hispanic	58 (87)
	Hispanic	4 (6)
	Black	2 (3)
	Asian	1 (2)
	Other	1 (2)
Sex	Female (%)	36 (54)
	Male	30 (46)
Education*	<High school (%)	4 (8)
	High school	20 (42)
	Some graduate	13 (27)
	College or more	11 (23)
Family income	<$10,000 (%)	6 (9)
	$10–25,000	9 (14)
	$25–50,000	17 (26)
	$50–75,000	13 (20)
	>$75,000	9 (14)
	Refused/unknown	12 (18)
Source of health insurance coverage	Own job (%)	26 (39)
	Spouse/parent	29 (44)
	Purchased own	6 (9)
	Medicare/medicaid	3 (5)
	unknown	2 (3)

*Education of subjects age ≥18.

TABLE III. Summary of Interview Results in a Study of HMO Members, July–September, 1995

	New-onset asthma N (%)[a]	Reactivated asthma N (%)	All N (%)
All cases[b]	23 (35)	43 (65)	66
DFP[c]	20 (87)	41 (95)	61 (92)
Aware of diagnosis	13 (57)	39 (91)[d]	52 (79)
Atopy	16 (70)	34 (79)	50 (76)
Chronic bronchitis	7 (30)	10 (23)	17 (26)
Current smoker	2 (9)	9 (21)	11 (17)
Ex-smoker	5 (22)	9 (21)	14 (21)

[a]Percent of column total except as indicated.
[b]Percent of row.
[c]Discriminative Function Predictor for the diagnosis of asthma [Burney et al., 1989].
[d]Significant difference between rates for new-onset and reactivated asthma cases ($P < 0.01$).

obtain their health insurance from their own employer but were enrolled through a family member's employer or by other means. The majority (62%) of patients interviewed had never smoked (Table III), 21% were current, and 17% were ex-smokers. Smokers averaged 16 pack-years. Of the never smokers, 70% were passively exposed to smoke at work, at home, or both.

New-onset asthma cases accounted for 35% of the interviewed subjects, and a total of 26 cases when noninterviewed cases with complete charts were included, for an annual incidence of 1.3/1,000 [95% CI 0.92–1.8]. The incidence of clinically significant asthma, including reactivated cases, was 3.7/1,000 [95% CI, 3.1–4.5]. As might be anticipated in a managed care setting, physicians used physiologic testing sparingly. Of the 67 cases with complete chart reviews, we found that seven had peak expiratory flows, seven underwent spirometry (including five with response to bronchodilator), and none had methacholine challenge testing results in the clinic chart. The DFP, a strong predictor of bronchial hyper-responsiveness, was positive in 92% of patients interviewed (Table III), suggesting that our case identification algorithm based on a physician diagnosis of asthma was highly specific for asthma. However, 14 (21%) of the cases did not recall being told by a physician that they had asthma. These patients fell disproportionately among the new-onset cases ($P = 0.003$). Chronic phlegm production was reported by 26%, suggest-

TABLE IV. Summary of Evidence for Asthma Attributable to Occupational Exposure in a Study of HMO Members, July–September, 1995

	New-onset asthma N (%)[a]	Reactivated asthma N (%)	All N (%)
RADS-like case	2 (9)	1 (2)	3 (5)
Strong evidence	1 (5)	4 (9)	5 (8)
Moderate evidence	3 (13)	3 (7)	6 (9)
Total attributable to occupational exposure[b]	6 (26)	8 (19)	14 (21)
Weak evidence	10 (43)	23 (53)	33 (50)
No evidence	7 (30)	12 (28)	19 (29)

[a]Percent of column total.
[b]Sum of Rads-like cases, strong evidence, and moderate evidence cases.

ing some overlap with chronic bronchitis, although we had specifically excluded persons for whom physicians had recorded this diagnosis. Chronic phlegm and atopy were equally frequent and smoking rates were not significantly different between the new-onset and reactivated cases.

Table IV summarizes the results of the analysis for evidence for attribution to occupational exposure. Exposures and other details of the cases are shown in Table V. There were two new-onset cases with RADS-like histories stemming from high-level irritant exposures at work prior to the index visit; one was a fighter and the other was exposed to concentrated fumes from a drain cleaner. Another case, an office worker with a history of childhood asthma, reported onset of symptoms following exposure to high levels of dust from construction in her office. Five patients had strong evidence and six additional cases had moderately strong evidence for asthma attributable to occupational exposure (attributable risk). Thus, including RADS-like cases, 14 (21%) [95% CI 12–32%] of the 66 interviewed cases were attributable to occupational exposure. The proportion was 19% [95% CI 11–29%] when the eight nonrespondents were included, and 23% [95% CI 10–41%] when only new-onset cases were included. An additional 33 patients had weak evidence that occupational exposures were involved in the onset or reactivation of their asthma.

The 14 cases of asthma attributable to occupational exposure gave an estimated annual incidence of 71/100,000 [95% CI 43–111]. Including only those cases with strong evidence of an occupational etiology or RADS-like histories, eight (12%) of the cases gave an incidence of 40/100,000 [95% CI 20–73]. Incidence was similar for women and men and was at least as high among adolescents ages 15–18 (100/100,000) as among the older age strata 19–30 (84/100,000) and 31–55 (62/100,000). Smoking habits were no more frequent among the cases attributable to occupational exposures than among the other asthmatics ($P = 0.76$).

Of 67 complete charts, ten (15%) documented a provider asking about occupational triggers and of those, three reported finding a positive association with work. All three were classified as weak evidence for occupational causes (i.e., not attributed to occupational exposure) based on the questionnaire data and none were diagnosed or coded as occupational asthma by the treating physician. In only two of the 14 cases we categorized as attributable to occupational exposure did the treating physician ask about work and in neither case did the physician note work-related symptoms. Worker's compensation insurance was not charged for care of any of these patients and none of the cases could be located in the list of reported cases on file with the state SENSOR program.

Twelve of the 67 cases were referred to an allergist or pulmonologist and none to the Department of Occupational Medicine. Allergists and pulmonologists asked about work-related asthma triggers in 50% of the referred cases, accounting for more than half of all cases with a record of being asked. Primary and urgent care physicians recorded asking about occupational triggers in only 7% of the cases. Allergy and pulmonary specialists also asked more frequently about exposure to pets (50%) and other home-based factors (67%) than did other physicians (2% and 44%, respectively).

DISCUSSION

The incidence of new, adult-onset asthma in this population (1.3/1,000) was in the middle of the range of previously reported rates from community-based studies of this age group (0.5 to 2.5/1,000) [Kivity et al., 1995; McWhorter et al., 1989; Yunginger et al., 1992], indicating that the automated search and chart review was a sensitive as well as specific method for identifying onset of clinically significant, physician-diagnosed asthma among the HMO members. The study included 19,801 person-years (237,611 person-months) by following 79,203 subjects at risk for one quarter (July–September), including two months with low rates of acute asthma and one with high rates [Schwartz et al., 1993]. Thus, seasonal variation introduced some uncertainty in the asthma incidence estimate. However, it is unlikely that occupational asthma incidence in the general population is significantly influenced by seasonal fluctuations. The incidence of asthma attributable to occupational exposure, 71/100,000, was significantly higher than incidence estimated from surveillance data.

The estimate of attributable risk from this study falls in the middle of the range of attributable risk estimates (6–33%) reported by recent cross-sectional studies of occupation and asthma in the general population [Blanc, 1987; Blanc et al., 1996; Kogevinas et al., 1996; Ng et al., 1994;

TABLE V. Occupational Asthma Cases in a Study of HMO Members, July–September, 1995

Age/sex	Exposure	Job	Earliest onset of asthma	Work-related symptom score	Exposure score[a]	Practitioner asked about work exposure
		RADS-like				
37/M	Fire smoke	Firefighter	1995[b]	0	1/1	No
40/F	Drain cleaner	Restaurant manager	1995[b]	2	0/2	No
		RADS-like exacerbation				
41/F	Dust from construction	Office worker	1960	2	2/2	No
		Strong evidence for occupational asthma:				
30/M	Red cedar dust	Carpenter	1995[b]	3	2/2	No
20/M	Welding fume	Student, technical school	1985	2	2/2	No
22/M	Rubber dust	Goggle maker	1974	2	2/2	No
49/F	Glues, wool dust	Hat maker	1993	3	0/2	—[c]
46/F	Cleaning fluids, cigarette smoke	Bartender	1990	3	0/2	—[c]
		Moderate evidence for occupational asthma				
37/M	Machining fluids	Assembler, tool manufacturing	1995[b]	1	2/2	Yes
50/F	Various	Hairdresser	1959	1	2/2	—[c]
15/M	Lacquer, epoxy	Archery repair	1990	1	1/1	No
19/F	Variety store	Retail clerk	1994[b]	1	1/1	No
16/M	Grass, pesticides	Golf course mower	1985	1	0/1	No
45/F	Household cleaners	Home-care attendant	1995[b]	1	0/1	Yes

[a]Sensitizer/irritant: Score is a composite of the industrial hygienists' judgment of likelihood, frequency, and intensity of exposure.
[b]New-onset asthma.
[c]Chart not available or insufficient information in chart.

Timmer and Rosenman, 1993; Xu and Christiani, 1993]. However, the incidence of asthma attributable to occupational exposure we observed was significantly greater than the incidence of occupational or work-related asthma reported by surveillance systems [Gannon and Burge, 1993; Kanerva et al., 1994; Keskinen et al., 1978; Meredith, 1993; Meredith et al., 1991; Provencher et al., 1997; Reijula et al., 1996; Rosenman et al., 1997].

Surveillance methods, the first of the three methods described in the Introduction, were used to estimate the annual incidence of occupational asthma from voluntary physician reports in the UK (0.9 to 6.5 cases/100,000) [Gannon and Burge, 1993; Meredith, 1993; Meredith et al., 1991]. In Finland, higher rates were found based on surveillance of insurance company reports (15/100,000) [Kanerva et al., 1994] than from voluntary physician reporting (3.6/100,000) [Keskinen et al., 1978]. A comparison of physician reported occupational asthma with the social insurance registry of all moderate to severe asthma gave a population attributable risk of 4.8% [Reijula et al., 1996]. In Quebec, Canada, voluntary physician reporting gave an estimated annual incidence of 7.9/100,000 among men and 4.2/100,000 among women [Provencher et al., 1997]. In Michigan, physician, hospital, and workers' compensation reports collected by the SENSOR (Sentinel Event Notification System for Occupational Risks) program gave an estimated incidence of 2.9/100,000 [Rosenman et al., 1997]. However, follow-up workplace investigations of fewer than half of the implicated workplaces found more cases of probable work-related asthma than the entire number reported from all workplaces. Analysis of UK data also suggested that community physicians may significantly underreport occupational asthma diagnoses [Gannon and Burge, 1993]. However, even insurance-based reporting may underestimate occupational asthma incidence if the condition is underdiagnosed.

The second method (analogous to the one used here), determining the proportion of asthma cases that meet an epidemiologic case definition of asthma attributable to occupational exposure was used in a Michigan hospital discharge study. Between 3 and 20% of hospitalized asthmatics had asthma attributable to workplace exposures [Timmer and Rosenman, 1993]. Using similar methods, studies of chronic asthma and disability found that between 6 and 17%

of prevalent asthma met an epidemiologic case definition of occupational asthma [Blanc, 1987; Blanc et al., 1996]. Our results are at the upper end of the range from these reports.

Finally, using the third method one can determine the excess prevalence of asthma among workers in exposed jobs by comparison with workers in unexposed jobs. This method was used in a study of Beijing residents, in which physician-diagnosed asthma was significantly more prevalent in persons with dust, gas, or chemical fume exposure at work than in their neighbors. Excess asthma among the exposed accounted for approximately 15% of all cases [Xu and Christiani, 1993]. A community clinic based case-control study in Singapore found that asthma cases were more likely than controls to have ever worked in service or production occupations, as compared with professional, managerial, and sales [Ng et al., 1994]. The population attributable risk of asthma due to exposures in the service and production sectors was 33%. A community based, cross-sectional study in Spain found that population-attributable risk of adult-onset asthma (using a strict definition, including documented bronchial hyperreactivity) from certain high-risk occupations was 6 to 9% [Kogevinas et al., 1996].

The increased risk of asthma in relation to occupational exposures, described by community-based studies using the third method, may not indicate an increased risk of clinical occupational asthma. This may occur because general workplace air pollution and irritant exposures may be causes of asthma, while not giving rise to cases with specific sensitization to workplace exposures, or otherwise clinically recognizable as occupational asthma [Beach et al., 1996; Flodin et al., 1996].

We found that, although we only studied patients with physician-diagnosed asthma, a significant proportion of asthma patients (43% of new-onset and 9% of reactivated cases) did not report having physician-diagnosed asthma in response to the standard questions about asthma history [Ferris, 1978]. Thus, studies using a questionnaire approach to determine the prevalence of asthma, especially if interest focuses on recent-onset asthma, may be subject to underreporting. Symptoms, as anticipated, were more sensitive.

Overall asthma incidence may have been underestimated in this study because patients seeking care outside of the health plan would not have been counted, and this may have been more likely for occupational asthma covered by workers' compensation. Cases lost due to outside-of-plan medical care would have biased toward lower incidence and attributable risk estimates. However, outside-of-plan care for new-onset or newly reactivated asthma seems unlikely. It is unlikely that cases of clinically significant, physician-diagnosed asthma treated through the HMO were missed due to use of medications or diagnosis codes not covered by the computerized search because we were able to identify and search the database for all brands of asthma medication available to HMO members, and all of the asthma and occupational asthma-related ICD codes. Any loss of sensitivity due to coding errors would have affected occupational and non-occupational cases similarly. Thus, lower sensitivity would underestimate occupational asthma incidence and have little or no impact on attributable risk.

Asthma attributable to occupational exposure could have been overestimated if our criteria were not sufficiently specific. Malo et al. [1991] reported that the history alone is not sufficient to diagnose occupational asthma in the setting of medical consultation to determine eligibility for workers' compensation. They found a 63% positive predictive value of history alone and an 83% negative predictive value. In the present study, however, subjects were not aware that the structured interview would be used to evaluate possible occupational causes, and patients were not seeking compensation. Thus, there was no incentive to report particular symptoms or exposures. Malo et al. used an unstructured interview and narrow definition of occupational asthma that excluded asthma resulting from irritants, from complex mixtures in which sensitizers could not be identified, and occupationally aggravated asthma. We also excluded work-aggravated asthma (as defined by Rosenman et al. [1997]). However, we used a broader definition of asthma attributable to occupational exposure based on the work-related asthma definition from the SENSOR programs. Because of this broader definition, a higher positive predictive value would be expected in the present study. If all our cases with evidence for an occupational etiology were evaluated by thorough workplace investigation and physiologic studies [Chan-Yeung, 1995], some cases with moderate evidence might not be confirmed. Conversely, it is likely that some cases with weak evidence would be confirmed. Furthermore, if the positive and negative predictive values in this study were 63% and 83%, respectively, then the true number of cases attributable to occupational exposure would have been 18, or four more than we actually identified (9 of 14 the cases that were attributed to occupational exposure and 9 of the remaining 43).

The carpenter we identified with incident asthma and exposure to red cedar represents a classic example of occupational asthma and an example of the importance of early diagnosis. Western red cedar workers have been extensively studied and it is estimated that 4–14% of workers exposed to the dust of this wood develop asthma [Chan-Yeung, 1994]. Plicatic acid, a low-molecular weight constituent of Western red cedar, is considered the responsible agent. A study of workers, who had been diagnosed and ceased exposure approximately four years earlier, found that those with persistent asthma at follow-up had been diagnosed later in the course of their disease than workers who had completely recovered [Chan-Yeung et al., 1987]. There is also evidence, based on patients with diisocyanate-induced occupational asthma, that early anti-inflammatory therapy may be useful [Paggiaro et al., 1994]. Thus, the case

of red cedar asthma identified by our epidemiologic methods emphasizes the point that primary care physicians may be able to improve the prognosis for adolescents and adults with new-onset asthma by taking an occupational history, urging the elimination of exposure, and initiating anti-inflammatory treatment.

The HMO participating in this study has an excellent record for quality of care. However, none of the cases we identified were reported to the Massachusetts SENSOR program, largely because physicians did not take the necessary history to make a diagnosis of occupational asthma—physicians documented asking about occupational factors in only 14% of the cases attributable to occupational exposure and did not refer any cases for investigation of possible occupational asthma. This serves to substantiate the fact that surveillance programs suffer from underreporting and cannot give reliable estimates of incidence, although they can identify sentinel events and may be able to measure changes in incidence over time. In addition, none of the medical care for these cases was charged to workers' compensation insurance. Given that approximately 20% of cases were probably occupational, this implies a significant loss of revenue. More importantly, prompt diagnosis is essential because early cessation of exposure and early anti-inflammatory treatment may improve the prognosis of occupational asthma.

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