

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)

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

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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, multi-specialty 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: de-

mographics (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

TABLE 1
Occupational Asthma Case Definition and Classification Matrix

| Expert Exposure Rating | Work-Related Symptom Score | | | |
|------------------------|----------------------------|----------|----------|----------|
| | 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.

interval [CI], 3.9–9.4) for sensitizers and 3.8 (3.0–4.8) for irritants.

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 Zhao¹³ 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 signifi-

TABLE 2
Population Demographics of Adult-Onset Asthma Cases

| | Respondents | | | Nonrespondents | All Cases |
|--------------------------------------|-------------|-------------|----------|----------------|-----------|
| | Incident | Reactivated | Total | | |
| 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) |

cantly 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 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 attrib-

utable 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)

| Age | Maximum Score, % (n) | | Irritant Score | | Sensitizer Score | |
|--------|----------------------|---------|----------------|---------|------------------|---------|
| | 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 | 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 | 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 surveil-

lance 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 studies³⁰ 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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ORIGINAL ARTICLE

The frequency of workplace exacerbation among health maintenance organisation members with asthma

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Objectives: Workplace conditions can potentially contribute to the worsening of asthma, yet it is unclear what percentage of adults with asthma experience workplace exacerbation of symptoms. The objective of this investigation was to determine the prevalence of workplace exacerbation of asthma (WEA).

Methods: Adults with asthma aged 18–44 were enrolled into the baseline survey of a longitudinal study. Members of a health maintenance organisation were considered candidates for participation if they fulfilled membership, diagnostic, and treatment criteria based on automated review of electronic billing, claims, and pharmacy records. Diagnosis and treatment were confirmed by manual review of medical records. A telephone questionnaire was administered. A work related symptom score was assigned to each participant based on responses to questions about work related asthma symptoms, medication use, and symptom triggers. Blinded to participants' answers to these questions, two researchers independently reviewed the self-reported work histories and assigned exposure ratings. A final exposure score was then calculated. Participants with sufficient evidence for work related symptoms and exposure were classified as having WEA.

Results: Of the 598 participants with complete data, 557 (93%) were working, and 136 (23%) fulfilled the criteria for WEA. Those with WEA were more likely to be male and to report that they had been bothered by asthma symptoms during the past seven days.

Conclusions: Workplace exacerbation of asthma was common in this study population, occurring in over a fifth of these adults with asthma. Physicians should consider that work can contribute to the exacerbation of symptoms when treating adults with asthma.

Work related asthma is the most common non-asbestos lung disease seen in occupational health clinics in the United States,^{1,2} as well as the most common occupational lung disease in many industrialised countries.^{3,4} Researchers in the US have estimated that from 3% to 21% of asthma among adults is attributable to workplace exposures.^{5–9} A recent review of the relevant literature by a committee of the American Thoracic Society concluded that 15% of asthma among adults can be attributed to occupation.⁹ Work related asthma includes individuals with new onset asthma caused by workplace exposure to sensitisers or irritants, as well as those with pre-existing asthma that is exacerbated by workplace exposures.¹⁰

The prevalence of workplace exacerbation of asthma (WEA) has been investigated using a variety of data sources. In the province of Ontario in Canada, the Worker Compensation Board reported that half of all asthma claims received between 1984 and 1988 involved exacerbation.^{11,12} Cohorts of patients with occupational asthma treated in occupational and environmental medicine clinics in Massachusetts and Washington included 18% and 27%, respectively, with WEA.^{13,14} The Sentinel Event Notification System for Occupational Risks (SENSOR) is a case based surveillance programme that has been applied to different diseases in the US. From SENSOR activities in four states during 1993–95, 19% of work related asthma cases were considered to be work aggravated asthma, with the rest classified as new onset cases.¹⁰

The prevalence of WEA can also be expressed as a percentage of all cases of adult asthma, an estimate that

can be derived by conducting population based (or quasi-population based) studies. From a community based sample of adults in Australia, 20% of respondents with asthma stated that their symptoms were worse as the result of work.¹⁵ From a study in Norway, 33% of the men and 18% of the women with asthma reported that they had ever had respiratory symptoms associated with work that abated on weekends or holidays.¹⁶ From an interview survey of adults with asthma enrolled in a health maintenance organisation (HMO) in the state of Colorado in the US, approximately 25% of the 1461 participants reported that their asthma was made worse by their current work environment.¹⁷ From a population based survey conducted in the state of Maine, 25% of 64 adults with asthma reported that their coughing or wheezing was worse at work.¹⁸

Although the existing population based surveys were informative, an in-depth study that used a more rigorous case definition was needed to provide a more accurate estimate of the prevalence of WEA and a better understanding of the circumstances that contributed to this problem. This additional information could then be used to plan preventive actions. Therefore, in 2000, the National Institute for Occupational Safety and Health (NIOSH) initiated the Workplace Exacerbation of Asthma Project to

Abbreviations: FCHP, Fallon Community Health Plan; HMO, health maintenance organisation; HSRB, Human Subjects Review Board; ICD-9, International Classification of Diseases, Ninth Revision; NIOSH, National Institute for Occupational Safety and Health; SENSOR, Sentinel Event Notification System for Occupational Risks; WEA, workplace exacerbation of asthma

investigate the frequency, causes, and consequences of WEA. This project was divided into three studies conducted over a five year period. Adults with asthma were enlisted and interviewed in the baseline study, and were re-interviewed approximately two years later in the follow up study. The validation study was intended to validate self-reported work related asthma symptoms in a subset of baseline study participants. Consistent with the intention of conducting a population based study, NIOSH contracted with a research department in an HMO to implement data collection.

In the current analyses, we used data from the baseline study to determine what percentage of adults with asthma fulfilled criteria for WEA.

METHODS

Human subjects review and approval

The NIOSH Human Subjects Review Board (HSRB) reviewed and approved the research protocol, as did the HSRB of the contracted HMO, Fallon Clinic, Inc, Research Department in Eastern and Central Massachusetts.

Identification of participants

Potential participants were selected from members of the Fallon Community Health Plan (FCHP). Almost all (99%) FCHP members were enrolled into the plan without health screening. Most (83%) entered as part of an employer based programme, but an additional 16% were Medicare or Medicaid patients. Study participants were enrolled if they met criteria applied using both automated review of electronic billing, claims, and pharmacy records, and manual chart review. These methods and their validity are discussed in a previous publication.¹⁹

1. Electronic records were scanned each month for 16 consecutive "index" months (that is, September 2000 to December 2001) to identify potential participants who met age and FCHP membership criteria:

(a) adult aged 18–44 years in index month

(b) enrolled with the FCHP for at least six months prior to the index month.

2. Next, exclusion criteria were applied to electronic records from the previous 12 months to identify the at-risk population. People were excluded if there was a recorded diagnosis of congestive heart failure (International Classification of Diseases, Ninth Revision (ICD-9) codes 428.0–428.9), bronchiectasis (ICD-9 494), emphysema (ICD-9 492.0–492.8), pulmonary embolism (ICD-9 415.0–415.9), or pulmonary hypertension (ICD-9 416.0–416.9). People were also excluded if they did not have one of the following in the previous 12 months: emergency room visit with a primary diagnosis of asthma (ICD-9 493.0–493.91), hospital admission with a primary diagnosis of asthma, diagnosis of dust pneumonopathy (ICD-9 504–507), diagnosis of red cedar asthma (ICD-9 495.88), diagnosis of detergent asthma (ICD-9 507.8), asthma diagnosis and outpatient nebulisation treatment, dispensing of any one of several types of long acting asthma controller medications (for example, beta-agonist, leukotriene inhibitor, theophylline, corticosteroid), diagnosis of asthma and dispensing of oral steroids, asthma diagnosis and dispensing of four or more beta-agonist metered dose inhalers.

3. The electronic records from the index month for the at-risk population were then scanned to identify which potential participants were receiving current treatment for asthma, according to whether they met one of the following criteria:

(a) emergency room visit for asthma (ICD-9 493.0–493.91), or

(b) hospital admission with a primary diagnosis of asthma, or

(c) outpatient diagnosis of asthma accompanied by one of the following:

i. dispensing of a minimum of one beta-agonist inhaler, or
ii. dispensing of a beta-agonist inhaler with theophylline,

or

iii. dispensing of a steroid or cromolyn inhaler, or

iv. dispensing of an oral steroid taper, or

v. an outpatient treatment with intravenous theophylline, or

vi. an outpatient treatment with nebulizer, or

vii. dispensing of a nebulizer to relieve airway obstruction,

or

viii. dispensing of a leukotriene inhibitor.

(d) diagnosis of dust pneumonopathy (ICD-9 504–507), or

(e) diagnosis of red cedar asthma (ICD-9 495.88), or

(f) diagnosis of detergent asthma (ICD-9 507.8), or

(g) dispensing of any one of several types of long acting asthma controller medications (for example, beta-agonist, leukotriene inhibitor, theophylline, corticosteroid), with or without a diagnosis of asthma.

4. A research nurse manually reviewed the medical records of all potential study participants to determine if there was a confirmed diagnosis of asthma with onset prior to the past year. During this review of records, the research nurse abstracted demographic and medical data, and assigned a level of severity.²⁰ The four levels of severity were mild intermittent, mild persistent, moderate persistent, and severe persistent.

The contractor contacted potential participants meeting criteria 1–4 by mailing each one a letter which explained the study. The letter was followed by a telephone call approximately two weeks later. Interviewing was conducted March 2001 through August 2002. Interviewers attempted to reach each potential respondent seven times at various times during the day and week before giving up. The next selection criterion was determined early in the telephone interview.

5. When reached by telephone, the potential participant reported "yes" to both of the following questions:

(a) Have you ever had asthma?

(b) Have you taken any medication for asthma or other breathing problems within the past 12 months?

If the potential participant provided the "yes" answers specified in criterion 5, the interviewer continued the telephone call by reviewing the purpose of the study, answering questions, and asking the individual to provide verbal informed consent. To compensate participants for their time, an honorarium of US\$20 was provided to each person who completed the questionnaire. Once efforts to contact someone were terminated, a code was assigned to indicate the final call disposition, such as questionnaire completed, refused to participate, or could not contact.

As a study of the exacerbation of existing asthma, it was necessary to ensure that participants did not have recent onset of their asthma. This was addressed during the review of medical records, in which we ascertained that onset was prior to the past year (criterion 4). To be certain that the person's asthma did not start during the past year, we required the following based on information gathered during the interview:

6. Participant reported that the date of their first asthma attack was at least 14 months before the date of interview.

Telephone interviews

The baseline questionnaire incorporated items from several other questionnaires.^{21–22} Responses to questions provided information on asthma history (for example, date of onset and suspected cause of asthma), severity of current asthma, and the asthma-work association. A series of validated questions were included to measure the social impact of

asthma.²³ Also, respondents were asked to provide detailed descriptions of jobs they had held during the previous 12 months.

We used a computerised assisted telephone interview system to administer the baseline questionnaire. Before starting the interviews, the NIOSH project manager trained six interviewers in basic interviewing techniques. Topics of instruction included the interviewers' role in the project, asking the questions, clarifying the questions, and probing for appropriate responses. All interviews were recorded on audiotape so that the NIOSH project manager could monitor the quality and accuracy of the data collection. After an interviewer was trained, the project manager reviewed the audiotapes from the first 10 questionnaires administered by the interviewer. Initial problems included not reading the questions as written and insufficient probing for appropriate responses. After the initial review of 10 questionnaires for each interviewer, a 20% sample of the remaining completed questionnaires were reviewed. The findings from these monitoring efforts were communicated back to the contractor's project manager in a timely manner in an effort to improve the interviewers' performance.

Criteria for workplace exacerbation of asthma

The definition of workplace exacerbation of asthma was based on a self-report of work related worsening of symptoms and a judgment by an expert panel that the participant was likely to have had exposure to asthmagenic agents (for example, sensitisers and irritants) at work.

A work related symptom score (0–3) was assigned to each participant based on responses to questionnaire items concerning the previous 12 months. One point was assigned for each of the following that were met: (1) asthma symptoms got better on weekends, vacations, or other times when away from work; (2) use of an inhaler or nebulizer was greater on work days; and (3) in response to an open-ended question about asthma triggers, the participant identified conditions at work that set off asthma symptoms or breathing trouble.

Review of the data revealed problems with how participants responded to the open-ended question about asthma triggers. In particular, some participants listed conditions that made their asthma worse, and then stated that these conditions bothered them everywhere they went, including at work. This broad assignment of location was less precise than desired, so two of the researchers independently re-evaluated the responses and assigned each reported work related trigger to one of five categories: (1) traditional work related asthma agents (for example, chemicals, dust, fumes, molds); (2) physical work related agents (for example, physical exertion, cold air, humidity, temperature change); (3) stress at work; (4) second hand smoke at work; (5) an infection or non-occupational allergy. After independently evaluating each of the responses, the two researchers compared their results and resolved disagreements on a case-by-case basis. Any work related triggers in the first four categories resulted in a "yes" response for the new workplace trigger variable. The results of this validation effort were the third element used to construct the final work related symptom score for each employed participant.

An industrial hygienist and an epidemiologist independently reviewed the detailed job descriptions and assigned exposure scores to each job held during the 12 months before interview. The description of each job was based on responses to 29 items in the questionnaire. The information gathered included job title and tasks, what the company did or manufactured, ventilation in the worksite, responses to an open-ended question about chemicals and materials used or contacted at work, and responses to a series of close-ended

Table 1 Protocol for assigning subscores for exposure to asthma agents

| Score | Probability | Intensity | Frequency |
|-------|---------------|-----------|------------------------|
| 0 | <50% | Low | Once per week or less |
| 1 | ≥50% but <80% | Moderate | Some part of most days |
| 2 | ≥80% | High | Most of the time |

questions about different types of exposures and conditions at work that could contribute to the exacerbation of asthma. The reviewers were blinded to any other information about the participant, including responses used to determine the work related symptom score. Both reviewers were familiar with asthma agents that occur in occupational settings. They relied on various reference materials to inform their judgments, including a published list of potential agents²⁴ and a list of occupational asthmagens compiled by the Association of Occupational and Environmental Clinics that is available on the internet.²⁵

Ratings were assigned separately for sensitiser and irritant exposures and ranged from 0 to 2. Three subscores were assigned, one each for probability, intensity, and frequency of exposure. The subscores followed the criteria presented in table 1. To arrive at a score for either sensitisers or irritants, the three subscores were tallied. The sum of subscores and the corresponding score were: sum = 0 or 1 then score = 0; sum = 2 or 3 then score = 1; sum = 4, 5, or 6 then score = 2. The scores from the two reviewers were added together to achieve separate summary scores for sensitisers and irritants. The sum of scores and corresponding summary score were: sum = 0 then summary score = 0; sum = 1 or 2 then summary score = 1; sum = 3 or 4 then summary score = 2. The final exposure score was the higher of the summarised sensitiser and irritant scores.

Our decision matrix for a work related pattern is closely modeled after the approach developed by Milton and colleagues.⁸ The final exposure score and work related symptom score were cross tabulated to determine strength of evidence for WEA. If someone had worked more than one job in the past 12 months, the exposure score was used for the most recent job or the job worked at most if there were multiple current jobs. Cases were classified as having no, weak, moderate, or strong evidence for workplace exacerbation based on a decision matrix. Participants with moderate or strong evidence were classified as having WEA. This group included all the participants with both exposure and symptom scores greater than 0, and those with a combination symptom/exposure score of 3/0.

Statistics

Data analyses were conducted using SAS statistical software for personal computers.²⁶ To test for statistical significance, we used χ^2 for comparisons involving categorical data, and in particular the continuity corrected χ^2 for data in 2-by-2 tables.²⁷ We used Student's *t* test for comparisons involving continuous data.²⁷ *p* values less than or equal to 0.05 were considered statistically significant.

RESULTS

There was a monthly average of approximately 48 000 people aged 18–44 years enrolled in the HMO during the study period. Based on review of the electronic patient records, 1251 individuals met selection criteria 1–3, of whom 978 also met criterion 4 that was based on manual chart review. The interviewers were not able to reach 322 (33%) of the 978 by telephone after seven attempts. Of the 656 contacted by telephone, 640 (65% of 978) agreed to participate and 16

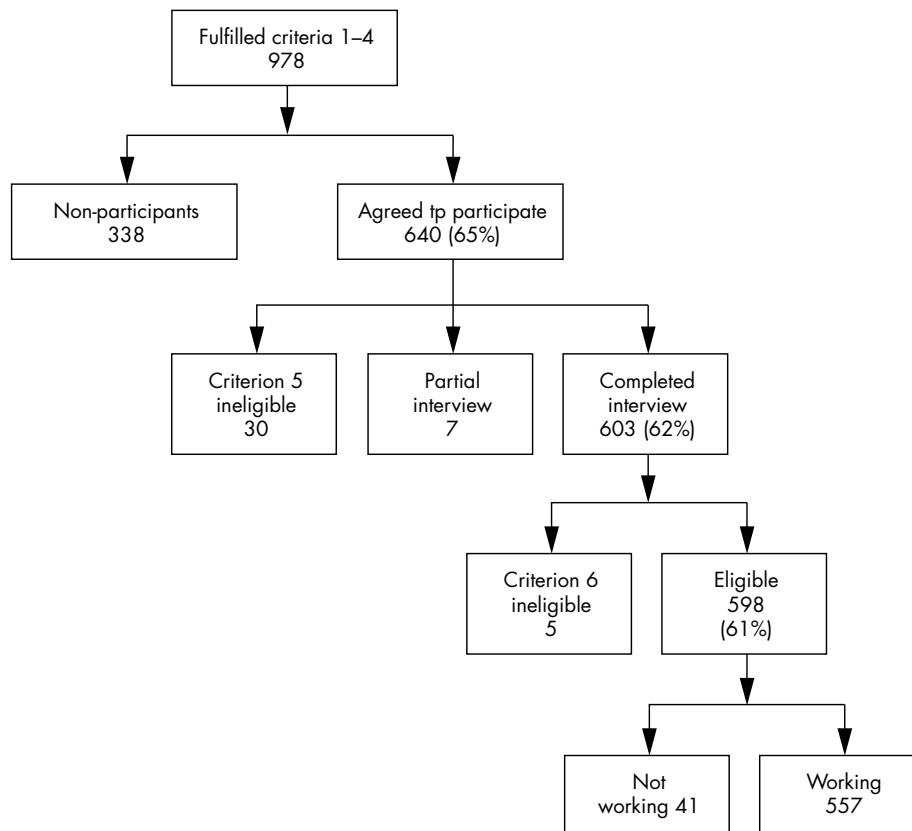


Figure 1 Disposition of candidates for study.

refused (fig 1). Another 30 potential participants reported they did not have asthma or did not use medications for asthma in the past 12 months (that is, did not fulfill selection criterion 5) and were not interviewed. Of the 610 who started the interview, seven completed only part of the baseline questionnaire and five were excluded due to recent onset of asthma (criterion 6). Data from the remaining 598 participants (that is, 61% of the 978 who fulfilled selection criteria 1–4) were included in the following statistical analyses and will be called participants.

The 380 non-participants were similar in age to the participants, but more likely to be male (44% v 31%, $p < 0.0001$). Members of both groups were about equally likely to have moderate or severe asthma (that is, 39% of participants, 38% of non-participants). However, the participants had proportionately more in the mild persistent category (30% v 23%) and fewer in the mild intermittent category (30% v 39%) than the non-participants ($p = 0.02$).

The study participants were overwhelmingly white (95%) and only 6% reported Hispanic ethnicity. Women (69%) outnumbered men (31%) by more than 2 to 1. By design, their ages ranged from 18 to 44 years in the index month when they were first identified as candidates for study, but

Table 2 Percentage of working participants judged to have had exposure to sensitizers and/or irritants at work, by age and gender*

| Age (years) | Male | Female |
|-------------|---------------|---------------|
| 18–25 | 62% (26/42) | 40% (36/91) |
| 26–35 | 61% (39/64) | 37% (42/113) |
| 36–45 | 61% (45/74) | 43% (75/173) |
| Total | 61% (110/180) | 41% (153/377) |

* $p < 0.05$ in each age category comparing males to females.

one of the participants had attained the age of 45 by the time he was interviewed. So, the 598 study participants ranged in age from 18 to 45 years when interviewed, with a mean of 32.8 years (SD 7.8). The participants included 19% current and 23% former cigarette smokers, and 37% had completed college. Of the 446 who answered the question about income, 52% earned a gross weekly salary of at least \$550.

The age at onset of asthma ranged from 1 to 42 years, the mean was 15.5 (SD 10.8), and 366 (61%) participants had onset before the age of 18. A family history of asthma was common, with 183 (31%) reporting that either their mother or father had asthma. When asked what they thought caused their asthma, many participants replied heredity, infections,

Table 3 Distribution of 598 baseline study participants by strength of evidence for workplace exacerbation of asthma

| Exposure score† | work related symptom score | | | | Total |
|-----------------|----------------------------|-----------|-----------|-----------|-------|
| | 0 | 1 | 2 | 3 | |
| 0 | 215‡ | 92 | 15 | 13 | 335 |
| 1 | None | Weak | Weak | Moderate* | 220 |
| | 121 | 66 | 22 | 11 | |
| 2 | Weak | Moderate* | Moderate* | Strong* | 43 |
| | 19 | 19 | 3 | 2 | |
| Total | 355 | 177 | 40 | 26 | 598 |

*23% ($n = 136$) of the 598 study participants had moderate or strong evidence, and were classified as having workplace exacerbation of asthma.

†Based on the higher of two scores for sensitizer and irritant agents, as independently assigned by two researchers after review of each participant's work history for the 12 months before interview.

‡Includes 41 participants who were unemployed during the 12 months before interview.

Table 4 Comparison of study participants with and without workplace exacerbation of asthma

| Descriptive variables* | Workplace exacerbation of asthma | | p Value |
|---|----------------------------------|--------------|---------|
| | Yes (n = 136) | No (n = 462) | |
| Race, % white | 96% | 94% | 0.44 |
| Ethnicity, % Hispanic | 7% | 6% | 0.91 |
| Gender, % male | 45% | 27% | <0.0001 |
| Age in years, mean (SEM) | 33.3 (0.7) | 32.6 (0.4) | 0.35 |
| Education, % college degree or more | 31% | 38% | 0.15 |
| Salary, % gross weekly income \geq \$550 | 47% | 53% | 0.32 |
| Cigarette smoking, % | | | 0.27 |
| Never | 53% | 61% | |
| Former | 26% | 21% | |
| Current | 21% | 18% | |
| Asthma onset before age 18 years, % | 58% | 62% | 0.45 |
| Asthma severity based on medical records, % | | | 0.32 |
| Mild intermittent | 28% | 31% | |
| Mild persistent | 27% | 31% | |
| Moderate or severe | 45% | 38% | |
| No of days bothered by asthma in past 7 days, mean (SEM) | 4.0 (0.2) | 3.1 (0.1) | 0.002 |
| No of treatments for acute asthma attacks in past 12 months, mean (SEM) | 1.4 (0.2) | 1.1 (0.1) | 0.15 |
| No of days missed work due to asthma in past 12 months, mean (SEM)† | 2.8 (0.7) | 1.9 (0.3) | 0.24 |

*There were missing values for several variables. Some participants refused to answer questions about their race (n = 2), Hispanic ethnicity (n = 2), and education (n = 1). For gross weekly salary, 446 provided answers, while the other 152 had no salary (for example, unemployed or student) or refused to answer.

†Limited to the 557 participants who were employed in the past 12 months.

or cigarette smoke. Among the 203 who were employed at the time of asthma onset, 20 (10%) reported they thought it was due, at least in part, to workplace exposures.

A total of 263 participants (44% of 598) had an exposure score >0. More participants were judged to have had exposure to sensitizers alone (n = 91, 15% of 598) than to irritants alone (n = 69, 12%), and 103 (17%) had exposure to both kinds of agents. The likelihood of having an exposure score >0 varied little with age (table 2). However, men were more likely than women to have worked in jobs that were judged to have had sensitizer and/or irritant exposures, regardless of age ($p \leq 0.05$).

The distribution of study participants by the decision matrix is presented in table 3, which includes 557 (93% of 598) participants who were employed in the year before interview, and 41 who were not employed and assigned to the combined exposure/symptom category of 0/0. There were 243 participants (41% of 598) with a work related symptom score >0, and they included 73 (12% of 598) who reported their asthma symptoms got better away from work, 57 (10%) who reported they used an inhaler or nebulizer more at work, and 205 (34%) who reported an asthma trigger at work. About two thirds of the 243 (n = 158) reported an asthma trigger but neither work related symptoms nor medication use. The percentage of working participants with a symptom score >0 increased with the exposure score: 41% (120/294) for exposure = 0, 45% (99/220) for exposure = 1, and 56% (24/43) for exposure = 2, with $p = 0.07$ by χ^2 test for trend.

A total of 136 (23% of 598) participants had either moderate or strong evidence for workplace exacerbation and, consequently, were classified as having WEA. The WEA participants included 123 (90% of 136) with both exposure and symptom scores >0, and 13 (10%) with a combined symptom/exposure score of 3/0. Approximately half (n = 66, 49%) of the 136 with WEA had a combined score of 1/1, and only 12% (n = 16) had strong evidence for WEA.

Of the 20 participants who reported that work contributed to the onset of their asthma, eight (40%) fulfilled the criteria for WEA. This percentage was greater than the 22% with WEA among all other study participants ($p = 0.10$). At

interview, seven of the eight were still working at the same job they had at asthma onset. One of these eight individuals had onset of asthma as recently as 1 year and 8 months before the survey interview. However, the other seven had had asthma onset earlier, ranging from 3 years and 7 months to 9 years and 7 months before interview.

Those with and without WEA were similar in terms of several descriptive features (table 4). However, the WEA participants were more likely to be male (45% v 27%, $p < 0.0001$). Among working participants, men were more likely than women to have an exposure score (see table 2) and a symptom score (48% v 41%, $p = 0.15$) greater than 0. The WEA and non-WEA participants did not differ substantially by severity of asthma as determined by medical records. Yet, those with WEA tended to self-report more severe asthma, as indicated by the last three rows in table 4. In particular, WEA participants reported being bothered by asthma on more days during the past seven days than their non-WEA counterparts ($p = 0.002$).

DISCUSSION

Potential selection bias

By conducting the study in an HMO, we did not include adults with asthma who were without medical care coverage. Based on a recent analysis of data from the 2003 National Health Interview Survey, 17.8% of employed people in the US did not have health insurance at the time of interview.²⁸ This segment of the population is likely working in some of the dirtiest jobs in the country. With this in mind, our findings may underestimate the percentage of asthmatic adults with WEA.

Among adults who were enrolled in the HMO, we used a relatively strict definition of asthma. For example, we required participants to have evidence of asthma based on a review of both their electronic (criteria 2 and 3) and paper (criterion 4) medical records. We also excluded potential participants who had not used medications for asthma in the past 12 months (second part of criterion 5), which meant we may have rejected some people with very mild asthma. While we may have excluded some people with asthma, we believe

that the study group was not contaminated with people who did not have asthma.

Work related exposure and symptom scores

We avoided using self-reported occupational exposure because of the potential for bias. Bias was demonstrated in a previous study of respiratory symptoms, in which researchers observed an inflation of the effect estimate when self-reported occupational exposure was used rather than a characterisation of exposure based on a structured occupational history.²⁹ Our use of a questionnaire combined with expert evaluation is a preferred approach to retrospective evaluation of occupational exposures.³⁰ The exposure score might still reflect errors due to incomplete or misleading information provided by the participant, or misjudgment by the researcher.

It is likely that some participants in the current study inaccurately perceived the work-relationship of their symptoms, medication use, or asthma triggers, resulting in either overreporting or underreporting. A common concern with occupational diseases is that workers will overreport work related symptoms in order to receive compensation.³¹ This type of overreporting was unlikely in the current study. First, participants were selected on the basis of their having asthma and not on whether they sought compensation. Second, the current study was not presented to the participants as a way to gain benefits by claiming work related worsening of asthma. Even in the absence of possible monetary gains, we cannot entirely rule out that reporting by some participants was influenced by a desire to blame or protect their employers.

Our criteria for WEA were not based solely on participants self-reporting that their asthma was made worse by work. They also had to have evidence of relevant work related exposures, as determined by two researchers who independently reviewed and scored the work histories, to fulfill our criteria for WEA. The one exception to the exposure requirement was for those participants with a combined exposure/symptom score of 0/3, who represented just 10% (n = 13) of all 136 WEA cases. At final count, a little over half (n = 136, 56%) of the 243 participants with a symptom score >0 also met the exposure criteria and were considered to have WEA.

Workplace exacerbation and severity of asthma

A recent publication presented characteristics of the 210 cases of work aggravated asthma that were identified during 1993–95 as part of the SENSOR surveillance programme conducted in four states in the US.³² The authors noted that work aggravated asthma cases were as likely as new onset work related asthma cases to report several adverse outcomes. We anticipated that participants in the current study who fulfilled the criteria for WEA would have more severe asthma than their non-WEA counterparts. Indeed, some of the findings from the current study were consistent with this expectation. For example, the WEA participants reported they were bothered by asthma symptoms on more days in the past seven days than the non-WEA participants (p = 0.002). The WEA group also reported more days missed from work because of asthma (p = 0.24), which would be expected if work were a source of troublesome exposures.

While the exacerbation of asthma due to workplace exposures could contribute to severity, it is also possible workplace exacerbation is more likely among individuals whose asthma is already severe. For example, in a longitudinal study of adults with asthma that included both new onset and work exacerbated cases of asthma, both baseline severity and workplace exposures were observed to be associated with partial or complete work disability.³³ Longitudinal follow up is needed to accurately determine

Main messages

- Cases of workplace exacerbation of asthma (WEA) were successfully identified using self-reported data on work related exposures and symptoms/medication use.
- WEA was common, occurring in 23% of adults with asthma in a health maintenance organisation.
- Among adults with asthma, those with WEA were more likely to be male and reported being bothered by asthma on more days during the past seven days.

Policy implications

- WEA is relatively common and should be considered by physicians when treating adults with asthma.

whether a severe asthma status preceded or followed work related exacerbation. We are following participants from the current study to determine whether WEA status predicts progression of disease over time.

WEA and gender

Women were twice as numerous as men in our study group of adults with asthma, but a disproportionate number of WEA cases were men. This reflects the fact that men were more likely to be employed in workplaces with exposures to agents of relevance to asthma, and to report work related problems with asthma. In a telephone survey of adults in Maine, men accounted for 47% of all respondents and for 75% of the respondents in jobs at higher risk for exacerbation of asthma.¹⁸ However, in a survey of adults with asthma enrolled in a HMO in Colorado, men and women were equally likely to report that their current work environment made their asthma worse.¹⁷

Conclusion

Physicians should consider that work can contribute to the exacerbation of symptoms when treating adults with asthma. Based on the current study, we conclude that workplace exacerbation of asthma is a relatively common occurrence, identified in 23% of adult asthma cases between the ages of 18 and 44 in this HMO population. The participants with WEA were more likely to be men than women. The WEA participants also reported being bothered by asthma on more days during the past seven days, but it is unclear whether this finding and other indicators of more severe asthma preceded or followed the start of WEA. In an ongoing follow up study, we will analyse data from the participants' medical records to determine whether those with WEA develop more severe asthma over time than those without WEA.

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Incidence of Work-Related Asthma in Members of a Health Maintenance Organization

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Objective: The objective of this study was to evaluate work-related asthma among health maintenance organization (HMO) members. Recent reports suggest that the incidence of work-related asthma may be much higher than Sentinel Event Notification Systems for Occupational Risks (SENSOR) data estimate. **Methods:** Using the HMO's electronic medical record, we identified 1747 persons with evidence of new or recurrent asthma. Interviews with 352 of them elicited information about workplace exposures, symptoms, and home environment. Industrial hygienists rated the potential asthmagenicity of the respondents' work environments. **Results:** Based on the industrial hygienist ratings and self-reported work-relatedness of asthma symptoms, we classified 33% of those interviewed as having potentially work-related asthma, suggesting an overall work-related asthma incidence/recurrence rate of 28 cases per 10,000. **Conclusions:** The contribution of occupation to the occurrence of adult onset asthma may be much higher than typically suggested in the literature. (J Occup Environ Med. 2005;47:1292-1297)

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Estimates of the proportion of asthma that is work-related typically range from 5% to 15%.¹⁻³ Reasons for the differences in estimates relate both to varying definitions for work-related and occupational asthma and to limitations in the methodologies for assessing it.³ Guidelines of the U.S. Centers for Disease Control and Prevention National Institute for Occupational Safety & Health (NIOSH)^{4,5} for the surveillance of work-related asthma recognize two distinct subclasses: new-onset work-related asthma and work-aggravated asthma (ie, preexisting asthma that is made worse by exposures in the workplace).⁵ New-onset work-related asthma results from exposure to a sensitizer (in which case asthma symptoms may not occur until after many years of exposure) or an irritant (in which case asthma symptoms typically occur within 24 hours of a high-level exposure, but may occur only after repeated, low-level exposure).⁶ The term occupational asthma, as used in the literature, typically equates with new-onset work-related asthma,^{7,8} although some authors limit the term to sensitizer-induced new-onset asthma.^{9,10} Thus, this article uses the term work-related asthma.

Relatively little population-based information about work-related asthma is available. In the United States, estimates of the average annual incidence of work-related asthma based on the Sentinel Event Notification Systems for Occupational Risks (SENSOR) have ranged

from five cases/10⁶ in Massachusetts¹¹ to 37 cases/10⁶ in Michigan.¹² The SENSOR data are assumed to be underestimates, however,⁵ and more refined estimates from Michigan suggest an incidence rate between 58 and 204 cases/10⁶.¹³ Outside the United States, estimates have ranged from as low as 21 cases/10⁶ in the United Kingdom to 191 cases/10⁶ in Finland.^{14–18}

Although NIOSH has published criteria for using its definition of work-related asthma,¹⁹ their use is limited from an epidemiologic perspective because the needed information is difficult to obtain. Recently, Milton and colleagues studied 79,204 health maintenance organization (HMO) members, aged 15 to 55, and estimated that 21% of incident asthma cases were work-related, an incidence of 71 per 100,000 in this population.²⁰ The Milton et al study is of particular interest because it used electronic medical records information, confirmed by chart review, to define asthma cases. It used a detailed interview, coupled with industrial hygiene evaluation, to assess both the work-relatedness of symptoms and the asthmagenicity of the work environment. The Milton protocol thereby attempts to address, in a reasonably rigorous manner, all three dimensions of the NIOSH definition.

This study evaluated all new cases of asthma occurring in 1 year among the working-aged members of a large HMO to determine the incidence of work-related asthma.

Materials and Methods

This study received Institutional Review Board approval. It was conducted in parallel with investigators from Harvard University as part of a joint award by NIOSH. The surveillance algorithm and the telephone questionnaire were developed collaboratively and were patterned after Milton's 1998 protocol.²⁰

Research Setting and Target Population

Kaiser Permanente Northwest (KPNW) is a large group-model HMO centered in Portland, Oregon, that provides comprehensive, pre-paid healthcare service. Its members' demographic characteristics correspond closely to the area population as a whole.^{21,22} We studied the approximately 255,000 members aged 15 to 55.

Most KPNW members receive coverage through work or are included in a household member's work-related coverage. The 50 largest employer groups contracting with KPNW belong to industries with known exposures to potential asthma triggers such as wood products, aluminum, electronics, and steel manufacturing.

Data Systems

Healthcare utilization data for this analysis were derived from administrative and clinical databases maintained by KPNW. These databases include information on inpatient admissions, emergency department services, general outpatient care, and medication dispensings from KPNW's outpatient pharmacies. Claims for services by non-KPNW facilities were also included.

Surveillance Algorithm

Initially, we identified the at-risk population by excluding individuals with prevalent asthma and other diagnoses that might be confused with asthma. Table 1 summarizes this algorithm. Further details on the predictive value of our prevalence algorithm have been published elsewhere.²³

Using the at-risk population, we applied the algorithm in Table 2 to identify potential incident cases. We captured only individuals who presented with asthma severe enough to trigger a medication dispensing. However, to exclude "ruleout" diagnoses, we required more than one beta-agonist inhaler dispensing to

TABLE 1

Algorithm for Identifying the 'At-Risk' Population

Inclusion criteria

- Aged 15–55 years as of the first day of the target month AND
- Continuous health plan eligibility for the prior 6 months

Exclusion criteria (any one of the following):

- Healthcare utilization in past year
- Outpatient or primary inpatient visit for any of the following
 - congestive heart failure
 - chronic obstructive pulmonary disease
 - bronchiectasis
- Chronic bronchitis
- sleep apnea
- Emergency department, urgency care, or primary inpatient visit for asthma
- Healthcare utilization in the past 2 yr
- Outpatient visit for asthma
- Medication dispensing in the past year
- ≥4 dispensings of beta-agonist inhalers
- (≥1 dispensing of either an inhaled corticosteroid or cromolyn) and (≥1 beta-agonist inhaler dispensing)

fulfill the medication requirement. The resulting algorithm may exclude some truly incident cases, but it also should (appropriately) exclude some

TABLE 2

Algorithm for Identification of Incident Asthma Cases*

Utilization criterion

Any one of the following healthcare contacts in the target month

- Emergency department visit for asthma
- Inpatient stay with primary diagnosis of asthma
- Outpatient clinic visit or urgent care clinic visit for asthma

Medication criterion†

Any of the following dispensing patterns in the target or subsequent month

- ≥2 dispensings of beta-agonist inhalers
- ≥1 dispensing of any asthma medication other than beta-agonists inhalers

*To be identified as a potential case, the person must meet *both* the utilization and the medication criteria.

†The following medications are considered when applying the medication criteria: beta-agonist inhaler, inhaled corticosteroid, cromolyn inhaler, theophylline, beta-agonist nebulizer, leukotriene inhibitor, prednisone, nebulization treatment.

individuals with mild, intermittent asthma who were incorrectly included in the at-risk pool.

As shown in Tables 1 and 2, our algorithm attempts to exclude from the at-risk population individuals with active asthma who require ongoing health care. It does not, however, exclude very mild asthmatics with no outpatient care in the past 2 years and only minimal beta-agonist use; and it does not exclude those with asthma that is no longer active. Thus, ours is a study of asthma incidence and recurrence rather than incidence alone. To assure that all participants were defined comparably, we divided our yearlong surveillance period into 12 months and applied the algorithm independently in each month.

All potentially incident cases thus identified were independently verified by medical record review by trained medical records technicians. Reviewers confirmed a provider diagnosis of asthma and prescription of either bronchodilators or steroids or instructions to refill an active prescription.

Assessment of Workplace Exposures and Work-Relatedness of Symptoms and Triggers

We attempted to telephone a subset of individuals with chart-confirmed incident asthma to assess the work-relatedness of symptoms and triggers and to gather information about potential workplace exposures. A work-relatedness score, ranging from 0 to 3, was defined as the sum of the following events: 1) the participant's chest symptoms or breathing troubles got better "on weekends, vacations, or other times when you are away from work"; 2) the participant used less reliever medication "on weekends, vacations, or other times when you are away from work"; and 3) the participant reported a trigger that was a problem at work. Information about triggers was

assessed through both closed- and open-ended questions.

Occupational exposures were assessed through a series of closed- and open-ended questions that asked about the work environment, ventilation in the work area, and the participant's particular job activities, including use of "tools, chemicals, or other materials" and exposure to "dust, smoke, gas, or chemical fumes" on the job. The questions were asked by lay staff trained by an industrial hygienist (IH), and the responses were then independently reviewed by IHs from Portland and NIOSH who were blinded to the work-relatedness questions. Each of the two industrial hygienists assigned every participant a three-point irritant score and a three-point sensitizer score, which were then averaged across hygienists and combined to yield a single three-point summary IH rating, scored as "0" (little or no asthmagenic potential), "1" (possible asthmagenic potential), or "2" (clear asthmagenic potential).

The overall assessment of whether the participant's asthma was work-related was determined by the joint distribution of the work-relatedness score and the summary IH score, as illustrated in Table 3. Participants classified as having moderate to strong evidence of work-related asthma were considered to have work-related asthma. We also defined as work-related asthma the one case of reactive airways dysfunction syndrome (RADS) that was associated with workplace exposures.

All participants provided oral consent before beginning the interview.

Statistical Methods

Incidence rates, expressed as number of incident cases per 10,000 person-years of observation, were calculated as the total number of incident cases identified during the 12-month surveillance period divided by the total number of person-years of eligibility (sum of the at-risk populations for each month divided by 12) times 10,000. The same approach was used to calculate both overall incidence rates and subgroup-specific rates. Statistical analysis of the incidence data, including calculation of confidence intervals and comparisons of rates across subgroups, was conducted using Poisson regression analysis.

Results

Across the 12-month surveillance interval, we identified 1916 suspected cases of new or recurrent asthma of a total of 203,701 person-years of observation. Of these, 1747 (91%) were validated based on chart review. Thus, the overall rate of occurrence of new or recurrent asthma (both work-related and nonwork-related) in this population was 86 per 10,000 person-years of observation. Table 4 summarizes the figures by gender and age. Rates were consistently higher for women than for men in each age group, and we observed no significant gender-by-age interaction. We attempted to contact 828 of the cases and successfully completed interviews on 387 (47%) of them. A further 35 denied having had a recent visit for breathing problems, despite our having

TABLE 3
Grid for Assessing Strength of Evidence for Work-Relatedness of Participant's Asthma

| Summary Industrial Hygienist Rating | Work-Relatedness Score | | | |
|--|------------------------|----------|----------|----------|
| | 0 | 1 | 2 | 3 |
| 0 = little or no asthmagenic potential | No | Weak | Weak | Moderate |
| 1 = possible asthmagenic potential | Weak | Moderate | Moderate | Strong |
| 2 = clear asthmagenic potential | Weak | Moderate | Strong | Strong |

Participants with moderate or strong evidence were classified as having work-related asthma.

TABLE 4
Rate of Occurrence of New and Recurrent Asthma Among Members Aged 15 to 55 of Kaiser Permanente Northwest for the year 2000

| | Age (yrs) | | | | Total |
|--|-----------|-------|-------|-------|-------|
| | 15-25 | 26-35 | 36-45 | 46-55 | |
| Size of at-risk population (1000 person-yr) | | | | | |
| Men | 25 | 20 | 26 | 28 | 98 |
| Women | 25 | 22 | 28 | 30 | 106 |
| Total | 50 | 42 | 54 | 57 | 204 |
| Validated cases of new or recurrent asthma | | | | | |
| Men | 160 | 148 | 164 | 155 | 627 |
| Women | 235 | 247 | 307 | 331 | 1120 |
| Total | 395 | 395 | 471 | 486 | 1747 |
| "Incidence" of new or recurrent asthma (per 10,000 person-yr) | | | | | |
| Men | 65 | 74 | 63 | 56 | 64 |
| Women | 92 | 111 | 109 | 111 | 106 |
| Total | 79 | 93 | 87 | 85 | 86 |

documented evidence of such a visit, and so were also excluded from the analysis. The remainder of this analysis focuses on the 352 individuals who acknowledged having breathing difficulties and completed the full telephone interview. Of these, 75 (21%; 95% confidence interval [CI], 17-26%) reported onset of symptoms within the past year, and thus presumably represent true incident asthma, as opposed to recurrence of dormant asthma. These results suggest that the true rate of occurrence of incident asthma in this population (both work-related and nonwork-related) was 18 per 10,000 person-years of observation. Compared with participants who completed the interview, nonrespondents were slightly younger (36 vs 38 years, $P = 0.004$) and were more likely to be male (40% vs 28%, $P < 0.001$).

Table 5 shows the proportion of incident cases whose asthma we classified as being potentially work-related. The data are expressed relative to the entire population, not only to those who had jobs. Overall, we estimate that 33% (95% CI = 28-38%) of the asthma in this population was potentially work-related, with estimates consistently (and significantly) higher for men than for women. Had we required strong evidence (Table 3) to classify

asthma as work-related, only 4.5% of the 352 incident/recurrent cases would have been classified as work-related.

Finally, Table 6 combines the information from Tables 4 and 5 to estimate the incidence of work-related and nonwork-related asthma

in this population. The estimated incidence of work-related asthma in the population overall was 28 per 10,000 person-years of observation and tended to be higher among those aged 26 and older relative to those aged 15 to 25. The incidence of nonwork-related asthma varied little by age and was consistently higher for women than for men. Although not shown, the proportion of work-related cases did not differ for those judged to have true incident versus recurrent asthma.

Discussion

This survey of the incidence and recurrence of work-related asthma in a young adult population estimated a higher contribution of occupation to adult-onset asthma than has typically been reported and at the same time illustrates the widely reported difficulties in the assessment of work-related asthma in field trials. We estimated that 33% of new-onset or recurrent asthma in the age range 15 to 55 years may be work-related with

TABLE 5
Proportion of Incident Asthma That Appears to be Work-Related

| | Age | | | | Total |
|-------|-----------|----------|----------|-----------|-----------|
| | 15-25 | 26-35 | 36-45 | 46-55 | |
| Men | 33% (24)* | 50% (26) | 44% (18) | 40% (30) | 42% (98) |
| Women | 11% (38) | 31% (48) | 29% (79) | 36% (89) | 29% (254) |
| Total | 19% (62) | 38% (74) | 32% (97) | 37% (119) | 33% (352) |

Males significantly greater than females based on logistic regression. No significant gender by age interaction.

*Denominator shown in parentheses.

TABLE 6
Estimated Incidence of Work-Related And Nonwork-Related Asthma (per 10,000 person-yr of observation) Among Members Aged 15 to 55 of Kaiser Permanente Northwest for the Year 2000

| | Age (yrs) | | | | Total |
|------------------------|-----------|-------|-------|-------|-------|
| | 15-25 | 26-35 | 36-45 | 46-55 | |
| Work-related asthma | | | | | |
| Men | 22 | 37 | 28 | 22 | 27 |
| Women | 10 | 35 | 32 | 40 | 31 |
| Total | 15 | 35 | 28 | 31 | 28 |
| Nonwork-related asthma | | | | | |
| Men | 43 | 37 | 35 | 34 | 37 |
| Women | 83 | 76 | 78 | 71 | 75 |
| Total | 64 | 58 | 59 | 53 | 58 |

an “incidence” of work-related asthma in this age range of 28 per 10,000 person-years of observation.

This study has several strengths. It made use of automated medical records information from a well-defined population and used industrial hygienist review of detailed information about the workplace and work exposures rather than simply the participant’s industry and occupation to classify the asthmagenicity of the work environment. It combined this latter information with self-reported work-relatedness of symptoms, medication use, and asthma triggers (all part of the NIOSH criteria for work-relatedness of asthma) to arrive at a final classification of whether a participant’s asthma was potentially work-related. In addition, because most individuals were interviewed within a few months of diagnosis, their recall of work tasks and exposures around the time of the diagnosis should have been reasonably accurate.

The study also has several potential limitations. First, although we are reasonably confident of our ability to identify prevalent asthma,²⁴ we are less confident of our ability to identify incident asthma because, by definition, it represents an initial diagnosis for which there are typically not subsequent encounters to further validate the diagnosis. For this reason, we used reasonably strict criteria to exclude likely “ruleout” diagnoses and also had a medical records technician review each suspected incident case. Nonetheless, 9% of those interviewed denied having had a recent healthcare visit for breathing problems. Second, although our IH assessment should represent a considerable improvement over traditional epidemiologic approaches, it is no substitute for a detailed industrial hygiene investigation of the workplace, which is the “gold standard” for determining workplace exposure to an asthmagenic agent. Third, our original work-relatedness score, as previously noted, may overestimate the

presence of work-related triggers. Finally, we completed full interviews on only 43% of those we attempted to reach. Work exposures for the remainder may differ systematically from those interviewed. We do know that nonresponders were slightly younger on average and were more likely to be male.

We believe our algorithm, originally proposed by Milton et al,²⁰ represents a rigorous attempt, from an epidemiologic perspective, to implement the NIOSH case definition algorithm.¹⁹ It incorporates a careful IH review of the participant’s work environment and information about the association of symptoms, medication use, and triggers with work. Still, it should not be used to attribute work-relatedness on an individual level. More accurately, it should be viewed as suggesting the potential for work-relatedness.

This study also raises a number of interesting methodological issues concerning the epidemiologic classification of work-related asthma. Had we used only the IH classifications, 142 individuals (40% of the sample) would have been classified as having possible or definite asthmagenic exposures at work, and yet 32 of these individuals (23%) scored zero on the work-relatedness score and thus should have a low likelihood of having work-related asthma. Even for the 58 individuals with an IH score of 2, 15 (26%) still had a work-relatedness score of zero. Similarly, 46% of individuals with a nonzero work-relatedness score had an IH score of zero (45% for those with work-relatedness scores of 2 or 3). This suggests the likelihood that both systems used alone are subject to considerable misclassification, and that use of both together results in a substantially improved estimate.

Even so, the fact that 52% of the suspected work-related cases fell into the most marginal evidence category, the (1,1) cell in Table 3, raises the likelihood that many of these individuals are still misclassified. Even if only half of these individuals

were misclassified, the proportion of individuals classified as having work-related asthma would drop from 33% to 24%. If we had classified this whole category as “weak” instead of “moderate” evidence, the proportion would be reduced further to 16%. We suspect that the lower figures may be more accurate, because one of the categories of the work-relatedness scale appears to lack specificity. For example, although only 12% of participants reported that their symptoms were better away from work and only 7% reported using their reliever medications less when they were away from work, 55% reported a work-related trigger. These latter individuals comprise 96% of those with a work-relatedness score of 1.

Furthermore, most of the individuals who reported a work-related trigger also reported that their trigger was a problem away from work. If we recomputed the work-relatedness score, counting work triggers as positive only if they were a problem only at work, the proportion of asthma that was work-related would be reduced to 9%. Although this figure almost certainly reflects an overly conservative estimate, these results illustrate the sensitivity of the estimates in Table 5 to changes in our classification algorithm. It would also be of interest to compare the IH scores using this methodology with those that would be obtained using more conventional systems based on job title and industry alone (with or without limited expert evaluation).

Although the question about work-related triggers may lack specificity, the alternative of requiring a trigger that is present only at work probably errs in the opposite direction. If someone is sensitized to an agent, we expect him or her to report responding to that same agent in more than one location, eg, at work and away from work. In a situation in which we are not sure whether the same exposure at home or at work was the causative agent, the weight of evidence is typically on the side of the

occupational exposure. For example, a person can grow up in contact with wheat and wheat products and yet, as seen with studies of baker apprentices, it is not until they enter the workplace that they develop extreme allergies to wheat. A person being interviewed in such a case would report responding to the same agent at home and at work.

Finally, it is of interest to compare our findings with those of Milton et al,²⁰ because we have essentially replicated their protocol on a larger scale and with a different population. Our estimate for the overall “incidence” of adult-onset asthma is more than twice that reported by Milton (86 vs 37 per 10,000), although our estimate of the proportion of these cases that truly represent new-onset asthma is lower than Milton’s (21% vs 35%). In both studies, the proportion of asthma estimated to be work-related is high relative to typical reports in the literature (Milton et al reported 21% vs our 33%, P value = 0.09), although they are consistent with estimates from a recent study from Finland (29% for men and 17% for women).²⁵ Even the revised estimates presented in our sensitivity analysis, although lower, were still generally higher than the typically reported range of 5% to 15%. Milton et al²⁶ recently reported in abstract form on initial results from a further study using their protocol and noted incidence figures that are almost twice those reported in their initial study of Boston-area residents (and hence more in line with the estimates reported here).

In summary, this study of adult-onset asthma among members of a large HMO in the northwest United States generally corroborates the findings from a similarly conducted analysis in the northeastern United States and suggests that the contribution of occupation to the occurrence of adult-onset asthma may be much higher than has typically been suggested in the literature.

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