SPECIAL ARTICLE

How Much Adult Asthma Can Be Attributed to Occupational Factors?

Paul D. Blanc, MD, MSPH, Kjell Toren, MD

PURPOSE: Many occupational factors can cause asthma or reactivate preexisting disease. We carried out a critical review and synthesis of the available literature to estimate the proportion of adult asthma that is attributable to workplace factors.

METHODS: We reviewed published citations from 1966 through May 1999 as well as recent abstracts of studies providing risk estimates for asthma among various occupations. We extracted published attributable risk estimates, derived others from published data, and extrapolated estimates from the incidence rates of occupational asthma. We used a semiquantitative score to rank studies based on their characteristics.

RESULTS: We obtained 43 attributable risk estimates from 19 different countries: 23 were published estimates, 8 were derived from published data, and 12 were extrapolated from incidence data. The median value for the attributable risk of occupationally associated asthma was 9% (25th to 75th interquartile range: 5% to 19%). The derived estimates (median attributable risk = 25%) were significantly greater than published values (median = 9%, $P = 0.002$), whereas the extrapolated estimates were significantly lower (median = 5%, $P = 0.04$). The 12 highest scored studies based on their characteristics yielded a median risk estimate of 15%.

CONCLUSION: Occupational factors are associated with about 1 in 10 cases of adult asthma, including new onset disease and reactivation of preexisting asthma. **Am J Med. 1999;107: 580–587.** ©1999 by Excerpta Medica, Inc.

Asthma is common among adults of working age, and its incidence appears to be increasing (1). Adult asthma includes persistent childhood asthma, early-onset asthma that reactivates in adulthood, and new-onset disease. Among the latter two groups, asthma is a sentinel health event that warrants a high index of suspicion for a potential work-related etiology (2). Many agents encountered in a wide variety of occupations can cause or reactivate asthma (3). Work-related asthma is one of the most common occupational lung diseases worldwide (4,5).

The proportion of disease that can be attributed to a risk factor is a critical measure of the adverse public health impact of that risk factor (6). The attributable risk, also called the population attributable risk or etiologic fraction, is a way to quantify this proportion. The attributable risk reflects the strength of the risk factor as well as the proportion of the population that is exposed to it. An attributable risk of 10%, for example, suggests that 1 in 10 cases of that disease would not have occurred were it not for that specific exposure, assuming that the exposure is causally related to the disease (7).

Given the potential association between occupational factors and asthma, the common nature of the exposures involved, and the frequency of asthma, the attributable risk for work-related factors in asthma has important public health implications. Several investigators, using a variety of analytic approaches, have estimated the attributable risk for occupational causes of asthma. For example, some studies have estimated the proportion of clinically manifest asthma (new and reactivated disease) to which occupational factors have contributed, while other studies included only patients with new adult-onset asthma. The goal of this study was to review and synthesize the literature in order to make a reliable estimate of the attributable risk of adult asthma that is associated with workplace exposures.

METHODS

Study Selection

We identified published citations by searching the computerized database Medline from January 1966 through May 1999 using the key words "asthma and risk and occupation(al)(ally)." We identified 396 entries for potential inclusion, 295 of which were published after 1989. After review of the relevant English language articles, we also selected appropriate reference citations and, in turn, retrieved their relevant citations. To identify recent stud-

From the Division of Occupational and Environmental Medicine (PDB), Department of Medicine and Cardiovascular Research Institute, University of California San Francisco, San Francisco, California; and the Department of Respiratory Medicine and Allergology and Department of Occupational and Environmental Medicine (KT), Sahlgrenska University Hospital, Goteborg, Sweden.

Supported by a Research Career Development Award KO4 HL03225 (PDB) and by the Swedish Council for Worklife Research (KT).

Requests for reprints should be addressed to Paul D. Blanc, MD, Box 0924, University of California San Francisco, San Francisco, California 94143-0924.

Manuscript submitted March 12, 1999, and accepted in revised form August 11, 1999.

0002-9343/99/$–see front matter
PII S0002-9343(99)00307-1

ies, we reviewed the published abstracts of the 1997 to 1999 international meetings of the American Thoracic Society and the American Academy of Allergy, Asthma and Immunology, and the 1997 to 1998 abstracts of the European Respiratory Society and the American College of Chest Physicians.

Reports fell into three broad categories: published estimates of occupational attributable risk for asthma; analyses that included a measure of the relative risk or odds ratio for asthma associated with occupational factors; and studies that reported a population-based incidence of occupationally related asthma. We included each type of study in our analysis. There were no exclusion criteria based on study size. We excluded reports that studied a single occupational or industrial risk group, even when defined by a broad category such as "farmers," because they did not permit an estimation of the attributable risk of asthma beyond the high-risk group studied.

Published Attributable Risk Estimates

If the term "attributable risk," "population attributable risk," or "etiologic fraction" was not used but the estimated proportion of cases due to occupational exposures was reported, we treated this as a reported attributable risk. Within studies, we recorded several attributable risk estimates if they were reported, such as those for narrower or broader categories of exposure, including broad occupational groups, job-linked exposure matrix, where risk is assumed a priori based on specific jobs, or self-reported exposures. When multiple estimates were presented in the same publication, we used the average of the highest and lowest value. If several definitions of asthma were used, we recorded the attributable risk estimate associated with the most specific criteria, such as disease defined by adult onset and confirmed by pulmonary function criteria.

Derived Attributable Risk Estimates

We identified several studies that reported an overall measure of work-associated risk for asthma by occupational categories but did not estimate the attributable risk. Those studies that also provided the prevalence of the exposure risk and the relative risk or odds ratio, however, allowed us to estimate the attributable risk as (8): proportion exposed $\times$ (relative risk $-$ 1) divided by (proportion exposed $\times$ [relative risk $-$ 1]) $+$ 1. We assumed that a reported odds ratio was a reasonable estimate of the relative risk. For case-control studies, we used the proportion of exposure among the controls to estimate the prevalence of the exposure in the population (8).

When risk was presented in gender-stratified analyses only, we weighted the attributable risk estimate based on the exposure proportions of the gender strata in the study. When risk estimates for several mutually exclusive occupational risk factors were presented, we estimated the attributable risk by summing their effects, based on the frequency of each exposure. If available, we used adjusted relative risk estimates in our calculations. We excluded studies in which the exposure proportion could not be determined or in which asthma-specific data were not provided (such as those that included patients with chronic obstructive lung disease).

Extrapolated Attributable Risk

Several studies did not report the attributable or relative risks of occupational exposures for asthma but did estimate the incidence of occupational asthma. We used these estimates to extrapolate an attributable risk estimate by assuming that the incidence of asthma among adults of working age was 100 per 100,000 person-years (9). Given that assumption, the attributable risk can be estimated as the ratio of the incidence of occupational asthma to total asthma incidence in the same age stratum.

Semiquantitative Assessment of Study Characteristics

We included studies that defined asthma by self-report, physician diagnosis, or symptoms combined with physiologic confirmation, such as measurement of airway responsiveness or variability of peak expiratory flow over time. Similarly, occupationally related disease included specialist physician diagnosis of occupationally related asthma, subject self-attribution of etiology, and presumed association based on occupational history or reported job exposures. To assess the varying characteristics of the studies semiquantitatively, we developed a priori scoring criteria to grade the attributable risk estimate that we used. (We did not score incidence-based extrapolations or published attributable risk values that reflected consensus statements.) The scoring schema had seven components reflecting the key differences among the studies. We calculated the score for a study based on the number of subjects with asthma ($<$100 patients $=$ 0, 100 to 499 patients $=$ 0.5, $\geq$500 patients $=$ 1.0); source of asthma diagnosis (self-report of asthma $=$ 0, physician diagnosis of asthma without physiologic criteria $=$ 0.5, standardized physiologic criteria of reversible airflow obstruction, variable peak expiratory flow, or nonspecific increased airway responsiveness $=$ 1); determination of occupational-relatedness (epidemiologic association based on job exposures or occupational category $=$ $-$0.5, self-report of attribution $=$ 0, attribution based on clinical assessment $=$ 1.0); study design and sampling method (clinical case series or convenience sample $=$ 0, community-based sample or surveillance system data $=$ 0.5, systematic population-based sampling $=$ 1); statistical adjustment for smoking (adjustment performed $=$ 0.5); age of asthma onset among subjects (any age $=$ 0, analysis

Table 1. Published Attributable Risk Estimates for Occupationally Related Asthma

Location (Reference)	Number with Asthma/ Total Number	Study Design	Attributable Risk*	Study Score†
Canada (10)	731/731	University referral clinic	7%	1.5
Canada (11)	383/2966	Random population survey	15%	2.0
Canada (12)	>500/>12,000	Random population survey	23%	0.5
Finland (13)	4717/4717	National incidence	5%	3.5
Japan (14)	813/813	Industry-based, men only	9% (3%, 15%)	1.5
New Zealand (15)	159/810	Random population survey	2% (2%, 3%)	3.0
Norway (16)	156/4492	Random population survey	19%	1.5
Singapore (17)	787/2378	Community clinic case-control	33%	2.0
Spain (18)	136/1415	Random population survey	9%	3.0
Spain (19)	81/899	Random population survey	20%	2.0
Sweden (20)	323/1787	Case-control study	11%	3.0
United Kingdom (21)	NA	Extrapolation from survey	2%	—
United Kingdom (22)	658/658	Case-control study, men only	2%	1.0
United States (23)	NA	Consensus statement	2%	—
United States (24)	468/6063	Weighted disability sample	15%	2.0
United States (25)	94/94	Hospitalized cases	14% (3%, 26%)	1.0
United States (26)	601/601	Community-based sample	12% (6%, 17%)	0.5
United States (27)	NA	Theoretical model	8%	—
United States (27,28)	1291/42,487	Weighted population sample	7%	1.0
United States (29)	68/72,204	Incident cases from HMO	21%	1.5
United States (30)	65/1226	Random survey, older women only	18% (15%, 20%)	1.0
Zambia (31)	580/580	University clinic	6%	1.5
International (32)	<500/8420	Random population survey	7% (5%, 10%)	3.0

* Attribute risk values in parentheses represent lowest and highest estimates reported within a given study based on differing assumptions (see Methods).
† Study characteristic scores (see Methods) were not estimated for non–data-based estimates.
HMO = health maintenance organization; NA = not available.

limited to adult onset cases = 0.5); publication type (peer-reviewed = 0, letter, abstract, or other = −1.0). The maximum score possible was 5.

Data Analysis

We estimated the attributable risk for each of the three categories: published estimates, values derived from published estimates of relative risks and exposure prevalence, and extrapolations from estimated incidence rates. For the published and derived attributable risks, we also estimated a weighted attributable risk by summing the product of each attributable risk with its study score and dividing by the sum of all the scores. We tested the differences in the estimated attributable risks between groups of studies using the Wilcoxon rank sum test. We used the Spearman rank correlation to measure the association between attributable risk and study characteristic score.

RESULTS

Published Population Attributable Risk Estimate Sources

There were 23 studies that estimated the attributable risk of asthma due to occupational exposures (Table 1) (10–32), including data from 17 countries. The estimates varied widely, from 2% to 33%. The median value for the attributable risks from all 23 studies was 9% (25th to 75th percentile: 6% to 18%); the mean (± SD) value was 12% ± 8%.

Three estimates were based on extrapolation (21), theoretical modeling (27), or consensus statement (23). Of the 20 remaining data-based studies, 10 studied adults with asthma who were identified using random population sampling (10,12,15,16,18,19,24,28,30,32). In the remaining 10 studies, patients with asthma were identified through various clinical or case-reporting techniques. The median attributable risk among the 10 population sampling-based estimates was 15%, compared with 9% among the 10 other studies ($P = 0.38$). There were seven reports of the proportion of adult-onset asthma attributable to occupation (11,13,15,18,20, 22,29). The median attributable risk among these studies was 9% and did not differ significantly from the median of 14% among the remaining data-based estimates ($P = 0.20$).

Six studies made more than one estimate of the attributable risk based on different assumptions or definitions. One study of 813 adults with asthma estimated that 3% were definitely of occupational origin and that an addi-

Table 2. Occupationally Related Attributable Risk for Asthma Derived from Published Data

Location (Reference)	Number with Asthma/ Total Number	Study Design	Attributable Risk	Study Score*
Canada (33)	62/1634	Random population survey	15%	1.0
China (34,35)	137/3606	Random population survey	17%	1.5
Finland (36)	41/1196	Regional prevalence	45%	2.0
France (37)	157/379	Case-control study	28%	0.5
France (38)	144/2406	Random population survey	30%	1.5
Italy (39)	<100/1635	Random population survey	26%	1.0
Sweden (40)	79/383	Case-control study	23%	2.0
United Kingdom (41)	24/241	Case-control study	20%	2.0

* See Methods for details of study characteristic scoring.

tional 12% were strongly suspected, for a total of 15% (14). Timmer and Rosenman (25), using hospital discharge data for 94 patients, estimated an attributable risk of 3% for probable occupational asthma, 18% based on possible combined with probable cases, and 26% based on self-report of work attribution. Forastiere et al (30) estimated an attributable risk of 15% as defined by reported exposures and 20% as defined by occupational group. Another study estimated an attributable risk of 6% as defined by reported exposure combined with an occupationally based exposure matrix, wherein certain jobs were assumed to be of greater asthma-causing risk on an a priori basis, and an attributable risk as high as 17% when the definition required either but not both criteria (26).

Attributable risk estimates from a multinational study ranged from 5% based on an occupational exposure matrix up to 10% based on occupational groups (32). Survey data from New Zealand yielded an attributable risk of 1.9% based on a high exposure categorization, without farmers and food processors, and 3.1% including those groups. That study defined asthma as increased bronchial reactivity and adult-onset wheezing rather than asthma per se. A report from Spain estimated an attributable risk of 9% based on high-risk occupational groups, defining asthma as increased bronchial reactivity, adult-onset asthma symptoms, or use of medication (15,18). Although data from New Zealand and Spain were also included in the multinational estimate (32), the two country-specific analyses differ because they were based on adult-onset disease.

Derived Attributable Risk Estimates

We identified 8 reports from 7 countries (Table 2) that provided data that allowed us to derive an estimate of the attributable risk for occupational asthma (33–41). The median attributable risk was 25% (25th to 75th percentile: 19% to 30%); mean 26% ± 10%. Four of the studies were random population surveys (33,34,38,39). Of the three case-control studies, two were population-based: One was nested within a longitudinal survey (41), and a second sampled all adults with asthma within a geographic region based on asthma medication prescriptions, identifying controls with a random survey (40). One report from Finland sampled the entire population aged 64 years and older within a geographically defined area (36). That study (attributable risk of 45%) and a French population survey that was limited to adults aged 65 years and older (attributable risk of 30%) (38) contributed the two greatest derived estimates of attributable risk. Overall, the attributable risk estimates that were derived from available data (Table 2) were significantly greater than the 23 values (Table 1) that were reported in the literature ($P = 0.002$).

Extrapolated Attributable Risk Based on Incidence of Occupational Asthma

The estimated incidence of occupational asthma varied widely among countries (Table 3) (21,42–52), from a low of 1.2 to a high of 17.4 per 100,000 person-years. The highest rate (in Finland) included asthma among farmers. Based on the 12 unique analyses represented in Table 3, the median incidence of occupational asthma is 4.7 cases per 100,000 person-years. Assuming an incidence for all asthma among adults of working age of 100 per 100,000 person-years, the estimated median attributable risk is 5% (25th to 75th percentile: 3% to 8%), significantly lower than the reported values in Table 1 ($P = 0.04$) and the estimated values in Table 2 ($P = 0.0003$).

Several case detection methods were used to estimate the incidence of occupational asthma in these studies (Table 4). The SWORD, SHIELD, SENSOR, and PROPULSE programs are public health surveillance schemes. Although the Swedish estimate based on compensation data is considerably greater than other insurance claim estimates, the data from Sweden do not exclude claims that may later have been denied.

Table 3. Studies of Occupational Asthma Incidence: Extrapolated Estimates of Attributable Risk

Location (Reference)	Total Number	System*	Time	Incidence per 100,000 Person-Years	Extrapolated Attributable Risk
British Columbia, Canada (42)	124	Surveillance	1991	9.2	9%
Quebec, Canada (21)	214	Compensation	1986–88	2.6	3%
Quebec, Canada (43)	287	PROPULSE	1992–93	6.3	6%
Finland (21)†	1038	Registry	1988,90,92	14.0	14%
Finland (44)	2602	Registry	1989–95	17.4	17%
Germany (45)	1900	Compensation	1995	5.1	5%
Sweden (46)	1010	Compensation	1990–92	8.0	8%
United Kingdom (21)	1282	Compensation	1989–92	1.2	1%
United Kingdom (47)†	1528	SWORD	1989–91	2.1	2%
United Kingdom (21)	1954	SWORD	1992–93	3.7	4%
Midlands, United Kingdom (48)†	129	SHIELD	1989–91	4.3	4%
Midlands, United Kingdom (49)	1097	SHIELD	1989–97	4.3	4%
California (50)	945	SENSOR	1993–96	2.5	3%
Michigan (51)	725	SENSOR	1988–94	2.9	3%
Michigan (52)	904	SENSOR	1988–95	8.0	8%

* Two rate estimates from Finland (21,44), two from the United Kingdom SWORD surveillance program (21,47), and two from the United Kingdom SHIELD program (48,49) are based on the same reporting systems and thus overrepresent these data sets. There are also two reports using the Michigan SENSOR surveillance system (51,52): both were used in estimating the incidence of occupational exposure since different analytic approaches were used to generate estimates.

† Not included in estimated attributable risk for this group of studies (see Results).

Gender-Specific Estimates

In the Finnish study, the attributable risk of occupational asthma was 6% among men and 4% among women (13). Similarly, the Swedish study estimated the attributable risk as 14% among men and 10% among women (20). In contrast, gender-specific estimates in the multinational analysis, stratified only for the occupationally defined overall risk of 9.9%, were lower for men (9.1%) than women (11.5%) (32). Gender-specific data from Spain gave similar estimates (about 5%) in men and women (18). Table 1 also includes two estimates based only on male subjects (14,22) and one limited to women (30).

It was possible to estimate the gender-specific attributable risk for two additional studies. The study by Viegi et al (39) yielded an estimate of 24% among men and 27% among women, whereas the data from Senthilselvan et al (33), in a rural sample, yielded an attributable risk of 22% among men and only 3% among women.

Work-Related Worsening of Asthma

Only one study (29) distinguished new-onset occupational asthma from asthma that was reactivated by workplace factors. In that study, reactivated asthma accounted for 43 of the 66 cases, of which 8 were considered occupationally related (an attributable risk of 19%), compared with 6 (26%) of the 23 cases with new-onset disease. Another study estimated that, in addition to the 2% of asthma caused by work, 4% of adult asthma was "made worse by work," including the general category of aggravated responses to workplace stimuli (21). About 20% of adults with asthma, however, report work-associated symptoms (53), which must be considered distinct from reactivated, previously quiescent, disease.

Table 4. Summary Estimates for the Attributable Risk of Asthma among Adults due to Occupation

Source of Estimate	Number of Studies	Attributable Risk Estimate	
		Median	Mean
Published estimates	23	9%	12%
Derived from published data	8	25%	26%
Extrapolated from incidence estimates	12	5%	6%
Weighted mean based on study score	28	—	15%
Estimates from reports with highest study scores	12	15%	17%
All studies	43	9%	13%

Semiquantitative Assessment of Study Characteristics

The median study characteristic score for the 28 studies that could be scored was 1.5 (25th to 75th percentile: 1 to 2). The median scores were similar for studies that published attributable risk values and those from which an attributable risk estimate was derived ($P > 0.4$). There was no association between study score and the attributable risks (Spearman rank correlation $= -0.17$; $P = 0.38$).

Summary Estimates of Attributable Risk

The summary value using all 43 studies provided a median estimate that 9% of adult asthma is associated with occupational factors (Table 4). When study quality was considered, either by weighting studies or by only considering studies with a score ≥ 2.0, the attributable risk was about 15%.

DISCUSSION

We identified many studies that measured the contribution of occupational factors to adult asthma. Although the studies involved more than 20 countries and varied in their characteristics, half of the attributable risk estimates were between 5% and 19%, with a median of 9%. The published estimates of the attributable risk were lower than those we derived from available data. This suggests that if publication bias exists, it may be toward lower estimates. In contrast, estimates of the attributable risk that were based on the incidence of occupational asthma yielded lower estimates of the attributable risk, probably because of underreporting of the incidence of occupational asthma.

There are important limitations to our study. A literature review and synthesis is not equivalent to a meta-analysis (54,55). Because of their heterogeneity, the studies we analyzed were not appropriate for meta-analysis, even with newer approaches that integrate different study designs (56). The semiquantitative study characteristic scoring scale that we used has not been independently validated. It can also be criticized for the values that it assigned. For example, perhaps studies that require physiologic criteria for asthma decrease case capture rates and should therefore be discounted. We also gave a higher score to a clinical assessment of occupational-relatedness compared with an epidemiologic association alone. Moreover, our discounting of non–peer-reviewed publication may be unnecessary.

We excluded some studies. For example, an analysis of surveillance data from Italy estimated that 250 (67%) of 373 patients with asthma might have work-related disease (57). The study, however, was based on patients who were referred because an occupational etiology was likely. A study of a Finnish twin cohort (58) that found that suspect workplace exposures were reported by 27% of 78 patients with asthma but only 9% of controls ($P < 0.05$) did not include enough data to estimate an attributable risk. Several studies (59–63) of wheezing or chronic airflow obstruction have found an association with occupation, but these findings are not asthma-specific and thus these studies were not included (59–63).

What are the implications for clinical practice if about 9% of asthma among adults is attributable to occupational factors? Most occupationally related diseases go unrecognized, and obtaining a detailed occupational history is often ill suited to general medical practice. Moreover, because those with occupational asthma often leave their initial job, the treating physician may be evaluating a patient many years after the inciting event. Clearly, addressing past and present occupational factors should be a priority in the assessment of adults with asthma.

The attributable risk of asthma due to occupational exposure incorporates various degrees of causation. In the most straightforward case, work-related exposures induce new-onset asthma in a patient without any previous history of reactive airways disease. In another scenario, workplace factors may reactivate asthma in someone who has been asymptomatic for many years. Occupational exposures may also aggravate preexisting disease, such that new medications or additional medical care is required, a scenario we have not addressed in this analysis. In each case, the ability to detect an occupational association with clinical disease depends on the study design used to estimate it.

Nonetheless, from a practical point of view, each scenario is equally relevant to clinical care. Identifying asthma triggers in the workplace has critical implications for management. Issues of compensation, disability evaluation, and prevention of additional cases are also all directly linked to a health care provider making the connection between occupation and asthma.

REFERENCES

1. Blanc PD. Characterizing the occupational impact of asthma. In: Weiss KB, Buist AS, Sullivan SD, eds. *Asthma's Impact on Society: The Social and Economic Burden. Lung Biology in Health and Disease.* New York: Marcel Dekker. 1999;55–75.
2. Rutstein DD, Mullan RJ, Frazier TM, et al. Sentinel health events (occupational): a basis for physician recognition and public health surveillance. *Am J Pub Health.* 1983;73:1054–1062.
3. Venables KM, Chan-Yeung M. Occupational asthma. *Lancet.* 1997; 349:1465–1469.
4. Beckett WS. The epidemiology of occupational asthma. *Eur Respir J.* 1994;7:161–164.
5. Nordman H. Occupational asthma—time for prevention. *Scand J Work Environ Health.* 1994;20:108–115.
6. Northridge MA. Annotation: public health methods—attributable risk as a link between causality and public health action. *Am J Pub Health.* 1995;85:1202–1204.
7. Levin ML. The occurrence of lung cancer in man. *Acta Unio Internat Contra Cancrum.* 1953;9:531–541.

8. Walter SD. Calculation of attributable risks from epidemiological data. *Int J Epidemiol.* 1978;7:175–182.
9. Toren K, Hermansson BA. Incidence rate of adult-onset asthma in relation to age, gender and smoking—a Swedish population-based study of 15,813 adults. *Int J Tuberculos Lung Dis.* 1999;3:192–197.
10. Tarlo S, Leung K, Broder I, et al. Prevalence and characterization of asthmatics symptomatically worse at work among a general asthma clinic population. *Chest.* 1997;112:133s. Abstract.
11. Johnson A, Dimich-Ward H, Manfreda J, et al. The prevalence of suspected occupational asthma (OA) in a population-based survey. *Am J Respir Crit Care Med.* 1998;157:A882. Abstract.
12. Becklake MR, Ernst P, Chan-Yeung M, et al. The burden of airway disease attributable to work exposures in Canada. *Am J Respir Crit Care Med.* 1996;153:A433. Abstract.
13. Reijula K, Haahtela T, Klaukka T, Rantanen J. Incidence of occupational asthma and persistent asthma in young adults has increased in Finland. *Chest.* 1996;110:50–61.
14. Kobayashi S. Different aspects of occupational asthma in Japan. In Frazier CA, ed. *Occupational Asthma.* New York: Van Nostrand Reinhold; 1980:229–244.
15. Fishwick D, Pearce N, D'Souza W, et al. Occupational asthma in New Zealanders: a population based survey. *Occup Environ Med.* 1997;54:301–306.
16. Bakke P, Eide GE, Hanoa R, Gulsvik A. Occupational dust or gas exposure and the prevalences of respiratory symptoms and asthma in the general population. *Eur Respir J.* 1991;4:273–278.
17. Ng TP, Hong CY, Goh LG, et al. Risks of asthma associated with occupations in a community-based case-control study. *Am J Ind Med.* 1994;25:709–718.
18. Kogevinas M, Anto JM, Soriano JB, et al. The risk of asthma attributable to occupational exposures. A population-based study in Spain. *Am J Respir Crit Care Med.* 1996;154:137–143.
19. Monso E, Munoz-Rino F, Izquierdo J, et al. Occupational asthma in the community: risk factors in a western Mediterranean population. *Arch Environ Health.* 1998;53:93–98.
20. Toren K, Balder B, Brisman J, et al. The risk of asthma in relation to occupational exposures: a case control study. *Eur Respir J.* 1999;13:496–501.
21. Meredith S, Nordman H. Occupational asthma: measures of frequency from four countries. *Thorax.* 1996;51:435–440.
22. Meredith SK, Cullinan P. Occupational asthma in east London. *Thorax.* 1995;50:432P. Abstract.
23. Salvaggio J, ed. *Occupational and Environmental Respiratory Disease in the NIAID Task Force Report: Asthma and Other Allergic Disease.* Washington DC: US Department of Health, Education and Welfare; NIH publication No. 79-387; 1979.
24. Blanc P. Occupational asthma in a national disability survey. *Chest.* 1987;92:613–617.
25. Timmer ST, Rosenman K. Occurrence of occupational asthma. *Chest.* 1993;104:816–820.
26. Blanc PD, Cisternas M, Smith S, Yelin E. Occupational asthma in a community-based survey of adult asthma. *Chest.* 1996;109:56–57s.
27. Blanc PD. Occupation and asthma: through a glass, darkly. *Chest.* 1996;110:3–5.
28. National Health Interview Survey, 1988. *Occupational Health Public Use Data Tape. National Center for Health Statistics.* Bethesda, Md. National Center for Health Statistics; 1992.
29. Milton DK, Solomon G, Rosiello RA, Herrick RF. Risk and incidence of asthma attributable to occupational exposure among HMO members. *Am J Ind Med.* 1998;33:1–10.
30. Forastiere F, Balmes J, Scarinci M, Tager IB. Occupation, asthma, and chronic respiratory symptoms in a community sample of older women. *Am J Respir Crit Care Med.* 1998;157:1864–1870.
31. Syabbalo N. Occupational asthma in a developing country. *Chest.* 1991;99:528. Letter.
32. Kogevinas M, Anto JM, Sunyer J, et al. Occupational asthma in Europe and other industrialized area: a population-based study. *Lancet.* 1999;353:1750–1754.
33. Senthilselvan A, Chen Y, Dosman JA. Predictors of asthma and wheezing in adults. *Am Rev Respir Dis.* 1993;148:667–670.
34. Xu X, Christiani DC. Occupational exposures and physician-diagnosed asthma. *Chest.* 1993;104:1364–1370.
35. Milton D, Christiani D. The risk of asthma attributable to occupational exposures: a population-based study in Spain. *Am J Respir Crit Care Med.* 1997;155:382. Letter.
36. Isoaha R, Puolijoki H, Huhti E, et al. Prevalence of asthma in elderly Finns. *J Clin Epidemiol.* 1994;47:10:1109–1118.
37. Le Moual N, Choudat D, Kennedy S, Kauffmann F. EGEA asthma case-control study: preliminary results of the role of occupational exposure to dust, gases and fumes. *Eur Respir J.* 1998;12(suppl 28):30s. Abstract.
38. Neijari C, Tessier JF, Letenneur L, et al. Prevalence of self-reported asthma symptoms in a French elderly sample. *Respir Med.* 1996;90:401–408.
39. Viegi G, Preediletto R, Paoletti P, et al. Respiratory effects of occupational exposure in a general population sample in North Italy. *Am Rev Respir Dis.* 1991;143:510–515.
40. Flodin U, Ziegler J, Jonsson P, Axelson O. Bronchial asthma and air pollution at workplaces. *Scand J Work Environ Health.* 1996;22:451–456.
41. Bodner CH, Ross S, Little J, et al. Risk factors for adult onset wheeze. *Am J Respir Crit Care Med.* 1998;157:35–42.
42. Contreras GR, Rosseau R, Chan-Yeung M. Occupational respiratory disease in British Columbia, Canada in 1991. *Occup Environ Med.* 1994;51:710–712.
43. Provencher S, LaBreche FP, De Guire L. Physician based surveillance for occupational respiratory diseases: the experience of PROPULSE, Quebec, Canada. *Occup Environ Med.* 1997;54:272–276.
44. Karjalainen A, Virtanen L, Tammilekto K, Kurppa K. Occupational asthma by industry in Finland in 1989–1995. *Eur Respir J.* 1998;12(suppl 28):30s. Abstract.
45. Baur X, Degens P, Weber K. Occupational obstructive diseases in Germany. *Am J Ind Med.* 1998;33:454–462.
46. Toren K. Self reported rate of occupational asthma in Sweden 1990–2. *Occup Environ Med.* 1996;53:757–761.
47. Meredith SK, McDonald JC. Work-related respiratory disease in the United Kingdom, 1989–1992: report of the SWORD project. *Occup Med.* 1994;44:183–189.
48. Ganon PFG, Burge PS. The SHIELD scheme in the West Midlands region, United Kingdom. *Br J Ind Med.* 1993;50:791–796.
49. Di Stefano F, Siriruttanapruk S, McCoach J, Burge PS. Asthma in the West Midlands (UK) from the SHIELD surveillance scheme. *Eur Respir J.* 1998;12(suppl 28):30s. Abstract.
50. Reinisch F, Cussler S, Harrison R. Occupational asthma surveillance in California 1993–1996. *Am J Respir Crit Care Med.* 1998;157:A882.
51. Rosenman KD, Reilly MJ, Kalinowski DJ. A state-based surveillance system for work-related asthma. *J Occup Environ Med.* 1997;39:415–425.
52. Hennenberg PK, Kreiss K, Rosenman KD, et al. An evaluation of the incidence of work-related asthma in the United States. *Int J Occup Environ Health.* 1999;5:1–8.
53. Abramson MJ, Kutin JJ, Rosier MJ, Bowes G. Morbidity, medication and trigger factors in a community sample of adults with asthma. *Med J Austral.* 1995;162:78–81.
54. Powe NR, Turner JA, Maklan CW, Ersek M. Alternative methods for formal literature review and meta-analysis in the AHCPR Patient Outcomes Research Teams. Agency for Health Care Policy and Research. *Med Care.* 1994;32:JS22–37.
55. D'Agostino RB, Weintraub M. Meta-analysis: a method for research. *Clin Pharmacol Ther.* 1995;58:605–616.

56. Austin H, Perkins LL, Martin DO. Estimating the relative risk across sparse case-control and follow-up studies: a method for meta-analysis. *Stat Med.* 1997;16:1005–1015.
57. Mastrangelo G, Bombana S, Priante E, et al. Repeated case-control studies as a method of surveillance for asthma in occupations. *J Occup Environ Med.* 1997;39:51–57.
58. Antti-Poika M, Nordman H, Koskenvuo M, et al. Role of occupational exposure to airway irritants in the development of asthma. *Int Arch Occup Environ Health.* 1992;64:195–200.
59. Leibowitz MD. Occupational exposures in relation to symptomatology and lung function in a community population. *Environ Res.* 1977;14:59–67.
60. Korn RJ, Dockery DW, Spizer FE, et al. Occupational exposures and chronic respiratory symptoms. *Am Rev Respir Dis.* 1987;136:298–304.
61. Krzyzanowski M, Kauffman F. The relation of respiratory symptoms and ventilatory function to moderate occupational exposure in a general population. *Int J Epidermiol.* 1988;17:397–406.
62. Heederik D, Pouwels H, Kromhout H, Kromhout D. Chronic non-specific occupational exposures estimated by means of a job exposure matrix: the Zutphen Study. *Int J Epidemiol.* 1989;18:382–389.
63. Krzyzanowski M, Jedrychowski J. Occupational exposure and incidence of chronic respiratory symptoms among residents of Cracow followed for 13 years. *Int Arch Occupy Environ Health.* 1990;62:311–317.