SPECIAL ARTICLE

How Much Adult Asthma Can Be Attributed to Occupational Factors?

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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%.


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)l(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-
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):

$$\text{attributable risk} = \frac{\text{proportion exposed} \times (\text{relative risk} - 1)}{1}$$

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

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

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

* 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).
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 $\geq 2.0$, 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 physiological 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 publications 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


