CORRESPONDENCE

Occupational asthma in New Zealanders: a population based study

EDITOR,—The community based study of asthma attributable to occupational exposures by Fishwick et al contributes to our appreciation for the types of occupations with increased risk for wheeze, asthma symptoms, and bronchial hyperreactivity (BHR). For computation of the proportion of asthma attributable to occupational exposures, the authors took care to initially define the groups that would be considered at risk. Thus, they avoided a positive bias in computing the attributable risk (AR) due to occupational exposures that would occur if the investigators had used a data based criterion for occupational risks—for example, considering occupational groups eventually exposed based on an AR of 50% if the AR was point cut off such as 1. However, by narrowly defining the at risk group, an appropriate strategy for measuring relative risk in the search for causal associations, they have introduced a negative bias in the measurement of AR. In this letter I examine the possible magnitude of this bias and issues of case definition and selection that may have impacted the reported AR estimates.

It is a characteristic of relative risk measures that, as the definition of exposure becomes less specific—that is, increasing numbers of unexposed people are non-differentially misclassified as exposed—the relative risk estimate will decline. It is also true that the AR will decrease as the relative risk decreases. However, it will also increase as the prevalence of exposure increases. Thus, the net effect of including larger populations in the definition of exposure may not be obvious. In a recent review, Wacholder et al show that non-differential misclassification of unexposed subjects as exposed does not change the AR. A mathematical proof of this fact has also been published. On the other hand, when exposed subjects are misclassified as unexposed, the AR and the relative risk are decreased. Based on these facts, Wacholder et al noted two key imperatives for the design of studies to obtain an unbiased measure of AR that apply provided that any misclassification is non-differential: (1) all exposed people must be classified as exposed; and (2) misclassifying unexposed people as exposed does not affect the point estimate of the AR, but does increase its SE.

The New Zealand study clearly shows that narrow definitions of exposure result in underestimation of the AR. Also, the AR of asthma did not reach the 38% found by the authors, the initial high risk group excluded several occupations with well known risks of asthma including farming, hairdressing, food processing, and woodworking. Of these known high risk groups, farm workers and food processors, were included as exposed, the AR for onset of wheeze after the age 15 increased from 1.9% to 3.1%. Ng et al also used a case-control design to study the AR of asthma due to occupational exposures. However, that study differed from the one of Fishwick et al in that the case definition was based on clinically diagnosed asthma rather than responses to a questionnaire, and Ng et al used a broad definition of exposure to compute the AR of asthma due to occupational exposures. The estimate by Ng et al for Singapore was more than 10 times higher than the AR reported for New Zealand. Although the different AR estimates may be largely due to different exposure prevalences in the two countries and to different methods for ascertaining case status, the definition of exposure may have contributed to these widely differing results.

The definitions for the control category in the two studies are similar. Therefore, it should be possible to compute the AR with the crude prevalence ratios from data in the tables of Fishwick et al to explore the effect of the narrow definition of exposure. Unfortunately, the authors report the tables report all wheeze, not just wheeze with onset after the age of 15. This points to an important problem with the reported odds ratios, which partly reflect the occupations chosen by people with childhood onset asthma rather than risk of asthma from occupational exposures. I have proceeded to compute the AR even with this crude data to make my point, but please note that these results are not adjusted for age, sex, and tobacco smoking, and because they also do not exclude people with childhood onset of wheeze, do not correspond to the AR reported in the paper. The crude AR for wheeze, based on the non-differentially exposed groups, is 0.63%. However, when all those not in group 1 are considered as potentially exposed, the AR is 2.3%. Thus, had the authors computed the age, sex, and smoking adjusted AR for wheeze onset after age 15 with this broad definition of exposure it is likely that they would have obtained a higher estimate of the risk attributable to occupational exposures.

In contrast to this increase in occupational AR when wheeze defined case status, the AR declined from 1.79% to 0.34% when bronchial hyperreactivity (BHR) defined case status and a broad definition of exposure was used. This reflected the fact that the risk for BHR in several groups, most notably the “other food processing” group, dropped so precipitously that these exposures seemed to be protective for BHR even when they had been significant for asthma for wheeze. These major changes in risk suggest that differential misclassification may have been introduced by two types of selection bias.

Firstly, the authors noted two key imperatives for the design of studies to obtain the detailed questionnaire and methacholine challenge tests; the attrition was only 38% of the target study population. Although the authors reported that women and ex-smokers were less likely to report BHR than men and non-smokers, they did not comment on the relation between wheeze or the combination of wheeze and occupation and testing BHR. It is also curious that one more spray painter participated in the BHR test than answered the questionnaire.

A low and uneven participation rate may be such that the conditions of non-differential misclassification would not be met, and therefore, that Wacholder’s suggestions for biased measurements of AR would not apply. This may be especially true in this three stage study from New Zealand where the final participation rate for methacholine challenge was only 38% of the target study population (70% of the 64% who returned the detailed questionnaire who were selected from among the 84% who responded to the initial brief questionnaire).

The second selection bias affecting relative risks and ARs for BHR is that people are unlikely to select occupations independent of their BHR status. Thus, people with pre-existing BHR may be less likely to choose jobs in dusty trades, and so reduce the apparent risk in a study of BHR prevalence. What is really of interest here is the onset of BHR—something that cannot be determined from a cross sectional case-control study.

Given the low participation rates and likely selection biases, the authors were correct to report AR only from the first or questionnaire stage of the study, and to compute it based on wheeze with onset after the age 15. The use of narrow definitions of exposure may have been justified to defend against selection bias resulting from the low and variable participation rates across occupations. However, given these limitations, we should not consider these definitive estimates of the attributable risk of asthma from occupational exposures in New Zealand. New study designs involving incident cases and capable of achieving higher participation rates across all occupational groups are needed to give us a clearer answer to the question how much of the asthma among adults is attributable to occupational exposures?

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Author’s reply—We thank Milton for, and read with interest, his comments concerning our recent publication in Occupational and Environmental Medicine. Indeed, the comments concerning our paper are valid and explore the variation in attributable risk (AR) of occupational asthma due to the use of varying definitions of asthma. We would like to respond particularly to two points made by Milton.

Firstly, he suggests that the AR for occupational asthma would have been higher for wheezing if we had adopted a broader definition of occupational asthma classified as being at high risk. In response, we would emphasise that we also expected this, and indeed our estimates of AR are likely to be an underestimate. In fact, we noted that the estimate would have been higher if we had examined food processors (other than bakers). However, we also reported the findings for the more restricted exposure group, so that they could be compared with the findings of the Spanish group.
Secondly, Milton makes the important point that the AR for bronchial hyperresponsiveness (BHR) dropped when a broader definition of exposure was used, and this may reflect possible types of selection bias. We similarly would agree with the possible biases he raises, but would counter that a further possible explanation could be the differences in the findings for wheezing and BHR due to differences in the findings for the control group (group 1) — that is, that group 1 had a particularly low prevalence of wheezing or a particularly high prevalence of BHR either by chance, or because of unknown selection factors or occupational exposures. We would also comment that Milton is assuming that wheezing and BHR should show the same patterns, but this is not necessarily the case as wheeze, BHR, and asthma are not synonymous.

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This conference is being hosted by the Workplace Safety and Health Division of Manitoba Labour and the InterAgency Committee on Agricultural Safety and Health.

The Planning Committee is represented by the Crop Protection Institute of Canada, Manitoba Labour, Manitoba Agriculture, Manitoba Hydro, Peak of the Market, the Prairie Implement Manufacturers’ Association, United Grain Growers, and the Workers Compensation Board of Manitoba.

All sessions and meetings are open to registrants. Children’s and spousal programmes will be provided.

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BOOK REVIEW

Book review editor: R I Maynard

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It is difficult to conceive of any book dealing better with the scientific aspects of tuberculosis. This is not entirely surprising, however, given the experience and expertise of the authors who are widely known and respected by clinical and public health bacteriologists. Furthermore, this book is timely as the subject is of increasing importance. Although the incidence of tuberculosis has, until recently, declined in industrialised countries, this has not been so elsewhere. Moreover, the association of the disease with HIV infections and AIDS, as well as multiple drug resistance, has led to what now, with an estimated 5000 deaths daily worldwide, is no less than a global emergency.

The authors are to be commended for covering the subject so comprehensively and concisely with excellent illustrations in little more than 100 pages. Despite its brevity, the book is a mine of essential information. After a brief historical introduction, the authors sort out clearly the tangle of mycobacterial nomenclature. Then, after a short clinical section, they describe the role and design of laboratories with special reference to their varying degrees of technical complexity. There is commendable emphasis on all aspects of safety which include not only the design of the laboratory but also the collection and transport of specimens as well as their handling and processing in the laboratory.

The section on training and motivation of staff is excellent. Of great importance also is the part dealing with sterilization and safe disposal of infected waste products.

Routine technical procedures from the fixation, staining, and microbiological examination of dried smears, through cultural methods, to the identification of isolates and drug susceptibility testing are described clearly in considerable detail. More advanced methods for detecting growth of mycobacteria and testing their drug susceptibility by radiometry and nucleic acid-base techniques are described also. For such measure, the final chapter deals briefly but succinctly with leprosy.

This book can be highly recommended to all students and professionals concerned with the prevention and treatment of tuberculosis as well as those people concerned with the occupational health of laboratory workers. Officers of the Health and Safety Executive would also find it of value. Considering the amount and quality of information together with the sound advice contained in this book, its cost at £25 is not excessive.

C E D Taylor