Letter to the editor

Scand J Work Environ Health 1980;6(1):80-82

doi:10.5271/sjweh.2630

A note on observational bias in case-referent studies in occupational health epidemiology.

by Axelson O

Refers to the following text of the Journal: 1979;5(2):91-99

Key terms: case-referent study; letter to the editor; observational bias; occupational health epidemiology

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/7384771

Scand j work environ health 6 (1980) 80—82

LETTER TO THE EDITOR

A note on observational bias in case-referent studies in occupational health epidemiology

Adequacy of information is an apparent requisite for the epidemiologic evaluation of potential health hazards. Assessing exposure especially tends to be difficult, whereas diseases or causes of death can be more explicitly characterized. Sometimes, occupational titles can be considered acceptable indicators of exposure, eg, painter with regard to solvent exposure, chimney sweeper with regard to soot, etc, whereas such titles as metal worker, wood worker and others similar are less useful for the characterization of exposure. It should be emphasized, however, that the goal of occupational epidemiology is not to associate the job as such with a certain health hazard but rather to pinpoint the responsible agent or process, which might then be eliminated or changed in order to avoid the hazard.

Observation of exposure

In case-referent studies, the frequency of a particular job among the cases and the referents might indicate exposure, but it is usually possible also to obtain rather specific information about each subject's exposure conditions over time from a factory or a trade union. The case-referent approach becomes particularly convenient if it is possible to find a setting in which a fairly large group of workers with the exposure in question live in a parish or a small town, for which a (local) population register of deaths or diseases (eg, a hospital register) is available [cf Axelson (1)].

However, many types of exposure tend to be scattered and widespread in society, and they usually require questionnaires and interviews for assessment. The situation then becomes much more problematic with regard to the adequacy of the information, since there could be a tendency, conscious or not, for those suffering from a particular disease, the cases, to exaggerate the exposure somewhat in comparison with healthy referents. Should the disease at issue be severe, resulting in deaths, it might be preferable also to utilize dead individuals as referents to achieve an inquiry situation similar to that of the cases. In general, it seems preferable to use diseased referents, as they might be apt to reply in a manner more similar to that of the cases than healthy individuals, who might find little interest in answering various questions about earlier exposures. On the other hand, one has to be careful with regard to the diagnoses chosen since reference entities must be unrelated (positively or negatively) to the exposure [cf Axelson (1)].

If interviewers are used, they should be blinded with regard to the subject's status as case or referent (again the benefit of using dead referents for dead cases is apparent); also the questions should cover various extraneous matters in addition to the specific exposure(s) under consideration. The same recommendation might be given when questionnaires are to be used.

Although certain measures should be taken in the design of the study to obtain adequate information, there is nevertheless always the suspicion that the observation of exposure might be biased if one has to rely on questionnaires or interviews. Interestingly, some evaluation of the adequacy of exposure information can be obtained from the data, if the information

0355-3140/80/010080-3

is not only about a specific exposure but also about other characteristics to which the exposure is related. A prerequisite is, however, that these other characteristics can be more precisely assessed than the exposure itself. For example, whereas an exposure which has occurred among some, but not all, individuals in a specific job or particular trade might be observed with various degrees of uncertainty through questionnaires or interviews, it is possible to achieve (almost) exact information about the individual's occupational title, eg, forestry worker, metal worker, etc. Then, if an increased risk ratio is obtained with regard to the specific exposure because of an inclination of the cases to exaggerate and/or the referents to underestimate their exposure, a tendency towards prevention should also appear among the nonexposed individuals within the specific job, trade, etc, to which the specific exposure belongs. This aspect is particularly relevant in situations with fairly high risk ratios, as often obtained in occupational health studies, whereas less credibility of such an evaluation can be achieved in situations of a slight or moderate increase in the risk ratio, say, of less than two or three. In addition this evaluation procedure fails if the actual exposure is relatively rare, say 10 % or less, even within the particular job, trade, etc, and the majority of the referents are apt to recall the exposure poorly.

Algebraic calculations

The issue might be further and more exactly illustrated as follows. Consider a case-referent study with the following structure and definitions:

Job/trade category	*Exposed*	*Nonexposed*
Within job/trade		
Cases	a_1	b_1
Referents	c_1	d_1
Outside job/trade		
Cases	—	b_0
Referents	—	d_0

Under the assumption that no hazard is associated with the exposure, ie, if the rate or risk ratio (odds ratio) is unity (2), one has for the total study

$$a_1 (d_1 + d_0)/c_1 (b_1 + b_0) = 1 \quad [1]$$

and also within the trade

$$a_1 d_1/c_1 b_1 = 1 \quad [2]$$

and then equation 1 might be substituted and rearranged as

$$(b_1 + b_0)/b_1 = (d_1 + d_0)/d_1 \quad [3]$$

and therefore

$$b_1/b_0 = d_1/d_0 \quad [4]$$

Now, if the exposure is inadequately observed in such a way that cases tend to be classified as exposed more often than they really are (by gaining a quantity from b_1, ie, Δb_1) and/or the exposure of the referents is underestimated (by losing a quantity from c_1, ie, Δc_1, being gained by d_1), then

$$\frac{(a_1 + \Delta b_1)(d_0 + d_1 + \Delta c_1)}{(b_0 + b_1 - \Delta b_1)(c_1 - \Delta c_1)} > 1 \quad [5]$$

is the expression for an increased risk ratio through biased observation. However, with regard to equation 4, the consequence will be

$$(b_1 - \Delta b_1)/b_0 < (d_1 + \Delta c_1)/d_0 \quad [6]$$

or a "prevention" among the nonexposed within the trade, since

$$(b_1 - \Delta b_1)\, d_0/b_0\, (d_1 + \Delta c_1) < 1, \quad [7]$$

where $(b_1 - \Delta b_1)$ represents the (inadequately observed) nonexposed cases and $(d_1 + \Delta c_1)$ the (also inadequately observed) nonexposed referents within the trade, etc.

These aspects make it possible to clarify somewhat the adequacy of observation in a case-referent study, ie, if the exposure, as obtained through interviews or questionnaires, can be included under a class of some other and more objectively observable entity, eg, job affiliation, etc, and given a reasonably high risk ratio, as well as a fairly common exposure within the job, etc. Only if, for some reason (other than the exposure at issue), there should be an elevated morbidity or mortality within this particular job, trade, etc, would an observational bias result in a normal

risk ratio for the nonexposed, together with an elevated hazard for the exposed. Such situations are less likely to occur, however, but are difficult to reveal, and judgements about such rare possibilities have to be based on information from outside the study.

References

1. Axelson O. The case-referent (case-control) study in occupational health epidemiology. Scand j work environ health 5 (1979) 91—99.
2. Miettinen OS. Estimability and estimation in case-referent studies. Am j epidemiol 103 (1976) 226—235

Olav Axelson
Department of Occupational Medicine
University Hospital
S-581 85 Linköping
Sweden