CORRESPONDENCE

Estimation of prevalence rate ratios for cross sectional data: an example in occupational epidemiology

Sir,—A cross sectional or prevalence study is often used in an occupational setting to assess whether an association exists between exposure in the workplace and some physiological state where information on exposure and physiological state are obtained contemporaneously. If the physiological state is dichotomised as "normal" or "pathological" the data can either be analysed by stratification, standardisation,[1] or by multiple logistic regression.[2] The last is an especially valuable statistical tool in that it allows statistical adjustment of several confounders as well as assessment of effect modification based on modest sample size. The drawback with logistic regression for cross sectional data is that the model estimates the prevalence odds ratio (POR) as effect measure. Under certain restricted conditions the POR approximates the incidence density ratio,[3 4] which makes it (arguably) a useful effect measure for causal inference. Nevertheless, because prevalence data lack time dimension—they do not establish that cause antecedes effect[5]—the usefulness of POR as an indicator of aetiology may be illusory.

In aetiological research, especially if the latent period (interval between exposure and occurrence of disease) is protracted and ill defined, a cross sectional study can only be used to assess a statistical association between exposure and a physiological state, leaving causal inference to an appropriate epidemiological design such as a prospective cohort or retrospective case-control that incorporates the time dimension. (Parenthetically the odds ratio is a more desirable effect measure in a case-control study than is generally realised, but it has more defects in a cohort study than are widely appreciated.)[4] Of course, cross sectional studies have other important applications—for example, in non-aetiological studies or in aetiological studies where the disease has a short and well defined latent period.[1 3]

As an epidemiological measure, the prevalence rate ratio or relative risk (PRR) is a better index than POR. Whereas PRR is easy to interpret and to communicate, POR lacks intelligibility—it does not possess a simple meaning.[6 7] As emphasised by Savitz, a desirable epidemiological measure must be one that is simply interpretable. As such, the odds ratio has no direct epidemiological utility except as an approximation of the rate ratio.[8]

Because cross sectional studies are not (or should not be) used for rare exposures or conditions, POR will generally be very discrepant from PRR. What is needed then is a statistical model that estimates PRR rather than POR yet preserves the advantages of logistic regression.

Cox's proportional hazards model[9] was originally developed for the estimation of instantaneous conditional hazards ratio based on complete or censored longitudinal data with varying follow up times. Subsequently, Breslow[10] showed that by imposing a condition of constant follow up time, Cox's model can be adapted for the estimation of rate ratios.

To illustrate the application of Breslow's modification of Cox's model for the estimation of PRR with adjustment of confounding, we consider a cross sectional study of 236 workers occupationally exposed to cadmium (data were collected by KSC). The data analytical goal is to estimate the crude and covariate adjusted PRR of urinary cadmium concentration (indirect estimate of exposure to cadmium) on probability of β_2 microglobulinuria (a dichotomised physiological state); potential confounders include sex, ethnicity, and age. Table 1 summarises the observed results. The PRRs estimated by the Breslow-Cox model (table 2) are very discrepant from the PORs estimated by the logistic regression model (table 3), thus underscoring the limitation of logistic regression for cross sectional data. The figure displays the model predicted probability of β_2 microglobulinuria as related to urinary cadmium concentration. All statistical analyses were

Table 1 Urinary cadmium concentration as a predictor for β_2 microglobulinuria in a cross sectional study of 236 workers occupationally exposed to cadmium

β_2 microglobulin (μg/g creatinine)	Urinary cadmium (μg/g creatinine)		
	<5	5 to <10	≥10
"Pathological" (>200)	3 (2%)	7 (17%)	32 (73%)
"Normal" (≤200)	147	35	12
Total	150	42	44

Table 2 Crude and adjusted rate ratio (relative risk) of urinary cadmium concentration (risk factor) on β_2 microglobulinuria (response): proportional hazard model*

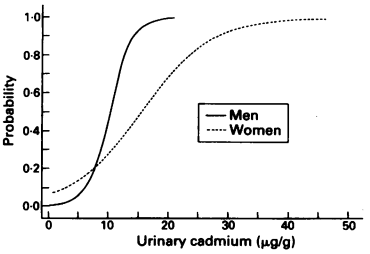
Urinary cadmium (μg/g creatinine)	Crude	Adjusted
	Rate ratio(95% CI)	Rate ratio(95% CI)
<5	1 (—)	1 (—)
5 to <10	8·3 (2·1–32·2)	6·4 (1·5–27·4)
≥10	36·4 (11·1–118·7)	40·6 (11·0–149·5)

*Statistically adjusted for ethnicity (Chinese, Malay, Indians), sex, and age.

Table 3 Crude and adjusted odds ratio of urinary cadmium concentration (risk factor) on β_2 microglobulinuria (response): logistic model*

Urinary cadmium (μg/g creatinine)	Crude	Adjusted
	Odds ratio(95% CI)	Odds ratio(95% CI)
<5	1 (—)	1 (—)
5 to <10	9·8 (2·4–39·8)	7·8 (1·6–37·2)
≥10	130·7 (34·8–489·9)	219·4 (38·5–1252·0)

*Statistically adjusted for ethnicity (Chinese, Malay, Indians), sex, and age.



Probability of β_2 microglobulinuria as related to urinary cadmium concentration.

carried out by SAS.[11 12] The programs and related information documenting the analytical process are available from JL. Please send a floppy diskette for storage.

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Chrysotile asbestos revisited

Sir,—It is difficult to find a material that has stimulated as much interest, and raised so much controversy, as asbestos. Mentions of health related effects in the literature date back almost to the beginning of this century. Yet results of recent studies are still on the agenda of international scientific meetings and published in current medical journals. Also, several if not most animal and in vitro studies on other fibrous materials include asbestos fibres as "positive controls" in their experimental design. The more recent human studies and updates on health related effects of occupational exposure to asbestos can now rely on longer periods of follow up, and on somewhat better defined exposure data to specific asbestos types.

A case in point is the recent update of the largest cohort of chrysotile asbestos workers ever undertaken.[1] The preliminary results were the subject of a presentation in September 1992 at the 9th International Symposium on Epidemiology in Occupational Health, held in Cincinnati. The status of this unique cohort had been reviewed four times, the latest follow up was in May 1992 and included 2827 additional deaths, bringing the total to 7312. Cancer risks were re-evaluated. For six classes of exposure up to 300 mpcf years, the authors were unable to detect any excess lung cancers. Applying a conservative estimate for conversion of 1 mpcf ~3 f/ml, the exposure levels below which no excess lung cancers were detected would be 900 f/ml. years, or ~45 f/ml for 20 years. While awaiting the publication of the full study later this year, this preliminary report should not be construed as an invitation to relax the exposure limit of 1 f/ml for chrysotile, as recommended by a group of experts convened by the World Health Organisation in 1989. It does indicate, however, that the recommended exposure limit was indeed a realistic and acceptable one.

I mentioned animal studies on man made fibrous materials, which sometimes include at least one asbestos fibre type as "positive control"; this is another area that needs to be revisited. For example, in a recent inhalation study on the allegedly minor health related effects of man made vitreous fibres (MMVFs), the authors include for comparison the results of concurrent studies on the allegedly severe effects from one refractory ceramic fibre sample, and from chrysotile asbestos.[2] Close scrutiny of the experimental design, however, reveals that the results reported are from animals exposed six hours a day, five days a week, for 24 months to ~250 f/ml for the MMVFs, ~180 f/ml for refractory ceramic fibre, and 10 000 f/ml for chrysotile asbestos!

Another report[3] indicates that after 24 months at a dose of 100 f/ml (~0·9 mg/m³), of aramid (Kevlor) fibres in rats fibrosis had developed along with cystic keratinising squamous tumours. In view of the other inhalation experiments on MMVFs mentioned, an interesting experiment (which has never been carried out) would be to test the effects of a 24 month inhalation exposure to chrysotile at similar fibre number dosage (see table). With regard to inhalation studies on rock and slag fibres, the International Labour Office report indicates that "Available data are insufficient to draw conclusions on the relative potency of various types, because the true exposure (number of respirable fibres) was not characterized in most studies."

It is worth going further into the details of the units of dosage used when reporting results. Coffin and colleagues have for many years warned against inappropriate comparison of the pathological potential of different fibre preparations when only gravimetric units were used to report biological effects. For instance, an in vitro study published in 1988 on the comparison of mass *v* number of fibres in the cytotoxic response of lung cells from Chinese hamsters to erionite, crocidolite, and chrysotile, showed that on the basis of fibre numbers, erionite required fewer fibres than crocidolite, and that chrysotile required a >50-fold higher number of fibres to produce cytotoxic effects similar to those obtained with crocidolite. By comparison with erionite, the difference was >300-fold.[4]

More recently, Coffin *et al*[5] reported the results of an in vivo study on induction of mesothelioma after intrapleural and intratracheal injections in the rat. Erionite was 500 to 800 times more tumorigenic, and crocidolite was 30 to 60 times more so than chrysotile on the basis of the ratio of tumours to numbers of fibres. The fibre preparations used contained $3{\cdot}3 \times 10^6$ f/mg for erionite, $8{\cdot}6 \times 10^6$ f/mg for crocidolite and 1090×10^6 f/mg for chrysotile.

It is worth mentioning that the summary of research recommendations of a National Institute of