

CORRESPONDENCE

SAS program for testing the difference between two correlated correlation coefficients

Sir,—Sometimes we need to statistically compare two product-moment correlation coefficients (r) that are correlated—that is, not statistically independent. We might, for example, wish to determine whether the correlation of urinary cadmium (X_1) on β_2 microglobulin (Y) is statistically different from the correlation of blood cadmium (X_2) on β_2 microglobulin (Y) in the same group of subjects. In a methodological study to validate two methods, say machine (X_1) *v* ascultatory (X_2), against a reliable invasive method (Y), for measuring blood pressure, we might compare the correlation of X_1 on Y with the correlation of X_2 on Y .

These correlation coefficients are correlated because they share the common variable Y measured from the same group of subjects, and any test of significance that ignores this non-independence will be inappropriate. Actually the problem has long been recognised and the test for comparing correlated correlation coefficients was first described by Hotelling in 1940.¹ Hotelling's t test has been used for many years and is still being used, even though the method has serious drawbacks.^{2,3} Improvements to the Hotelling test have been considered by several authors.²⁻⁶

Here I describe an SAS program⁷ to compare two correlated correlation coefficients. The program uses the statistical procedure given by Meng *et al*⁶ and it outputs the Z value (standard normal deviate) and the two sided significance probability pertaining to the statistical difference of the two correlated correlation coefficients. To enhance user friendliness, the program is packaged as an SAS macro named %MACRO CCORR (appendix). The macro requires four user supplied parameters: rx1y (correlation of X_1 on Y), rx2y (correlation of X_2 on Y), rx1x2 (correlation of X_1 on X_2), and n (number of subjects in the sample). If you stored the macro with filename and extension as "ccorr.mac" in C:/MYSAS, then the entire SAS program will consist of as few as two statements, one to invoke the macro and the other to supply the four parameters to the macro. Here is an example of a complete SAS program:

```
%INCLUDE 'C:/MYSAS/CCORR.MAC';
%CCORR (0.72, 0.55, 0.22, 50)
%CCORR (0.25, -0.14, 0.18, 60)
```

The first test gives $Z = 1.4282$ with the two sided probability value = 0.15319; the second test gives $Z = 2.3085$ with the two sided probability value = 0.02097.

Appendix: listing of the SAS codes

```
%MACRO CCORR (rx1y, rx2y, rx1x2, n);
*% stored as 'CCORR.MAC';
OPTIONS nocenter.nodate;
DATA _null_;
z1 = 0.5*log((1 + &rx1y)/(1 - &rx1y));
z2 = 0.5*log((1 + &rx2y)/(1 - &rx2y));
rs = (&rx1y*&rx1y + &rx2y*&rx2y)/2;
f = (1 - &rx1x2)/(2*(1 - rs));
if f > 1 then f = 1;
h = (rs*(1 - f)/(1 - rs)) + 1;
zdiff = z1 - z2;
den = 2*h*(1 - &rx1x2);
Z = zdiff*((&n - 3)/den)*0.5;
prob = (1 - probnorm(abs(Z)))**2;
put @5 'Z' = 'Z 8.4' 2-sided p value =
'prob 7.5;
*Note: output is shown on the 'LOG
WINDOW';
run;
%MEND CCORR;
```

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Reproductive risks associated with diving

Sir,—Raymond (1993;50:1055-6) considers the risks to reproduction from convective heat exposure among divers who use hyperbaric chambers. It is worth noting that they may be presumed to be at risk not only from the heat, but also from the pressure.

Röckert *et al*¹ reported that the plasma testosterone concentrations of rats exposed to a hyperbaric environment of air were significantly and substantially (about 50%) reduced. Röckert and Haglid² reported that preliminary results from the determination of plasma testosterone in human divers showed it to decrease after diving.

I have hypothesised that the sex ratio (proportion of males) of mammalian (including human) offspring is affected by the hormone concentrations of both parents at the time of conception; high concentrations of testosterone being associated with subsequent births of boys and high concentrations of gonadotrophin with subsequent births of girls.³ This suggestion is supported by the findings of Lyster⁴ and Röckert⁵ who reported highly significant low sex ratios in the offspring of Australian abalone divers and Swedish navy divers. It is also supported by the finding of a significantly low sex ratio in the offspring of men who were exposed to the nematocide DBCP⁶; such men have been reported to have high

gonadotrophin but normal testosterone concentrations.⁷

Workers in industrial medicine might consider using the sex ratios of offspring as a criterion of reproductive risk. Unusual sex ratios of offspring are characteristic of a number of diseases—for example, prostatic cancer,⁸ hepatitis B,⁹ multiple sclerosis,¹⁰ otosclerosis,¹¹ and non-Hodgkin's lymphoma.¹²

Meanwhile it might be prudent to re-examine the testicular function and sex ratios of offspring of further samples of divers.

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Occupational exposure to dust and lung disease among sheet metal workers

Sir,—The study *Occupational exposure to dust and lung disease among sheet metal workers* by Hunting and Welch (1993;50: 432-42) was an ambitious undertaking. This correspondence considers the modelling and selection techniques employed, the validity of the work history and exposure modelling, the potential impact of possible selection bias, and the appropriateness of the industrial hygiene evaluation on the fibreglass insulation findings.

In terms of the modelling and variable selection techniques, the final analyses of exposure *v* chronic bronchitis were not age adjusted even though the confounding effects of age are ubiquitous and universally recognised in epidemiological research. Age should have been included in the regression equation "regardless of statistical significance if such inclusion changes the estimated coefficients of the risk variables by any appreciable degree."¹ Without such an adjustment, the statistical significance of the association between chronic bronchitis and high level fibreglass exposure (ripout) may

be entirely due to the association between age and the lifetime odds of having performed ripout.

Asbestos exposure (which was modelled as adjusted years of exposure) was treated differently from fibreglass exposure (ever/never had a high exposure) in the multiple logistic regression analyses. The tables and text indicate that a fibreglass exposure index based on either the adjusted years of fibreglass exposure or none/moderate/high fibreglass exposure would not have indicated any association between fibreglass exposure and chronic bronchitis.

The median duration of exposure in the "high level" fibreglass group is zero years, and 75% of this group had less than one year of experience at the "high level". It is not biologically plausible that such a fleeting exposure is responsible for symptoms of chronic bronchitis.

Work history and exposure modelling are not adequately considered. It is questioned whether the exposure models are truly able to distinguish qualitatively and/or quantitatively between the exposures of asbestos, welding, and fibreglass, given the high degree of correlation among them. No attempt was made to validate the self reported work histories (which are open to recall bias) nor to validate the models of fibreglass and asbestos exposure. More should have been done to validate the exposure modelling assumptions because the paper's conclusions are based on these assumptions (see industrial hygiene comments later).

The overall design of the survey raises important questions about the potential impact of selection bias on the study. This includes the representativeness of the results and the validity of generalising these results beyond the sample.

The survey's results are based on less than 40% of those eligible and invited to participate. It relied on data from a previous medical screening in which only 47% of those invited agreed to participate (12 454 of 26 329 sheet metal workers). Of this, 407 (47%) eligible workers were selected from United States Sheet Metal and Air Conditioning National Association locals in the southeast sun belt and west coast states. Only 333 (82%) of these 407 completed the interviews.

Unanswered, yet most important questions remain. How did survey eligibility criteria affect results? Are there health related selection factors that influenced eligibility—for example, worked in the sheet metal shop for at least 70% of his working career, did removal for at least 40% of his working career, or welding for less than 20% of his working career? What sort of self selection operated over time to eventually impact eligibility, exposure, or health?

An important industrial hygiene consideration and a major issue in this study is the assignment of "high", "medium" and "low" concentration designations. No actual airborne fibre measurements were made of the occupational tasks. Rather, exposures were derived from several published reports. Also, the questionnaire only obtained "average percentage times" spent working in four broad areas of sheet metal work—namely, shop work, welding, job site installation, and ripout. Unless the exposure history is accurate, in terms of the actual work tasks, airborne concentrations, duration of exposure, and other airborne expo-

sure at the work site, any analysis will be of very limited value.

For example, the designation of "high" exposure was given to any fibreglass ripout operation. There were no ripout exposure concentration values referenced. One can not draw analogies from asbestos ripout operations with regard to the amount of fibre fly. A limited amount of sampling data (there is not that much fibreglass torn out) shows that fibreglass ceiling board ripout resulted in airborne fibre exposures with an average of 0.29 fibres/ml for all fibres, using the NIOSH 7400A method (which would be somewhat similar, but not identical to the method used by Balzer *et al*⁴ and Fowler *et al*⁵).

When the 7400B method (respirable fibres) was used, total fibre concentration was 0.14 fibres/ml, with further analyses revealing only 0.041 fibres/ml of respirable glass fibres. For pipe insulation ripout the airborne exposure concentrations were 0.126, and 0.046 fibres/ml for all respirable fibres and respirable glass fibres, respectively.²

The fibre concentrations reported by Balzer, Copper, and Fowler, as well as being total fibre counts, did not differentiate between glass and other fibrous materials.^{3,5} Further, the average airborne fibre diameters were well above the respirable range, suggesting that respirable fibre exposure would be lower.

Using NIOSH 7400B analytical methods, airborne average exposure concentrations for a wide variety of fabrication and installation operations including pipe insulation, range assembly, duct assembly, duct board installation, water heater assembly, and flex duct assembly ranged from 0.006 fibres/ml (duct board assembly) to 0.087 fibres/ml (general fabrication) for all fibres and 0.002 (duct board installation) to 0.071 fibres/ml (general fabrication) for glass fibres. In no instance did the 95th percentile individual concentration exceed 0.12 fibres/ml.² These respirable fibreglass exposure concentrations are similar to average concentrations recently noted in insulation wool manufacturing plants (all fibres, 0.03 fibres/ml⁶ and all fibres, 0.025 fibres/ml⁷) Because of these low uniform exposure values, it is not reasonable to divide the sheet metal workers' exposures into high, medium, and low categories.

It then follows that it is difficult to attribute the apparent excess of chronic bronchitis to overexposure to fibreglass. The authors are then faced with the same issues which confronted and confounded Engholm, and Von Schmalensee³ and Engholm *et al*.⁹

Based on the data presented, the paper's conclusion that high intensity exposure to fibreglass causes chronic bronchitis is unwarranted.

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Authors' reply

Konzen makes a number of criticisms of our study's finding that sheet metal workers with chronic bronchitis were 2.28 times as likely to have performed tasks involving high level fibreglass exposure (that is, ripout of fibreglass materials). We would like to take this opportunity to clarify our methods and provide additional information.

Konzen has a concern about selection bias. He correctly notes that only 47% of invited sheet metal workers participated in the initial medical examinations from which our sample for interview was drawn. For this study, 407 workers were selected from among those 12 454 initially examined, and 333 (82%) completed a telephone interview. Forty of the 74 non-participants were decreased or otherwise lost to follow up; of those actually contacted, 90.7% completed an interview.

To look indirectly at possible selection bias, we compared baseline (medical examination) characteristics of participants and non-participants from this study; the prevalence of chronic bronchitis was 15% in both groups. Notably, the non-participants (rather than the participants) had spent significantly more time doing job site installation and ripout work, which generally involve more dust exposure than shop work. Thus it is unlikely that the association between chronic bronchitis and ripout exposures would be biased by participation factors.

Konzen also questions whether our selection criteria may have biased the results. We selected workers who reported at the baseline medical examination doing primarily shop work (>70% of career) or doing ripout for >40% of their careers. These selection criteria were established to obtain a range of asbestos and fibreglass exposure among participants, with shop workers having more fibreglass and less asbestos exposure, and other workers having a variety of exposures, including high level exposures to both substances. We excluded workers who reported welding more than 20% of the time, in order to exclude this exposure as a major confounder. We do not believe that there would have been exposure and health selection factors simultaneously operating among the workers we selected. An example of how such a selection bias could occur would be if workers with lung disease switched from job site installation work to (often) less demanding shop work as they developed symptoms. These workers, however, would not have worked at least 70% of their careers in the shop, and thus would not have been included in this study. We