

THE AUTHOR REPLIES

I thank Drs. van der Gulden and Verbeek (1) for applying my shortcut method (2) to calculation of the confidence interval of a proportionate mortality rate (PMR). As I pointed out in an earlier letter (3), approximation of the exact limits of a 95 percent confidence interval can be further improved by using the formula

$$(\sqrt{O+1} + z_{0.95}/2)^2 = (\sqrt{O+1} + 0.98)^2 \quad (1)$$

instead of $(\sqrt{O+1} + 1)^2$, with O = the observed number of events.

For PMRs as well as for SMRs based on less than 10 cases, the approximated limits are more precise using equation 1. For example, for van der Gulden and Verbeek's first three disease sites where the observed numbers are 8 or less, the approximated upper limits are decreased to $A = 5.70$, $B = 2.92$, and $C = 3.77$. The reductions are about 50 percent of the differences between the

exact limits and the approximated limits, as van der Gulden and Verbeek (1) pointed out.

REFERENCES

1. van der Gulden JWJ, Verbeek ALM. Re: "A simple method to calculate the confidence interval of a standardized mortality ratio (SMR)." (Letter). *Am J Epidemiol* 1992;136:1170-1.
2. Ulm K. A simple method to calculate the confidence interval of a standardized mortality ratio (SMR). *Am J Epidemiol* 1990;131:373-5.
3. Ulm K. Re: "A simple method to calculate the confidence interval of a standardized mortality ratio (SMR)." (Letter). *Am J Epidemiol* 1991;133:212-14.

Kurt Ulm
*Institute for Medical Statistics
 and Epidemiology
 Technical University Munich
 Ismaninger Strasse 22
 D-8000 Munich 80
 Germany*

RE: "TESTS FOR TREND AND DOSE RESPONSE: MISINTERPRETATIONS AND ALTERNATIVES"

We would like to correct a possible misinterpretation that Maclure and Greenland (1) conveyed to readers regarding the analysis of our case-control study of occupational bladder cancer among women (2). It is important to note the difference between a duration effect (dose response) and a statistically significant result of the Mantel extension test. Indeed, for this reason, we made a clear distinction between a statistically significant trend test result and a consistent pattern of risk by duration of employment in the third paragraph on p. 457 of our paper (2). As we indicated in that paragraph, of the seven occupations with a significant trend test result (positive or negative) (table 4), we considered credible only those findings for which the pattern of risk by duration among the exposed was consistent. That is, we discounted the three occupations for which the p value for the trend test was significant but the risk among the exposed either reversed direction or remained unchanged with increasing duration. Thus, the only occupations mentioned in the abstract of our paper were the three manufacturing occupations out of the four that had "incremental relative risks" greater than or less than 1 (Maclure and Greenland's terminology).

Maclure and Greenland indicated that only one of the "incremental relative risks" was statistically significant because of our "sparse data" (1, p. 103). In our opinion, the search for occupa-

tional hazards in this study should not depend only on statistical significance, but should rely more on coherent patterns of risk. Our study is the largest study of bladder cancer conducted to date; it included over 10 times more female cases than the only other study we are aware of that focused on occupational bladder cancer in women (3). Thus, we believe that any consistent evidence of a hazard should be highlighted for further scrutiny, and particular attention should be given to those occupations in which workers have been found to have an increased risk of bladder cancer (e.g., metal workers and chemical workers).

REFERENCES

1. Maclure M, Greenland S. Tests for trend and dose response: misinterpretations and alternatives. *Am J Epidemiol* 1992;135:96-104.
2. Silverman DT, Levin LI, Hoover RN. Occupational risks of bladder cancer among white women in the United States. *Am J Epidemiol* 1990;132:453-61.
3. Maffi L, Vineis P. Occupation and bladder cancer in females. *Med Lav* 1986;77:511-14.

Debra T. Silverman
 Robert N. Hoover
*Epidemiology and Biostatistics Program
 National Cancer Institute
 Bethesda, MD 20892*

proximated limits, as van k (1) pointed out.

REFERENCES
 Verbeek ALM. Re: "A simple method to calculate the confidence interval of a ratio (SMR)." (Letter). *Am J Epidemiol* 1990;131:373-5.
 Verbeek ALM. A simple method to calculate the confidence interval of a standardized mortality ratio. *Am J Epidemiol* 1991;133:373-5.

Ulm
 Institute for Medical Statistics
 and Epidemiology
 Technical University Munich
 Biedersteiner Strasse 22
 80634 Munich 80
 Germany

STATEMENTS AND

Our study should not depend on the significance of trends of risk. Our study is a case-control study of bladder cancer conducted to determine whether there are more female cases than we are aware of that suggest that any consistent trend in bladder cancer in women should be highlighted for particular attention should be given to occupations in which workers have an increased risk of bladder cancer and chemical

REFERENCES
 Hoover RN. Tests for trend and dose response: misinterpretations and alternatives. *Am J Epidemiol* 1992;135:96-104.
 Levin LI, Hoover RN. Occupational risks of bladder cancer among white women in the United States. *Am J Epidemiol* 1990;132:453-61.

Occupation and bladder cancer among white women. *Am J Epidemiol* 1986;77:511-14.
 Silverman DT, Hoover RN. Occupational risks of bladder cancer among white women in the United States. *Am J Epidemiol* 1990;132:453-61.
 Maclure M, Greenland S. Tests for trend and dose response: misinterpretations and alternatives. *Am J Epidemiol* 1992;135:96-104.
 Department of Biostatistics Program
 Harvard School of Public Health
 665 Huntington Ave
 Boston, MA 02115
 20892

THE AUTHORS REPLY

We thank Drs. Silverman and Hoover (1) for their observations. However, in our paragraph on the paper by Silverman et al. (2), we did not use the words "statistically significant." We said that if Silverman et al. "had excluded the unexposed subjects (over 90 percent), they would have found the data too sparse to test their duration hypotheses" (3, p. 103).

In their abstract, Silverman et al. concluded that "punch and stamping press operatives had a significant trend in risk with increasing duration of employment ($p = 0.012$) . . . chemical processing workers [had] a significant, positive trend in risk with increasing duration of employment ($p = 0.042$) . . . [and] textile workers [had] a significant, negative trend in risk with increasing duration of employment ($p = 0.031$)" (2, p. 453). Table 1 shows data and relative risks from Silverman et al.'s table 4. We also show our estimates of the incremental relative risks and crude 95 percent confidence intervals for each increment in duration of exposure. Contrary to the statement of Silverman and Hoover, only the chemical processing workers show a "coherent

pattern of risk" (in the sense of monotonic trend), and even here the data are compatible with many other possibilities. We thus maintain that Silverman et al.'s data were too sparse to justify their original conclusions.

REFERENCES

1. Silverman DT, Hoover RN. Re: "Tests for trend and dose response: misinterpretations and alternatives." (Letter). *Am J Epidemiol* 1992;136:1172.
2. Silverman DT, Levin LI, Hoover RN. Occupational risks of bladder cancer among white women in the United States. *Am J Epidemiol* 1990;132:453-61.
3. Maclure M, Greenland S. Tests for trend and dose response: misinterpretations and alternatives. *Am J Epidemiol* 1992;135:96-104.

Malcolm Maclure
 Department of Epidemiology
 Harvard School of Public Health
 Boston, MA 02115

Sander Greenland
 Department of Epidemiology
 School of Public Health
 University of California
 Los Angeles, CA 90024-1772

TABLE 1. Relative risks (RRs) and incremental relative risks (iRRs) of bladder cancer for white females in specified occupations, by duration of employment: National Bladder Cancer Study*

Occupation and duration (years) of employment	No. of cases	No. of controls	RR	iRR† (95% CI‡)
Punch and stamping press operative				
<5	3	8	0.6	
≥5	9	3	5.6	9.3 (1.4-60)
Chemical processing worker				
<5	7	7	1.9	
≥5	6	5	2.2	1.2 (0.24-5.6)
Textile worker				
<5	6	19	0.6	
6-9	5	15	0.7	1.2 (0.30-4.6)
≥10	3	14	0.4	0.57 (0.11-2.5)

* Based on table 4 of Silverman et al. (2).
 † Incremental relative risk is the ratio of two successive relative risks.
 ‡ Crude 95 percent confidence interval (using the variance of the log of the crude exposure odds ratio).

National Library of Medicine: IGM Full Record Screen



[Order Documents](#) [Log off IGM](#)

[Next Record](#) [Details Of Search](#) [Return to Results](#) [Return to Search Screen](#) [Previous Record](#)



Related Articles

TITLE: Re: "Tests for trend and dose response: misinterpretations and alternatives" [letter; comment]

AUTHORS: Silverman DT; Hoover RN

SOURCE: Am J Epidemiol 1992 Nov 1;136(9):1172-3

CITATION IDS: PMID: 1462979 UI: 93098180

COMMENT: Comment on: Am J Epidemiol 1992 Jan 1;135(1):96-104

MAIN MESH HEADINGS: *Epidemiologic Methods

ADDITIONAL MESH HEADINGS: Bladder Neoplasms/epidemiology
Female
Human
Occupational Diseases/epidemiology
Risk
1992/11
1992/01 00:00

PUBLICATION TYPES: COMMENT
LETTER

LANGUAGES: Eng



[Order Documents](#) [Log off IGM](#)

[Next Record](#) [Details Of Search](#) [Return to Results](#) [Return to Search Screen](#) [Previous Record](#)