CORRESPONDENCE

Reporting of occupational and environmental research: use and misuse of statistical and epidemiological methods

Rushton's recent article[1] on the reporting of occupational and environmental research raises several useful points that all researchers would do well to remember when writing up epidemiological findings for publication. Without expressly intending to do so, however, the article also emphasises the hazards of establishing formal criteria or checklists for the evaluation of scientific work. Good epidemiological practices certainly exist, but one of the pitfalls inherent in attempts to codify them is that, by their nature, lists of the features of "good" research tend to impose a "one size fits all" standard, which—like clothing of the same description—fits nothing particularly well.

The prospect of developing formal guidelines for reporting analyses based on multivariable models illustrates the difficulties. Science involves many kinds of activities, but the significant advances come about through the creative application of human intellect, rather than by rote repetition of the familiar. Like other aspects of science, epidemiological data analysis blends attention to factual detail with creativity, intuition, judgement, and even aesthetics. From the initial choice of model form to the final specification of covariates and interaction terms, there may be many reasonable ways to model a given data set. Researchers should be at liberty to analyze their data according to their individual scientific insights. In subsequent evaluations of methods and results, reviewers likewise should be encouraged to apply their scientific judgement, rather than following a recipe.

The opportunity cost involved in complying with guidelines for good practice may also be considerable, as Rushton suggests.[1] Between the growing fear of litigation and mounting demands for accountability, especially in the United States, epidemiologists may soon spend more time documenting adherence to protocol than doing science.

My particular fear, however, is that guidelines will be used to assail sound research on the grounds that it fails to comply with supposed standards of good science. The misuse of Hill's ideas about causality illustrates the danger. Hill intended his suggestions as an aid to researchers, not as evaluative standards for critics; he wrote: "I do not believe…that we can usefully lay down some hard-and-fact rules of evidence that *must* be obeyed before we accept cause and effect. None of my nine viewpoints … can be required as a *sine qua non*. What they can do, with greater or less strength, is help us to make up our minds on the fundamental question."[2] Yet Hill's ideas are often presented as criteria that must be fulfilled for a study's evidence to be accepted.[3] The involvement of such obviously self interested groups as the Chemical Manufacturers Association in promoting "good epidemiological practices" makes the potential misuse of guidelines to suppress good research seem all too likely.

I do not mean to suggest that all epidemiological research should be published or accepted at face value, far from it. There will always be a need for review to ensure the quality of published work and to protect the public from policies based on unsound science. I am convinced, however, that peer review coupled with the opportunity for criticism and debate in open publications provide the best pathway to this goal. By contrast with standardised criteria, these processes allow multiple, independent readers' perspectives on the methodological quality, and the substantive importance of research to be heard. As a result, they reduce the chances that unconventional but valuable views will be suppressed or that an interested group could gain control over the process for their own purposes.

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1 Rushton L. Reporting of occupational and environmental research: use and misuse of statistical and epidemiological methods. *Occup Environ Med* 2000;**57**:1–9.
2 Hill AB. The environment and disease: association or causation? *Proc R Soc Med* 1965;**58**: 295–300.
3 Gamble JF. $PM_{2.5}$ and mortality in long term prospective cohort studies: cause-effect or statistical association? *Environ Health Perspect* 1998;**106**:535–49.

L Rushton replies

Loomis draws attention to the potential dangers of the rigid use of checklists and guidelines to judge occupational and environmental research. I agree with these sentiments, in particular the concerns about the increasing number of papers which use compliance with these guidelines as a justification for conclusions on causality. There is, however, one rapidly expanding area of research which would benefit from the development of minimum standards for presentation of results. This is the field of epidemiological meta-analysis, in which data are generally abstracted from published papers. Difficulties can arise in deriving a common set of definitions for variables. For example, in a meta-analysis of use of oral contraceptives and risk of breast cancer,[1] 42 different categories of duration of use of oral contraceptive were published in the 24 papers analysed for this variable. Debate within the scientific community is needed to decide categorisations which would be most useful. Editors could then encourage authors either to use these in their papers or at least be prepared to make them available on request.

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1 Rushton L, Jones DR. Oral contraceptive use and breast cancer risk: a meta- analysis of variations with age at diagnosis, parity and total duration of oral contraceptive use. *Br J Obstet Gynecol* 1992;**99**:239–46.

Occupational exposures and pancreatic cancer: a meta-analysis

A meta-analysis that was recently published in this *Journal*[1] suggested an association between excess pancreatic cancer risk and exposure to nickel and nickel compounds (meta-risk ratio 1.9, 95% confidence interval (95% CI) 1.2 to 3.2, based on four studies). Through correspondence with the authors (Ojajärvi *et al*), I learned that their analysis excluded the many epidemiological studies that had been conducted on workers in the nickel refining and alloy production industries. Although most of these studies could not contribute to the meta-analysis due to a failure to specifically examine risk of pancreatic cancer, I found two studies of nickel workers that provide relevant data.

I think that one of these studies, which examined mortality in 11 500 nickel mining and smelting workers,[2] should have been included in the meta-analysis by Ojajärvi *et al*,[1] based on the criteria used for study selection. Another study of more than 30 000 workers exposed to nickel and nickel compounds in the production of nickel alloys[3] was published a few months after the May 1998 cut off that Ojajärvi *et al* used to establish the data base for their meta-analysis. The results from these studies[2 3] add substantially to data used in the analysis by Ojajärvi *et al*[1].

Combining the data from all of these studies with the meta-analysis random effects model used by Ojajärvi *et al*[1] produces a meta-risk ratio (MRR) of 1.3 (95% CI 0.9 to 1.9). Interestingly, the two studies designed specifically to detect excess cancer risks associated with occupational exposure to nickel[2 3] show the lowest relative risks for pancreatic cancer and differ substantially from the MRR for nickel exposure calculated by Ojajärvi *et al* (1.9). Moreover, the estimated relative risk (0.9) from the study of nickel alloy workers[3] is significantly smaller ($p<0.05$) than even the lower 95% confidence limit (1.2) for the MRR of Ojajärvi *et al*.[1]

The fact that the MRR of Ojajärvi *et al*[1] for nickel related pancreatic cancer significantly overestimates the risk found in a large cohort of nickel workers indicates that their meta-analysis risk estimates should be viewed with an appropriate degree of caution. These results of the meta-analysis may be considerably biased because of limitations of the studies on which they are based. In studies that relate to nickel, the potential for misclassification bias is strong because of the complete confounding of nickel exposure with known carcinogenic hazards such as cadmium,[5] or asbestos, polycyclic aromatic hydrocarbons, chromium, beryllium, polychlorinated biphenyls, and hydrazine.[4] Similarly, in the meta-analysis of Ojavarvi *et al*[1] the case-control study[7] that contributed the most substantial evidence of a risk of pancreatic cancer related to nickel provides equally strong statistical evidence of associations between excess pancreatic cancer and expo-

Table 1 Cancer risks in studies of workers exposed to nickel and its compounds

Study	*Study type*	*Included in Ojajärvi et al*[1]	*Pancreatic cancer deaths*	*RR*	*95% CI**
Thermoelectric plant workers[4]	Cohort	Yes	1	3.6	0.1 to 19.9
Cadmium/nickel battery workers[5]	Cohort	Yes	3	1.7	0.3 to 4.9
Los Angeles workplaces[6]	Case-control	Yes	6	1.5	0.4 to 5.7
Montreal workplaces[7]	Case-control	Yes	12	2.1	1.1 to 3.9
Nickel mining and smelting workers[2]	Cohort	No	12	1.3	0.7 to 2.3
Nickel alloy production workers[3]	Cohort	No	131	0.9	0.8 to 1.1

*SMR/100 for cohort studies.

sures to 10 other substances, some of which are likely to be correlated with occupational exposure to nickel.

Although Ojajärvi *et al*[1] are to be congratulated on their investigation of the aetiology of pancreatic cancer, it is my opinion that their results are most appropriately viewed as hypotheses that require further investigation, rather than compelling evidence that links substances to the induction of pancreatic cancer. As Ojajärvi *et al*[1] correctly suggest, research to test these hypotheses requires large studies and more refined measures of exposure. With respect to nickel and nickel compounds, data from large studies that were not included in the analysis of Ojajärvi *et al*[1] call into question the veracity of a hypothesis that links nickel exposure to increased risk of pancreatic cancer.

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1 Ojajärvi IA, Partanen TJ, Ahlbom A, *et al*. Occupational exposures and pancreatic cancer: a meta-analysis. *Occup Environ Med* 2000;**97**:316–24.
2 Shannon HS, Walsh C, Jadon N, *et al*. Mortality of 11 500 nickel workers: extended follow up and relationship to environmental conditions. *Toxicol Ind Health* 1988;**4**:277–94.
3 Arena VC, Sussman NB, Redmond CK, *et al*. Using alternative comparison populations to assess occupation-related mortality risk. *J Occup Environ Med* 2000;**40**:907–16.
4 Cammarano G, Crosignani P, Berrino H, *et al*. Additional follow up of cancer mortality among workers in a thermoelectric power plant. *Scand J Work Environ Health* 1986;**12**: 631–2.
5 Andersson K, Elinder CG, Hogstedt C, *et al*. Mortality among cadmium and nickel-exposed workers in a Swedish battery factory. *Current Topics in Environmental and Toxicological Chemistry* 1985;**8**:399–408.
6 Mack TM, Peters JM, Yu MC, *et al*. Pancreas cancer is unrelated to the workplace in Los Angeles. *Am J Ind Med* 1985;**7**:253–6.
7 Siemiatycki J. *Risk factors for cancer in the workplace*. Boca Raton, FL: CRC Press, 1991.

Ojajärvi and Partanen reply

We thank Seilkop for his comment and have, in essence, not much to add to it. The study by Shannon *et al*[1] had obviously been overlooked and the study by Arena *et al*[2] was published after our deadline for the inclusion of studies.

Seilkop's table has errors for the study by Andersson *et al*.[3] The number of pacreatic cancer deaths should be 2; relative risk should be 1.2; and 95% confidence interval should be 0.1 to 4.5.

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1 Shannon HS, Walsh C, Jadon N, *et al*. Mortality of 11 500 nickel workers - extended follow up and relationship to environmental conditions. *Toxicol Ind Health* 1991;7:277–94.
2 Arena VC, Sussman NB, Redmond CK, *et al*. Using alternative comparison populations to assess occupation-related mortality risk. *J Occup Environ Med* 1998;**40**:907–16.
3 Andersson VC, Elinder CG, Hogstedt C, *et al*. Mortality among cadmium and nickel-exposed workers in a Swedish battery factory. *Current Topics in Environmental and Toxicological Chemistry* 1985;399–408.

Air pollution research databases

I write to inform your readers that the MRC Institute for Environment and Health is compiling two databases on research in air pollution (including indoor air pollution). These databases are designed to provide funding bodies and policy makers with an up to date source of information which they may use to:

- Identify people and groups with expertise in particular aspects of air pollution research
- Obtain information on current topics of air pollution research
- Identify gaps in research on air pollution
- Identify new advances in the air pollution field
- Assist in the prioritisation of future research on air pollution.

We encourage all researchers in the field to submit information on their work for inclusion in either or both these databases:

- *The air pollution research database* (APRED). This will hold data on research into indoor and outdoor air pollution within the United Kingdom. Its particular focus is on the individual researchers, their expertise and areas of interest. It is being prepared on behalf of the United Kingdom Department of Health and the Department of the Environment, Transport, and Regions.
- *The CEFIC database*. This will hold data on research being done on indoor air pollution in Europe, including the United Kingdom. Its primary intention is to identify all current research projects in the area. It is being prepared on behalf of the European Chemical Industry Council (CEFIC).

During development the databases will be held within the Institute, but in due course they will be made available through an internet website, in a searchable format.

The Institute is currently in the process of identifying the names and contact details of researchers in the United Kingdom so that they may be sent a questionnaire seeking certain information to enter onto the databases—for example, details about their research, project abstracts, research interests of each person, and details about their organisation.

All interested people should please go to the website address: *http://www.le.ac.uk/ieh/update/update.html#database* which gives a brief outline of the projects, and describes how to obtain a questionnaire and more information on the databases.

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CORRECTION

Personal exposures of children to nitrogen dioxide relative to concentrations in outdoor air. C H LINAKER, A J CHAUHAN, H M INSKIP, S T HOLGATE, D COGGON. 2000;**57**:472–6

Unfortunately an authors' error occurred in this paper in the conversion of concentrations of outdoor nitrogen dioxide (NO_2) from ppb to $\mu g/m^3$. As a consequence, all of the NO_2 measurements that were reported in outdoor air should be multiplied by a factor of 3.53. The correlations with personal NO_2 measurements are unchanged, as is the interpretation of our findings. Although higher than originally indicated, the outdoor NO_2 concentrations were nevertheless relatively low.

NOTICES

Nordic and National Training Centres Courses and Symposia 2001

Work and stress: somatic effects of physical and mental work
18-23 February, 2001, Geilo Hotel, Geilo, Norway
From intensive work systems to sustainable work systems
13-16 March, 2001, Ljungbergsgården, Tyningö, (Stockholm), Sweden
Challenges of ageing of the workforce
2-8 April, 2001, Hotel Riekonlinna, Saariselkä, Lapland, Finland
Research dissemination
22-26 April, 2001, Ljungbergsgården, Tyningö (Stockholm), Sweden
Safety research
10-15 June, 2001, Metalworkers' Murikka Institute, Tampere, Finland
Bullying and harassment at work
11-15 June, 2001, Hotel Eckerö, Åland, Finland
Introduction to occupational epidemiology
21-25 August, 2001, Hotel Gentofte, (Copenhagen), Denmark
Occupational exposure limits: approaches and criteria
23-28 September, 2001, Hotel Linné, Uppsala, Sweden
Occupational dermatology
11-16 September, 2001, Sokos Hotel Kuusamo, Kuusamo, Finland
Molecular toxicology: molecular epidemiology
14-19 October, 2001, Tallinn, Estonia
Intervention projects in the health care sector
21-25 October, 2001, Nordic School of Public Health, Gothenburg, Sweden
Risk assessment as a basis for the selection of personal protective equipment
28 October - 2 November, 2001, Medical Academy of Latvia, Riga, Latvia

A sister organisation to NIVA is the Nordic School of Public Health.
For more information about NIVA, visit our web-site: www.niva.org
For further information about their courses and seminars, please contact: Nordic School of Public Health, Box 12 133, SE-402 42 Göteborg, Sweden. Tel 0046 31 69 39 00; fax 0046 31 69 17 77; www.nhv.se

5th Annual Conference on Self Directed Learning in General Practice. 24th April 2001. London, UK.

Organised by the Open Learning Unit, University College London, and sponsored by the British Medical Journal. The conference will be organised around the themes of:

- Revalidation
- Web based learning resources for self directed learning.

The day will be based around small group workshops, with some offering hands on training in the use of on line learning resources. Places will therefore be strictly limited and allocated on a first come, first served basis.