

Confounding in epidemiological studies

EDITOR,—George Davey Smith and Andrew N Phillips draw attention to the problems of confounding, especially residual confounding, in epidemiological studies.¹ This is poorly understood and has led to many serious misunderstandings. It should always be considered as an explanation of any epidemiological association, but in some cases observational studies cannot resolve the issue, and one should not conclude that possibly confounded exposures should be ignored. When this impasse is reached it may be more appropriate to consider intervention studies.

The example of smoking and cervical cancer is a case in point. Early observations of this association were played down because of possible confounding with sexual behaviour. The relation was not, however, weakened when attempts were made to adjust more carefully for this—a procedure that often indicates residual confounding—and now dozens of carefully designed studies have found a strong relation. Clearly, randomising young women to smoke or not would be both ridiculous and unethical. We are attempting to study the effects of stopping smoking on untreated but carefully monitored mild cervical disease, with reference to both clinical and immunological variables. Studies of this kind may prove useful in resolving the problems of confounding.

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1 Davey Smith G, Phillips AN. Confounding in epidemiological studies: why "independent" effects may not be all they seem. *BMJ* 1992;305:757-9. (26 September.)

EDITOR,—George Davey Smith and Andrew N Phillips lay into our fellow epidemiologists with gusto,¹ but in their zeal to preserve us from false hopes of aetiological discovery and so of prevention they may have overreacted in the case of at least one of their prime examples.

Lack of physical activity, they say, is related to obesity (presumably they intend overweight); "obesity" is a powerful risk factor in its own right for diabetes (presumably they intend non-insulin dependent diabetes); ergo, the relation of lack of physical activity to the incidence of diabetes—now shown in prospective studies of three different populations and using two different methods of assessing physical activity^{2,3} could be due merely to confounding with obesity. Several points may be made.

Overweight and lack of physical activity are indeed closely and complexly interrelated. For example, a common route to weight gain in middle age is failure to adjust energy intake to declining energy output. Which component is effective "in its own right" and which doesn't matter? How much "lack of physical activity" does obesity contain? And so on.

In studies of non-insulin dependent diabetes in men the greatest reduction of incidence with physical activity occurred in the heaviest subjects, scarcely to be expected on a null hypothesis. Imprecision in self assessment of height and weight could of course be material even in University of Pennsylvania male graduates,⁴ American women nurses,⁵ and American male physicians,⁶ who were surveyed, but would it be imprecise enough to wipe out such trends? It would be worth demonstrating. A check in the study of nurses was reassuring.

Moreover, in the studies of doctors and nurses (but not the graduates) total estimates of energy output, so relevant to body weight, were not analysed. Instead their index was the report of

vigorous exercise long enough to work up a sweat. (Vigorous sports were also the most protective in the study of graduates.) Such vigorous exercise could be activating other physiological mechanisms of possible protection than those of energy balance.⁷

The point that Davey Smith and Phillips raise about "biological plausibility" is well taken. Too often there is a whiff of circular argument when this is deployed. Be that as it may, after 20 years* of repeated observations that exercise favourably affects glucose tolerance and insulin resistance, what would really have been interesting is a failure to show some protection by exercise against the occurrence of non-insulin dependent diabetes. This protection is estimated as "at least 25 per cent" from the American physicians study.

In short, the evidence of lower incidence of non-insulin dependent diabetes with exercise surely stands, one of considerable promise in so serious and common a disease, 5% of our (European) population over 40 years of age.⁷

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- 3 Manson JE, Rimm EB, Stampfer MJ, Golditz GA, Willett WC, Knowleski AS, et al. Physical activity and incidence of non-insulin dependent diabetes mellitus in women. *Lancet* 1991; 338:774-8.
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Large volume plastic spacers

EDITOR,—I wish to add a further comment on the use of large volume plastic spacers, discussed by Duncan Keeley.¹ In our genitourinary medicine clinics we frequently see patients who are taking inhaled pentamidine monthly as prophylaxis against pneumocystis pneumonia and always use a bronchodilator before the inhalation treatment. As the patients are being treated only once a month they do not become adept at using the pressurised aerosol inhalers, and instructing them on how to use one at each return visit can be time consuming. We now use the large volume plastic spacers and have found a considerable improvement. Showing patients how to use them is simple, and a lot of instruction time is saved. We can be confident of adequate bronchodilatation before treatment. Moreover, the patients feel more relaxed about coming to the clinic for their treatment knowing that they are not going to have to perform an intricate coordination manoeuvre. A spacer is labelled with the patient's name and number and kept for his or her use only.

Adequate bronchodilatation may also reduce the likelihood of coughing during the pentamidine treatment. This may be important, particularly as Fischl *et al* recently reported transmission of tuberculosis among HIV positive patients attending clinics in the United States and implicated inhalation treatment as one environmental factor that may have contributed to an outbreak.²

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1 Keeley D. Large volume plastic spacers in asthma. *BMJ* 1992;305:598-9. (12 September.)

2 Fischl MA, Uttamchandani RB, Daikos GL, Poblete RB, Moreno JN, Reyes RR, et al. An outbreak of tuberculosis caused by multidrug-resistant bacilli among patients with HIV infection. *Ann Intern Med* 1992;117:177-83.

Poor training in rheumatology

EDITOR,—Philip Steadman is concerned about disabled people not applying for the disability living allowance because of their fears of a medical examination.¹ In Arthritis Care's experience the reason for this and similar problems—for example, with applications for orange badges (indicating disability) and arranging transport to hospital—is the poor understanding of arthritis among many general practitioners.

General practitioners spend little time on rheumatology during their training, and they often seem not to understand the problems of people with arthritis. Many members of Arthritis Care tell us that their general practitioners do not appreciate how much the pain and mobility in arthritis vary from day to day and how much damage can be caused to affected joints by inappropriate walking or, indeed, by sitting in the same position for long periods. A person who seems to be able to walk quite well one day may barely be able to get out of bed the next. Arthritis Care would be grateful for the BMA's support in its efforts to improve medical education in rheumatology and arthritis.

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1 Steadman P. Applying for disability living allowance. *BMJ* 1992;305:893. (10 October.)

Assisted conception for infertility

EDITOR,—M G R Hull and colleagues have obtained excellent results in their assisted conception programme.¹ In our view, however, their expectations of assisted conception for infertility are not realistic.

A critical factor in the calculation of the Kaplan-Meier curve for estimating cumulative pregnancy rates—the method the authors used—is the assumption that couples who stop treatment after the first or following cycles will have had the same chance of conceiving by assisted conception as couples who continue treatment. From the data presented it is impossible to conclude whether this assumption is met, and the authors do not indicate whether they are aware of this methodological trap. Couples who do not become pregnant but decide to continue treatment in the next cycle may well represent selection of more favourable cases.

To analyse this we studied all couples who participated in our in vitro fertilisation programme from 1985 until 1990 for a first (n=525), second (n=309), third (n=190), and fourth (n=100) attempt at in vitro fertilisation. After each cycle three groups were distinguished: couples who achieved a pregnancy, couples who did not achieve a pregnancy and continued treatment in another cycle, and couples who did not achieve a pregnancy and decided to stop treatment. We analysed the second and third groups, looking at some factors of potential prognostic importance: a favourable indication (tubal factor or unexplained infertility) or unfavourable indication (male factor) for in vitro fertilisation, total fertilisation failure, fertilisation rate, and age of the woman. Continuous data were analysed by analysis of variance and the discrete data by the Mantel-Haenszel χ^2 test.

The differences between the couples who stopped and who continued treatment were significant for total fertilisation failure (p=0.0008)

and fertilisation rate ($p=0.001$) but not for indication ($p=0.08$) or age ($p=0.9$). The group who stopped treatment had a higher rate of total fertilisation failure, a lower fertilisation rate, and a generally more unfavourable indication for in vitro fertilisation. These results indicate that the assumption of the life table method is not met because patients who decide to stop treatment are likely to have less chance of conceiving by in vitro fertilisation than patients who continue.

Few studies giving cumulative pregnancy rates after several cycles of in vitro fertilisation evaluate possible selection bias in the couples who continue treatment. To avoid too high expectations people should be aware of the possibility of such selection, particularly in a study with the objective "to provide reliable prognostic information for couples seeking assisted conception."

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Hull MGR, Eddowes HA, Fahy U, Abuzeid MI, Mills MS, Cahill DJ, *et al.* Expectations of assisted conception for infertility. *BMJ* 1992;304:1465-9. (6 June.)

Reaccrediting general practice

EDITOR,—John Russell reports a small number of problems with assessment visits in general practice about which he has been informed anecdotally.¹ Against this, however, must be set the view of over 24 000 general practitioners, who responded "Disagree or strongly disagree" to the statement "There is no need for the profession to consider the possibility of a system of professional accreditation and re-accreditation at the present time" as follows: general practitioners with "no involvement with training"—49.1%; general practitioners with "training provided in the practice"—60.9%; general practitioners who "provide training personally"—70.1%.² It is therefore still logical to conclude that those general practitioners who have had personal experience of the trainer system, which involves about a quarter of all general practices in Britain, are more in favour of reaccreditation than those who have not.

Chris Nancollas emphasises the importance of consultation.³ The General Medical Services Committee represents all general practitioners in the NHS and regularly communicates with all local medical committees in the country. Similarly, the Royal College of General Practitioners is committed to its local faculties, which cover the whole of Britain.⁴

Developments in medicine worldwide have placed greater emphasis on continuing education and assessment or reaccreditation, or both, for all health professionals. It seems wise for the medical profession to continue to work on this, and it is encouraging that both Russell and Nancollas also believe that assessment of general practitioners through peer review is preferable to other methods, such as re-examination.

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1 Russell J. Reaccrediting general practice. *BMJ* 1992;305:835. (3 October.)

2 General Medical Services Committee. *Your choices for the future. A survey of GP opinion. UK report.* London: Electoral Reform Ballot Services, 1992.

3 Nancollas C. Reaccrediting general practice. *BMJ* 1992;305:835. (3 October.)

4 Royal College of General Practitioners. *A college plan. Priorities for the future.* London: RCGP, 1990. (Occasional paper 49.)

Guidance on guidelines

EDITOR,—Andrew Haines and Gene Feder's editorial on clinical guidelines draws attention to issues that need to be resolved if Britain is to avoid the American experience of producing thousands of guidelines of unproved efficacy.¹ Many of these issues were raised last year at a conference to assess the progress made in developing guidelines in Britain.² Three crucial issues surfaced: how guidelines can be produced and owned locally but not be perceived as being inferior to guidelines published by national bodies; how to ensure that they are updated regularly; and how to ensure their effective dissemination and use.

A national "clearing house" may seem to be an attractive means of collating and disseminating information. The experience of the King's Fund Centre in setting up a centralised system for collating details of good practice in medical audit, however, suggests that this process in isolation is of limited value (personal communication). The research and development initiative provides an alternative model, in which the provision is organised at a regional level.³

Guidelines are an important component of the development of explicit standards of care and thus are intimately connected with medical audit. It may be opportune, therefore, to integrate the "guideline industry" with the medical audit initiative; a strong medical audit structure already exists at regional level. In South West Thames, on the basis of 13 years' experience of producing hospital guidelines, we have established a treatment guidelines centre at St George's Hospital Medical School. This unit will disseminate information on national and local guidelines and also provide a publishing service for individual units. Its aim is to facilitate the development of local guidelines rather than to standardise practice across the region.

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1 Haines A, Feder G. Guidance on guidelines. *BMJ* 1992;305:785-6. (3 October.)

2 Collier J, Ismail I, Littlejohns P. Guidelines for treatment in NHS hospitals. *Medical Audit News* 1992;2:141-3.

3 Richardson J. Treatment guidelines and medical audit. *Lancet* 1991;338:877.

4 *Research for health: a research and development strategy for the NHS.* London: HMSO, 1991.

The death penalty

EDITOR,—In his editorial Richard J Bonnie mentions a recommendation of a BMA working party that certification of death should always take place away from the site of an execution.¹

That is not enough. The certifying doctor has to be removed from the execution with regard to both place and time (so as not to monitor the execution by, for example, electronically transmitted electrocardiography). Certification should be issued for medicolegal purposes only at a time and place where there is no longer any non-medical doubt about death having occurred.

The reason for this requirement is the sad fact that doctors are probably always present at executions (in the United States and elsewhere). Their "certification of death" amounts in many cases to active participation in the execution itself (monitoring heartbeats, etc and then accordingly ordering more voltage or more intravenous poison if deemed necessary) until they can certify that death has occurred and the executional process can be stopped, thereby making them de facto the chief executioners.

The request for certification was meant to be for the issuing of a medicolegal (written) statement

that death had irrevocably occurred at some earlier time. Instead, many doctors have twisted "certification" into meaning "certain making," from the original Latin meaning of the word *certificare*, thereby allowing them the actions mentioned above.

The Council of Judicial and Ethical Affairs of the American Medical Association is working on a new and stricter resolution, hopefully much along the lines of the resolution adopted by the Nordic medical associations in 1986, which in part reads: "For a physician to prepare, administer or monitor any procedure with a view to injuring a human being or to train others to do so would be a perversion of medical knowledge and skill and of the physician's responsibility to and role in society. Thus the medical associations of the Nordic countries... declare it indefensible for any physician to participate in any act connected to and necessary for the administration of capital punishment."

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1 Bonnie RJ. The death penalty. *BMJ* 1992;305:381-2. (15 August.)

Health checks for people over 75

EDITOR,—We were disturbed to read about the inadequacies in the system of annual health checks for people over 75, especially those relating to the detection of dementia.^{1,2} The shortcomings included lack of follow up of people not responding to the offer of a health check, the fact that inexperienced nurses performed the assessments, and a lack of national guidelines.

Detecting early dementia is important as it probably lessens the need for crisis intervention for patients' and relatives' support and because treatments likely to be available soon will depend on early diagnosis for best effect. Regular screening of elderly people is potentially useful for detecting dementia. We recently canvassed 37 local practices to examine what cognitive assessment was carried out in their checks of people over 75.

We received replies from 26 of the 37 practices (70%): three were completed by general practitioners, who indicated that they did most of their practice's assessments, and the rest by practice nurses. All 26 respondents reported assessing mental function, 16 informally and 10 formally. Of those who assessed it formally, four used a test and six used specific questions, one going on to use a test if this was indicated. Three different tests were being used, most commonly the abbreviated mental test score.³ This was usually provided by the Alzheimer's Disease Society. In an open question only three of the respondents who formally tested cognition indicated that the presence of physical or sensory problems affected their interpretation of performance. Five respondents spontaneously requested advice regarding the use of suitable tests.

Detection of dementia is unlikely to be achieved effectively by informal assessment by untrained staff. Screening instruments would enhance detection if training was given in their administration and interpretation. The abbreviated mental test score is appropriate as it is short and is effective at detecting dementia⁴ and at discriminating between organic and functional illness,⁵ which is probably important. Patients who perform poorly or whose test score has decreased should subsequently be assessed by their general practitioner. Cognitive screening of people over 75 in an average practice of 2000 people would produce around 17 people needing medical assessment, though in the second year of a screening programme the number should be lower.