The alleged roles of passive smoking in causing lung cancer and excess salt in causing hypertension have been endorsed by many medical bodies, incorporated into public policy, and presented to the public as scientific facts that should be acted on. It is a revealing commentary on the intellectual status of public health epidemiology that the statistical fiction on which this and similar misleading advice is derived should have gone unchallenged for so long.

JAMES LE FANU
General practitioner

Mawbey Brough Health Centre,
London SW8 2UD

- 1 Egger M, Davey Smith G. Misleading meta-analysis. *BMJ* 1995;310:752-4. (25 March.)
- 2 Wald NJ, Nanchahal K, Thompson SG, Cuckle HS. Does breathing other people's tobacco cause lung cancer? *BMJ* 1986;293:1217-21.
- 3 Heath CW. Environmental tobacco smoking and lung cancer. *Lancet* 1993;341:526.
- 4 Law MR, Frost CD, Wald NJ. Analysis of data from the trials of salt reduction. *BMJ* 1991;302:819-24.
- 5 Swales JD. Dietary salt: the role of meta-analysis. *J Hypertens* 1991;9(suppl 6):S42-8.

Registers for clinical trials already exist

EDITOR,—In their editorial on misleading meta-analyses, Matthias Egger and George Davey Smith point out that bias is a major cause of error because of the tendency for negative trials to disappear from view.¹ They call for registers of clinical trials to be established. The Medical Research Council already runs a register for cancer trials, and the national research and development programme has a project register system, which can do the job for other trials.

Ethics committees should ensure that investigators intend to publish their trial, perhaps requiring all patients to be informed that registration and publication will occur so that they can be reassured that their participation will benefit others. The project register system can then register the trials so that even the smallest negative trial, which is most likely to be the subject of publication bias, will be available to meta-analysis of the future.

J A MUIR GRAY
Director of research and development

NHS Executive, Anglia and Oxford,
Oxford OX3 7LF

- 1 Egger M, Davey Smith G. Misleading meta-analysis. *BMJ* 1995;310:752-4. (25 March.)

Variability among studies should be investigated

EDITOR,—Matthias Egger and George Davey Smith explain how pooling of smaller studies can turn out to be misleading after the subsequent publication of larger trials and suggest that meta-analyses of small trials should now be distrusted, even if their combined effect reaches significance.¹ Yet they also point out that evidence from mega-trials will continue to be unavailable for most medical interventions, and hence meta-analyses of smaller trials remain the only apparent way of appraising available evidence.

The various statistical manoeuvres that the authors suggest to remedy this situation ignore one important focus of meta-analysis—namely, the degree of variability, or spread, among different studies. One way of analysing this is to perform a χ^2 test of deviations of individual studies from the overall mean achieved by pooling the studies.² A significant P value for this test suggests a considerable amount of variability around the summary result. This approach could provide a more precise statistical test of whether meta-analysis of results of small trials should be distrusted or questioned.

Interestingly, the next issue of the *BMJ* con-

tained a meta-analysis of the efficacy of tricyclic drugs in treating child and adolescent depression in which a χ^2 test of heterogeneity of the different studies' results (as measured by changes in outcome score) was performed; this was significant at $P=0.05$.² This significant variability across studies was largely ignored in that paper. This, alongside the neglect of measures of dispersion in Egger and Davey Smith's editorial, testifies to a current tendency to overlook the issue of variability across results of studies in meta-analysis.

Obviously if all studies give the same result there is no point in a meta-analysis; such a statistical exploration becomes of interest only in the context of variability among studies. But widely differing findings across many studies surely demand an exploration of the reason for the variability, not just an attempt to derive a mean result. In the case of drug trials in particular, in which significant heterogeneity in results may be accounted for by different drug doses used, accounting for variation may be a better purpose for meta-analysis than merely deriving an average result.

A PERRY
Senior house officer in psychiatry
R PERSAUD
Consultant psychiatrist

Westways,
West Croydon,
Surrey CR9 2RR

- 1 Egger M, Davey Smith G. Misleading meta-analysis. *BMJ* 1995;310:752-4. (25 March.)
- 2 Hazell P, O'Connell D, Heathcote D, Robertson J, Henry D. Efficacy of tricyclic drugs in treating child and adolescent depression: a meta-analysis. *BMJ* 1995;310:897-900. (1 April.)

Fish oils and cardiovascular disease

EDITOR,—In their editorial B N C Pritchard and colleagues concluded that fish oils have beneficial effects on lipids and the haemostatic system, but they pressed for more studies in diseases related to atherosclerosis.¹ We wish to reinforce this recommendation, particularly in relation to diabetes.

Two studies in which we have been involved have suggested possible adverse effects on the coagulation system. In the case of patients with insulin dependent diabetes a randomised trial showed significant increases in fibrinogen and clotting factor X concentrations in the group that took a fish oil supplement.² In a separate trial in patients with non-insulin dependent diabetes factor VII concentration increased significantly in the group receiving the fish oil preparation; this group also showed worsening glycaemic control.³ Fibrinogen and factor VII may be risk factors for ischaemic heart disease.⁴ Thus these apparently adverse effects on the coagulation system may outweigh other potentially beneficial effects on platelet function. We are therefore concerned that the use of fish oil in diabetic subjects should be reserved for those participating in well designed trials to investigate further the effect of fish oils on the risk of ischaemic heart disease.

ANDREW HAINES
Head of department

Department of Primary Care,
University College London Medical School,
Whittington Hospital,
Archway Site,
London N19 5NF

Department of Medicine,
University College London Medical School,
G Block, Archway Wing,
Whittington Hospital,
London N19 3UA

JOHN S YUDKIN
Professor of medicine

- 1 Pritchard BNC, Smith CCT, Ling KLE, Betteridge DJ. Fish oils and cardiovascular disease. *BMJ* 1995;310:819-20. (1 April.)
- 2 Haines AP, Sanders TAB, Imeson JD, Mahler RF, Martin J, Mistry M, et al. Effects of a fish oil supplement on platelet function hemostatic variables and albuminuria in insulin dependent diabetics. *Thromb Res* 1986;43:643-55.

- 3 Hendra TJ, Britton ME, Roper DR, Wagaine-Twabwe D, Jeremy JY, Dandona P, et al. Effects of fish oil supplements in NIDDM subjects—controlled study. *Diabetes Care* 1990;13: 821-9.

- 4 Meade TW, Brozovic M, Chakrabarti RR, Haines AP, Imeson JD, Mellows S, et al. Haemostatic function and ischaemic heart disease: principal results of the Northwick Park heart study. *Lancet* 1986;i:533-7.

Advance directives

Approved guidelines are now required

EDITOR,—While it is useful to know that the Law Commission has followed the House of Lords in appearing to support the concept of advance directives,^{1,2} it is disappointing that more formal guidelines have not been suggested or approved. Keeping concepts in loose terms may satisfy the lawyers, who may in turn make incomes out of the loopholes, but this will not help our patients. Who will define capacity and the ability to consent or withhold consent? At present the final arbiter is the law, but recent cases suggest that this is muddled and not helpful to medical practitioners or patients.

We like to believe that adults without mental illness have a right to self determination, yet Re T and Re S both indicate that this is not so.^{3,4} Re T concerned a Jehovah's Witness who refused blood transfusion: the courts decided that her decision had been made and her religious persuasion determined under coercion and rejected her autonomous choice not to be given a transfusion when she could not defend herself against that decision.³ Re S concerned a woman whom the court ordered to have a caesarean section against her will.⁴ In contrast, in another recent case, Re C, a patient with paranoid schizophrenia in hospital, who thought that he was a medical practitioner, refused treatment and was deemed competent by the court to do so.⁵

If competent people refuse treatment in the present then the ability of an advance directive to be binding in the future must be severely compromised. In addition, if an incarcerated psychotic patient can be granted full competence on medical matters then presumably demented or other equally compromised patients will be able to make full autonomous decisions, upheld by the courts, irrespective of any existing directive. The only thing that will be achieved will be further legal intrusions into clinical decision making; patients do not stand to benefit.

PAULA J HARDY
Consultant anaesthetist

Gloucestershire Royal Hospital,
Gloucester GL1 3NN

- 1 Doyal L. Advance directives. *BMJ* 1995;310:612-3. (11 March.)
- 2 House of Lords Select Committee on Medical Ethics. *Report*. London: HMSO, 1994. (HL paper 21.)
- 3 Re T [1992] 9 BMLR 46.
- 4 Re S [1992] 9 BMLR 69.
- 5 Re C [1993] 15 BMLR 77.

Law Commission's report makes no provision for dissenting doctors

EDITOR,—There is more to some advance directives than the extension of autonomy by a once competent patient. That of the Voluntary Euthanasia Society, for example, requires that insulin is withheld when required from a signatory who develops presenile dementia. If that advance directive were legally enforceable the doctor would have to give way to a patient's wish to have death brought forward by unreasonable measures.

Len Doyal¹ does not mention a serious deficiency in the Law Commission's draft legislation—namely, the lack of any provision for a doctor to dissent for medical or moral reasons from implementing an advance directive. If the document cannot require doctors to act unlawfully, as the Law Commission claims, then it should not require them to act unethically either.