methods by which changes in these variables can be measured, and the authority and legal standing of guidelines on clinical practice.

All of these initiatives will have a pivotal role in accelerating the development of modern clinical care and in replacing clinical opinion with clinical evidence.

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1 Davidoff F, Haynes B, Sackett D, Smith R. Evidence based medicine. *BMJ* 1995;310:1085-6. (29 April.)

2 Esmail A. Evidence-based general practice: a critical reader [book review]. *BMJ* 1995;310:1146-7. (29 April.)

3 Miles A, Ligon M. *Effective clinical practice*. London: Blackwell Science (in press).

Accurate references are important

EDITOR,—William Rosenberg and Anna Donald praise the concept of evidence based medicine, but in their example they ignore the evidence.¹ They say, "It was decided to set a target international normalised ratio of 1.5-2.0." This is based on four references, three of which I have checked to find that they aimed at ratios of 2.8-4.2,² 1.4-2.8,³ and 2-4.5.⁴ Rosenberg and Donald do not provide the evidence supporting their choice of a lower ratio.

The search for evidence is helped by accurate references: two of these three are incorrect.

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1 Rosenberg W, Donald A. Evidence based medicine: an approach to clinical problem solving. *BMJ* 1995;310:1122-6. (29 April.)

2 Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B. Placebo controlled randomised trial of warfarin and aspirin for the prevention of thrombo-embolic complications in chronic atrial fibrillation. *Lancet* 1989;i:175-9.

3 Ezekowitz MD, Bridgers SL, James KE, Carlner NH, Colling CL, Gornick CC, et al. Warfarin in the prevention of stroke associated with non-rheumatic atrial fibrillation. *N Engl J Med* 1992;327:1406-12.

4 Stroke Prevention in Atrial Fibrillation Investigators. Warfarin versus aspirin for prevention of thromboembolism in atrial fibrillation: stroke prevention in atrial fibrillation II study. *Lancet* 1994;343:687-91.

Authors' reply

EDITOR,—We are pleased that David A Fitzmaurice admires our efforts. By forcing us to be explicit, the practice of evidence based medicine often identifies issues over which reasonable doctors can disagree, such as the therapeutic range. The fourth step of evidence based medicine, "acting on the evidence," involves clinical freedom and encourages the appropriate use of clinical responsibility, specifically to use the best available evidence when taking decisions about individual patients that consider all aspects of their care. Evidence based medicine does not force compliance with guidelines produced externally. With regard to an elderly woman at increased risk of haemorrhage, we disagree with Fitzmaurice's recommendation. The British Society of Haematology's guidelines are based on an earlier review,¹ which amplifies the flaws in evidence available at the time of their use. The more recent trials cited in our article provide far more reliable evidence of benefit from anticoagulant treatment, with international normalised ratios in the range 1.4-4.5. We believe the lower range to be safer for the patient, and our local anticoagulation laboratory recommends the narrow target range of 1.5-2.0.

Bruce G Charlton provides us with the opportunity of correcting the common misunderstanding that evidence based medicine is merely the mindless application of the results of megatrials. Evidence based medicine uses many forms of evidence, some of which come from the basic medical sciences and

some from large trials (surely a form of medical science). Trials (of whatever size is appropriate to the question they address) are unparalleled in providing estimates of efficacy, but in acting on the evidence thoughtful clinicians add their own estimates of susceptibility and, most important, patient utility to individualise the evidence. Charlton's accusations of non-randomness and selection bias are equally applicable to the case series of experienced clinicians and randomised controlled trials.

Malcolm Griffiths's letter allows us to re-emphasise the necessity to update systematic reviews of health care periodically. This is emphasised in the opening page of the reference he cites as well as its successor, the *Cochrane Database of Systematic Reviews*. We urge Griffiths to accept the database's invitation to identify additional evidence and suggest additional reviews for the update now under way.

In answer to Oliver Dearlove and colleagues, when we consider patients rather than procedures, over half the patients treated in a busy general medical service in Britain receive interventions that are based on randomised controlled trials or meta-analyses and an additional third receive interventions whose value is self evident.² Two other studies show the efficacy of teaching evidence based medicine, one of which we cited in our article.^{3,4}

Glenn W Jones and Stephen M Sagar have a narrow view of evidence based medicine. We strongly disagree with their assertion that randomised controlled trials provide the only form of evidence to be used in evidence based medicine, nor do we believe that other forms of evidence are heavily discounted by evidence based medicine. As pragmatic clinicians we aim to use the best available evidence, of whatever type of source. Jones and Sagar overlook two fundamental steps in evidence based medicine: critical appraisal and the application of evidence to clinical practice. Critical appraisal of evidence does not value randomised controlled trials while rejecting all other forms of evidence. Well conducted randomised controlled trials generate valuable, high quality evidence for some questions but not others, and in some areas the results of randomised controlled trials are not available. In either situation we must use other types of critically appraised evidence when forming clinical decisions.

Jones and Sagar suggest that the practice of evidence based medicine necessitates blind application of the results of large trials; this is a common misconception. Patients' preferences and their individual characteristics, as well as doctors' preferences, play a part in the fourth step in evidence based medicine—applying the evidence to clinical practice. Jones and Sagar state that evidence based medicine "cannot make decisions for us." We advocate freedom to make clinical decisions informed by the best available evidence and regard that as the practice of evidence based medicine.

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1 Hirsh J, Poller L, Deykin D, Levine M, Dalen JE. Optimal therapeutic range for oral anticoagulants. *Chest* 1989; 95(suppl):5-11S.

2 Ellis J, Mulligan I, Rowe J, Sackett DL. Inpatient general medicine is evidence-based. *Lancet* (in press).

3 Bennett KJ, Sackett DL, Haynes RB, Neufeld VR. A controlled trial of teaching critical appraisal of the literature to medical students. *JAMA* 1987;257:2451-4.

4 Shin J, Hance R, Johnston ME. Effect of problem-based, self-directed undergraduate education on life-long learning. *Can Med Assoc J* 1993;148:969-76.

Compliance with medication among elderly people

Study of self medication on elderly people was flawed

EDITOR,—Self medication programmes and compliance among elderly people are important.¹ Caution needs to be exercised, however, before we accept Catherine Lowe and colleagues' conclusion that a self medication programme improves compliance. The patients clearly knew which group they belonged to in the experiment; it is unclear whether investigator EAC (who followed up the patients) was blind to the patients' experimental status. Absence of blindness coupled with use of an unvalidated interview may have biased the results. For patients taking more than one tablet, a mean compliance score was calculated; these mean scores were later used in the statistical analysis to show a difference between the two groups. As the median number of drugs received by patients was four, the use of mean scores may be statistically inexact and inaccurately assume a normal distribution.

Compliance was high in both groups. This is hardly surprising as patients likely to comply poorly were excluded from the experiment at the outset. It would have been interesting if such patients had been included.

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1 Lowe CJ, Raynor DK, Courtney EA, Purvis J, Teale C. Effects of self medication programme on knowledge of drugs and compliance with treatment in elderly patients. *BMJ* 1995;310: 1229-31. (13 May.)

Author's reply

EDITOR,—A K Shah raises several points about our study. Firstly, the investigator (EAC) was not blind to the patient groups but collected data with a standard questionnaire to remove bias. Secondly, median numbers of medicines were quoted in table I as this was thought to be more appropriate than describing patients as taking fractions of tablets. Thirdly, compliance scores were compared with the Mann-Whitney U test, which is valid for non-normal distributions. This test ranked the mean compliance scores for each patient and did not compare means for the two groups. Finally, as stated and discussed in the paper, we excluded only patients not responsible for taking their medicine and terminally ill patients, who were clearly not appropriate for the study.

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Prophylactic aspirin and peptic ulcer bleeding

Patients warned of a bleed may be more vigilant

EDITOR,—John Weil and colleagues, in their large case-control study, do not mention that they have taken the possibility that their aspirin using subjects could have been more likely to spot a bleeding peptic ulcer because they would have been warned of the risk, and may therefore have had a lower threshold for detecting gastrointestinal haemorrhage.¹ If this factor was a material consideration then the extra bleeds detected and reported would have been of small size, and would presumably have been melaenas rather than haematemeses.

A minimum of 50 ml of blood is required to