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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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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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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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

produce a tarry stool.² If there are, as it would be reasonable to expect, a fairly large number of small gastrointestinal bleeds then those who were alerted about what to look for could expect to detect a few more. Aspirin prophylaxis is only recommended to be undertaken on medical advice. Presumably most doctors giving such advice would warn the patient of possible gastrointestinal bleeding and give advice on reporting it, if it occurs. The control groups would not be expected to have had similar advice.

John Weil and colleagues could throw light on whether this confounding factor could be material to their results, by showing the breakdown of melaena and haematemesis in each of the three groups they studied.

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Author's reply

EDITOR,—We cannot check on the proportions of overt haematemesis to melaena without going back to original records. We think it unlikely that Dr Fryer's explanation will account for the trends observed. If doctors had warned patients to watch for the ill effects of aspirin on the upper gut then we would not have expected to see the steadily increasing risk with aspirin dose. Also, very low dose aspirin was believed to be safe and therefore precautions are unnecessary, so warnings by doctors about the possible hazards of low dose aspirin will have been unlikely.

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Treatment of childhood asthma

EDITOR,—The study of Fiona Bryce and colleagues is elegantly designed to test the effects of an audit facilitator on treatment and diagnosis of childhood asthma by randomising within practices.¹

It is a pity, however, given the large number of time related significant changes in treatment found for both intervention and control groups, that the study did not have a control group of children from practices where no intervention was made. This would better confirm the conclusion that intervention increased the likelihood of diagnosis of childhood asthma and planned review but did not make major changes in treatment. From the evidence presented, time related changes for both groups (decrease in use of oral bronchodilators, theophyllines, antibiotics, and cough linctus; increase in inhaled and oral steroids) suggest that practice prescribing was also influenced for children in the control group. In support of the conclusion that practices were changing habits at this time, it may be of interest that over much the same period, in the neighbouring Grampian and Highland regions, a similar decrease in use of oral bronchodilators and increase in use of inhaled steroids was found for adults.²

None the less, we all need to remember that studies which introduce management interventions for (randomly) selected patients within a practice are not as "clean" as clinical trials of procedures or drug treatment. The same doctors and nurses whose behaviour is being changed in relation to the intervention group are also managing the control group. Without a completely

independent control group it is difficult to interpret findings if few differences are found between intervention and control.

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Mineralocorticoid effects of high dose hydrocortisone

EDITOR,—In their recent Lesson of the Week B H Ramsahoye and colleagues highlight the mineralocorticoid effect of high dose hydrocortisone as the principal factor that resulted in the fall in serum potassium concentrations (2.9 to 2.0 mmol/l) in their patient.¹ The episodes of ventricular fibrillation which followed were attributed to this fall in serum potassium concentration. Whereas intravenous hydrocortisone certainly contributed to the reduction in serum concentration of potassium, we suggest that other factors responsible for this change were a combination of inadequate supplementation, inappropriate cessation of potassium supplementation (at a serum concentration of 2.9 mmol/l), and, perhaps most importantly, significant continued urinary losses of potassium in the face of magnesium depletion.

The authors suggest that a reduction in serum potassium concentration of 1 mmol/l represents depletion in total body potassium of 100-200 mmol. Other workers would put the figure at twice this, with serum potassium concentrations of 3.0 mmol/l and 2.0 mmol/l representing total body potassium deficits of 350 and 700 mmol respectively.^{2,4} Thus, potassium supplementation of 40-80 mmol per day, in the face of such a large deficit and continuing losses, was inadequate. This case illustrates clearly the need for substantial intravenous potassium supplementation in patients with potassium depletion.

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Interventions in OXCHECK study waste resources

EDITOR,—The OXCHECK study showed significant reductions in total cholesterol concentration (3.1%) and blood pressure (2.5/1.5 mm Hg) with health checks over three years.¹ The reductions in cholesterol concentration are in line with responses shown in previous controlled trials.² The authors

seem in some doubt about whether these effects are large enough to justify the cost of the health checks. This may be clearer when the projected benefits are considered in absolute rather than relative terms.

When the Framingham parametric model is used to estimate risk³ with the mean blood pressure and mean total cholesterol concentration in the OXCHECK study, assuming a mean age of 50 and with weighting for the proportion of smokers, the risk of coronary death in the control group is about 0.075% a year in non-diabetic men without electrocardiographic evidence of left ventricular hypertrophy. In the intervention group the estimated rate of coronary death is lowered to 0.066% a year. This is a reduction in risk of 12% in relative terms, but in absolute terms 11 000 men would need to have health checks for one coronary death to be prevented each year. For women the reduction in relative risk seems even more impressive, at 25%, but over 80 000 women would need health checks for one coronary death to be prevented each year. If the study population had only a single initial health check lasting one hour and no follow up visits, seven practice nurses would be employed full time for one year to prevent one coronary death in men, and an additional 41 would need to be employed to prevent one death on women.

It is important to advise opportunistically on measures such as stopping smoking and increasing exercise, but whether the time and resources needed to implement these measures systematically, as tested in the OXCHECK study, can be justified is doubtful. It seems more appropriate to concentrate resources on lowering cholesterol with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors after myocardial infarction⁴ and in patients with other forms of coronary heart disease.⁵

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Assessing coronary risk

EDITOR,—Steven A Grover and colleagues compared estimates by doctors of gains in life expectancy as a result of a reduction in risk factors with those estimated from their computer model of prevention of coronary heart disease.¹ The model they used is based on logistic regression analyses, using data from the Framingham heart study, the Canada health survey, and Canadian life tables.² They calculated potential gains in life expectancy with intervention by applying to such a statistical model the levels of the risk factors before and after the intervention.

Three major problems are inherent in this approach. Firstly, the benefits of a reduction in risk factors may not be immediately apparent, since there is a substantial lag period before full benefits are achieved.³ Secondly, there may be irreversible damage to blood vessels or irreversible side effects of drugs. Finally, there is some