If we are to succeed in reducing the number of pregnancies in which the fetus has a neural tube defect we must adopt a policy of fortification of food. This approach is both simple and cheap and most likely to serve those at risk.

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Folate has potential to cause harm

EDITOR,—Nicholas J Wald and Carol Bower favour a population strategy rather than a selective strategy to prevent 1000 neural tube defects annually in the United Kingdom, with compulsory fortification of flour with folic acid.¹ They could perhaps have strengthened their case by referring to other potential benefits of their proposal—for example, in mental health, especially in psychiatric and geriatric populations.² Instead, however, they rather undermine their case by inaccurately minimising the disadvantages of their policy.

Their statement that "even in large doses folic acid has not been shown to cause harm" should not pass unchallenged. Although they acknowledge that folic acid may mask the anaemia of pernicious anaemia, they fail to emphasise that it may precipitate neurological complications in this context, as colleagues and I have shown.³ This can occur in the absence of anaemia, macrocytosis, or even a low serum vitamin B-12 concentration. The authors suggest that the problem of masking pernicious anaemia could be resolved by education, but apparently they do not favour a selective educational approach to prevent neural tube defects.

The risk that seizures may increase in patients with epilepsy⁴ is rather casually dismissed by the suggestion that higher doses of antiepileptic drugs might be needed, as if this in itself did not carry any risk.

A wider and more detailed consideration of all the advantages and disadvantages of the authors' proposals would be appropriate.

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Evidence based medicine

Example was flawed

EDITOR,—While I admire the intended efforts of evidence based medicine to reinforce clinical practice with up to date research, the article by William Rosenberg and Anna Donald highlights the flaws in this system.¹ The example that the

authors cite—of an elderly woman with non-rheumatic atrial fibrillation—is interesting. The risk-benefit analysis outlined makes no mention of therapeutic reference ranges, which are inextricably linked to any analysis of outcome measures associated with management with oral anti-coagulants. Thus, after it has been established that the patient would be more likely to benefit from treatment with warfarin, the clinical decision to have a target international normalised ratio of 1.5-2.0 is apparently picked out of thin air. This therapeutic range is too narrow to be of practical use and does not agree with the British Society of Haematology's current guidelines.² If strong advocates of evidence based medicine make such experientially based decisions, what chance do the rest of us have?

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Megatrials are subordinate to medical science

EDITOR,—Evidence based medicine started life as a flawed but marvellously refreshing approach to clinical practice and continuing education.¹ Unfortunately, it has recently been taken up by politicians and managers and is currently being packaged and promoted as a panacea, at the expense of medical science.

The main defining feature of evidence based medicine is its assertion that randomised controlled trials, especially "megatrials," should serve as the basis for clinical practice. For instance, William Rosenberg and Anna Donald deplore "the gaps between research evidence and clinical practice,"² as if megatrials told clinicians what to do and the job of clinicians was simply to do it.

But this whole notion of a gap between research and practice is misconceived. The results of megatrials—even in the rare circumstances that they are available and have been replicated—offer knowledge only at the population level.³ To apply this to the care of individual patients would be a classic example of the ecological fallacy: group averages tell us nothing about causal processes in the individuals who compose that group.

Furthermore, the population sampling achieved by a megatrial is non-random and subject to large selection bias. Megatrials are typically performed in specialised research settings. Despite this, some trials have included fewer than 10% of eligible patients.⁴ Even after admission, drop outs and crossovers between the comparison groups inevitably occur.⁵

The result of a megatrial cannot be extrapolated to a target population without substantial adjustments being made, and these adjustments will need to be based on contextual scientific knowledge. The epidemiological emphasis of evidence based medicine is mistaken. Science provides the innovations, the causal hypotheses, and the framework within which megatrials have their function.

Megatrials have an important role, but it is subordinate to medical science and consists mostly of checking predictions and refining protocols. If we needed to make a choice between medical science and megatrials as the basis of clinical practice then we would have to choose science.⁶

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Must be applied critically

EDITOR,—William Rosenberg and Anna Donald make a clear case for evidence based medicine.¹ Logically one would assume that there could be no case against such an approach. They describe a relatively tedious method of gathering evidence to answer a clinical question. Their method entails performing appropriate searches from scratch. Developments in systematic reviews—particularly in maternity care—have led to the gathering of evidence being simplified. In short, someone else's meta-analysis has already answered your question. Problems can arise when results of meta-analysis are not viewed critically and in an informed manner. I am aware that one purchaser refused to fund ultrasound scanning for anomalies in the second trimester because meta-analysis had shown that it detected only largely lethal anomalies.

In the development of a policy for induction of labour in our unit I suggested routine "cervical stretch and sweep" for pregnancies proceeding beyond term. I was challenged because a recently published book, summarising several meta-analyses, states that "there is too little evidence to assess the effectiveness of this technique."² This statement is supported by reference to a meta-analysis in the *Cochrane Database of Systematic Reviews*.³ This review was performed in 1989 and last amended more than three years ago. Since then a well conducted randomised controlled trial has been published,⁴ accompanied by a favourable review article.⁵ The compilers of the Cochrane database have not yet updated their meta-analysis to take account of these publications, and the book² has not been updated either, leading to a false interpretation of the value of a useful clinical intervention.

Purchasers and other decision makers should avoid adopting the findings of incomplete or out of date meta-analysis uncritically. Is there scope for a trial of evidence based medicine, assessing all outcomes and with full economic data?

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Many questions cannot be answered by evidence based medicine

EDITOR,—We envisage that databases for evidence based medicine would answer the question "What is best practice?" and that hospital based audit would check that best practice is being achieved. Our audit programme has examined pain relief for tonsillectomy. In the 58 children audited, nine tonsillar blocks were performed; additional oral

pain relief was required earlier in these nine children than in the children who had alternative intraoperative analgesia (n=9) (3.3 h v 7.6 h).

A conflict therefore arises over whether we should persist with tonsillar block and improve our performance even though we know that some children will be in pain while we are improving or whether we should abandon it for the method that gives better analgesia in our hands. We would now have difficulty in gaining the approval of an ethical committee for a trial of tonsillar block, so such a trial would not be included in an evidence based database even though it would answer a useful question. We also thought that parents would not consent to a trial investigating a method that we had shown to be inferior. This means that the question of pain relief may not be amenable to investigation with the criteria that have been imposed for evidence based medicine. Many more questions of interest would also be unanswerable.

Side effects of drugs come squarely into this category. Parke *et al*'s report of deaths after administration of propofol in children did not meet the criteria for inclusion in an evidence based database.² In our hospital an early death occurred after administration of propofol. We were told that there were so many confounding factors in our case that no inference was possible: Parke *et al*'s report certainly changed our practice. We conclude that some questions cannot be decided by the rigours of evidence based medicine and that, for others, answers are provided only after an unacceptable delay.

We challenge Frank Davidoff and colleagues to apply their criteria for evidence based medicine to the change of practice that they are advocating: is there any good evidence that evidence based practice works? The issue of the *BMJ* containing Davidoff and colleagues' editorial also contains a letter that investigates use of the Cochrane database.³ A more relevant question, however, is whether the outcome data for doctors who use the Cochrane database are better or worse than the data for those who do not.

Although evidence based medicine is a good way of deciding some issues, it is not the only way forward. If we use it as the only way forward we should recognise that we will not be able to answer some questions for which we will need to know the answers.

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No guidance is provided for situations for which evidence is lacking

EDITOR,—The paradigm of evidence based medicine provides clear guidance for making decisions about the delivery of health care in populations.^{1,2} Therefore, it must be qualified so that it can be used for managing specific patients.

Evidence based medicine finds answers only to those questions open to its techniques; randomised controlled trials are its capstone. Other types of evidence, including natural observations and pathophysiological principles, are ranked lower and heavily discounted. Nevertheless, for many

rare disorders and an increasing number of subgroups of patients we will never have higher levels of evidence. Evidence based medicine does not provide guidance when one is trying to make sense of situations for which better types of evidence are lacking. Even when we have better evidence it is difficult to apply it to a particular patient. When one treatment is shown to be better than another on a population basis this does not mean that it is the best treatment for the patient. Only when we cannot reliably predict which patient will benefit from each treatment option should we take the general conclusion for the population and apply it to the individual patient.³ Establishing predictive assays and baseline variables to stratify for risk and benefit may help to match treatment options to subgroups of patients. The evidence for this, however, is likely to be of a lower level, partly because of increasingly small sample sizes.

Furthermore, we present treatment options to a patient to elicit informed consent. Some patients may prefer to receive a treatment that has been classified as less efficacious by evidence based medicine. Some doctors may be willing to give the treatment, and some taxpayers may be willing to pay for it, to empower the patient by offering a meaningful choice. Also, patients have to compare different procedures of techniques and trade off the chances of benefits and of toxicities, the severities of outcomes, and their temporal relationships. Each patient will do this slightly differently and may prefer a treatment option that evidence based medicine and its derivatives (practice guidelines⁴ and economic analyses) suggest should be abandoned.

We enjoy using evidence based medicine in our practice and research efforts but believe that it fails to address how individual, public, and social choices are made. It is useful in the design and appraisal of studies, which can provide us with quality data about multiple treatment options. While high quality evidence based medicine definitely informs us, however, it cannot make decisions for our patients.

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Quality cannot always be quantified

EDITOR,—William Rosenberg and Anna Donald examine some of the disadvantages of evidence based medicine but, for each "threat," argue that an overall "opportunity" to improve existing practice ensues (with the implication that the debate is more polarised than perhaps it is).¹ One important disadvantage is not addressed, though it is encapsulated in another context earlier in the article where the effectiveness of evidence based medicine is considered: "the approach is difficult to evaluate . . . since many [outcomes] are difficult to quantify."

Surely this is a problem with evidence based medicine. Most outcomes of health care are multifactorial, and it is mainly those outcomes that lend themselves to direct quantitative assessment that are used in randomised controlled trials—measuring the measurable. To extrapolate from

the example given in the article, it is important to consider all the effects on a patient of initiating a lifelong course of warfarin; these include the inconvenience of daily treatment and regular monitoring and review; disruption of existing and future drug treatment because of drug interactions; and potential psychological morbidity resulting from imposition of the sick role by treatment of an asymptomatic condition. These outcomes cannot be measured, but the risk of haemorrhage and reduction in the risk of stroke can be, so these are the figures on which decisions are to be based, argue the authors.

Where gaps in evidence are likely to exist we are exhorted to surmount the problem by attempting to answer only questions "for which there is likely to be good evidence" and awaiting the results of future research. There are no suggestions on how our practice relating to unmeasurable aspects is to be guided.

An analogy might be where hospital managers are tempted to highlight waiting time for patients at outpatient clinics as an indicator of the clinics' performance. As doctors and patients we believe that the content of the eventual consultation is more important than the waiting time, but the measurement is easy and relatively precise. Neither of the implicit assumptions—that patients' satisfaction equates with their waiting time and that quality of health care given equates with patients' satisfaction—can be made.

The principle of critical appraisal is laudable in all branches of higher education and professional practice and may have been deficient in medical education and practice. The wholesale adoption of evidence based medicine, given the current limitations of comprehensive outcome measures, is premature. A gradual and integrated introduction may be more appropriate.

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Journal of Evaluation in Clinical Practice will start publication in September

EDITOR,—The "Editor's choice" in the issue of 29 April welcomes the publication of the new journal, *Evidence Based Medicine*, which is described more fully in Frank Davidoff and colleagues' editorial.¹ In addition, Aneez Esmail reviews a new textbook entitled *Evidence-based General Practice*.² These are important contributions to the inexorable development of evidence based health care.

I wish to draw attention to a new clinical journal that is similarly dedicated to evidence based medicine but within the broader context of multidisciplinary clinical care and analysis. The *Journal of Evaluation in Clinical Practice*, whose first edition will be published in September, will focus on systematic reviews of research on clinical effectiveness; the implementation of evidence based care in routine clinical practice; systematic medical and clinical audit; methodologies for quantifying clinical benefit from audit and after the implementation of evidence based care; systematic reviews of the current status of audit and its development in medicine, nursing, midwifery, and the range of professions allied to medicine; and the functional integration of clinical audit, research and development, and quality assurance in health care organisations.

A textbook focusing on such central issues in modern medicine, *Effective Clinical Practice*, will be published in November³ and is concerned with clinical effectiveness, clinical appropriateness, the efficiency of the delivery of clinical services, the