screening would raise, or the costs of providing a service for women who would not consider termination of pregnancy. We may be able to screen, and might potentially be able to do it cost effectively, but should we do it and, if so, how?

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Authors' reply

EDITOR,—Counselling is an important component of screening, but unless an appropriate level is adopted the cost will be unsupportable. Therefore in our analysis we used two levels: a low cost option (basic information in a leaflet, which was reinforced by a midwife or general practitioner) for all people who might be screened, and expensive genetic counselling (by a nurse specialist) for carrier couples. Unlike David J H Brock, Joan Morris, and Richard A Doherty and colleagues, we are not convinced that the expensive option is needed for carrier women whose partners have yet to be tested. Carrier couples have a 1 in 4 chance of having an affected pregnancy, and the next step is to consider having an invasive diagnostic procedure with the possibility of subsequently terminating the pregnancy. In contrast, carrier women have only a 1 in 199 chance of having an affected pregnancy, and the next step is simply to test their partner. Since this step is implicit in the woman's agreement to be screened we costed only repeating the original information to the partner—the approach taken in the Yorkshire pilot study of over 6000 women.[1]

Done this way, sequential screening will be more cost effective than couple screening even if, as Morris claims, only 4% of women change partners between pregnancies. Other options short of full genetic counselling are possible, but more research would be needed to determine their cost effectiveness. Our preferred strategy is disclosure couple screening, which costs no more than sequential screening but retains some of the advantages of full couple screening.[2]

The marginal (or incremental) costs of detecting mutations additional to ΔF508 were included in our results. These are much higher than the average costs of the single mutation test, provided that under 10% more carriers are detected, and so a full analysis was not included. The incremental cost quoted by David J Torgerson is incorrect: 90% detection of carriers and 75% uptake of screening yields 486 affected pregnancies in 1 000 000 women (400×75%×90%×90%×2), not 432, and would cost £158 000, not £332 000. Torgerson's suggestion that screening should be restricted to women already undergoing invasive prenatal diagnosis would be relatively cheap but is unattractive to health planners as it would have little impact on birth prevalence.

Sarah Walters seems to confuse cost effectiveness and cost benefit analysis—for example, lifetime medical costs do not affect the cost effectiveness of detecting an affected fetus. As we stated in our discussion, we chose cost effectiveness because the valuation of life is difficult and involves ethical issues, which fall outside the realm of economics. Others can build on our results to develop a more comprehensive decision analytical model incorporating the valuation of all outcomes and costs including treatment.

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Clinical trials and rare diseases

Statistical results should be expressed in different ways, depending on circumstances

EDITOR,—Since the *BMJ* requested that, when possible, the statistical analysis of results should give confidence intervals, the relevance of many studies has become clearer. In recommending a bayesian approach to clinical trials in rare diseases Richard J Lilford and colleagues point out that power calculations are based on the probability of the proposed hypothesis being true, even though the frequentist test giving the P value (the possibility that the null hypothesis is true) is almost always used to justify the results.[1] Perhaps the *BMJ* should encourage authors to present results as the likelihood of the hypothesis being true, whenever this is appropriate.

In some situations the appropriate test is to consider the possibility that the conclusion is wrong (here, a low P value indicates significance), while in others it is to consider the probability that the conclusion is right (here, the higher the P value the greater the significance). On the one hand, when a new discovery is made it is appropriate to consider the possibility that the effect has arisen by chance and to test a null hypothesis. On the other hand, when two treatments are known to be effective the relevant statement is the probability that one is superior to the other by a certain amount. Should we not express our findings in this way?

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1 Lilford RJ, Thornton JG, Braunholtz D. Clinical trials and rare diseases: a way out of a conundrum. *BMJ* 1995;311:1621-5. (16 December.)

Trials of adequate size are possible with the right organisation

EDITOR,—Richard J Lilford and colleagues have opened the debate on the difficult problem of clinical trials in rare diseases with insight and clarity.[1] We are concerned, however, that some of the messages conveyed in their article may be open to misinterpretation.

Firstly, readers should not accept that a trial that is not powerful enough to provide a definitive answer is as good (that is, clinically useful) as one that is appropriately sized. There is a hierarchy of evidence, with some forms of evidence carrying more weight than others. A trial that can produce reliable evidence must be better than one that cannot, although we agree that some evidence from a small trial is usually preferable to non-randomised evidence, even if this is based on large numbers.

Secondly, different parties may interpret the word "rare" in different ways. The authors quote the example of a trial of fetal surgery, which, if it was to be capable of producing a definitive answer, would need to recruit from a population of 12 million pregnant women. They imply that this would be impossible, which we do not accept. A trial of this size has not yet been done in this field, but that is not to say that it is impossible. Examples of trials in rare diseases show that widespread international collaboration is possible. A trial of the management of posthaemorrhagic ventricular dilatation in neonates is currently recruiting from 137 centres in 26 countries. This condition is very rare, and, although recruitment will take several years, the size of the trial has been calculated so that it will be capable of providing a definitive answer to the question being posed. If the main barriers to conducting large collaborative trials in rare diseases are organisational should we not be investing our scarce resources in overcoming these barriers to collaboration rather than relying on evidence from trials of inadequate size that may provide misleading evidence?

We agree with the authors that "any randomised evidence is better than none." We are concerned, however, that this approach may encourage researchers and funding bodies to support inadequately sized trials when trials that may provide definitive answers are possible with the right organisation and commitment from participating centres.

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GMSC's advice on intrapartum care is unhelpful

EDITOR,—The General Medical Services Committee recently issued guidance stating, "We think that practitioners who are going to provide intrapartum care should be the relatively few GPs [general practitioners] who are highly skilled and practised in this area . . . these GPs are referred to as GP obstetricians. Only they should undertake home deliveries and deliveries in GP units."[1,2]

We believe that this advice is unhelpful as it is likely to reduce the number of general practitioners prepared to attend women in labour. Few would be prepared to have their professional skills judged against some hypothetical standard of "general practitioner obstetrician," would describe themselves as "highly skilled and practised in this area," or would ever exercise obstetric skills at home. It might be argued that this advice seeks only to regulate the current position, but such general practitioners have never argued that they are doing anything more than exercising the skills that all general practitioners should have. The advice is counter to that in *Changing Childbirth* and that of the Royal Colleges of Midwives and General Practitioners,[3,4] which says that those general practitioners keen to provide care to women in