was unaware of the outcome for this group. When the government's threshold of 35 points for bypass surgery was introduced in May 1996, 130 of the 264 patients then on the waiting list at our hospital were removed because they did not reach the entry threshold. In the 18 months that followed 59 patients received surgery within the public system because of worsening symptoms and regrading, nine had operations done privately, and one was treated by angioplasty. Three patients died without receiving coronary surgery.

Finally, the weekly combined conference with our surgical colleagues concentrates on difficult and controversial cases. Neither inhospital emergencies (about two thirds of the workload) nor straightforward cases are usually discussed. Emergency cases are operated on urgently after appropriate consultation and straightforward cases are booked for bypass surgery by the referring cardiologist. For these reasons the conference may give a misleading impression to a visiting surgeon. We believe that the overall pattern of referrals is somewhat less adversely weighted than Bridgewater has appreciated.

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How should different life expectancies be valued?

Existential model may be better than scale that uses quality adjusted life years

EDITOR—Problems with the valuation of life expectancy and quality adjusted life years[1] can be traced to the underlying philosophical paradigm. The quality adjusted life year paradigm is based on 19th century classical utilitarianism. The greatest good is perfect health, which is valued at 1; being dead (and the event of death) has the value of 0. Other states are given values of <1; states judged worse than death may be given negative values.[2]

This century, philosophers such as Martin Heidegger and Sir Karl Popper have put forward ideas that differ from those of the utilitarians and suggest an alternative model of how to value health. Heidegger's premise is that we are unaware of things when they are normal; our conscious concern is with the abnormal. For example, we are not aware of using a door handle when we enter a room unless it is broken.[3] We are not consciously aware that our body is healthy; we become aware of our body only when we are ill, injured, or dying. This existential approach directs attention to aspects of health that we are aware of, such as distress, disability, and impending death.

Valuations when scale based on quality adjusted life years (QALYs) and existential model based on Heidegger's and Popper's premises is used

	Scale based on QALYs	Existential model
Healthy for one year	1	0
Illness for one year	<1	>0
Event of death	0	>0
Dead for one year	0	0

Popper exhorts us to minimise misery and misfortune, not seek to maximise good. These are not symmetrical. One person's suffering cannot be traded for another person's happiness. There is an analogy here with Popper's premise that the task of science is to eliminate false theories, not to attain ultimate truth.[4]

Deaths at different ages and in different circumstances have different consequences and should be valued differently. Once one is dead one has ceased to exist (at least for direct health care). This distinction, between the event of death and the state of being dead, is ignored in the literature about quality adjusted life years.

The table compares the valuations when the QALY scale and an existential model are used. It shows fundamental asymmetry. The task of commissioners of health care is to allocate resources in order to minimise the overall consequences of morbidity and death for their population. An existential model provides a direct indicator of these consequences. Unfortunately, the scale that uses quality adjusted life years creates a utilitarian distortion.

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Diminishing marginal utility and discounting future effects have similar consequences

EDITOR—Waugh and Scott propose that health effects should be tripled or doubled when total life expectancy is below 6 months or 12 months, respectively, when the duration of lifetime left is taken into account in economic evaluations.[1] Economic theory may be of help in the issues that they raise.

Firstly, the principle of attaching more weight to benefits gained when life expectancy is short corresponds to the economic principle of diminishing marginal utility, reflecting the idea that giving an additional sandwich to someone who has little to eat is preferable to giving it to someone with a lot to eat. This principle implies that giving an additional quality adjusted life year to a person with a quality adjusted life expectancy of 20 years is less valuable than giving one to a person with a life expectancy of only 3 months. This notion is already used implicitly: lifesaving lung transplantation, with huge costs per quality adjusted life year, is considered worthwhile, whereas prevention programmes aimed at people with high cholesterol concentrations, with much lower costs per quality adjusted life year, are not considered cost effective. The same notion may explain the acceptance of high costs in the last year(s) of life, when potential health gains and life expectancy are often low. Waugh and Scott's proposal to triple or double health effects is as arbitrary as is making no adjustment, and more research is needed to find the appropriate weights.

Secondly, correcting for diminishing marginal utility may partly solve the fact that people with a short life expectancy may be more willing to accept a poor quality of life than people with a longer life expectancy. This relates to one of the principles underlying quality adjusted life years—that of constant proportional trade off; this means that equivalence between 10 years in health state A and 5 years in health state B implies equivalence between 10 months in A and 5 months in B. Again, more research is needed to indicate how the concept of quality adjusted life years should be adapted for situations involving short life expectancies.

Finally, Waugh and Scott mention discounting future effects. Discounting and diminishing marginal utility are two different subjects, with similar consequences, but from completely different backgrounds. Thus they should be treated separately.

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When can odds ratios mislead?

Odds ratios should be used only in case-control studies and logistic regression analyses

EDITOR—Expressing the results of clinical trials and systematic reviews in terms of odds ratios can be more seriously misleading than Davies et al advise us.[1] They gave a correct analysis of situations in which odds ratios are used to describe increases in event rates, but their consideration of the more common situation, in which treatments reduce event rates, is short sighted. Here, effectiveness is more commonly expressed as the percentage relative risk reduction $(100\times(1-\text{relative risk})\%)$ than the actual relative risk. The discrepancy between a relative risk reduction and the equivalent relative odds reduction $(100\times(1-\text{odds ratio})\%)$ can be misleading.

When event rates are high (commonly the case in trials and systematic reviews) the relative odds reduction can be many times larger than the equivalent relative risk reduction.

For example, Brent et al report results of a trial of a programme aimed at increasing the duration of breast feeding.[2] By three months 32/51(63%) women had stopped breast feeding in the intervention group, compared with 52/57(91%) in the control group. Whereas the relative risk reduction is 31% the relative odds reduction is 84%: nearly three times as large. The same problem can occur in systematic reviews: a summary of the results of seven trials of antimicrobial treatment on premature rupture of membranes showed a 49% relative odds reduction of delivery by seven days, whereas the relative risk reduction was only 19%.[3]

Although relative odds and relative risk reductions always go in the same direction, these discrepancies in magnitude are large enough to mislead. Good estimates of treatment effects are essential for clinicians to be able to balance the relative probabilities of the good and bad outcomes that could be caused by a treatment.

The only safe use of odds ratios is in case-control studies and logistic regression analyses, where they are the best estimates of relative risks that can be obtained. Theoretical mathematical arguments for using odds ratios in other circumstances have not been supported by empirical studies.

In clinical trials and systematic reviews of trials there is no reason for compromising interpretation by reporting results in terms of odds rather than risks.[4,5] Authors and journal editors should ensure that the results of trials and systematic reviews are reported as relative risks unless there is a convincing argument otherwise.

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Avoidable systematic error in estimating treatment effects must not be tolerated

EDITOR—Davies et al conclude that "qualitative judgments based on interpreting odds ratios as though they were relative risks are unlikely to be seriously in error."[1] Statisticians may be satisfied with qualitative judgments, but doctors and patients must make quantitative judgments.

Relative risk and its complement, relative risk reduction, are widely used and well understood measures of treatment effect. Only case-control studies do not permit direct calculation of relative risk. Why then, when measures of treatment effect come from research that uses stronger designs, would clinicians accept odds ratios as being roughly equivalent to relative risks rather than demand to know the relative risk itself? If our goal is to provide as valid an estimate of a treatment effect as possible, why introduce any unnecessary systematic error?

Davies et al suggest that there is no important concern in interpreting an odds ratio of 0.66 (reduction in death after management in specialist stroke units) as if it were the relative risk (the true relative risk was 0.81 in their example). We disagree. How treatment effects are described influences doctors' perceptions of efficacy.[2,3] Moreover, the number needed to treat, a statistic widely used to express the clinical importance of treatment effects,[4] is seriously underestimated (by 45%) when the odds ratio is interpreted as the relative risk (in their example, it would be calculated erroneously as 5.3 rather than the true 9.7).

Knowing the number of patients one needs to treat to prevent one patient having the adverse target event is particularly useful in deciding whether to treat. Clinicians will treat patients when the number needed to treat is lower than a threshold number at which benefits of treatment wholly offset adverse events attributable to it.[5] Interpreting an odds ratio as if it were a relative risk introduces a systematic error in the estimation of the number needed to treat and hence in decisions on treatment: treatment will be recommended when it should not be.

The table shows the number needed to treat calculated erroneously from misinterpretation of the odds ratio as if it were the relative risk and correctly from the true relative risk. The calculations are done at high control event rates and over a range of odds ratios. When the control event rate is high, interpretation of the odds ratio as the relative risk results in a systematic and important underestimate of the number needed to treat.

When relative risk can be directly calculated, it should be. There is no reason to tolerate avoidable systematic error in estimating treatment effects.

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Number needed to treat calculated from misinterpretation of odds ratio (OR) as if it were relative risk (RR) and from true RR

	Number needed to treat			
	Control event rate 50%		Control event rate 80%	
OR	When OR used as RR	When true RR used	When OR used as RR	When true RR used
0.5	4.0	6.0	2.5	7.5
0.6	5.0	8.0	3.1	10.6
0.7	6.7	11.4	4.2	15.6
0.8	10.0	18.0	6.3	26.2
0.9	20.0	40.0	12.5	57.5

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Authors' reply

EDITOR—Both letters make interesting points about odds ratios but do not actually uncover any shortcomings in our paper. We did not advocate the use of odds ratios. Instead our paper addressed the issue of how common events must be, and how big effect sizes must be, before the odds ratio becomes a misleading estimate of the relative risk. Our main aim was to put to rest the widespread misconception that the odds ratio is a good approximation to the relative risk only when rare events are being dealt with. Our conclusion was that "serious divergence between the odds ratio and the relative risk only occurs with large effects on groups at high initial risk."

In our paper we clarified this. So long as the event rate in both the intervention and the control groups is less than 30% and the effect size is no more than moderate (say, a halving or a doubling of risk) then interpreting an odds ratio as a relative risk will overestimate the size of the effect by less than one fifth. This is a far cry from the requirement that events be rare. The authors of the letters confirm that problems can arise with higher event rates—all their examples use unusually high rates of between 50% and 91%.

In the paper we were quite clear that we were concerned with broad qualitative judgments of treatment effects and not precise quantitative estimates of the size of any effect. Though it is true, as Bracken and Sinclair state, that "doctors and patients must make quantitative judgments" we should be wary of invoking too great a precision in making these judgments. Many factors may influence the observed effect size of a treatment—for example, the nature of the group of patients studied, variations in the healthcare setting and concomitant care, and, of course, the play of chance.

On one thing we are in clear agreement: odds ratios can lead to confusion and alternative measures should be used when these are available. Authors reporting on

prospective studies should be encouraged to report the actual relative risk or relative risk reduction. Better still, as Bracken and Sinclair point out, numbers needed to treat (which measure absolute benefit) are more useful when treatment decisions are made than either relative risks or odds ratios (which measure only relative benefit). Nevertheless, when odds ratios are encountered, guidance on their interpretation is of more use than outright rejection.

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Long term pharmacotherapy of depression

Tricyclic antidepressants should not be first line treatment

EDITOR—In his editorial Edwards correctly points out the high rate of recurrence of disease among patients with major depression and the importance of long term treatment.[1] We dispute his advice to use tricyclic antidepressants as first line treatment.

He states that the dropout rate in clinical trials is 1-5% less in patients given selective serotonin reuptake inhibitors than in patients given tricyclic antidepressants. A meta-analysis of 62 randomised controlled trials found that the total discontinuation rate was 10% lower with selective serotonin reuptake inhibitors and the dropout rate due to side effects 25% lower.[2] These dropout rates imply that patients are being inadequately treated with tricyclic antidepressants and may require further psychiatric treatment and possibly admission to hospital.

Edwards admits that death is more likely to result from overdoses of older tricyclic antidepressants than from overdoses of newer compounds. He quotes a single questionnaire study to back up his claim that this difference may be due to doctors prescribing older antidepressants to patients who are more prone to suicide. The *Health of the Nation* sets a target for reducing the rate of suicide by 15% by 2000 and suggests that this may be achieved by reducing the availability of means to do so.[3] The famous reduction in suicide rates that followed the introduction of natural gas as well as more recent research supports this policy.[4]

Edwards calculates the average net ingredient cost of an NHS prescription for a selective serotonin reuptake inhibitor in 1995 to be £27.21. Our calculations based on figures obtained from a 1995 edition of the *British National Formulary* show it to be £23.43. He uses his figures to extrapolate the increase in cost that would be seen if selective serotonin reuptake inhibitors were used as first line treatment for all patients currently prescribed tricyclic antidepressants. The cost of drugs is only around 11% of the total cost of treating depression.[5] A review of research on cost effectiveness concluded that newer antidepressants were more cost effective than older drugs when all the costs of depression were taken into account.[5]

Edwards recommends that newer antidepressants should be used to treat patients who are more prone to suicide or accidents. Although risk factors for suicide exist, predicting who will do it is impossible. Accident proneness is a vague term that is impossible to assess and use as a means of deciding which drug patients will receive.

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Impact of side effects of treatment is important in older patients

EDITOR—The editorial by Edwards on the long term pharmacotherapy of depression[1] warrants further comment. The trials from the American National Institute of Mental Health showed that antidepressants given at full therapeutic doses and continued as maintenance treatment were significantly more beneficial than placebo after five years.[2] The benefit for maintenance treatment with antidepressants can thus be seen for five years after an index episode of depression and, indeed, for as long as follow up trials have been continued.

In comparing older tricyclic with newer antidepressants, a substantial advantage of preparations such as selective serotonin reuptake inhibitors is that for many of these products the starting dose is likely to be an effective therapeutic dose. This is not the case with tricyclic antidepressants. Many studies in primary care have shown that general practitioners continue to prescribe subtherapeutic doses of tricyclic antidepressants[3] and that patients receiving subtherapeutic doses consult their doctors more often. Donoghue et al showed an increase in antidepressant prescribing at therapeutic doses in primary care that seemed to be associated with an increase in prescribing of selective serotonin reuptake inhibitors.[4]

The comparatively small advantage associated with selective serotonin reuptake inhibitors compared with tricyclic antidepressants in dropout rates from meta-analyses cannot be assumed to be a valid reflection of daily clinical practice. Patients participating in clinical trials may be more likely to comply with their treatment. Many tricyclic antidepressants are prescribed as twice or thrice daily doses. In practice better compliance with taking the newer antidepressant drugs, many of which can be given once a day, might reasonably be expected.

The impact of side effects from antidepressant treatment on older patients is important. Anticholinergic, antiadrenergic, and antihistaminergic side effects associated with amitriptyline may lead to falls and fractures, which may lead to substantially greater illness than the predominantly gastrointestinal side effects associated with newer preparations.

The time may be ripe for large scale surveys of patient preferences and quality of life measures associated with the side effects of antidepressants to add a further dimension to the debate.

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Patients can help doctors decide on treatment

EDITOR—Edwards has written an editorial full of "shoulds,"[1] which had it been written about asthma would have concluded that beclomethasone and salbutamol should be prescribed for those who cannot tolerate isoprenaline and Do-Do tablets. Patients with major depression are not just found in outpatients departments. In the past five years alone, I have treated over 900 such patients in my suburban practice—cases that were diagnosed by history, examination, and using the questionnaires that hospital specialists such as Edwards have developed. Of course, general practitioners see "milder, heterogeneous cases," but they are in addition to, not a substitute for, the real thing.

Neither is it difficult to know why patients stop their treatment. I have been asking them for years and been using that information often to unlearn so much of what I was taught by specialists and academics. In diabetes, asthma, and depression the patient can become the specialist and help the doctor decide whether any form of treatment is still required and how much. Furthermore, if newer antidepressants should be prescribed for "patients who cannot tolerate older antidepressants [and I am talking therapeutic doses here] and/or who have a high risk of suicide by overdose ... [and to those] who are prone to accidents or have cardiovascular disease," I would be prescribing them for nearly all the patients I see anyway, even assuming I knew how to continually identify those at risk or welcomed the extra workload that would be required.

As one result of continued prescribing of tricyclic antidepressants, suicides will continue to occur ("only about 4%," so I guess we shouldn't be too bothered), as will