weekly consumption than 21 units. Common sense and scientific evidence suggest that some of these problems are more strongly associated with extreme consumption on single occasions than total consumption over a particular period (N Kreitman and J C Duffy, eighth annual alcohol epidemiology symposium, Helsinki, 1982).

It might be argued that as there is no scientific basis for the limits of 21 and 14 units a week new scientific information can be regarded as irrelevant. Such an attitude is short sighted and ultimately counterproductive, allowing legitimate public health interests and health advocacy to be portrayed as either ill informed or incompetent. Greater public health gain might result from giving advice that is both coherent and credible.

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- 1 Kemm J. Alcohol and heart disease: the implications of the U-shaped curve. *BMJ* 1990;307:1373-4. (27 November.)
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Wine glass holds more than one unit

EDITOR,—Patients are often accused of underestimating the amount of alcohol they drink, but do we as a profession not collude with this by stating that a glass of wine equals one unit of alcohol? Only wine with 8% alcohol fulfils this. As most wine is 12% or 13% alcohol and most people are liberal pourers would it not be more honest to say that a glass of wine is almost two units? Increasingly, beer and lager in cans and bottles is 6% to 8% alcohol. Should we not change our statements about these drinks too?

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- 1 Kemm J. Alcohol and heart disease: the implications of the U-shaped curve. *BMJ* 1993;307:1373-4. (27 November.)

Informed consent

Consent requires a flexible approach

EDITOR,—We wish to respond to the correspondents who replied to our article on the distress that fully informed consent for randomised trials of treatment of cancer can create.^{1,2} We are disappointed that some of them have concluded that we are against informed consent. We emphasised throughout our article that we are in favour of informed consent; it is the nature and degree of consent for individual patients that concern us. We advocate a flexible approach, but several correspondents have not fully understood this.

Mark Emberton and colleagues misrepresent our position. They quote studies that purport to show that patients want more detailed information and are not harmed by receiving it. They miss the point with the examples they quote. Fallowfield *et al*'s study concerned only those patients accepting randomisation and did not address the issue we raised. The other example they quote is of consent

in a randomised trial of surgery for hernia, which is clearly not comparable and is therefore unhelpful. These studies of patients' attitudes do not simulate the clinical situation in which a patient with newly diagnosed cancer faces discussion of a complex randomisation (sometimes with more than two alternative treatments). Patients are not a homogeneous group in this situation and should not be treated as if they are. They are individual people with a right to as much information as they want at that moment. The difficulty is to ascertain this without the doctor imposing his or her own view (which is usually the case in routine practice outside trials). We do not "use the argument that seeking normal consent . . . results in confusion and distress" in order to "challenge informed consent." Still less do we "pretend that the solution to the issue lies in not informing at all." We are in favour of informed consent and spend our professional lives talking to patients about their treatment. We believe that patients can be overwhelmed by too much information at the wrong time. Emberton and colleagues should not therefore misrepresent our view in the way that they do.

Laurence Gerlis says that we have "missed the boat" and quotes the current bureaucratic guidelines in the United States and Europe. It is never too late for common sense. Laws and ethical guidelines can be changed. Josephine G Wong is wrong to state that there is a conflict between the scientific needs of a randomised trial and a doctor's obligation to act in his or her patient's best interest. The whole point is that the trial position must be ethical to begin with. Again we refute her suggestion that we wish to "deprive the patient of information." We agree with her that gaining consent to treatment, whether in a trial or not, takes considerable time and effort. It is those patients who are damaged and upset by an insistence on inappropriate methods of imparting information who concern us.

J P Walsworth-Bell proposes a quasipsychiatric interpretation of our perceived distress, but we do not accept the explanation that we are unhappy at questioning the potential of a new treatment. We enjoy doing just that and believe profoundly in the scientific imperative for randomisation since new does not always equal better. We agree that doctors need help in how to approach the problem of informed consent and other aspects of communication with patients with cancer. For this reason, both of us participated in the production of a successful series of training programmes based on videos, for senior oncologists.

O A Adedeji states that patients would be told "less and less" if flexibility in the timing, wording, and degree of informed consent was adopted. We believe that the reverse would be the case. At present most patients are treated outside trials, sometimes because of these difficulties in gaining informed consent. How does Adedeji know what this overwhelming majority of patients are told? Do they have the full disclosure that Adedeji advocates? We doubt it.

Finally, the patient (Hazel Thornton) and the parent (Richard Keatinge) show that patients are indeed prepared to accept that they are not all the same and that advice about treatment outside trials may sometimes conceal dogmatic or ignorant medical attitudes. There are no ethical guidelines or legislation for fully informed consent for patients in this far more common situation.

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- 1 Tobias J, Souhami R. Fully informed consent can be needlessly cruel. *BMJ* 1993;307:1199-201. (6 November.)
- 2 Correspondence. Informed consent in clinical trials. *BMJ* 1993;307:1494-7. (4 December.)

Reactionary approach inhibits progress

EDITOR,—I suppose it was predictable that the paper by Jeffrey S Tobias and Robert L Souhami would provoke a barrage of ill informed and hostile comment.¹ I particularly took exception to the letter by Emberton and colleagues,² which cited work from my own group³ to justify their reactionary position.

The Cancer Research Campaign trial for the surgical management of primary breast cancer set out to recruit 2000 patients randomised between mastectomy and breast conserving techniques. After three years we had to admit defeat, as only 150 patients had been recruited. This small subset was used for the psychological inventory at long term follow up to determine the qualitative outcomes of these radically different therapeutic regimens.³

The real issue is what happened to the 1850 patients who should have been recruited and presumably were refused entry into the trial and, furthermore, what happened to the 75 000 women who developed breast cancer in the United Kingdom during that period and were treated by mastectomy or breast conserving techniques according to the whim of the general surgeon. During this period in the late '70s and early '80s, when there was genuine equipoise as to the relative merits of these two approaches, patients outside the trial were kept in the dark and not offered a choice, whereas those patients fully informed about the uncertainty were frightened off entry into the trial or forced to make decisions that, on the one hand, could lead to the unnecessary loss of their breasts and, on the other hand, the unnecessary loss of their life.

It is truly disingenuous of Emberton *et al* to compare this with a randomised trial looking at different techniques for the repair of an inguinal hernia.⁴ I would imagine that most patients would be totally indifferent to the surgical techniques used, particularly as the groin is hardly a zone of sexual attraction or sexual identity.

Furthermore, the leisurely contemplation of the anatomy of the inguinal canal cannot be compared with the agonising decision facing a middle aged man with crushing chest pain when the politically correct position demands fully informed consent before he can be randomised into a trial of clot busting drugs.

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Methods of consent should be tested experimentally

EDITOR,—Jeffrey S Tobias and Robert L Souhami use their clinical experiences to argue that inviting patients to make informed decisions may not be what patients want and sometimes results in more harm than good.¹ There is some empirical evidence to support this supposition. People vary in the role they wish to have in decisions regarding treatment. Some of this variation is due to individual differences in coping style.² Recent research suggests that a more important influence is the severity of the threat being faced. While most people in the general population think that they would want to play a part in determining their own treatment if they developed cancer, most patients with cancer want a doctor to make decisions on their behalf.³

Tobias and Souhami go further and suggest that

deciding what to tell patients should be left to the clinical judgment of the doctor. The main problem with this is that doctors have a poor track record in assessing the information needs and emotional needs of patients⁵ and judging their own skills in communication.⁵

Randomised controlled trials are generally considered to be the best antidote to clinical uncertainty. When there is behavioural uncertainty, such as over how to inform patients about trials, randomised controlled trials should again be the method of choice. Such studies would compare the effects on different groups of patients of different methods of informing them about trials. These methods could vary in the amount and type of information provided, the training of the person providing the information, and the period over which information was given and decisions sought. The impact of these different approaches on emotions, thinking, and decisions could then be assessed.

Tobias and Souhami may be correct in their clinical impressions that the practice of obtaining informed consent serves ethical principles more than the needs of patients. These impressions should be tested experimentally.

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Consent difficult in paediatric oncology

EDITOR,—Neil McIntosh's comments with regard to the difficulty of obtaining fully informed consent for treatment for neonatal problems are a useful contribution to the current debate.¹ They also ring true for paediatric oncologists, who, although committed to the concept of entering patients into randomised trials, often find it difficult to obtain truly informed consent from parents who are emotionally devastated by the recently acquired knowledge that their child has a life threatening condition. Frequently, requests for consent are met with blank stares, anger, or even the comment, "You do whatever you think right; we can't make a decision." The parents are angry not because the child is being put into a trial but because we are asking them to make an impossible decision at such an emotional time.

A recent study in which we audited parents' reactions to being informed that their child had cancer showed that a fifth denied having had a long discussion with the doctor up to a week after the original diagnosis and nearly three fifths remained confused or in doubt about factual information that had been imparted despite multiple (up to 20) discussions with doctors and supportive staff. The parents' previous life experiences, their educational achievements, but, most importantly, their emotional state seemed to determine their ability to receive information and to cope with it. To ask parents who are so distressed to give truly informed consent is extremely difficult, yet we must try to get at least assent. For so many of the diseases we are treating we do not know what the optimal treatment is and we must ask important therapeutic questions if we are to increase the survival of children with cancer and leukaemia further.

The sceptics who deny the need for trials must remember, for example, that before the Medical Research Council started its trials in childhood leukaemia in Britain in the late 1960s the median survival of a child with acute lymphoblastic leukaemia was barely six months. Now 65% of patients are alive at five years and beyond, free of disease, and most of those will be cured of their disease. That dramatic improvement is due to therapeutic trials, but I doubt if most of the parents of those cured patients will remember having given consent for their child to enter into a therapeutic trial even though they had it carefully explained and gave their so called informed consent.

Like McIntosh, I agree that you can obtain consent by getting a signature on paper, but that doesn't mean informed consent. McIntosh's suggestion of expanding the useful role of an ethical committee to give "society's" approval of a study should be explored further. It is one way of ensuring that only ethically acceptable studies are carried out.

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- 1 McIntosh N. Informed consent in clinical trials. *BMJ* 1993;307:1496. (4 December.)

Early treatment of Parkinson's disease

Open studies are unreliable

EDITOR,—We wish to comment on the article by the Parkinson's Disease Research Group in the United Kingdom on early treatment of the disease.¹

Firstly, the study was open; open studies may undermine the reliability of clinical trials. The comparability of the three groups over time is a major concern in this trial: in the bromocriptine group there was a 69% drop out rate, whereas in the two other groups the drop out rate was around 30%. This may have diminished the comparability of the groups with time.

The difference in the mean dose of levodopa after one year between the group given selegiline plus levodopa and the group given levodopa alone was only about 70 mg. What were the doses of levodopa after three years of treatment? In a double blind trial by Myllylä *et al* the difference in the daily dose of levodopa between a group given selegiline and a group given placebo was about 130 mg after one year and 185 mg after two years ($P < 0.001$).² In this study there were no significant differences in the parkinsonian disability between the two groups as expected because both groups were treated similarly to maintain the optimal clinical condition. Similar results were obtained in a double blind study by Sivertsen *et al*³ and in an open follow up study by Rinne.⁴ In the British study the patients were treated until a "satisfactory" clinical condition was achieved, rather than the optimal condition that was achieved in the three other studies. This may explain the difference in the doses of levodopa between the studies.

The authors do not report the changes in the number of doses of levodopa given daily. What was the average daily frequency of dosing after three years? The common strategy for maintaining constant concentrations of levodopa is to increase the frequency of doses. The type of oscillations in performance should also be more clearly stated in the paper. Furthermore, the percentage of oscillations is calculated per total number of patients; we suggest that calculating the percentage over time, taking into consideration the number of patients still in the study, might have given a more reliable picture.

One of the original aims and primary end points of the British study was to follow up mortality in the three treatment arms, which would offer valuable new information. Gaining this information may prove to be difficult as the patients were allowed to be rerandomised to one of the two other treatment arms of the trial. How can the final mortality figures be analysed in such a study?

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Authors' reply

EDITOR,—The Parkinson's Disease Research Group in the United Kingdom is aware of the disadvantages of an open prospective study, but a double blind trial would not have been possible at the time that the study started as the group's aim was to follow up a large number of patients from the early stages of the disease to death.

As a result of Vilho Myllylä and Esa Heinonen's queries we have analysed our data further. At three years' follow up the median dose of levodopa was 500 mg in arm 1 (levodopa alone) and 375 mg in arm 2 (levodopa plus selegiline) and the mean doses were 566 mg and 423 mg respectively. A mean difference of 143 mg of levodopa between the two arms is significant ($P < 0.05$) and confirms the mild levodopa sparing effect of selegiline. Why this effect was not evident after one year is unclear, but it may reflect the mild disability of the patients at this stage rather than any difference in therapeutic strategy.

We agree with Myllylä and Heinonen that it would have been useful to take account of the time of follow up when we analysed the side effects. We have reworked the data to express the incidence of dyskinesias and motor oscillations in rates per 1000 person years; the pattern of results is still the same, with no difference for oscillations and a greater incidence of dyskinesia in arm 2 than arm 1. Furthermore, the daily frequency of doses of levodopa after three years did not differ between arm 1 (mean 4 doses/day, range 3-8) and arm 2 (mean 4 doses/day, range 2-11).

Our main findings are based on an intention to treat analysis, in which patients were assigned to their initial treatment group. We stated in our paper that we used this method precisely because biases would arise if analysis was restricted only to patients receiving treatment. The figures of 69% for arm 3 (bromocriptine alone) and 30% for arms 1 and 2 refer to withdrawals from initial treatment and not "drop outs." Table II shows that only 30 of the 782 patients have been lost to follow up.

A high withdrawal rate from arm 3 was anticipated at the start of the trial, and for this reason the design allowed for rerandomisation. The trial is assessing whether early use of bromocriptine followed by a change to levodopa if necessary is preferable to starting with levodopa.

We disagree that rerandomisation invalidates the future analysis of mortality. Patients would have been withdrawn anyway, and rerandomising