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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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